Cancer and (AI) Research Literatures

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Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies.
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1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

The following introduces recent reports as references in the related studies.

Abas Mohamed, Y., et al. (2025). "Decoding the black box: Explainable AI (XAI) for cancer diagnosis, prognosis, and treatment planning-A state-of-the art systematic review." Int J Med Inform **193**: 105689.

OBJECTIVE: Explainable Artificial Intelligence (XAI) is increasingly recognized as a crucial tool in cancer care, with significant potential to enhance diagnosis, prognosis, and treatment planning. However, the holistic integration of XAI across all stages of cancer care remains underexplored. This review addresses this gap by systematically evaluating the role of XAI in these critical areas, identifying key challenges and emerging trends. MATERIALS AND METHODS: Following the PRISMA guidelines, a comprehensive literature search was conducted across Scopus and Web of Science, focusing on publications from January 2020 to May 2024. After rigorous screening and quality assessment, 69 studies were selected for in-depth analysis. RESULTS: The review identified critical gaps in the application of XAI within cancer care, notably the exclusion of clinicians in 83% of studies, which raises concerns about real-world applicability and may lead to explanations that are technically sound but clinically irrelevant. Additionally, 87% of studies lacked rigorous evaluation of XAI explanations, compromising their reliability in clinical practice. The dominance of post-hoc visual methods like SHAP, LIME and Grad-CAM reflects a trend toward explanations that may be inherently flawed due to specific input perturbations and simplifying assumptions. The lack of formal evaluation metrics and standardization constrains broader XAI adoption in clinical settings, creating a disconnect between AI development and clinical integration. Moreover, translating XAI insights into actionable clinical decisions remains challenging due to the absence of clear guidelines for integrating these tools into clinical workflows. CONCLUSION: This review highlights the need for greater clinician involvement, standardized XAI evaluation metrics, clinician-centric interfaces, context-aware XAI systems, and frameworks for integrating XAI into clinical workflows for informed clinical decision-making and improved outcomes in cancer care.

Abdul-Rida, N. A., et al. (2021). "A novel pregnene analogs: synthesis, cytotoxicity on prostate cancer of PC-3 and LNCPa-AI cells and in silico molecular docking study." Mol Divers **25**(2): 661-671.

New pregnene analogs of N-hydroxamic acid 6, imino-propane hydrazides 7 and 8 as well as the aryl amides 9-11, oxadiazole, pyrazole and sulfinyl analogs 13-15, via the hydrazide analog 5 of methyl ((5-pregnen-3beta,17beta-diol-15alpha-yl)thio)propanoate (4) were synthesized. The in vitro cytotoxic activities of selected synthesized steroids against two human prostate cancer cell lines (PC-3, and LNCaP-AI) were evaluated by MTT assay.

Compound 10 was the most active cytotoxic agent among these steroids against PC-3 and LNCaP-AI cell lines with inhibition of 96.2%, and 93.6% at concentration levels of 10.0 muM and 91.8%, and of 79.8% at concentration of 1.0 muM, respectively. Molecular docking study of 10 showed a hydrogen bonding with the amino acid Asn705 residue of the receptor 1E3G, together with hydrophobic interactions. Therefore, compound 10 can be considered as a promising anticancer agent due to its potent cytotoxic activity.

Abreu, A. A., et al. (2024). "Enhancing Readability of Online Patient-Facing Content: The Role of AI Chatbots in Improving Cancer Information Accessibility." J Natl Compr Canc Netw **22**(2 D).

BACKGROUND: Internet-based health education is increasingly vital in patient care. However, the readability of online information often exceeds the average reading level of the US population, limiting accessibility and comprehension. This study investigates the use of chatbot artificial intelligence to improve the readability of cancer-related patient-facing content. METHODS: We used ChatGPT 4.0 to rewrite content about breast, colon, lung, prostate, and pancreas cancer across 34 websites associated with NCCN Member Institutions. Readability was analyzed using Fry Readability Score, Flesch-Kincaid Grade Level, Gunning Fog Index, and Simple Measure of Gobbledygook. The primary outcome was the mean readability score for the original and artificial intelligence (AI)-generated content. As secondary outcomes, we assessed the accuracy, similarity, and quality using F1 scores, cosine similarity scores, and section 2 of the DISCERN instrument, respectively. RESULTS: The mean readability level across the 34 websites was equivalent to a university freshman level (grade 13+/-1.5). However, after ChatGPT's intervention, the AI-generated outputs had a mean readability score equivalent to a high school freshman education level (grade 9+/-0.8). The overall F1 score for the rewritten content was 0.87, the precision score was 0.934, and the recall score was 0.814. Compared with their original counterparts, the AI-rewritten content had a cosine similarity score of 0.915 (95% CI, 0.908-0.922). The improved readability was attributed to simpler words and shorter sentences. The mean DISCERN score of the random sample of AI-generated content was equivalent to "good" (28.5+/-5), with no significant differences compared with their original counterparts. CONCLUSIONS: Our study demonstrates the potential of AI chatbots to improve the readability of patient-facing content while maintaining content quality. The decrease in requisite literacy after AI revision emphasizes the potential of this technology to reduce health care disparities caused by a mismatch between educational resources available to a patient and their health literacy.

Abuzinadah, N., et al. (2023). "Improved Prediction of Ovarian Cancer Using Ensemble Classifier and Shaply Explainable AI." Cancers (Basel) **15**(24).

The importance of detecting and preventing ovarian cancer is of utmost significance for women's overall health and wellness. Referred to as the "silent killer," ovarian cancer exhibits inconspicuous symptoms during its initial phases, posing a challenge for timely identification. Identification of ovarian cancer during its advanced stages significantly diminishes the likelihood of effective treatment and survival. Regular screenings, such as pelvic exams, ultrasound, and blood tests for specific biomarkers, are essential tools for detecting the disease in its early, more treatable stages. This research makes use of the Soochow University ovarian cancer dataset, containing 50 features for the accurate detection of ovarian cancer. The proposed predictive model makes use of a stacked ensemble model, merging the strengths of bagging and boosting classifiers, and aims to enhance predictive accuracy and reliability. This combination harnesses the benefits of variance reduction and improved generalization, contributing to superior ovarian cancer prediction outcomes. The proposed model gives 96.87% accuracy, which is currently the highest model result obtained on this dataset so far using all features. Moreover, the outcomes are elucidated utilizing the explainable artificial intelligence method referred to as SHAPly. The excellence of the suggested model is demonstrated through a comparison of its performance with that of other cutting-edge models.

Adachi, M., et al. (2024). "AI Use in Mammography for Diagnosing Metachronous Contralateral Breast Cancer." J Imaging **10**(9).

Although several studies have been conducted on artificial intelligence (AI) use in mammography (MG), there is still a paucity of research on the diagnosis of metachronous bilateral breast cancer (BC), which is typically more challenging to diagnose. This study aimed to determine whether AI could enhance BC detection, achieving earlier or more accurate diagnoses than radiologists in cases of metachronous contralateral BC. We included patients who underwent unilateral BC surgery and subsequently developed contralateral BC. This retrospective study evaluated the AI-supported MG diagnostic system called FxMammo. We evaluated the capability of FxMammo (FathomX

Pte Ltd., Singapore) to diagnose BC more accurately or earlier than radiologists' assessments. This evaluation was supplemented by reviewing MG readings made by radiologists. Out of 1101 patients who underwent surgery, 10 who had initially undergone a partial mastectomy and later developed contralateral BC were analyzed. The AI system identified malignancies in six cases (60%), while radiologists identified five cases (50%). Notably, two cases (20%) were diagnosed solely by the AI system. Additionally, for these cases, the AI system had identified malignancies a year before the conventional diagnosis. This study highlights the AI system's effectiveness in diagnosing metachronous contralateral BC via MG. In some cases, the AI system consistently diagnosed cancer earlier than radiological assessments.

Aganja, R. P., et al. (2024). "AI-2 quorum sensing controlled delivery of cytolysin-A by tryptophan auxotrophic low-endotoxic Salmonella and its anticancer effects in CT26 mice with colon cancer." J Adv Res **61**: 83-100.

INTRODUCTION: The limitations of conventional cancer therapies necessitate target-oriented, highly invasive, and safe treatment approaches. Hence, the intrinsic anti-tumor activity of Salmonella can offer better options to combat cancers. OBJECTIVES: This study aims to utilize attenuated Salmonella and deliver cytolytic protein cytolysin A (ClyA) under quorum sensing (QS) signaling for precise localized expression in tumors but not in healthy organs. METHODS: The therapeutic delivery strain was imposed with tryptophan auxotroph for selective colonization in tumors by trpA and trpE deletion, and lipid-A and O-antigen were altered by pagL and rfaL deletions using lambda red recombination method. The strain was transformed with the designed QS-controlled ClyA expression vector which was validated by western blot. The in vivo passaged therapeutic strain was used for treatment four times at a weekly interval, with a dose of 5 x 10(6) CFU/mouse for cancer therapy. RESULTS: The attenuated strain induced minimal endotoxicity-related cytokines TNF-alpha, IL-1beta, and IFN-gamma and exhibited adequate colonization despite earlier exposure in mice. The QS-controlled ClyA expression was confirmed by western blot from bacterial cultures grown at different cell densities. The results demonstrated that the in vivo passaged strain preferentially colonized the tumor after vacating the spleen, liver, and lung, leaving no outward histological scars. The anti-cancer effect of the designed construct was evaluated in the murine CT26 colon cancer model. The expression of ClyA increased tumoricidal activity by 67 % compared to vector control. CONCLUSION: Hence, the anti-tumor effect of the engineered Salmonella strain was improved by ClyA expression via QS activation after achieving the threshold bacterial cell density. Further, immunohistochemical staining of the tumor and other organs corroborated the QS-controlled tumor-specific expression of ClyA. Overall, the results imply that the developed anti-cancer Salmonella has low endotoxicity and QS-controlled expression of ClyA as beneficial safety elements and supports recurrent Salmonella inoculation by O-antigen deficiency.

Aguilar, C., et al. (2023). "Monitoring Methodology for an AI Tool for Breast Cancer Screening Deployed in Clinical Centers." Life (Basel) **13**(2).

We propose a methodology for monitoring an artificial intelligence (AI) tool for breast cancer screening when deployed in clinical centers. An AI trained to detect suspicious regions of interest in the four views of a mammogram and to characterize their level of suspicion with a score ranging from one (low suspicion) to ten (high suspicion of malignancy) was deployed in four radiological centers across the US. Results were collected between April 2021 and December 2022, resulting in a dataset of 36,581 AI records. To assess the behavior of the AI, its score distribution in each center was compared to a reference distribution obtained in silico using the Pearson correlation coefficient (PCC) between each center AI score distribution and the reference. The estimated PCCs were 0.998 [min: 0.993, max: 0.999] for center US-1, 0.975 [min: 0.923, max: 0.986] for US-2, 0.995 [min: 0.972, max: 0.998] for US-3 and 0.994 [min: 0.962, max: 0.982] for US-4. These values show that the AI behaved as expected. Low PCC values could be used to trigger an alert, which would facilitate the detection of software malfunctions. This methodology can help create new indicators to improve monitoring of software deployed in hospitals.

Ahmad, A., et al. (2024). "A Qualitative Study with Informal Caregivers and Healthcare Professionals for Individuals with Head and Neck Cancer on the Usage of AI Chatbots." Stud Health Technol Inform **316**: 751-755.

Informal caregivers (ICs), including the patient's spouse, close relatives, or friends, play an important role in caregiving individuals with head and neck cancer (HNC). AI-based chatbots might offer information and assistance related to caregiving. This study presents the viewpoints of ICs and healthcare professionals (HCPs) on using AI-based chatbots in caring for individuals with HNC. A total of six focus groups were conducted with 15 ICs and

13 HCPs from three Swedish university hospitals. The study uncovers a widespread hesitancy toward the intention to use AI-based chatbots among ICs and HCPs. Factors contributing to this reluctance include their distrust in chatbot-provided information, negative past experiences of using chatbots, and lack of human connection in chatbot interactions. Embracing a holistic approach is crucial when designing chatbots, ensuring active user engagement and incorporating their perspectives into the design process.

Ahmad, R. M., et al. (2024). "AI-derived comparative assessment of the performance of pathogenicity prediction tools on missense variants of breast cancer genes." Hum Genomics **18**(1): 99.

Single nucleotide variants (SNVs) can exert substantial and extremely variable impacts on various cellular functions, making accurate predictions of their consequences challenging, albeit crucial especially in clinical settings such as in oncology. Laboratory-based experimental methods for assessing these effects are time-consuming and often impractical, highlighting the importance of in-silico tools for variant impact prediction. However, the performance metrics of currently available tools on breast cancer missense variants from benchmarking databases have not been thoroughly investigated, creating a knowledge gap in the accurate prediction of pathogenicity. In this study, the benchmarking datasets ClinVar and HGMD were used to evaluate 21 Artificial Intelligence (AI)-derived in-silico tools. Missense variants in breast cancer genes were extracted from ClinVar and HGMD professional v2023.1. The HGMD dataset focused on pathogenic variants only, to ensure balance, benign variants for the same genes were included from the ClinVar database. Interestingly, our analysis of both datasets revealed variants across genes with varying penetrance levels like low and moderate in addition to high, reinforcing the value of disease-specific tools. The top-performing tools on ClinVar dataset identified were MutPred (Accuracy = 0.73), Meta-RNN (Accuracy = 0.72), ClinPred (Accuracy = 0.71), Meta-SVM, REVEL, and Fathmm-XF (Accuracy = 0.70). While on HGMD dataset they were ClinPred (Accuracy = 0.72), MetaRNN (Accuracy = 0.71), CADD (Accuracy = 0.69), Fathmm-MKL (Accuracy = 0.68), and Fathmm-XF (Accuracy = 0.67). These findings offer clinicians and researchers valuable insights for selecting, improving, and developing effective in-silico tools for breast cancer pathogenicity prediction. Bridging this knowledge gap contributes to advancing precision medicine and enhancing diagnostic and therapeutic approaches for breast cancer patients with potential implications for other conditions.

Ahmed, S. R., et al. (2024). "Assessing generalizability of an AI-based visual test for cervical cancer screening." PLOS Digit Health **3**(10): e0000364.

A number of challenges hinder artificial intelligence (AI) models from effective clinical translation. Foremost among these challenges is the lack of generalizability, which is defined as the ability of a model to perform well on datasets that have different characteristics from the training data. We recently investigated the development of an AI pipeline on digital images of the cervix, utilizing a multi-heterogeneous dataset of 9,462 women (17,013 images) and a multi-stage model selection and optimization approach, to generate a diagnostic classifier able to classify images of the cervix into "normal", "indeterminate" and "precancer/cancer" (denoted as "precancer+") categories. In this work, we investigate the performance of this multiclass classifier on external data not utilized in training and internal validation, to assess the generalizability of the classifier when moving to new settings. We assessed both the classification performance and repeatability of our classifier model across the two axes of heterogeneity present in our dataset: image capture device and geography, utilizing both out-of-the-box inference and retraining with external data. Our results demonstrate that device-level heterogeneity affects our model performance more than geography-level heterogeneity. Classification performance of our model is strong on images from a new geography without retraining, while incremental retraining with inclusion of images from a new device progressively improves classification performance on that device up to a point of saturation. Repeatability of our model is relatively unaffected by data heterogeneity and remains strong throughout. Our work supports the need for optimized retraining approaches that address data heterogeneity (e.g., when moving to a new device) to facilitate effective use of AI models in new settings.

Alqahtani, S. (2024). "Systematic Review of AI-Assisted MRI in Prostate Cancer Diagnosis: Enhancing Accuracy Through Second Opinion Tools." Diagnostics (Basel) **14**(22).

BACKGROUND: Prostate cancer is a leading cause of cancer-related deaths in men worldwide, making accurate diagnosis critical for effective treatment. Recent advancements in artificial intelligence (AI) and machine learning (ML) have shown promise in improving the diagnostic accuracy of prostate cancer. OBJECTIVES: This systematic review aims to evaluate the effectiveness of AI-based

tools in diagnosing prostate cancer using MRI, with a focus on accuracy, specificity, sensitivity, and clinical utility compared to conventional diagnostic methods. METHODS: A comprehensive search was conducted across PubMed, Embase, Ovid MEDLINE, Web of Science, Cochrane Library, and Institute of Electrical and Electronics Engineers (IEEE) Xplore for studies published between 2019 and 2024. Inclusion criteria focused on full-text, English-language studies involving AI for Magnetic Resonance Imaging (MRI) -based prostate cancer diagnosis. Diagnostic performance metrics such as area under curve (AUC), sensitivity, and specificity were analyzed, with risk of bias assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. RESULTS: Seven studies met the inclusion criteria, employing various AI techniques, including deep learning and machine learning. These studies reported improved diagnostic accuracy (with AUC scores of up to 97%) and moderate sensitivity, with performance varying based on training data quality and lesion characteristics like Prostate Imaging Reporting and Data System (PI-RADS) scores. CONCLUSIONS: AI has significant potential to enhance prostate cancer diagnosis, particularly when used for second opinions in MRI interpretations. While these results are promising, further validation in diverse populations and clinical settings is necessary to fully integrate AI into standard practice.

Alsayed, A. A., et al. (2024). "Assessing the quality of AI information from ChatGPT regarding oral surgery, preventive dentistry, and oral cancer: An exploration study." Saudi Dent J **36**(11): 1483-1489.

AIM: Evaluation of the quality of dental information produced by the ChatGPT artificial intelligence language model within the context of oral surgery, preventive dentistry, and oral cancer. METHODOLOGY: This study adopted quantitative methods approach. The experts prepared 50 questions (including dimensions of, risk factors, preventive measures, diagnostic methods, and treatment options) that would be presented to ChatGPT, and its responses were rated for their accuracy, completeness, relevance, clarity or comprehensibility, and possible risks using a standardized rubric. To carry out the assessment of the responses by ChatGPT, a standardized scoring rubric was used. Evaluation process included feedback concerning the strengths, weaknesses, and potential areas of improvement in the responses provided by ChatGPT. RESULTS: While achieving the highest score for preventive dentistry at 4.3/5 and being able to communicate the complex information coherently, the tool showed lower accuracy for oral surgery and oral cancer, scoring 3.9/5 and 3.6/5, respectively, with several gaps for post-operative instructions, personalized risk assessments, and specialized diagnostic methods. Potential risks, such as a lack of individualized advice, were shown in 53% of the oral cancer and in 40% of the oral surgery. While showing promise in some domains, ChatGPT had important limitations in specialized areas that require nuanced expertise. CONCLUSION: The findings point to the need for professional supervision while using AI-generated information and ongoing evaluation as capabilities evolve, for the assurance of responsible implementation in the best interest of patient care.

Alsubai, S. (2024). "Transfer learning based approach for lung and colon cancer detection using local binary pattern features and explainable artificial intelligence (AI) techniques." PeerJ Comput Sci **10**: e1996.

Cancer, a life-threatening disorder caused by genetic abnormalities and metabolic irregularities, is a substantial health danger, with lung and colon cancer being major contributors to death. Histopathological identification is critical in directing effective treatment regimens for these cancers. The earlier these disorders are identified, the lesser the risk of death. The use of machine learning and deep learning approaches has the potential to speed up cancer diagnosis processes by allowing researchers to analyse large patient databases quickly and affordably. This study introduces the Inception-ResNetV2 model with strategically incorporated local binary patterns (LBP) features to improve diagnostic accuracy for lung and colon cancer identification. The model is trained on histopathological images, and the integration of deep learning and texture-based features has demonstrated its exceptional performance with 99.98% accuracy. Importantly, the study employs explainable artificial intelligence (AI) through SHapley Additive exPlanations (SHAP) to unravel the complex inner workings of deep learning models, providing transparency in decision-making processes. This study highlights the potential to revolutionize cancer diagnosis in an era of more accurate and reliable medical assessments.

Anaby, D., et al. (2023). "'Earlier than Early' Detection of Breast Cancer in Israeli BRCA Mutation Carriers Applying AI-Based Analysis to Consecutive MRI Scans." Cancers (Basel) **15**(12).

Female BRCA1/BRCA2 (=BRCA) pathogenic variants (PVs) carriers are at a substantially higher risk for developing breast cancer (BC) compared with the average risk population. Detection of BC at an early stage significantly improves prognosis. To facilitate early BC detection, a surveillance scheme is offered to BRCA PV carriers from age 25-30 years that includes annual

MRI based breast imaging. Indeed, adherence to the recommended scheme has been shown to be associated with earlier disease stages at BC diagnosis, more in-situ pathology, smaller tumors, and less axillary involvement. While MRI is the most sensitive modality for BC detection in BRCA PV carriers, there are a significant number of overlooked or misinterpreted radiological lesions (mostly enhancing foci), leading to a delayed BC diagnosis at a more advanced stage. In this study we developed an artificial intelligence (AI)-network, aimed at a more accurate classification of enhancing foci, in MRIs of BRCA PV carriers, thus reducing false-negative interpretations. Retrospectively identified foci in prior MRIs that were either diagnosed as BC or benign/normal in a subsequent MRI were manually segmented and served as input for a convolutional network architecture. The model was successful in classification of 65% of the cancerous foci, most of them triple-negative BC. If validated, applying this scheme routinely may facilitate 'earlier than early' BC diagnosis in BRCA PV carriers.

Andreeva, V., et al. (2021). "Preoperative AI-Driven Fluorescence Diagnosis of Non-Melanoma Skin Cancer." Diagnostics (Basel) **12**(1).

The diagnosis and treatment of non-melanoma skin cancer remain urgent problems. Histological examination of biopsy material-the gold standard of diagnosis-is an invasive procedure that requires a certain amount of time to perform. The ability to detect abnormal cells using fluorescence spectroscopy (FS) has been shown in many studies. This technique is rapidly expanding due to its safety, relative cost-effectiveness, and efficiency. However, skin lesion FS-based diagnosis is challenging due to a number of single overlapping spectra emitted by fluorescent molecules, making it difficult to distinguish changes in the overall spectrum and the molecular basis for it. We applied deep learning (DL) algorithms to quantitatively assess the ability of FS to differentiate between pathologies and normal skin. A total of 137 patients with various forms of primary and recurrent basal cell carcinoma (BCC) were observed by a multispectral laser-based device with a built-in neural network (NN) "DSL-1". We measured the fluorescence spectra of suspected non-melanoma skin cancers and compared them with "normal" skin spectra. These spectra were input into DL algorithms to determine whether the skin is normal, pigmented normal, benign, or BCC. The preoperative differential AI-driven fluorescence diagnosis method correctly predicted the BCC lesions. We obtained an average sensitivity of 62% and average specificity of 83% in our experiments. Thus, the presented "DSL-1" diagnostic device can be a viable tool for the real-time diagnosis and guidance of non-melanoma skin cancer resection.

Annan, A., et al. (2024). "Using AI and Social Media to Understand Health Disparities for Transgender Cancer Care." JAMA Netw Open **7**(8): e2429792.

This qualitative study used an artificial intelligence (AI) large language model and social media to investigate challenges encountered by transgender individuals during breast and gynecological cancer care.
eng fees from GSK and AstraZeneca outside the submitted work. Dr Sun reported owning stock from Merck and Co and UnitedHealth Group outside the submitted work. No other disclosures were reported.

Arasu, V. A., et al. (2023). "Comparison of Mammography AI Algorithms with a Clinical Risk Model for 5-year Breast Cancer Risk Prediction: An Observational Study." Radiology **307**(5): e222733.

Background Although several clinical breast cancer risk models are used to guide screening and prevention, they have only moderate discrimination. Purpose To compare selected existing mammography artificial intelligence (AI) algorithms and the Breast Cancer Surveillance Consortium (BCSC) risk model for prediction of 5-year risk. Materials and Methods This retrospective case-cohort study included data in women with a negative screening mammographic examination (no visible evidence of cancer) in 2016, who were followed until 2021 at Kaiser Permanente Northern California. Women with prior breast cancer or a highly penetrant gene mutation were excluded. Of the 324 009 eligible women, a random subcohort was selected, regardless of cancer status, to which all additional patients with breast cancer were added. The index screening mammographic examination was used as input for five AI algorithms to generate continuous scores that were compared with the BCSC clinical risk score. Risk estimates for incident breast cancer 0 to 5 years after the initial mammographic examination were calculated using a time-dependent area under the receiver operating characteristic curve (AUC). Results The subcohort included 13 628 patients, of whom 193 had incident cancer. Incident cancers in eligible patients (additional 4391 of 324 009) were also included. For incident cancers at 0 to 5 years, the time-dependent AUC for BCSC was 0.61 (95% CI: 0.60, 0.62). AI algorithms had higher time-dependent AUCs than did BCSC, ranging from 0.63 to 0.67 (Bonferroni-adjusted P < .0016). Time-dependent AUCs for combined BCSC and AI models were slightly higher than AI alone (AI with BCSC time-dependent AUC range, 0.66-0.68; Bonferroni-adjusted P < .0016). Conclusion When using a negative screening examination, AI algorithms

performed better than the BCSC risk model for predicting breast cancer risk at 0 to 5 years. Combined AI and BCSC models further improved prediction. (c) RSNA, 2023 Supplemental material is available for this article.

Augusto, T. V., et al. (2021). "Effects of PI3K inhibition in AI-resistant breast cancer cell lines: autophagy, apoptosis, and cell cycle progression." Breast Cancer Res Treat **190**(2): 227-240.

INTRODUCTION: Breast cancer is the leading cause of cancer death in women. The aromatase inhibitors (AIs), Anastrozole (Ana), Letrozole (Let), and Exemestane (Exe) are a first-line treatment option for estrogen receptor-positive (ER(+)) breast tumors, in postmenopausal women. Nevertheless, the development of acquired resistance to this therapy is a major drawback. The involvement of PI3K in resistance, through activation of the PI3K/AKT/mTOR survival pathway or through a cytoprotective autophagic process, is widely described. MATERIALS AND METHODS: The involvement of autophagy in response to Ana and Let treatments and the effects of the combination of BYL-719, a PI3K inhibitor, with AIs were explored in AI-resistant breast cancer cell lines (LTEDaro, AnaR, LetR, and ExeR). RESULTS: We demonstrate that Ana and Let treatments do not promote autophagy in resistant breast cancer cells, contrary to Exe. Moreover, the combinations of BYL-719 with AIs decrease cell viability by different mechanisms by nonsteroidal vs. steroidal AIs. The combination of BYL-719 with Ana or Let induced cell cycle arrest while the combination with Exe promoted cell cycle arrest and apoptosis. In addition, BYL-719 decreased AnaR, LetR, and ExeR cell viability in a dose- and time-dependent manner, being more effective in the ExeR cell line. This decrease was further exacerbated by ICI 182,780. CONCLUSION: These results corroborate the lack of cross-resistance between AIs verified in the clinic, excluding autophagy as a mechanism of resistance to Ana or Let and supporting the ongoing clinical trials combining BYL-719 with AIs.

Auzine, M. M., et al. (2024). "Development of an ensemble CNN model with explainable AI for the classification of gastrointestinal cancer." PLoS One **19**(6): e0305628.

The implementation of AI assisted cancer detection systems in clinical environments has faced numerous hurdles, mainly because of the restricted explainability of their elemental mechanisms, even though such detection systems have proven to be highly effective. Medical practitioners are skeptical about adopting AI assisted diagnoses as due to the latter's inability to be transparent about decision making processes. In this respect, explainable artificial intelligence (XAI) has emerged to provide explanations for model predictions, thereby overcoming the computational black box problem associated with AI systems. In this particular research, the focal point has been the exploration of the Shapley additive explanations (SHAP) and local interpretable model-agnostic explanations (LIME) approaches which enable model prediction explanations. This study used an ensemble model consisting of three convolutional neural networks(CNN): InceptionV3, InceptionResNetV2 and VGG16, which was based on averaging techniques and by combining their respective predictions. These models were trained on the Kvasir dataset, which consists of pathological findings related to gastrointestinal cancer. An accuracy of 96.89% and F1-scores of 96.877% were attained by our ensemble model. Following the training of the ensemble model, we employed SHAP and LIME to analyze images from the three classes, aiming to provide explanations regarding the deterministic features influencing the model's predictions. The results obtained from this analysis demonstrated a positive and encouraging advancement in the exploration of XAI approaches, specifically in the context of gastrointestinal cancer detection within the healthcare domain.

Ayling, R. M. and F. Cotter (2024). "Diagnostic application of the ColonFlag AI tool in combination with faecal immunochemical test in patients on an urgent lower gastrointestinal cancer pathway." BMJ Open Gastroenterol **11**(1).

OBJECTIVE: Colorectal cancer (CRC) is the fourth most common cancer in the UK. Patients with symptoms suggestive of CRC should be referred for urgent investigation. However, gastrointestinal symptoms are often non-specific and there is a need for suitable triage tools to enable prioritisation of investigations. In this study, the performance of the faecal immunochemical test (FIT), anaemia and the artificial intelligence algorithm ColonFlag were retrospectively examined and evaluated for their potential clinical benefits in patients who had been referred on an urgent lower gastrointestinal cancer pathway. DESIGN: All patients aged over 40 years referred in a 12-month period were included. After 6 months, clinical outcomes were determined and the performance of the triage tests was evaluated. RESULTS: A total of 3822 patients completed investigations and received a diagnosis. 143 had CRC, 126 high-risk adenomas (HRA). ColonFlag would have missed 27 CRC and 29 HRA. Faecal haemoglobin (f-Hb) at a cut-off of 10 microg/g

would have missed 10 CRC and 26 HRA; f-Hb in combination with anaemia would have missed 2 CRC and 14 HRA. Using f-Hb in combination with ColonFlag would have missed only 1 CRC and 5 HRA and would have reduced the need for urgent referral by over 400 patients. CONCLUSION: ColonFlag has potential to assist detection of CRC and HRA, alone where no faecal sample is present and in combination with FIT and to reduce the need for urgent referral.

Ayyad, S. M., et al. (2021). "Role of AI and Histopathological Images in Detecting Prostate Cancer: A Survey." Sensors (Basel) **21**(8).

Prostate cancer is one of the most identified cancers and second most prevalent among cancer-related deaths of men worldwide. Early diagnosis and treatment are substantial to stop or handle the increase and spread of cancer cells in the body. Histopathological image diagnosis is a gold standard for detecting prostate cancer as it has different visual characteristics but interpreting those type of images needs a high level of expertise and takes too much time. One of the ways to accelerate such an analysis is by employing artificial intelligence (AI) through the use of computer-aided diagnosis (CAD) systems. The recent developments in artificial intelligence along with its sub-fields of conventional machine learning and deep learning provide new insights to clinicians and researchers, and an abundance of research is presented specifically for histopathology images tailored for prostate cancer. However, there is a lack of comprehensive surveys that focus on prostate cancer using histopathology images. In this paper, we provide a very comprehensive review of most, if not all, studies that handled the prostate cancer diagnosis using histopathological images. The survey begins with an overview of histopathological image preparation and its challenges. We also briefly review the computing techniques that are commonly applied in image processing, segmentation, feature selection, and classification that can help in detecting prostate malignancies in histopathological images.

Batra, U., et al. (2024). "AI-based pipeline for early screening of lung cancer: integrating radiology, clinical, and genomics data." Lancet Reg Health Southeast Asia **24**: 100352.

BACKGROUND: The prognosis of lung carcinoma has changed since the discovery of molecular targets and their specific drugs. Somatic Epidermal Growth Factor Receptor (EGFR) mutations have been reported in lung carcinoma, and these mutant proteins act as substrates for targeted therapies. However, in a resource-constrained country like India, panel-based next-generation sequencing cannot be made available to the population at large. Additional challenges such as adequacy of tissue in case of lung core biopsies and locating suitable tumour tissues as a result of innate intratumoral heterogeneity indicate the necessity of an AI-based end-to-end pipeline capable of automatically detecting and learning more effective lung nodule features from CT images and predicting the probability of the EGFR-mutant. This will help the oncologists and patients in resource-limited settings to achieve near-optimal care and appropriate therapy. METHODS: The EGFR gene sequencing and CT imaging data of 2277 patients with lung carcinoma were included from three cohorts in India and a White population cohort collected from TCIA. Another cohort LIDC-IDRI was used to train the AIPS-Nodule (AIPS-N) model for automatic detection and characterisation of lung nodules. We explored the value of combining the results of the AIPS-N with the clinical factors in the AIPS-Mutation (AIPS-M) model for predicting EGFR genotype, and it was evaluated by area under the curve (AUC). FINDINGS: AIPS-N achieved an average AP50 of 70.19% in detecting the location of nodules within the lung region of interest during validation and predicted the score of five lung nodule properties. The AIPS-M machine learning (ML) and deep learning (DL) models achieved AUCs ranging from 0.587 to 0.910. INTERPRETATION: The AIPS suggests that CT imaging combined with a fully automated lung-nodule analysis AI system can predict EGFR genotype and identify patients with an EGFR mutation in a cost-effective and non-invasive manner. FUNDING: This work was supported by a grant provided by Conquer Cancer Foundation of ASCO [2021IIG-5555960128] and Pfizer Products India Pvt. Ltd.

Bernstein, M. H., et al. (2023). "Can incorrect artificial intelligence (AI) results impact radiologists, and if so, what can we do about it? A multi-reader pilot study of lung cancer detection with chest radiography." Eur Radiol **33**(11): 8263-8269.

OBJECTIVE: To examine whether incorrect AI results impact radiologist performance, and if so, whether human factors can be optimized to reduce error. METHODS: Multi-reader design, 6 radiologists interpreted 90 identical chest radiographs (follow-up CT needed: yes/no) on four occasions (09/20-01/22). No AI result was provided for session 1. Sham AI results were provided for sessions 2-4, and AI for 12 cases were manipulated to be incorrect (8 false positives (FP), 4 false negatives (FN)) (0.87 ROC-AUC). In the Delete AI (No Box) condition, radiologists were told AI results would not be saved for the evaluation. In Keep AI (No Box) and Keep AI

(Box), radiologists were told results would be saved. In Keep AI (Box), the ostensible AI program visually outlined the region of suspicion. AI results were constant between conditions. RESULTS: Relative to the No AI condition (FN = 2.7%, FP = 51.4%), FN and FPs were higher in the Keep AI (No Box) (FN = 33.0%, FP = 86.0%), Delete AI (No Box) (FN = 26.7%, FP = 80.5%), and Keep AI (Box) (FN = to 20.7%, FP = 80.5%) conditions (all ps < 0.05). FNs were higher in the Keep AI (No Box) condition (33.0%) than in the Keep AI (Box) condition (20.7%) (p = 0.04). FPs were higher in the Keep AI (No Box) (86.0%) condition than in the Delete AI (No Box) condition (80.5%) (p = 0.03). CONCLUSION: Incorrect AI causes radiologists to make incorrect follow-up decisions when they were correct without AI. This effect is mitigated when radiologists believe AI will be deleted from the patient's file or a box is provided around the region of interest. CLINICAL RELEVANCE STATEMENT: When AI is wrong, radiologists make more errors than they would have without AI. Based on human factors psychology, our manuscript provides evidence for two AI implementation strategies that reduce the deleterious effects of incorrect AI. KEY POINTS: * When AI provided incorrect results, false negative and false positive rates among the radiologists increased. * False positives decreased when AI results were deleted, versus kept, in the patient's record. * False negatives and false positives decreased when AI visually outlined the region of suspicion.

Bhattacharya, S., et al. (2023). "Advances and challenges in thyroid cancer: The interplay of genetic modulators, targeted therapies, and AI-driven approaches." Life Sci **332**: 122110.

Thyroid cancer continues to exhibit a rising incidence globally, predominantly affecting women. Despite stable mortality rates, the unique characteristics of thyroid carcinoma warrant a distinct approach. Differentiated thyroid cancer, comprising most cases, is effectively managed through standard treatments such as thyroidectomy and radioiodine therapy. However, rarer variants, including anaplastic thyroid carcinoma, necessitate specialized interventions, often employing targeted therapies. Although these drugs focus on symptom management, they are not curative. This review delves into the fundamental modulators of thyroid cancers, encompassing genetic, epigenetic, and non-coding RNA factors while exploring their intricate interplay and influence. Epigenetic modifications directly affect the expression of causal genes, while long non-coding RNAs impact the function and expression of micro-RNAs, culminating in tumorigenesis. Additionally, this article provides a concise overview of the advantages and disadvantages associated with pharmacological and non-pharmacological therapeutic interventions in thyroid cancer. Furthermore, with technological advancements, integrating modern software and computing into healthcare and medical practices has become increasingly prevalent. Artificial intelligence and machine learning techniques hold the potential to predict treatment outcomes, analyze data, and develop personalized therapeutic approaches catering to patient specificity. In thyroid cancer, cutting-edge machine learning and deep learning technologies analyze factors such as ultrasonography results for tumor textures and biopsy samples from fine needle aspirations, paving the way for a more accurate and effective therapeutic landscape in the near future.

Bhattacharya, S., et al. (2024). "Empowering precision medicine: regenerative AI in breast cancer." Front Oncol **14**: 1465720.

Regenerative AI is transforming breast cancer diagnosis and treatment through enhanced imaging analysis, personalized medicine, drug discovery, and remote patient monitoring. AI algorithms can detect subtle patterns in mammograms and other imaging modalities with high accuracy, potentially leading to earlier diagnoses. In treatment planning, AI integrates patient-specific data to predict individual responses and optimize therapies. For drug discovery, generative AI models rapidly design and screen novel molecules targeting breast cancer pathways. Remote monitoring tools powered by AI provide real-time insights to guide care. Examples include Google's LYNA for analyzing pathology slides, Kheiron's Mia for mammogram interpretation, and Tempus's platform for integrating clinical and genomic data. While promising, challenges remain, including limited high-quality training data, integration into clinical workflows, interpretability of AI decisions, and regulatory/ethical concerns. Strategies to address these include collaborative data-sharing initiatives, user-centered design, explainable AI techniques, and robust oversight frameworks. In developing countries, AI tools like MammoAssist and Niramai's thermal imaging system are improving access to screening. Overall, regenerative AI offers significant potential to enhance breast cancer care, but judicious implementation with awareness of limitations is crucial. Coordinated efforts across the healthcare ecosystem are needed to fully realize AI's benefits while addressing challenges.

Bhattacharya, T., et al. (2019). "AI Meets Exascale Computing: Advancing Cancer Research With Large-Scale High Performance Computing." Front Oncol **9**:

984.

The application of data science in cancer research has been boosted by major advances in three primary areas: (1) Data: diversity, amount, and availability of biomedical data; (2) Advances in Artificial Intelligence (AI) and Machine Learning (ML) algorithms that enable learning from complex, large-scale data; and (3) Advances in computer architectures allowing unprecedented acceleration of simulation and machine learning algorithms. These advances help build in silico ML models that can provide transformative insights from data including: molecular dynamics simulations, next-generation sequencing, omics, imaging, and unstructured clinical text documents. Unique challenges persist, however, in building ML models related to cancer, including: (1) access, sharing, labeling, and integration of multimodal and multi-institutional data across different cancer types; (2) developing AI models for cancer research capable of scaling on next generation high performance computers; and (3) assessing robustness and reliability in the AI models. In this paper, we review the National Cancer Institute (NCI) -Department of Energy (DOE) collaboration, Joint Design of Advanced Computing Solutions for Cancer (JDACS4C), a multi-institution collaborative effort focused on advancing computing and data technologies to accelerate cancer research on three levels: molecular, cellular, and population. This collaboration integrates various types of generated data, pre-exascale compute resources, and advances in ML models to increase understanding of basic cancer biology, identify promising new treatment options, predict outcomes, and eventually prescribe specialized treatments for patients with cancer.

Bhattarai, S., et al. (2024). "Advancing Peptide-Based Cancer Therapy with AI: In-Depth Analysis of State-of-the-Art AI Models." J Chem Inf Model **64**(13): 4941-4957.

Anticancer peptides (ACPs) play a vital role in selectively targeting and eliminating cancer cells. Evaluating and comparing predictions from various machine learning (ML) and deep learning (DL) techniques is challenging but crucial for anticancer drug research. We conducted a comprehensive analysis of 15 ML and 10 DL models, including the models released after 2022, and found that support vector machines (SVMs) with feature combination and selection significantly enhance overall performance. DL models, especially convolutional neural networks (CNNs) with light gradient boosting machine (LGBM) based feature selection approaches, demonstrate improved characterization. Assessment using a new test data set (ACP10) identifies ACPred, MLACP 2.0, AI4ACP, mACPred, and AntiCP2.0_AAC as successive optimal predictors, showcasing robust performance. Our review underscores current prediction tool limitations and advocates for an omnidirectional ACP prediction framework to propel ongoing research.

Bidzinska, J. and E. Szurowska (2023). "See Lung Cancer with an AI." Cancers (Basel) **15**(4).

A lot has happened in the field of lung cancer screening in recent months. The ongoing discussion and documentation published by the scientific community and policymakers are of great importance to the entire European community and perhaps beyond. Lung cancer is the main worldwide killer. Low-dose computed tomography-based screening, together with smoking cessation, is the only tool to fight lung cancer, as it has already been proven in the United States of America but also European randomized controlled trials. Screening requires a lot of well-organized specialized work, but it can be supported by artificial intelligence (AI). Here we discuss whether and how to use AI for patients, radiologists, pulmonologists, thoracic surgeons, and all hospital staff supporting screening process benefits.

Bifarin, O. O. and F. M. Fernandez (2023). "Automated machine learning and explainable AI (AutoML-XAI) for metabolomics: improving cancer diagnostics." bioRxiv.

MOTIVATION: Metabolomics generates complex data necessitating advanced computational methods for generating biological insight. While machine learning (ML) is promising, the challenges of selecting the best algorithms and tuning hyperparameters, particularly for non-experts, remain. Automated machine learning (AutoML) can streamline this process; however, the issue of interpretability could persist. This research introduces a unified pipeline that combines AutoML with explainable AI (XAI) techniques to optimize metabolomics analysis. RESULTS: We tested our approach on two datasets: renal cell carcinoma (RCC) urine metabolomics and ovarian cancer (OC) serum metabolomics. AutoML, using auto-sklearn, surpassed standalone ML algorithms such as SVM and random forest in differentiating between RCC and healthy controls, as well as OC patients and those with other gynecological cancers (Non-OC). Auto-sklearn employed a mix of algorithms and ensemble techniques, yielding a superior performance (AUC of 0.97 for RCC and 0.85 for OC). Shapley Additive Explanations (SHAP) provided a global ranking of feature importance, identifying dibutylamine and ganglioside GM(d34:1) as the top discriminative metabolites for RCC and OC, respectively. Waterfall

plots offered local explanations by illustrating the influence of each metabolite on individual predictions. Dependence plots spotlighted metabolite interactions, such as the connection between hippuric acid and one of its derivatives in RCC, and between GM3(d34:1) and GM3(18:1_16:0) in OC, hinting at potential mechanistic relationships. Through decision plots, a detailed error analysis was conducted, contrasting feature importance for correctly versus incorrectly classified samples. In essence, our pipeline emphasizes the importance of harmonizing AutoML and XAI, facilitating both simplified ML application and improved interpretability in metabolomics data science. AVAILABILITY: https://github.com/obifarin/automl-xai-metabolomics.

Bifarin, O. O. and F. M. Fernandez (2024). "Automated Machine Learning and Explainable AI (AutoML-XAI) for Metabolomics: Improving Cancer Diagnostics." J Am Soc Mass Spectrom **35**(6): 1089-1100.

Metabolomics generates complex data necessitating advanced computational methods for generating biological insight. While machine learning (ML) is promising, the challenges of selecting the best algorithms and tuning hyperparameters, particularly for nonexperts, remain. Automated machine learning (AutoML) can streamline this process; however, the issue of interpretability could persist. This research introduces a unified pipeline that combines AutoML with explainable AI (XAI) techniques to optimize metabolomics analysis. We tested our approach on two data sets: renal cell carcinoma (RCC) urine metabolomics and ovarian cancer (OC) serum metabolomics. AutoML, using Auto-sklearn, surpassed standalone ML algorithms like SVM and k-Nearest Neighbors in differentiating between RCC and healthy controls, as well as OC patients and those with other gynecological cancers. The effectiveness of Auto-sklearn is highlighted by its AUC scores of 0.97 for RCC and 0.85 for OC, obtained from the unseen test sets. Importantly, on most of the metrics considered, Auto-sklearn demonstrated a better classification performance, leveraging a mix of algorithms and ensemble techniques. Shapley Additive Explanations (SHAP) provided a global ranking of feature importance, identifying dibutylamine and ganglioside GM(d34:1) as the top discriminative metabolites for RCC and OC, respectively. Waterfall plots offered local explanations by illustrating the influence of each metabolite on individual predictions. Dependence plots spotlighted metabolite interactions, such as the connection between hippuric acid and one of its derivatives in RCC, and between GM3(d34:1) and GM3(18:1_16:0) in OC, hinting at potential mechanistic relationships. Through decision plots, a detailed error analysis was conducted, contrasting feature importance for correctly versus incorrectly classified samples. In essence, our pipeline emphasizes the importance of harmonizing AutoML and XAI, facilitating both simplified ML application and improved interpretability in metabolomics data science.

Binzagr, F. (2024). "Explainable AI-driven model for gastrointestinal cancer classification." Front Med (Lausanne) **11**: 1349373.

Although the detection procedure has been shown to be highly effective, there are several obstacles to overcome in the usage of AI-assisted cancer cell detection in clinical settings. These issues stem mostly from the failure to identify the underlying processes. Because AI-assisted diagnosis does not offer a clear decision-making process, doctors are dubious about it. In this instance, the advent of Explainable Artificial Intelligence (XAI), which offers explanations for prediction models, solves the AI black box issue. The SHapley Additive exPlanations (SHAP) approach, which results in the interpretation of model predictions, is the main emphasis of this work. The intermediate layer in this study was a hybrid model made up of three Convolutional Neural Networks (CNNs) (InceptionV3, InceptionResNetV2, and VGG16) that combined their predictions. The KvasirV2 dataset, which comprises pathological symptoms associated to cancer, was used to train the model. Our combined model yielded an accuracy of 93.17% and an F1 score of 97%. After training the combined model, we use SHAP to analyze images from these three groups to provide an explanation of the decision that affects the model prediction.

Biswas, N. and S. Chakrabarti (2020). "Artificial Intelligence (AI)-Based Systems Biology Approaches in Multi-Omics Data Analysis of Cancer." Front Oncol **10**: 588221.

Cancer is the manifestation of abnormalities of different physiological processes involving genes, DNAs, RNAs, proteins, and other biomolecules whose profiles are reflected in different omics data types. As these bio-entities are very much correlated, integrative analysis of different types of omics data, multi-omics data, is required to understanding the disease from the tumorigenesis to the disease progression. Artificial intelligence (AI), specifically machine learning algorithms, has the ability to make decisive interpretation of "big"-sized complex data and, hence, appears as the most effective tool for the analysis and understanding of multi-omics data for patient-specific observations. In this review, we have

discussed about the recent outcomes of employing AI in multi-omics data analysis of different types of cancer. Based on the research trends and significance in patient treatment, we have primarily focused on the AI-based analysis for determining cancer subtypes, disease prognosis, and therapeutic targets. We have also discussed about AI analysis of some non-canonical types of omics data as they have the capability of playing the determiner role in cancer patient care. Additionally, we have briefly discussed about the data repositories because of their pivotal role in multi-omics data storing, processing, and analysis.

Bluethmann, S. M., et al. (2021). "Study design and methods for the using exercise to relieve joint pain and improve AI adherence in older breast cancer survivors (REJOIN) trial." J Geriatr Oncol **12**(7): 1146-1153.

BACKGROUND: Aromatase Inhibitors (AIs) are recommended for survival in post-menopausal breast cancer survivors (BCS) with hormone-sensitive disease. AI Adherence is suboptimal, especially in older BCS. Joint pain is a common AI-related symptom that is associated with low AI adherence. The Using Exercise to Relieve Joint Pain in Older Breast Cancer Survivors (REJOIN) Trial will evaluate the efficacy of a self-management intervention (exercise + education) to increase knowledge/self-efficacy for symptom management, reduce joint pain and potentially increase AI adherence in older BCS planning to take AIs. METHODS: This randomized controlled pilot trial will include sedentary BCS, 65 years and older, diagnosed with stage I-III hormone-sensitive breast cancer, who have completed primary cancer treatment and are planning to initiate AIs. We will adapt an evidence-based physical activity program for older adults that includes bi-weekly, supervised exercise sessions plus 30 min of education. The 16-week intervention program includes: 8-weeks of supervised sessions plus 8-weeks of self-guided home sessions with periodic phone coaching. We will conduct geriatric assessments plus measurements of exercise, joint pain, and AI adherence (baseline, 4, 6 and 12 months). DISCUSSION: REJOIN is one of the first trials to exclusively target older BCS using a self-management intervention, informed by geriatric assessment and exercise physiology, to improve health outcomes in survivorship. The REJOIN trial could lay the foundation for transdisciplinary research that bridges the gap between clinical and public health perspectives in healthy aging, with the opportunity to translate clinical interventions into non-pharmacological tools for a growing, yet underserved population of older survivors. TRIAL REGISTRATION: NCT03955627.

Bonmati, L. M., et al. (2022). "CHAIMELEON Project: Creation of a Pan-European Repository of Health Imaging Data for the Development of AI-Powered Cancer Management Tools." Front Oncol **12**: 742701.

The CHAIMELEON project aims to set up a pan-European repository of health imaging data, tools and methodologies, with the ambition to set a standard and provide resources for future AI experimentation for cancer management. The project is a 4 year long, EU-funded project tackling some of the most ambitious research in the fields of biomedical imaging, artificial intelligence and cancer treatment, addressing the four types of cancer that currently have the highest prevalence worldwide: lung, breast, prostate and colorectal. To allow this, clinical partners and external collaborators will populate the repository with multimodality (MR, CT, PET/CT) imaging and related clinical data. Subsequently, AI developers will enable a multimodal analytical data engine facilitating the interpretation, extraction and exploitation of the information stored at the repository. The development and implementation of AI-powered pipelines will enable advancement towards automating data deidentification, curation, annotation, integrity securing and image harmonization. By the end of the project, the usability and performance of the repository as a tool fostering AI experimentation will be technically validated, including a validation subphase by world-class European AI developers, participating in Open Challenges to the AI Community. Upon successful validation of the repository, a set of selected AI tools will undergo early in-silico validation in observational clinical studies coordinated by leading experts in the partner hospitals. Tool performance will be assessed, including external independent validation on hallmark clinical decisions in response to some of the currently most important clinical end points in cancer. The project brings together a consortium of 18 European partners including hospitals, universities, R&D centers and private research companies, constituting an ecosystem of infrastructures, biobanks, AI/in-silico experimentation and cloud computing technologies in oncology.

Borrelli, F., et al. (2023). "AI-aided holographic flow cytometry for label-free identification of ovarian cancer cells in the presence of unbalanced datasets." APL Bioeng **7**(2): 026110.

Liquid biopsy is a valuable emerging alternative to tissue biopsy with great potential in the noninvasive early diagnostics of cancer. Liquid

biopsy based on single cell analysis can be a powerful approach to identify circulating tumor cells (CTCs) in the bloodstream and could provide new opportunities to be implemented in routine screening programs. Since CTCs are very rare, the accurate classification based on high-throughput and highly informative microscopy methods should minimize the false negative rates. Here, we show that holographic flow cytometry is a valuable instrument to obtain quantitative phase-contrast maps as input data for artificial intelligence (AI)-based classifiers. We tackle the problem of discriminating between A2780 ovarian cancer cells and THP1 monocyte cells based on the phase-contrast images obtained in flow cytometry mode. We compare conventional machine learning analysis and deep learning architectures in the non-ideal case of having a dataset with unbalanced populations for the AI training step. The results show the capacity of AI-aided holographic flow cytometry to discriminate between the two cell lines and highlight the important role played by the phase-contrast signature of the cells to guarantee accurate classification.

Borrelli, P., et al. (2021). "AI-based detection of lung lesions in [(18)F]FDG PET-CT from lung cancer patients." EJNMMI Phys **8**(1): 32.

BACKGROUND: [(18)F]-fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET-CT) is a well-established modality in the work-up of patients with suspected or confirmed diagnosis of lung cancer. Recent research efforts have focused on extracting theragnostic and textural information from manually indicated lung lesions. Both semi-automatic and fully automatic use of artificial intelligence (AI) to localise and classify FDG-avid foci has been demonstrated. To fully harness AI's usefulness, we have developed a method which both automatically detects abnormal lung lesions and calculates the total lesion glycolysis (TLG) on FDG PET-CT. METHODS: One hundred twelve patients (59 females and 53 males) who underwent FDG PET-CT due to suspected or for the management of known lung cancer were studied retrospectively. These patients were divided into a training group (59%; n = 66), a validation group (20.5%; n = 23) and a test group (20.5%; n = 23). A nuclear medicine physician manually segmented abnormal lung lesions with increased FDG-uptake in all PET-CT studies. The AI-based method was trained to segment the lesions based on the manual segmentations. TLG was then calculated from manual and AI-based measurements, respectively and analysed with Bland-Altman plots. RESULTS: The AI-tool's performance in detecting lesions had a sensitivity of 90%. One small lesion was missed in two patients, respectively, where both had a larger lesion which was correctly detected. The positive and negative predictive values were 88% and 100%, respectively. The correlation between manual and AI TLG measurements was strong (R(2) = 0.74). Bias was 42 g and 95% limits of agreement ranged from -736 to 819 g. Agreement was particularly high in smaller lesions. CONCLUSIONS: The AI-based method is suitable for the detection of lung lesions and automatic calculation of TLG in small- to medium-sized tumours. In a clinical setting, it will have an added value due to its capability to sort out negative examinations resulting in prioritised and focused care on patients with potentially malignant lesions.

Bradley, J. D., et al. (2006). "Comparison of helical, maximum intensity projection (MIP), and averaged intensity (AI) 4D CT imaging for stereotactic body radiation therapy (SBRT) planning in lung cancer." Radiother Oncol **81**(3): 264-268.

BACKGROUND AND PURPOSE: To compare helical, MIP and AI 4D CT imaging, for the purpose of determining the best CT-based volume definition method for encompassing the mobile gross tumor volume (mGTV) within the planning target volume (PTV) for stereotactic body radiation therapy (SBRT) in stage I lung cancer. MATERIALS AND METHODS: Twenty patients with medically inoperable peripheral stage I lung cancer were planned for SBRT. Free-breathing helical and 4D image datasets were obtained for each patient. Two composite images, the MIP and AI, were automatically generated from the 4D image datasets. The mGTV contours were delineated for the MIP, AI and helical image datasets for each patient. The volume for each was calculated and compared using analysis of variance and the Wilcoxon rank test. A spatial analysis for comparing center of mass (COM) (i.e. isocenter) coordinates for each imaging method was also performed using multivariate analysis of variance. RESULTS: The MIP-defined mGTVs were significantly larger than both the helical- (p=0.001) and AI-defined mGTVs (p=0.012). A comparison of COM coordinates demonstrated no significant spatial difference in the x-, y-, and z-coordinates for each tumor as determined by helical, MIP, or AI imaging methods. CONCLUSIONS: In order to incorporate the extent of tumor motion from breathing during SBRT, MIP is superior to either helical or AI images for defining the mGTV. The spatial isocenter coordinates for each tumor were not altered significantly by the imaging methods.

Brattoli, B., et al. (2024). "A universal immunohistochemistry analyzer for generalizing AI-

driven assessment of immunohistochemistry across immunostains and cancer types." NPJ Precis Oncol **8**(1): 277.

Immunohistochemistry (IHC) is the common companion diagnostics in targeted therapies. However, quantifying protein expressions in IHC images present a significant challenge, due to variability in manual scoring and inherent subjective interpretation. Deep learning (DL) offers a promising approach to address these issues, though current models require extensive training for each cancer and IHC type, limiting the practical application. We developed a Universal IHC (UIHC) analyzer, a DL-based tool that quantifies protein expression across different cancers and IHC types. This multi-cohort trained model outperformed conventional single-cohort models in analyzing unseen IHC images (Kappa score 0.578 vs. up to 0.509) and demonstrated consistent performance across varying positive staining cutoff values. In a discovery application, the UIHC model assigned higher tumor proportion scores to MET amplification cases, but not MET exon 14 splicing or other non-small cell lung cancer cases. This UIHC model represents a novel role for DL that further advances quantitative analysis of IHC.

Burrell, A. (2024). "Yonder: Improving connections, AI in reflective practice, lung cancer diagnosis, and euthanasia aftercare." Br J Gen Pract **74**(748): 508.

Caliskan, M. and K. Tazaki (2023). "AI/ML advances in non-small cell lung cancer biomarker discovery." Front Oncol **13**: 1260374.

Lung cancer is the leading cause of cancer deaths among both men and women, representing approximately 25% of cancer fatalities each year. The treatment landscape for non-small cell lung cancer (NSCLC) is rapidly evolving due to the progress made in biomarker-driven targeted therapies. While advancements in targeted treatments have improved survival rates for NSCLC patients with actionable biomarkers, long-term survival remains low, with an overall 5-year relative survival rate below 20%. Artificial intelligence/machine learning (AI/ML) algorithms have shown promise in biomarker discovery, yet NSCLC-specific studies capturing the clinical challenges targeted and emerging patterns identified using AI/ML approaches are lacking. Here, we employed a text-mining approach and identified 215 studies that reported potential biomarkers of NSCLC using AI/ML algorithms. We catalogued these studies with respect to BEST (Biomarkers, EndpointS, and other Tools) biomarker sub-types and summarized emerging patterns and trends in AI/ML-driven NSCLC biomarker discovery. We anticipate that our comprehensive review will contribute to the current understanding of AI/ML advances in NSCLC biomarker research and provide an important catalogue that may facilitate clinical adoption of AI/ML-derived biomarkers.

Cao, K., et al. (2023). "Can AI-based body composition assessment outperform body surface area in predicting dose-limiting toxicities for colonic cancer patients on chemotherapy?" J Cancer Res Clin Oncol **149**(15): 13915-13923.

PURPOSE: Gold standard chemotherapy dosage is based on body surface area (BSA); however many patients experience dose-limiting toxicities (DLT). We aimed to evaluate the effectiveness of BSA, two-dimensional (2D) and three-dimensional (3D) body composition (BC) measurements derived from Lumbar 3 vertebra (L3) computed tomography (CT) slices, in predicting DLT in colon cancer patients. METHODS: 203 patients (60.87 +/- 12.42 years; 97 males, 47.8%) receiving adjuvant chemotherapy (Oxaliplatin and/or 5-Fluorouracil) were retrospectively evaluated. An artificial intelligence segmentation model was used to extract 2D and 3D body composition measurements from each patients' single mid-L3 CT slice as well as multiple-L3 CT scans to produce a 3D BC report. DLT was defined as any incidence of dose reduction or discontinuation due to chemotherapy toxicities. A receiver operating characteristic (ROC) analysis was performed on BSA and individual body composition measurements to demonstrate their predictive performance. RESULTS: A total of 120 (59.1%) patients experienced DLT. Age and BSA did not vary significantly between DLT and non-DLT group. Females were significantly more likely to experience DLT (p = 4.9 x 10(-3)). In all patients, the predictive effectiveness of 2D body composition measurements (females: AUC = 0.50-0.54; males: AUC = 0.50-0.61) was equivalent to that of BSA (females: AUC = 0.49; males: AUC = 0.58). The L3 3D skeletal muscle volume was the most predictive indicator of DLT (AUC of 0.66 in females and 0.64 in males). CONCLUSION: Compared to BSA and 2D body composition measurements, 3D L3 body composition measurements had greater potential to predict DLT in CRC patients receiving chemotherapy and this was sex dependent.

Cao, K., et al. (2024). "Improving the prediction of chemotherapy dose-limiting toxicity in colon cancer patients using an AI-CT-based 3D body composition of the entire L1-L5 lumbar spine." Support Care Cancer **33**(1): 45.

PURPOSE: Chemotherapy dose-limiting

toxicities (DLT) pose a significant challenge in successful colon cancer treatment. Body composition analysis may enable tailored interventions thereby supporting the mitigation of chemotherapy toxic effects. This study aimed to evaluate and compare the effectiveness of using three-dimensional (3D) CT body composition measures from the entire lumbar spine levels (L1-L5) versus a single vertebral level (L3), the current gold standard, in predicting chemotherapy DLT in colon cancer patients. METHODS: Retrospective analysis of 184 non-metastatic colon cancer patients receiving adjuvant chemotherapy was performed. DLT was defined as any occurrence of dose reduction or discontinuation due to chemotherapy toxicity. Using artificial intelligence (AI) auto-segmentation, 3D body composition measurements were obtained from patients' L1-L5 levels on CT imaging. The effectiveness of patients' 3D L3 body composition measurement and incorporating data from the entire L1-L5 (including L3) region in predicting DLT was examined. RESULTS: Of the 184 patients, 112 (60.9%) experienced DLT. Neuropathy was the most common toxicity (49/112, 43.8%) followed by diarrhea (35.7%) and nausea/vomiting (33%). Patients with DLT had lower muscle volume at all lumbar levels compared to those without. The machine learning model incorporating L1-L5 data and patient clinical data achieved high predictive performance (AUC = 0.75, accuracy = 0.75), outperforming the prediction using single L3 level (AUC = 0.65, accuracy = 0.65). CONCLUSION: Evaluating a patient's body composition allowed prediction of chemotherapy toxicities for colon cancer. Incorporating fully automated body composition analysis of CT slices from the entire lumbar region offers promising performance in early identification of high-risk individuals, with the ultimate aim of improving patient's quality of life.

Cao, X. L., et al. (2017). "[Downregulation of PTTG1 expression inhibits the proliferation and invasiveness and promotes the apoptosis of human prostate cancer LNCaP-AI cells]." Zhonghua Nan Ke Xue **23**(7): 589-597.

OBJECTIVE: To investigate the effects of down-regulation of PTTG1 expression on the proliferation, invasiveness and apoptosis of androgen-independent human prostate cancer LNCaP-AI cells and their sensitivity to androgen antagonists. METHODS: Human prostate cancer LNCaP-AI cells were transfected with siRNA targeting the PTTG1 gene using the Lipofectamine 2000 transfection reagent. The proliferation, invasiveness and apoptosis of the cells were detected by MTT, Transwell assay and flow cytometry, respectively. The protein expressions of PTTG1, p-Akt, and p-ERK were determined by Western blot and the mRNA expression of PTTG1 measured by agarose gel electrophoresis. RESULTS: The siRNA expression vector markedly down-regulated the expression of PTTG1, which effectively suppressed the proliferation of the LNCaP-AI cells, with the inhibition rates of (19.47 +/- 2.12), (24.01 +/- 2.13) and (48.02 +/- 2.22)% at 24, 48 and 72 hours, respectively, after transfection, with statistically significant differences among the three groups (P <0.05). The number of the cells passing through the polycarbonate film was remarkably decreased at 24, 48 and 72 hours (74.67 +/- 9.85, 56.44 +/- 8.66 and 37.33 +/- 6.14) as compared with the baseline (111.11 +/- 13.47) (P <0.01), while the apoptosis rate of the cells was significantly increased at 24, 48 and 72 hours (18.32 +/- 0.94), (19.94 +/- 1.30) and (21.73 +/- 1.88)% in comparison with the baseline ([2.17 +/- 0.49] %), (P <0.05). PTTG1 siRNA combined with androgen antagonist flumatide exhibited even more significant effects in inhibiting the proliferation and promoting the apoptosis of the LNCaP-AI cells than either used alone, and in a flumatide dose-dependent manner. The inhibition and apoptosis rates of the LNCaP-AI cells treated with 50 nmol/L flumatide were (27.13 +/- 3.52) and (3.94 +/- 0.48)%, and those treated with siRNA + 50 nmol/L flumatide were (67.51 +/- 5.13) and (19.93 +/- 1.72)%, respectively, both with statistically significant differences between the two groups (P <0.05). The inhibition and apoptosis rates of the cells treated with 100 nmol/L flumatide were (43.72 +/- 3.90) and (5.33 +/- 0.66)%, and those treated with siRNA + 100 nmol/L flumatide were (73.19 +/- 4.78) and (23.43 +/- 1.76)%, respectively, both with statistically significant differences between the two groups (P <0.05). CONCLUSIONS: The siRNA expression vector can down-regulate the expression of PTTG1, which can inhibit the proliferation and invasiveness of LNCaP-AI cells, promote their apoptosis, and increase their sensibility to androgen antagonists. Suppressing the expression of PTTG1 may enhance the effect of androgen-deprivation therapy on advanced prostate cancer.

Capobianco, E. (2022). "High-dimensional role of AI and machine learning in cancer research." Br J Cancer **126**(4): 523-532.

The role of Artificial Intelligence and Machine Learning in cancer research offers several advantages, primarily scaling up the information processing and increasing the accuracy of the clinical decision-making. The key enabling tools currently in use in Precision, Digital and Translational Medicine, here named as 'Intelligent Systems' (IS), leverage

unprecedented data volumes and aim to model their underlying heterogeneous influences and variables correlated with patients' outcomes. As functionality and performance of IS are associated with complex diagnosis and therapy decisions, a rich spectrum of patterns and features detected in high-dimensional data may be critical for inference purposes. Many challenges are also present in such discovery task. First, the generation of interpretable model results from a mix of structured and unstructured input information. Second, the design, and implementation of automated clinical decision processes for drawing disease trajectories and patient profiles. Ultimately, the clinical impacts depend on the data effectively subjected to steps such as harmonisation, integration, validation, etc. The aim of this work is to discuss the transformative value of IS applied to multimodal data acquired through various interrelated cancer domains (high-throughput genomics, experimental biology, medical image processing, radiomics, patient electronic records, etc.).

Chan, H. P., et al. (2020). "CAD and AI for breast cancer-recent development and challenges." Br J Radiol **93**(1108): 20190580.

Computer-aided diagnosis (CAD) has been a popular area of research and development in the past few decades. In CAD, machine learning methods and multidisciplinary knowledge and techniques are used to analyze the patient information and the results can be used to assist clinicians in their decision making process. CAD may analyze imaging information alone or in combination with other clinical data. It may provide the analyzed information directly to the clinician or correlate the analyzed results with the likelihood of certain diseases based on statistical modeling of the past cases in the population. CAD systems can be developed to provide decision support for many applications in the patient care processes, such as lesion detection, characterization, cancer staging, treatment planning and response assessment, recurrence and prognosis prediction. The new state-of-the-art machine learning technique, known as deep learning (DL), has revolutionized speech and text recognition as well as computer vision. The potential of major breakthrough by DL in medical image analysis and other CAD applications for patient care has brought about unprecedented excitement of applying CAD, or artificial intelligence (AI), to medicine in general and to radiology in particular. In this paper, we will provide an overview of the recent developments of CAD using DL in breast imaging and discuss some challenges and practical issues that may impact the advancement of artificial intelligence and its integration into clinical workflow.

Chandrashekar, M., et al. (2024). "Path-BigBird: An AI-Driven Transformer Approach to Classification of Cancer Pathology Reports." JCO Clin Cancer Inform **8**: e2300148.

PURPOSE: Surgical pathology reports are critical for cancer diagnosis and management. To accurately extract information about tumor characteristics from pathology reports in near real time, we explore the impact of using domain-specific transformer models that understand cancer pathology reports. METHODS: We built a pathology transformer model, Path-BigBird, by using 2.7 million pathology reports from six SEER cancer registries. We then compare different variations of Path-BigBird with two less computationally intensive methods: Hierarchical Self-Attention Network (HiSAN) classification model and an off-the-shelf clinical transformer model (Clinical BigBird). We use five pathology information extraction tasks for evaluation: site, subsite, laterality, histology, and behavior. Model performance is evaluated by using macro and micro F(1) scores. RESULTS: We found that Path-BigBird and Clinical BigBird outperformed the HiSAN in all tasks. Clinical BigBird performed better on the site and laterality tasks. Versions of the Path-BigBird model performed best on the two most difficult tasks: subsite (micro F(1) score of 72.53, macro F(1) score of 35.76) and histology (micro F(1) score of 80.96, macro F(1) score of 37.94). The largest performance gains over the HiSAN model were for histology, for which a Path-BigBird model increased the micro F(1) score by 1.44 points and the macro F(1) score by 3.55 points. Overall, the results suggest that a Path-BigBird model with a vocabulary derived from well-curated and deidentified data is the best-performing model. CONCLUSION: The Path-BigBird pathology transformer model improves automated information extraction from pathology reports. Although Path-BigBird outperforms Clinical BigBird and HiSAN, these less computationally expensive models still have utility when resources are constrained.

Chang, L., et al. (2022). "AI-Driven Synthetic Biology for Non-Small Cell Lung Cancer Drug Effectiveness-Cost Analysis in Intelligent Assisted Medical Systems." IEEE J Biomed Health Inform **26**(10): 5055-5066.

According to statistics, in the 185 countries' 36 types of cancer, the morbidity and mortality of lung cancer take the first place, and non-small cell lung cancer (NSCLC) accounts for 85% of lung cancer (International Agency for Research on Cancer, 2018), (Bray et al., 2018). Significantly in many developing countries, limited medical resources and excess population seriously affect the diagnosis and

treatment of alung cancer patients. The 21st century is an era of life medicine, big data, and information technology. Synthetic biology is known as the driving force of natural product innovation and research in this era. Based on the research of NSCLC targeted drugs, through the cross-fusion of synthetic biology and artificial intelligence, using the idea of bioengineering, we construct an artificial intelligence assisted medical system and propose a drug selection framework for the personalized selection of NSCLC patients. Under the premise of ensuring the efficacy, considering the economic cost of targeted drugs as an auxiliary decision-making factor, the system predicts the drug effectiveness-cost then. The experiment shows that our method can rely on the provided clinical data to screen drug treatment programs suitable for the patient's conditions and assist doctors in making an efficient diagnosis.

Chang, Y. C., et al. (2024). "Generative Artificial Intelligence (AI) to Uncover Insights From Breast Cancer Patients' Perceptions to Mindfulness-Based Stress Reduction (MBSR) Interventions." Holist Nurs Pract.

The study's central objective is to harness the power of generative Artificial Intelligence (AI), in particular based on Large Language Models, as a valuable resource for delving deeper into the insights offered by patients with breast cancer (BC) who actively participated in a Mindfulness-Based Stress Reduction (MBSR) program. In a 6-week MBSR program, each session lasted 2 hours and encompassed a range of techniques, including sitting meditation, body scan, Hatha yoga, and walking meditation. A total of 25 participants were enrolled in the study. The majority of these participants reported a high level of satisfaction with the mindfulness course. The application of generative AI enabled a comprehensive analysis of the participants' responses, revealing distinct subgroups among them. The MBSR program was found to be beneficial for most participants, serving as a valuable tool in managing the psychological stresses associated with BC.

Chang, Y. W., et al. (2022). "Artificial Intelligence for Breast Cancer Screening in Mammography (AI-STREAM): A Prospective Multicenter Study Design in Korea Using AI-Based CADe/x." J Breast Cancer **25**(1): 57-68.

PURPOSE: Artificial intelligence (AI)-based computer-aided detection/diagnosis (CADe/x) has helped improve radiologists' performance and provides results equivalent or superior to those of radiologists' alone. This prospective multicenter cohort study aims to generate real-world evidence on the overall benefits and disadvantages of using AI-based CADe/x for breast cancer detection in a population-based breast cancer screening program comprising Korean women aged >/= 40 years. The purpose of this report is to compare the diagnostic accuracy of radiologists with and without the use of AI-based CADe/x in mammography readings for breast cancer screening of Korean women with average breast cancer risk. METHODS: Approximately 32,714 participants will be enrolled between February 2021 and December 2022 at 5 study sites in Korea. A radiologist specializing in breast imaging will interpret the mammography readings with or without the use of AI-based CADe/x. If recall is required, further diagnostic workup will be conducted to confirm the cancer detected on screening. The findings will be recorded for all participants regardless of their screening status to identify study participants with breast cancer diagnosis within both 1 year and 2 years of screening. The national cancer registry database will be reviewed in 2026 and 2027, and the results of this study are expected to be published in 2027. In addition, the diagnostic accuracy of general radiologists and radiologists specializing in breast imaging from another hospital with or without the use of AI-based CADe/x will be compared considering mammography readings for breast cancer screening. DISCUSSION: The Artificial Intelligence for Breast Cancer Screening in Mammography (AI-STREAM) study is a prospective multicenter study that aims to compare the diagnostic accuracy of radiologists with and without the use of AI-based CADe/x in mammography readings for breast cancer screening of women with average breast cancer risk. AI-STREAM is currently in the patient enrollment phase. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT05024591.

Cheng, T., et al. (2015). "Correlation of apolipoprotein A-I kinetics with survival and response to first-line platinum-based chemotherapy in advanced non-small cell lung cancer." Med Oncol **32**(1): 407.

The aim of this study was to determine whether apolipoprotein A-I (ApoA-I) kinetics predict the overall survival in patients with advanced-stage non-small cell lung cancer (NSCLC) during platinum-based first-line therapy. A total of 125 NSCLC patients from January 2008 to September 2014 were retrospectively reviewed. Serum ApoA-I level was measured at baseline and thereafter at the start of each palliative chemotherapy cycle for all patients. Patients were divided into four groups according to ApoA-I kinetics. Patients whose ApoA-I >/= 1.01 g/L and never decreased during treatment, patients whose ApoA-I >/= 1.01 g/L and decreased

(ApoA-I < 1.01 g/L) at least one time during treatment, patients whose ApoA-I < 1.01 g/L and normalized (ApoA-I >/= 1.01) at least one time during treatment, and patients whose ApoA-I < 1.01 g/L and never normalized during treatment were assigned to non-decreased, decreased, normalized, and non-normalized ApoA-I groups, respectively. Overall survival rates were significantly different between the four groups, with 2-year survival rates of 88.6 and 17.5 % for the non-decreased and the decreased ApoA-I groups, respectively, and none survived 2 years later in the normalized and the non-normalized ApoA-I groups. When compared with the non-decreased group, the hazard ratios of death were 0.05, 0.44, and 1.73 in the normalized, decreased, and non-normalized groups, respectively (P < 0.001). Normalization of ApoA-I was associated with a low risk of progression, whereas patients with a decreased level of ApoA-I showed a progression of disease in most cases. ApoA-I can be a novel, widely available biomarker for patients with NSCLC.

Cheraghi, H., et al. (2024). "Continuous distribution of cancer cells in the cell cycle unveiled by AI-segmented imaging of 37,000 HeLa FUCCI cells." Heliyon **10**(9): e30239.

Classification of live or fixed cells based on their unlabeled microscopic images would be a powerful tool for cell biology and pathology. For such software, the first step is the generation of a ground truth database that can be used for training and testing AI classification algorithms. The Application of cells expressing fluorescent reporter proteins allows the building of ground truth datasets in a straightforward way. In this study, we present an automated imaging pipeline utilizing the Cellpose algorithm for the precise cell segmentation and measurement of fluorescent cellular intensities across multiple channels. We analyzed the cell cycle of HeLa-FUCCI cells expressing fluorescent red and green reporter proteins at various levels depending on the cell cycle state. To build the dataset, 37,000 fixed cells were automatically scanned using a standard motorized microscope, capturing phase contrast and fluorescent red/green images. The fluorescent pixel intensity of each cell was integrated to calculate the total fluorescence of cells based on cell segmentation in the phase contrast channel. It resulted in a precise intensity value for each cell in both channels. Furthermore, we conducted a comparative analysis of Cellpose 1.0 and Cellpose 2.0 in cell segmentation performance. Cellpose 2.0 demonstrated notable improvements, achieving a significantly reduced false positive rate of 2.7 % and 1.4 % false negative. The cellular fluorescence was visualized in a 2D plot (map) based on the red and green intensities of the FUCCI construct revealing the continuous distribution of cells in the cell cycle. This 2D map enables the selection and potential isolation of single cells in a specific phase. In the corresponding heatmap, two clusters appeared representing cells in the red and green states. Our pipeline allows the high-throughput and accurate measurement of cellular fluorescence providing extensive statistical information on thousands of cells with potential applications in developmental and cancer biology. Furthermore, our method can be used to build ground truth datasets automatically for training and testing AI cell classification. Our automated pipeline can be used to analyze thousands of cells within 2 h after putting the sample onto the microscope.

Choi, G., et al. (2021). "AI-Based Drug Discovery of TKIs Targeting L858R/T790M/C797S-Mutant EGFR in Non-small Cell Lung Cancer." Front Pharmacol **12**: 660313.

Lung cancer has a high mortality rate, and non-small cell lung cancer (NSCLC) is the most common type of lung cancer. Patients have been observed to acquire resistance against various anticancer agents used for NSCLC due to L858R (or Exon del19)/T790M/C797S-EGFR mutations. Therefore, next-generation drugs are being developed to overcome this problem of acquired resistance. The goal of this study was to use artificial intelligence (AI) to discover drug candidates that can overcome acquired resistance and reduce the limitations of the current drug discovery process, such as high costs and long durations of drug design and production. To generate ligands using AI, we collected data related to tyrosine kinase inhibitors (TKIs) from accessible libraries and used LSTM (Long short term memory) based transfer learning (TL) model. Through the simplified molecular-input line-entry system (SMILES) datasets of the generated ligands, we obtained drug-like ligands via parameter-filtering, cyclic skeleton (CSK) analysis, and virtual screening utilizing deep-learning method. Based on the results of this study, we are developing prospective EGFR TKIs for NSCLC that have overcome the limitations of existing third-generation drugs.

Choi, S. H., et al. (2024). "Automated Organ Segmentation for Radiation Therapy: A Comparative Analysis of AI-Based Tools Versus Manual Contouring in Korean Cancer Patients." Cancers (Basel) **16**(21).

BACKGROUND: Accurate delineation of tumors and organs at risk (OARs) is crucial for intensity-modulated radiation therapy. This study aimed to evaluate the performance of OncoStudio, an AI-based auto-segmentation tool developed for

Korean patients, compared with Protege AI, a globally developed tool that uses data from Korean cancer patients. METHODS: A retrospective analysis of 1200 Korean cancer patients treated with radiotherapy was conducted. Auto-contours generated via OncoStudio and Protege AI were compared with manual contours across the head and neck and thoracic, abdominal, and pelvic organs. Accuracy was assessed using the Dice similarity coefficient (DSC), mean surface distance (MSD), and 95% Hausdorff distance (HD). Feedback was obtained from 10 participants, including radiation oncologists, residents, and radiation therapists, via an online survey with a Turing test component. RESULTS: OncoStudio outperformed Protege AI in 85% of the evaluated OARs ($p < 0.001$). For head and neck organs, OncoStudio achieved a similar DSC (0.70 vs. 0.70, $p = 0.637$) but significantly lower MSD and 95% HD values ($p < 0.001$). In thoracic organs, OncoStudio performed excellently in 90% of cases, with a significantly greater DSC (male: 0.87 vs. 0.82, $p < 0.001$; female: 0.95 vs. 0.87, $p < 0.001$). OncoStudio also demonstrated superior accuracy in abdominal (DSC 0.88 vs. 0.81, $p < 0.001$) and pelvic organs (male: DSC 0.95 vs. 0.85, $p < 0.001$; female: DSC 0.82 vs. 0.73, $p < 0.001$). Clinicians favored OncoStudio in 70% of cases, with 90% endorsing its clinical suitability for Korean patients. CONCLUSIONS: OncoStudio, which is tailored for Korean patients, demonstrated superior segmentation accuracy across multiple anatomical regions, suggesting its suitability for radiotherapy planning in this population.

Chugh, V., et al. (2024). "Employing nano-enabled artificial intelligence (AI)-based smart technologies for prediction, screening, and detection of cancer." Nanoscale **16**(11): 5458-5486.

Cancer has been classified as a diverse illness with a wide range of subgroups. Its early identification and prognosis, which have become a requirement of cancer research, are essential for clinical treatment. Patients have already benefited greatly from the use of artificial intelligence (AI), machine learning (ML), and deep learning (DL) algorithms in the field of healthcare. AI simulates and combines data, pre-programmed rules, and knowledge to produce predictions. Data are used to improve efficiency across several pursuits and tasks through the art of ML. DL is a larger family of ML methods based on representational learning and simulated neural networks. Support vector machines, convulsion neural networks, and artificial neural networks, among others, have been widely used in cancer research to construct prediction models that enable precise and effective decision-making. Although using these innovative methods can enhance our comprehension of how cancer progresses, further validation is required before these techniques can be used in routine clinical practice. We cover contemporary methods used in the modelling of cancer development in this article. The presented prediction models are built using a variety of guided ML approaches, as well as numerous input attributes and data collections. Early identification and cost-effective detection of cancer's progression are equally necessary for successful treatment of the disease. Smart material-based detection techniques can give end consumers a portable, affordable instrument to easily detect and monitor their health issues without the need for specialized knowledge. Owing to their cost-effectiveness, excellent sensitivity, multimodal detection capacity, and miniaturization aptitude, two-dimensional (2D) materials have a lot of prospects for clinical examination of various compounds as well as cancer biomarkers. The effectiveness of traditional devices is moving faster towards more useful techniques thanks to developments in 2D material-based biosensors/sensors. The most current developments in the design of 2D material-based biosensors/sensors-the next wave of cancer screening instruments-are also outlined in this article.

Chyrmang, G., et al. (2024). "Insights into AI advances in immunohistochemistry for effective breast cancer treatment: a literature review of ER, PR, and HER2 scoring." Curr Med Res Opin: 1-31.

Breast cancer is a significant health challenge, with accurate and timely diagnosis being critical to effective treatment. Immunohistochemistry (IHC) staining is a widely used technique for the evaluation of breast cancer markers, but manual scoring is time-consuming and can be subject to variability. With the rise of Artificial Intelligence (AI), there is an increasing interest in using machine learning and deep learning approaches to automate the scoring of ER, PR and HER2 biomarker in IHC-stained images for effective treatment. In this narrative literature review, we focus on AI-based techniques for the automated scoring of breast cancer markers in IHC-stained images, specifically Allred, Histochemical (H-Score), and HER2 scoring. We aim to identify the current state-of-the-art approaches, challenges, and potential future research prospect for this area of study. By conducting a comprehensive review of the existing literature, we aim to contribute to the ultimate goal of improving the accuracy and efficiency of breast cancer diagnosis and treatment.

Clunie, D., et al. (2024). "Summary of the National Cancer Institute 2023 Virtual Workshop on Medical

Image De-identification-Part 2: Pathology Whole Slide Image De-identification, De-facing, the Role of AI in Image De-identification, and the NCI MIDI Datasets and Pipeline." J Imaging Inform Med.

De-identification of medical images intended for research is a core requirement for data sharing initiatives, particularly as the demand for data for artificial intelligence (AI) applications grows. The Center for Biomedical Informatics and Information Technology (CBIIT) of the United States National Cancer Institute (NCI) convened a two half-day virtual workshop with the intent of summarizing the state of the art in de-identification technology and processes and exploring interesting aspects of the subject. This paper summarizes the highlights of the second day of the workshop, the recordings and presentations of which are publicly available for review. The topics covered included pathology whole slide image de-identification, de-facing, the role of AI in image de-identification, and the NCI Medical Image De-Identification Initiative (MIDI) datasets and pipeline.

Damiani, C., et al. (2023). "Evaluation of an AI Model to Assess Future Breast Cancer Risk." Radiology **307**(5): e222679.

Background Accurate breast cancer risk assessment after a negative screening result could enable better strategies for early detection. Purpose To evaluate a deep learning algorithm for risk assessment based on digital mammograms. Materials and Methods A retrospective observational matched case-control study was designed using the OPTIMAM Mammography Image Database from the National Health Service Breast Screening Programme in the United Kingdom from February 2010 to September 2019. Patients with breast cancer (cases) were diagnosed following a mammographic screening or between two triannual screening rounds. Controls were matched based on mammography device, screening site, and age. The artificial intelligence (AI) model only used mammograms at screening before diagnosis. The primary objective was to assess model performance, with a secondary objective to assess heterogeneity and calibration slope. The area under the receiver operating characteristic curve (AUC) was estimated for 3-year risk. Heterogeneity according to cancer subtype was assessed using a likelihood ratio interaction test. Statistical significance was set at P < .05. Results Analysis included patients with screen-detected (median age, 60 years [IQR, 55-65 years]; 2044 female, including 1528 with invasive cancer and 503 with ductal carcinoma in situ [DCIS]) or interval (median age, 59 years [IQR, 53-65 years]; 696 female, including 636 with invasive cancer and 54 with DCIS) breast cancer and 1:1 matched controls, each with a complete set of mammograms at the screening preceding diagnosis. The AI model had an overall AUC of 0.68 (95% CI: 0.66, 0.70), with no evidence of a significant difference between interval and screen-detected (AUC, 0.69 vs 0.67; P = .085) cancer. The calibration slope was 1.13 (95% CI: 1.01, 1.26). There was similar performance for the detection of invasive cancer versus DCIS (AUC, 0.68 vs 0.66; P = .057). The model had higher performance for advanced cancer risk (AUC, 0.72 >/=stage II vs 0.66 <stage II; P = .037). The AUC for detecting breast cancer in mammograms at diagnosis was 0.89 (95% CI: 0.88, 0.91). Conclusion The AI model was found to be a strong predictor of breast cancer risk for 3-6 years following a negative mammographic screening. (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Mann and Sechopoulos in this issue.

de Souza, L. A., Jr., et al. (2021). "Convolutional Neural Networks for the evaluation of cancer in Barrett's esophagus: Explainable AI to lighten up the black-box." Comput Biol Med **135**: 104578.

Even though artificial intelligence and machine learning have demonstrated remarkable performances in medical image computing, their level of accountability and transparency must be provided in such evaluations. The reliability related to machine learning predictions must be explained and interpreted, especially if diagnosis support is addressed. For this task, the black-box nature of deep learning techniques must be lightened up to transfer its promising results into clinical practice. Hence, we aim to investigate the use of explainable artificial intelligence techniques to quantitatively highlight discriminative regions during the classification of early-cancerous tissues in Barrett's esophagus-diagnosed patients. Four Convolutional Neural Network models (AlexNet, SqueezeNet, ResNet50, and VGG16) were analyzed using five different interpretation techniques (saliency, guided backpropagation, integrated gradients, input x gradients, and DeepLIFT) to compare their agreement with experts' previous annotations of cancerous tissue. We could show that saliency attributes match best with the manual experts' delineations. Moreover, there is moderate to high correlation between the sensitivity of a model and the human-and-computer agreement. The results also lightened that the higher the model's sensitivity, the stronger the correlation of human and computational segmentation agreement. We observed a relevant relation between computational learning and experts' insights, demonstrating how human knowledge may

influence the correct computational learning.

Derangere, V., et al. (2022). "Combination of CDX2 H-score quantitative analysis with CD3 AI-guided analysis identifies patients with a good prognosis only in stage III colon cancer." Eur J Cancer **172**: 221-230.

AIM: Stratification of colon cancer (CC) of patients with stage II and III for risk of relapse is still needed especially to drive adjuvant therapy administration. Our study evaluates the prognostic performance of two known biomarkers, CDX2 and CD3, standalone or their combined information in stage II and III CC. PATIENTS AND METHODS: CDX2 and CD3 expression was evaluated in Prodige-13 study gathering 443 stage II and 398 stage III primary CC on whole slide colectomy. We developed for this study an H-score to quantify CDX2 expression and used our artificial intelligence (AI)-guided tissue analysis ColoClass to detect CD3 in tumour core and invasive margin. Association between biomarkers and relapse-free survival was investigated. RESULTS: Univariate analysis showed that the combined variable CD3-TC and CD3-IM was associated with prognosis in both stage II and stage III. CDX2, on the contrary, was associated with prognosis only in stage III. We subsequently associated CDX2 and combined immune parameters only in stage III. This multivariate analysis allowed us to distinguish a proportion of stage III CC harbouring a high CDX2 expression and a high immune infiltration with a particularly good prognosis compared to their counterpart. CONCLUSION: This study validated the prognostic role of CDX2 and CD3 evaluated with immunohistochemistry procedures in stage III but not in stage II. This association would be conceivable in a routine pathology laboratory and could help oncologist to consider chemotherapy de-escalation for a part of stage III patients.

Derevianko, A., et al. (2023). "The Use of Artificial Intelligence (AI) in the Radiology Field: What Is the State of Doctor-Patient Communication in Cancer Diagnosis?" Cancers (Basel) **15**(2).

BACKGROUND: In the past decade, interest in applying Artificial Intelligence (AI) in radiology to improve diagnostic procedures increased. AI has potential benefits spanning all steps of the imaging chain, from the prescription of diagnostic tests to the communication of test reports. The use of AI in the field of radiology also poses challenges in doctor-patient communication at the time of the diagnosis. This systematic review focuses on the patient role and the interpersonal skills between patients and physicians when AI is implemented in cancer diagnosis communication. METHODS: A systematic search was conducted on PubMed, Embase, Medline, Scopus, and PsycNet from 1990 to 2021. The search terms were: ("artificial intelligence" or "intelligence machine") and "communication" "radiology" and "oncology diagnosis". The PRISMA guidelines were followed. RESULTS: 517 records were identified, and 5 papers met the inclusion criteria and were analyzed. Most of the articles emphasized the success of the technological support of AI in radiology at the expense of patient trust in AI and patient-centered communication in cancer disease. Practical implications and future guidelines were discussed according to the results. CONCLUSIONS: AI has proven to be beneficial in helping clinicians with diagnosis. Future research may improve patients' trust through adequate information about the advantageous use of AI and an increase in medical compliance with adequate training on doctor-patient diagnosis communication.

Ding, T., et al. (2024). "AI-based automated breast cancer segmentation in ultrasound imaging based on Attention Gated Multi ResU-Net." PeerJ Comput Sci **10**: e2226.

Breast cancer is a leading cause of death among women worldwide, making early detection and diagnosis critical for effective treatment and improved patient outcomes. Ultrasound imaging is a common diagnostic tool for breast cancer, but interpreting ultrasound images can be challenging due to the complexity of breast tissue and the variability of image quality. This study proposed an Attention Gated Multi ResU-Net model for medical image segmentation tasks, that has shown promising results for breast cancer ultrasound image segmentation. The model's multi-scale feature extraction and attention-gating mechanism enable it to accurately identify and segment areas of abnormality in the breast tissue, such as masses, cysts, and calcifications. The model's quantitative test showed an adequate degree of agreement with expert manual annotations, demonstrating its potential for improving early identification and diagnosis of breast cancer. The model's multi-scale feature extraction and attention-gating mechanism enable it to accurately identify and segment areas of abnormality in the breast tissue, such as masses, cysts, and calcifications, achieving a Dice coefficient of 0.93, sensitivity of 93%, and specificity of 99%. These results underscore the model's high precision and reliability in medical image analysis.

Ding, Y., et al. (2021). "[AI-assisted Prediction of Lymph Node Metastasis of Breast Cancer: Current and Prospective Research]." Sichuan Da Xue Xue

Bao Yi Xue Ban **52**(2): 162-165.

One of the most important application of artificial intelligence (AI) in pathology is prediction, using morphological features, of patient prognosis and response to specific treatments. As one of the most common kinds of malignancies in the world and the crucial important cause of death due to malignant tumor among women, breast cancer has become the center of attention in clinical services. Axillary lymph node metastasis is an important prognostic factor in breast cancer. The accuracy of the assessment of axillary lymph node metastasis bears heavily on clinical diagnosis and treatment. At present, based on the principle of non-invasive procedures, many studies have been done to develop models that can be used to predict sentinel lymph node metastasis of breast cancer. However, different clinical and pathological parameters are used in these predictive models. How to analyze the clinical and pathological data of breast cancer patients in a more comprehensive way and how to establish a prediction model with better precision have become the future direction of development. In this paper, we describe the research progress of AI in pathology and the current status of its use in breast cancer research. We have conducted in-depth reflection and looked into the future of ways to predict effectively breast cancer lymph node metastasis and to establish more accurate and effective deep-learning algorithm based on AI assistance so as to continuously improve the diagnosis and treatment of breast cancer.

Dlamini, Z., et al. (2020). "Artificial intelligence (AI) and big data in cancer and precision oncology." Comput Struct Biotechnol J **18**: 2300-2311.

Artificial intelligence (AI) and machine learning have significantly influenced many facets of the healthcare sector. Advancement in technology has paved the way for analysis of big datasets in a cost- and time-effective manner. Clinical oncology and research are reaping the benefits of AI. The burden of cancer is a global phenomenon. Efforts to reduce mortality rates requires early diagnosis for effective therapeutic interventions. However, metastatic and recurrent cancers evolve and acquire drug resistance. It is imperative to detect novel biomarkers that induce drug resistance and identify therapeutic targets to enhance treatment regimes. The introduction of the next generation sequencing (NGS) platforms address these demands, has revolutionised the future of precision oncology. NGS offers several clinical applications that are important for risk predictor, early detection of disease, diagnosis by sequencing and medical imaging, accurate prognosis, biomarker identification and identification of therapeutic targets for novel drug discovery. NGS generates large datasets that demand specialised bioinformatics resources to analyse the data that is relevant and clinically significant. Through these applications of AI, cancer diagnostics and prognostic prediction are enhanced with NGS and medical imaging that delivers high resolution images. Regardless of the improvements in technology, AI has some challenges and limitations, and the clinical application of NGS remains to be validated. By continuing to enhance the progression of innovation and technology, the future of AI and precision oncology show great promise.

Dong, Z., et al. (2023). "Exploring the challenge of early gastric cancer diagnostic AI system face in multiple centers and its potential solutions." J Gastroenterol **58**(10): 978-989.

BACKGROUND: Artificial intelligence (AI) performed variously among test sets with different diversity due to sample selection bias, which can be stumbling block for AI applications. We previously tested AI named ENDOANGEL, diagnosing early gastric cancer (EGC) on single-center videos in man-machine competition. We aimed to re-test ENDOANGEL on multi-center videos to explore challenges applying AI in multiple centers, then upgrade ENDOANGEL and explore solutions to the challenge. METHODS: ENDOANGEL was re-tested on multi-center videos retrospectively collected from 12 institutions and compared with performance in previously reported single-center videos. We then upgraded ENDOANGEL to ENDOANGEL-2022 with more training samples and novel algorithms and conducted competition between ENDOANGEL-2022 and endoscopists. ENDOANGEL-2022 was then tested on single-center videos and compared with performance in multi-center videos; the two AI systems were also compared with each other and endoscopists. RESULTS: Forty-six EGCs and 54 non-cancers were included in multi-center video cohort. On diagnosing EGCs, compared with single-center videos, ENDOANGEL showed stable sensitivity (97.83% vs. 100.00%) while sharply decreased specificity (61.11% vs. 82.54%); ENDOANGEL-2022 showed similar tendency while achieving significantly higher specificity (79.63%, $p < 0.01$) making fewer mistakes on typical lesions than ENDOANGEL. On detecting gastric neoplasms, both AI showed stable sensitivity while sharply decreased specificity. Nevertheless, both AI outperformed endoscopists in the two competitions. CONCLUSIONS: Great increase of false positives is a prominent challenge for applying EGC diagnostic AI in multiple centers due to high heterogeneity of negative cases. Optimizing AI by adding samples and using novel algorithms is promising to overcome this

challenge.

Dwivedi, K., et al. (2023). "An explainable AI-driven biomarker discovery framework for Non-Small Cell Lung Cancer classification." Comput Biol Med **153**: 106544.

Non-Small Cell Lung Cancer (NSCLC) exhibits intrinsic heterogeneity at the molecular level that aids in distinguishing between its two prominent subtypes - Lung Adenocarcinoma (LUAD) and Lung Squamous Cell Carcinoma (LUSC). This paper proposes a novel explainable AI (XAI)-based deep learning framework to discover a small set of NSCLC biomarkers. The proposed framework comprises three modules - an autoencoder to shrink the input feature space, a feed-forward neural network to classify NSCLC instances into LUAD and LUSC, and a biomarker discovery module that leverages the combined network comprising the autoencoder and the feed-forward neural network. In the biomarker discovery module, XAI methods uncovered a set of 52 relevant biomarkers for NSCLC subtype classification. To evaluate the classification performance of the discovered biomarkers, multiple machine-learning models are constructed using these biomarkers. Using 10-Fold cross-validation, Multilayer Perceptron achieved an accuracy of 95.74% (+/-1.27) at 95% confidence interval. Further, using Drug-Gene Interaction Database, we observe that 14 of the discovered biomarkers are druggable. In addition, 28 biomarkers aid the prediction of the survivability of the patients. Out of 52 discovered biomarkers, we find that 45 biomarkers have been reported in previous studies on distinguishing between the two NSCLC subtypes. To the best of our knowledge, the remaining seven biomarkers have not yet been reported for NSCLC subtyping and could be further explored for their contribution to targeted therapy of lung cancer.

Dy, A., et al. (2024). "AI improves accuracy, agreement and efficiency of pathologists for Ki67 assessments in breast cancer." Sci Rep **14**(1): 1283.

The Ki-67 proliferation index (PI) guides treatment decisions in breast cancer but suffers from poor inter-rater reproducibility. Although AI tools have been designed for Ki-67 assessment, their impact on pathologists' work remains understudied. 90 international pathologists were recruited to assess the Ki-67 PI of ten breast cancer tissue microarrays with and without AI. Accuracy, agreement, and turnaround time with and without AI were compared. Pathologists' perspectives on AI were collected. Using AI led to a significant decrease in PI error (2.1% with AI vs. 5.9% without AI, $p < 0.001$), better inter-rater agreement (ICC: 0.70 vs. 0.92; Krippendorff's alpha: 0.63 vs. 0.89; Fleiss' Kappa: 0.40 vs. 0.86), and an 11.9% overall median reduction in turnaround time. Most pathologists (84%) found the AI reliable. For Ki-67 assessments, 76% of respondents believed AI enhances accuracy, 82% said it improves consistency, and 83% trust it will improve efficiency. This study highlights AI's potential to standardize Ki-67 scoring, especially between 5 and 30% PI-a range with low PI agreement. This could pave the way for a universally accepted PI score to guide treatment decisions, emphasizing the promising role of AI integration into pathologist workflows.

Elsanhoury, R., et al. (2023). "AI & experimental-based discovery and preclinical IND-enabling studies of selective BMX inhibitors for development of cancer therapeutics." Int J Pharm **645**: 123384.

The current work aims to design and provide a preliminary IND-enabling study of selective BMX inhibitors for cancer therapeutics development. BMX is an emerging target, more notably in oncological and immunological diseases. In this work, we have employed a predictive AI-based platform to design the selective inhibitors considering the novelty, IP prior protection, and drug-likeness properties. Furthermore, selected top candidates from the initial iteration of the design were synthesized and chemically characterized utilizing (1)H NMR and LC-MS. Employing a panel of biochemical (enzymatic) and cancer cell lines, the selected molecules were tested against these assays. In addition, we used artificial intelligence to predict and evaluate several critical IND-focused physicochemical and pharmacokinetics values of the selected molecules. A secondary objective of the current work was also to validate the sole role of BMX in animal models known to be mediated by BMX. More than 50 molecules were designed in the present study employing five novel discovered scaffolds. Two molecules were nominated for further IND-focused studies. Compound II showed promising in-vitro activity against BMX in both enzymatic assays compared to other kinases and in cancer cell lines with known BMX overexpression. Interestingly, compound II showed very favorable physicochemical and pharmacokinetics properties as predicted by the used platforms. The animal study further confirmed the sole role of BMX in the disease model. The current work provides promising data on a selective BMX inhibitor as a potential lead for therapeutics development, and the asset is currently in the optimization stage. Notably, the current study shows a framework for a combined approach employing both AI and experimentation that can be used by academic labs in their research programs to more streamline programs into IND-focused to be

bridged easily for further clinical development with industrial partners.

Enstrom, C., et al. (2024). "Visualizing Future Breast Cancer Prognosis by Generative AI." Stud Health Technol Inform **316**: 724-725.

In Sweden, 30 percent of breast cancer cases are detected between screenings, leading to later staged cancer diagnoses. Aileen Health is preventing later staged cancers by making a breast cancer prognosis with generative AI. This study investigates how breast radiologists perceive AI-generated images and their usability as cancer prognosis. Through literature review and formative usability testing, the research study emphasizes the challenges when integrating AI-generated medical images into clinical decision-making. Furthermore, our findings stress the importance of avoiding cognitive overload and following mental models. Future research should focus on radiologists' use of breast cancer prognosis at various urgency levels, as well as AI accuracy of generated images.

Erdas, C. B. (2024). "Computer-aided colorectal cancer diagnosis: AI-driven image segmentation and classification." PeerJ Comput Sci **10**: e2071.

Colorectal cancer is an enormous health concern since it is among the most lethal types of malignancy. The manual examination has its limitations, including subjectivity and data overload. To overcome these challenges, computer-aided diagnostic systems focusing on image segmentation and abnormality classification have been developed. This study presents a two-stage approach for the automatic detection of five types of colorectal abnormalities in addition to a control group: polyp, low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, serrated adenoma, adenocarcinoma. In the first stage, UNet3+ was used for image segmentation to locate the anomalies, while in the second stage, the Cross-Attention Multi-Scale Vision Transformer deep learning model was used to predict the type of anomaly after highlighting the anomaly on the raw images. In anomaly segmentation, UNet3+ achieved values of 0.9872, 0.9422, 0.9832, and 0.9560 for Dice Coefficient, Jaccard Index, Sensitivity, Specificity respectively. In anomaly detection, the Cross-Attention Multi-Scale Vision Transformer model attained a classification performance of 0.9340, 0.9037, 0.9446, 0.8723, 0.9102, 0.9849 for accuracy, F1 score, precision, recall, Matthews correlation coefficient, and specificity, respectively. The proposed approach proves its capacity to alleviate the overwhelm of pathologists and enhance the accuracy of colorectal cancer diagnosis by achieving high performance in both the identification of anomalies and the segmentation of regions.

Eriksson, M., et al. (2024). "European validation of an image-derived AI-based short-term risk model for individualized breast cancer screening-a nested case-control study." Lancet Reg Health Eur **37**: 100798.

BACKGROUND: Image-derived artificial intelligence (AI)-based risk models for breast cancer have shown high discriminatory performances compared with clinical risk models based on family history and lifestyle factors. However, little is known about their generalizability across European screening settings. We therefore investigated the discriminatory performances of an AI-based risk model in European screening settings. METHODS: Using four European screening populations in three countries (Italy, Spain, Germany) screened between 2009 and 2020 for women aged 45-69, we performed a nested case-control study to assess the predictive performance of an AI-based risk model. In total, 739 women with incident breast cancers were included together with 7812 controls matched on year of study-entry. Mammographic features (density, microcalcifications, masses, left-right breast asymmetries of these features) were extracted using AI from negative digital mammograms at study-entry. Two-year absolute risks of breast cancer were predicted and assessed after two years of follow-up. Adjusted risk stratification performance metrics were reported per clinical guidelines. FINDINGS: The overall adjusted Area Under the receiver operating characteristic Curve (aAUC) of the AI risk model was 0.72 (95% CI 0.70-0.75) for breast cancers developed in four screening populations. In the 6.2% [529/8551] of women at high risk using the National Institute of Health and Care Excellence (NICE) guidelines thresholds, cancers were more likely diagnosed after 2 years follow-up, risk-ratio (RR) 6.7 (95% CI 5.6-8.0), compared with the 69% [5907/8551] of women classified at general risk by the model. Similar risk-ratios were observed across levels of mammographic density. INTERPRETATION: The AI risk model showed generalizable discriminatory performances across European populations and, predicted approximately 30% of clinically relevant stage 2 and higher breast cancers in approximately 6% of high-risk women who were sent home with a negative mammogram. Similar results were seen in women with fatty and dense breasts. FUNDING: Swedish Research Council.

Fan, J. L., et al. (2024). "A thousand and one tumors: the promise of AI for cancer biology." Nat Methods **21**(8): 1403-1406.

Fang, C., et al. (2022). "The Prognostic Value of Serum Apolipoprotein A-I Level and Neutrophil-to-Lymphocyte Ratio in Colorectal Cancer Liver Metastasis." J Oncol **2022**: 9149788.

BACKGROUND: Colorectal cancer liver metastasis (CRLM) is a high degree of malignancy with rapid disease progression and has a poor prognosis. Both serum apolipoprotein A-I (ApoA-I) and neutrophil-to-lymphocyte ratio (NLR) play key roles in anti-inflammation and antitumor. This study is aimed at evaluating the implication of serum ApoA-I level in combination with NLR in the prognosis of CRLM. METHODS: We retrospectively analyzed the serum ApoA-I level and NLR in 237 patients with CRLM. Cox regression analyses were used to identify the independent prognostic significance of these indicators. Kaplan-Meier method and Log-rank test were applied to compute overall survival (OS). Both the ApoA-I and NLR were divided into three levels, according to their medians. A risk-stratified prediction model was established to evaluate the prognosis of patients with CRLM. The ROC curve AUC values were applied to evaluate the capability of the model. RESULTS: Higher levels of ApoA-I and lower NLR were strongly associated with prolonged OS (Log-rank test, $P < 0.05$). The patients were then grouped into three queues according to the ApoA-I level and NLR. There was a crucial diversity in the OS ($P < 0.001$) between the high-risk (ApoA - I </= 1.03 g/L and NLR > 3.24), medium-risk (ApoA - I > 1.03 g/L or NLR </= 3.24) and low-risk groups (ApoA - I > 1.03 g/L and NLR </= 3.24). The AUC value of the prediction model (AUC = 0.623, 95% CI: 0.557-0.639, $P = 0.001$) was higher than other individual indicators (including ApoA-I, NLR, cT classification, and cN classification). Additionally, the association of the prediction model and cTN classification (AUC = 0.715, 95% CI: 0.606-0.708, $P < 0.001$) was better than the model and cTN classification alone. CONCLUSION: The combination of ApoA-I level and NLR could be a prognostic indicator for CRLM.

Fang, J. S., et al. (2024). "Elucidation of the Anti-Lung Cancer Mechanism of Xiao'ai Jiedu Prescription Based on Network Pharmacology and Molecular Docking." Altern Ther Health Med.

OBJECTIVE: Network pharmacology is an emerging discipline that applies computational methods to understand drug actions and interactions with multiple molecular targets. Xiao'ai Jiedu is a valued traditional Chinese medicine preparation for which the mechanism of action is not yet established. This study aims to explore the mechanism of Xiao'ai Jiedu in treating lung cancer through network pharmacology. METHODS: First, the Traditional Chinese Medicine Systems Pharmacology (TCMSP) data platform was used to analyze the target treatment results of different medicinal materials in Mr. Zhou's cancer prescriptions. Then, functional enrichment analysis was performed to conduct a secondary analysis of the dissemination of cancer biological and pharmacological information in the human body. The Cancer Genome Atlas (TCGA) was used to obtain several cancer-aggressive target groups, and their transcription RNA was extracted for collection. The CIBERSORT evaluation method was used to conduct a Spearman correlation analysis on the data processing results. Then the matching degree between the experimental cells and the principle of drug treatment was analyzed to improve the statistical analysis. RESULTS: Pharmacology research results showed that the network can accurately eliminate cancer detoxification targeted target correlation set, and through the data interpretation found that four different gene transcription have significant influence on lung cancer. The findings also confirmed that the degree of immune cell infiltration has a key role in lung cancer The study summarizes the active ingredients and their targets and mechanisms of action of the elimination of Xiao'ai Jiedu formula for the treatment of lung cancer. CONCLUSION: Network pharmacology can carry on the processing of the data, find the key to conform to the goal of research data, and the corresponding results are obtained, and the development of network pharmacology is not limited to, the study of lung cancer.

Feng, F., et al. (2020). "Xiao-ai-ping injection adjunct with platinum-based chemotherapy for advanced non-small-cell lung cancer: a systematic review and meta-analysis." BMC Complement Med Ther **20**(1): 3.

BACKGROUND: Xiao-ai-ping injection (XAPI), as patented Chinese medicine, has shown promising outcomes in non-small-cell lung cancer (NSCLC) patients. This meta-analysis investigated the efficacy and safety of XAPI in combination with platinum-based chemotherapy. METHODS: A comprehensive literature search was conducted to identify relevant studies in Pubmed, EMBASE, the Cochrane Library, Chinese National Knowledge Infrastructure, Wangfang Database, VIP Database, and Chinese Biology Medical Database from the date of their inception to September 2018. The RevMan 5.3 software was applied to calculate the risk ratio (RR) and mean difference (MD) with 95% confidence interval (CI). RESULTS: We included and analyzed 24 randomized controlled trials. The meta-analysis showed that XAPI adjunctive to platinum-based chemotherapy had better outcomes in

objective tumor response rate (ORR) (RR: 1.27, 95% CI, 1.14-1.40); improved Karnofsky performance scores (KPS) (RR: 1.70, 95% CI, 1.48-1.95); reduction in occurrence of grade 3/4 leukopenia (RR: 0.49, 95% CI, 0.38-0.64), anemia (RR: 0.63, 95% CI, 0.46-0.87) and thrombocytopenia (RR: 0.53, 95% CI, 0.38-0.73), nausea and vomiting (RR: 0.57, 95% CI, 0.36-0.90); and enhanced immune function (CD8(+) [MD: 4.96, 95% CI, 1.16-8.76] and CD4(+)/CD8(+) [MD: 2.58, 95% CI, 1.69-3.47]). However, it did not increase dysregulated liver and kidney function, diarrhea, constipation, and fatigue. Subgroup analysis of ORR and KPS revealed that dosage, treatment duration, and methodological quality did not affect the outcome significantly. CONCLUSIONS: Our meta-analyses demonstrated that XAPI in combination with platinum-based chemotherapy had a better tumor response, improved the quality of life, attenuated adverse side effects, and enhanced immune function, which suggests that it might be used for advanced NSCLC. Moreover, low dosage (< 60 ml/d) and long-term treatment of XAPI might be a choice for advanced NSCLC patients.

Feretzakis, G., et al. (2024). "Emerging Trends in AI and Radiomics for Bladder, Kidney, and Prostate Cancer: A Critical Review." Cancers (Basel) **16**(4).

This comprehensive review critically examines the transformative impact of artificial intelligence (AI) and radiomics in the diagnosis, prognosis, and management of bladder, kidney, and prostate cancers. These cutting-edge technologies are revolutionizing the landscape of cancer care, enhancing both precision and personalization in medical treatments. Our review provides an in-depth analysis of the latest advancements in AI and radiomics, with a specific focus on their roles in urological oncology. We discuss how AI and radiomics have notably improved the accuracy of diagnosis and staging in bladder cancer, especially through advanced imaging techniques like multiparametric MRI (mpMRI) and CT scans. These tools are pivotal in assessing muscle invasiveness and pathological grades, critical elements in formulating treatment plans. In the realm of kidney cancer, AI and radiomics aid in distinguishing between renal cell carcinoma (RCC) subtypes and grades. The integration of radiogenomics offers a comprehensive view of disease biology, leading to tailored therapeutic approaches. Prostate cancer diagnosis and management have also seen substantial benefits from these technologies. AI-enhanced MRI has significantly improved tumor detection and localization, thereby aiding in more effective treatment planning. The review also addresses the challenges in integrating AI and radiomics into clinical practice, such as the need for standardization, ensuring data quality, and overcoming the "black box" nature of AI. We emphasize the importance of multicentric collaborations and extensive studies to enhance the applicability and generalizability of these technologies in diverse clinical settings. In conclusion, AI and radiomics represent a major paradigm shift in oncology, offering more precise, personalized, and patient-centric approaches to cancer care. While their potential to improve diagnostic accuracy, patient outcomes, and our understanding of cancer biology is profound, challenges in clinical integration and application persist. We advocate for continued research and development in AI and radiomics, underscoring the need to address existing limitations to fully leverage their capabilities in the field of oncology.

Fernandez, G., et al. (2022). "Development and validation of an AI-enabled digital breast cancer assay to predict early-stage breast cancer recurrence within 6 years." Breast Cancer Res **24**(1): 93.

BACKGROUND: Breast cancer (BC) grading plays a critical role in patient management despite the considerable inter- and intra-observer variability, highlighting the need for decision support tools to improve reproducibility and prognostic accuracy for use in clinical practice. The objective was to evaluate the ability of a digital artificial intelligence (AI) assay (PDxBr) to enrich BC grading and improve risk categorization for predicting recurrence. METHODS: In our population-based longitudinal clinical development and validation study, we enrolled 2075 patients from Mount Sinai Hospital with infiltrating ductal carcinoma of the breast. With 3:1 balanced training and validation cohorts, patients were retrospectively followed for a median of 6 years. The main outcome was to validate an automated BC phenotyping system combined with clinical features to produce a binomial risk score predicting BC recurrence at diagnosis. RESULTS: The PDxBr training model (n = 1559 patients) had a C-index of 0.78 (95% CI, 0.76-0.81) versus clinical 0.71 (95% CI, 0.67-0.74) and image feature models 0.72 (95% CI, 0.70-0.74). A risk score of 58 (scale 0-100) stratified patients as low or high risk, hazard ratio (HR) 5.5 (95% CI 4.19-7.2, $p < 0.001$), with a sensitivity 0.71, specificity 0.77, NPV 0.95, and PPV 0.32 for predicting BC recurrence within 6 years. In the validation cohort (n = 516), the C-index was 0.75 (95% CI, 0.72-0.79) versus clinical 0.71 (95% CI 0.66-0.75) versus image feature models 0.67 (95% CI, 0.63-071). The validation cohort had an HR of 4.4 (95% CI 2.7-7.1, $p < 0.001$), sensitivity of 0.60, specificity 0.77, NPV 0.94, and PPV 0.24 for predicting BC recurrence within 6 years. PDxBr also

improved Oncotype Recurrence Score (RS) performance: RS 31 cutoff, C-index of 0.36 (95% CI 0.26-0.45), sensitivity 37%, specificity 48%, HR 0.48, p = 0.04 versus Oncotype RS plus AI-grade C-index 0.72 (95% CI 0.67-0.79), sensitivity 78%, specificity 49%, HR 4.6, p < 0.001 versus Oncotype RS plus PDxBr, C-index 0.76 (95% CI 0.70-0.82), sensitivity 67%, specificity 80%, HR 6.1, p < 0.001. CONCLUSIONS: PDxBr is a digital BC test combining automated AI-BC prognostic grade with clinical-pathologic features to predict the risk of early-stage BC recurrence. With future validation studies, we anticipate the PDxBr model will enrich current gene expression assays and enhance treatment decision-making.

Fukuda, M., et al. (1999). "[Sequential changes in hormone levels in postmenopausal breast cancer patients under long-term treatment with an aromatase inhibitor. Kanagawa AI Study Group]." Gan To Kagaku Ryoho **26**(14): 2201-2208.

Sequential changes in hormone levels were assessed for one year in postmenopausal breast cancer patients administered the aromatase inhibitor fodrozole hydrochloride hydrate (Afema) in order to evaluate its efficacy and safety in long-term treatment. Forty patients received Afema alone as postoperative adjuvant therapy, while 30 received it with 5-FU. Plasma estrone and estradiol levels decreased significantly in both groups (p < 0.001) and were not affected by body mass index (BMI). Plasma androstenedione and testosterone levels increased within the normal range. Aldosterone levels hit bottom 3 months after treatment was started, and tended to return to the pre-treatment baseline thereafter. Plasma cortisol levels increased significantly within the normal range. FDP and alpha 2-PIPC, parameters related to blood coagulation and fibrinolysis, showed no significant change. Adverse reactions, mainly nausea and elevation of LDH levels, were all slight. Thus, long-term administration of Afema resulted in significant decreases in estrogen levels with few adverse reactions regardless of the BMI, suggesting that it can be safely used as effective postoperative adjuvant therapy.

Futane, A., et al. (2024). "Aptamer-functionalized MOFs and AI-driven strategies for early cancer diagnosis and therapeutics." Biotechnol Lett **46**(1): 1-17.

Metal-Organic Frameworks (MOFs) have exceptional inherent properties that make them highly suitable for diverse applications, such as catalysis, storage, optics, chemo sensing, and biomedical science and technology. Over the past decades, researchers have utilized various techniques, including solvothermal, hydrothermal, mechanochemical, electrochemical, and ultrasonic, to synthesize MOFs with tailored properties. Post-synthetic modification of linkers, nodal components, and crystallite domain size and morphology can functionalize MOFs to improve their aptamer applications. Advancements in AI and machine learning led to the development of nonporous MOFs and nanoscale MOFs for medical purposes. MOFs have exhibited promise in cancer therapy, with the successful accumulation of a photosensitizer in cancer cells representing a significant breakthrough. This perspective is focused on MOFs' use as advanced materials and systems for cancer therapy, exploring the challenging aspects and promising features of MOF-based cancer diagnosis and treatment. The paper concludes by emphasizing the potential of MOFs as a transformative technology for cancer treatment and diagnosis.

Gaube, S., et al. (2024). "Comparing preferences for skin cancer screening: AI-enabled app vs dermatologist." Soc Sci Med **349**: 116871.

BACKGROUND AND AIM: Skin cancer is a major public health issue. While self-examinations and professional screenings are recommended, they are rarely performed. Mobile health (mHealth) apps utilising artificial intelligence (AI) for skin cancer screening offer a potential solution to aid self-examinations; however, their uptake is low. Therefore, the aim of this research was to examine provider and user characteristics influencing people's decisions to seek skin cancer screening performed by a mHealth app or a dermatologist. METHODS: Two forced-choice conjoint experiments with N(main) = 1591 and N(replication) = 308 participants from the United States were conducted online to investigate preferences for screening providers. In addition to the provider type (mHealth app vs dermatologist), the following provider attributes were manipulated: costs, expertise, privacy policy, and result details. Subsequently, a questionnaire assessed various user characteristics, including demographics, attitudes toward AI technology and medical mistrust. RESULTS: Outcomes were consistent across the two studies. The provider type was the most influential factor, with the dermatologist being selected more often than the mHealth app. Cost, expertise, and privacy policy also significantly impacted decisions. Demographic subgroup analyses showed rather consistent preference trends across various age, gender, and ethnicity groups. Individuals with greater medical mistrust were more inclined to choose the mHealth app. Trust, accuracy, and quality ratings were higher for the dermatologist, whether selected or not. CONCLUSION: Our results offer valuable

insights for technology developers, healthcare providers, and policymakers, contributing to unlocking the potential of skin cancer screening apps in bridging healthcare gaps in underserved communities.

Gong, J., et al. (2023). "The application of lightweight AI algorithms in postoperative rehabilitation of breast cancer." Comput Methods Biomech Biomed Engin: 1-12.

The prevalence of breast cancer as a major global cancer has underscored the importance of postoperative recovery for breast cancer patients. Among the issues, postoperative patients are prone to spinal deformities, including scoliosis, which has drawn significant attention from healthcare professionals. The primary aim of this study is to design a postoperative recovery platform for breast cancer patients that can effectively detect posture changes, provide feedback and support to medical staff, assist doctors in formulating recovery plans, and prevent spinal deformities. The feasibility of the recovery platform is also validated through experiments. The development and validation of the experimental recovery platform. The recovery platform includes instrument design, patient data collection, model training and fine-tuning, and postoperative body posture evaluation by comparing preoperative and postoperative conditions. The evaluation results are provided to doctors to facilitate the formulation of personalized postoperative recovery plans. This paper comprehensively designs and implements the recovery platform and verifies its feasibility through simulation experiments. Statistical methods were employed for the validation of the rehabilitation platform in simulated experiments, with a significance level of $p < 0.05$. In comparison to static assessments like CT scans, this paper introduces a dynamic detection method that provides a more insightful analysis of body posture. The experiments also demonstrate the preventive capability of this method against post-operative spinal deformities, ultimately enhancing patients' self-image, restoring their confidence, and enabling them to lead more fulfilling lives.

Guo, S. P., et al. (2021). "Serum Apolipoprotein A-I Predicts Response of Rectal Cancer to Neoadjuvant Chemoradiotherapy." Cancer Manag Res **13**: 2623-2631.

BACKGROUND: Serum lipids have been reported as prognosticators for malignancies, including rectal cancer (RC). Yet, their value in predicting the response of RC to neoadjuvant chemoradiotherapy (NACRT) remains unknown. This study aimed to assess the predictive abilities of serum lipids for a bad response, and to build a serum lipid-based prediction model. METHODS: In total, 751 patients diagnosed with stage cII-III RC and treated with NACRT plus surgery from January 2007 to August 2018 were retrospectively reviewed and randomly divided into two data sets, in a ratio of 1:1. Receiver operating characteristics (ROC) analysis was conducted in the development set to select possible predictors of bad NACRT response from pathoclinical factors, including serum lipids. Multivariate logistic regression was conducted to further determine independent predictors, which were then used to develop a prediction index (PI). Finally, the PI was verified in the validation set, through ROC analysis and chi-squared test. RESULTS: Five independent predictors were identified: tumor length >/=4 cm, cT4 stage, carcinoembryonic antigen >/=5.0 ng/mL, irradiation with three-dimensional conformal radiotherapy technique, and apolipoprotein A-I </=1.20 g/L. Each of them was assigned a number of points. In the validation set, the area under the curve of PI appeared as 0.642 (95% confidence interval 0.586-0.697). The sensitivity, specificity, positive and negative predictive values, and concordance were 72.3%, 52.3%, 63.8%, 61.9%, and 63.0%, respectively. CONCLUSION: Serum apolipoprotein A-I was found to correlate negatively with the RC response to NACRT. It could serve as a biomarker for guiding individualized treatment and a potential target for improving sensitivity to chemoradiation.

Hamamoto, R., et al. (2022). "Introducing AI to the molecular tumor board: one direction toward the establishment of precision medicine using large-scale cancer clinical and biological information." Exp Hematol Oncol **11**(1): 82.

Since U.S. President Barack Obama announced the Precision Medicine Initiative in his New Year's State of the Union address in 2015, the establishment of a precision medicine system has been emphasized worldwide, particularly in the field of oncology. With the advent of next-generation sequencers specifically, genome analysis technology has made remarkable progress, and there are active efforts to apply genome information to diagnosis and treatment. Generally, in the process of feeding back the results of next-generation sequencing analysis to patients, a molecular tumor board (MTB), consisting of experts in clinical oncology, genetic medicine, etc., is established to discuss the results. On the other hand, an MTB currently involves a large amount of work, with humans searching through vast databases and literature, selecting the best drug candidates, and manually confirming the status of available clinical trials. In addition, as personalized medicine advances,

the burden on MTB members is expected to increase in the future. Under these circumstances, introducing cutting-edge artificial intelligence (AI) technology and information and communication technology to MTBs while reducing the burden on MTB members and building a platform that enables more accurate and personalized medical care would be of great benefit to patients. In this review, we introduced the latest status of elemental technologies that have potential for AI utilization in MTB, and discussed issues that may arise in the future as we progress with AI implementation.

He, X. R., et al. (2016). "Injectable Chinese herbal formula Kang'ai for nonsmall cell lung cancer: Trial sequential analysis of 2,259 participants from 31 randomized controlled trials." J Cancer Res Ther **12**(2): 735-743.

OBJECTIVE: The aim was to evaluate the efficacy and safety of Kang' ai (KA) injection for patients with nonsmall cell lung cancer (NSCLC). Furthermore, to identify if more trials are needed before reliable conclusions could be drawn with regard to these outcomes. MATERIALS AND METHODS: We searched the Cochrane library, PubMed, EMBASE, VIP, CBMdisc, and CNKI in September 2012, and then an additional updated search was conducted in January 2013. Only relevant randomized controlled trials (RCTs) on KA injection plus first-line cisplatin-based chemotherapy in the treatment of NSCLC were identified. Trials' data was reviewed and extracted by two reviewers independently. The quality of included studies was assessed according to a statement from Cochrane Handbook. RevMan 5 Software and Trial sequential analysis (TSA) software were applied for data analyses. RESULTS: A total of 31 RCTs involving 2259 patients were included. The results of meta-analysis showed that compared with chemotherapy alone, the combination of KA injection plus chemotherapy had a statistically significant benefit in improving clinical response rate (relative risk [RR] =1.29, 95% confidence interval [CI]: 1.17-1.41, P < 0.00001), clinical benefit rate (RR = 1.19, 95% CI: 1.14-1.25, P < 0.00001) and quality of life (RR = 1.79, 95% CI: 1.63-1.98, P < 0.00001); hematological toxicity (white blood cell) (RR = 0.71, 95% CI: 0.66-0.76, P < 0.00001) and nonhematological toxicity (nausea and vomiting) (RR = 0.73, 95% CI: 0.65-0.83, P < 0.00001) were improved as well. TSA showed that all cumulative Z-score crossed their monitoring boundaries, demonstrating that no more trials are needed before reliable conclusions could be drawn. CONCLUSION: Current evidence presented that KA injection might improve the therapeutic effect when combined with chemotherapy. Moreover, no more trials are needed in future according to TSA. Nevertheless, additional randomized studies investigating KA injection are needed to be further evaluated.

Higuchi, T., et al. (2016). "Contribution of Estrone Sulfate to Cell Proliferation in Aromatase Inhibitor (AI) -Resistant, Hormone Receptor-Positive Breast Cancer." PLoS One **11**(5): e0155844.

Aromatase inhibitors (AIs) effectively treat hormone receptor-positive postmenopausal breast cancer, but some patients do not respond to treatment or experience recurrence. Mechanisms of AI resistance include ligand-independent activation of the estrogen receptor (ER) and signaling via other growth factor receptors; however, these do not account for all forms of resistance. Here we present an alternative mechanism of AI resistance. We ectopically expressed aromatase in MCF-7 cells expressing green fluorescent protein as an index of ER activity. Aromatase-overexpressing MCF-7 cells were cultured in estrogen-depleted medium supplemented with testosterone and the AI, letrozole, to establish letrozole-resistant (LR) cell lines. Compared with parental cells, LR cells had higher mRNA levels of steroid sulfatase (STS), which converts estrone sulfate (E1S) to estrone, and the organic anion transporter peptides (OATPs), which mediate the uptake of E1S into cells. LR cells proliferated more in E1S-supplemented medium than did parental cells, and LR proliferation was effectively inhibited by an STS inhibitor in combination with letrozole and by ER-targeting drugs. Analysis of ER-positive primary breast cancer tissues showed a significant correlation between the increases in the mRNA levels of STS and the OATPs in the LR cell lines, which supports the validity of this AI-resistant model. This is the first study to demonstrate the contribution of STS and OATPs in E1S metabolism to the proliferation of AI-resistant breast cancer cells. We suggest that E1S metabolism represents a new target in AI-resistant breast cancer treatment.

Hill, H., et al. (2024). "Cost-Effectiveness of AI for Risk-Stratified Breast Cancer Screening." JAMA Netw Open **7**(9): e2431715.

IMPORTANCE: Previous research has shown good discrimination of short-term risk using an artificial intelligence (AI) risk prediction model (Mirai). However, no studies have been undertaken to evaluate whether this might translate into economic gains. OBJECTIVE: To assess the cost-effectiveness of incorporating risk-stratified screening using a breast cancer AI model into the United Kingdom (UK) National Breast Cancer Screening Program.

DESIGN, SETTING, AND PARTICIPANTS: This study, conducted from January 1, 2023, to January 31, 2024, involved the development of a decision analytical model to estimate health-related quality of life, cancer survival rates, and costs over the lifetime of the female population eligible for screening. The analysis took a UK payer perspective, and the simulated cohort consisted of women aged 50 to 70 years at screening. EXPOSURES: Mammography screening at 1 to 6 yearly screening intervals based on breast cancer risk and standard care (screening every 3 years). MAIN OUTCOMES AND MEASURES: Incremental net monetary benefit based on quality-adjusted life-years (QALYs) and National Health Service (NHS) costs (given in pounds sterling; to convert to US dollars, multiply by 1.28). RESULTS: Artificial intelligence-based risk-stratified programs were estimated to be cost-saving and increase QALYs compared with the current screening program. A screening schedule of every 6 years for lowest-risk individuals, biannually and triennially for those below and above average risk, respectively, and annually for those at highest risk was estimated to give yearly net monetary benefits within the NHS of approximately pound60.4 (US $77.3) million and pound85.3 (US $109.2) million, with QALY values set at pound20 000 (US $25 600) and pound30 000 (US $38 400), respectively. Even in scenarios where decision-makers hesitate to allocate additional NHS resources toward screening, implementing the proposed strategies at a QALY value of pound1 (US $1.28) was estimated to generate a yearly monetary benefit of approximately pound10.6 (US $13.6) million. CONCLUSIONS AND RELEVANCE: In this decision analytical model study of integrating risk-stratified screening with a breast cancer AI model into the UK National Breast Cancer Screening Program, risk-stratified screening was likely to be cost-effective, yielding added health benefits at reduced costs. These results are particularly relevant for health care settings where resources are under pressure. New studies to prospectively evaluate AI-guided screening appear warranted.

Hillis, E., et al. (2024). "Evaluating Generative AI's Ability to Identify Cancer Subtypes in Publicly Available Structured Genetic Datasets." J Pers Med **14**(10).

BACKGROUND: Genetic data play a crucial role in diagnosing and treating various diseases, reflecting a growing imperative to integrate these data into clinical care. However, significant barriers such as the structure of electronic health records (EHRs), insurance costs for genetic testing, and the interpretability of genetic results impede this integration. METHODS: This paper explores solutions to these challenges by combining recent technological advances with informatics and data science, focusing on the diagnostic potential of artificial intelligence (AI) in cancer research. AI has historically been applied in medical research with limited success, but recent developments have led to the emergence of large language models (LLMs). These transformer-based generative AI models, trained on vast datasets, offer significant potential for genetic and genomic analyses. However, their effectiveness is constrained by their training on predominantly human-written text rather than comprehensive, structured genetic datasets. RESULTS: This study reevaluates the capabilities of LLMs, specifically GPT models, in performing supervised prediction tasks using structured gene expression data. By comparing GPT models with traditional machine learning approaches, we assess their effectiveness in predicting cancer subtypes, demonstrating the potential of AI models to analyze real-world genetic data for generating real-world evidence.

Horesh, D., et al. (2022). "Virtual Reality Combined with Artificial Intelligence (VR-AI) Reduces Hot Flashes and Improves Psychological Well-Being in Women with Breast and Ovarian Cancer: A Pilot Study." Healthcare (Basel) **10**(11).

BACKGROUND AND AIMS: Breast and ovarian cancers affect the lives of many women worldwide. Female cancer survivors often experience hot flashes, a subjective sensation of heat associated with objective signs of cutaneous vasodilatation and a subsequent drop in core temperature. Breast and Ovarian cancer patients also suffer from sleep difficulties and mental health issues. The present study aimed to assess the effectiveness of Bubble, a novel artificial intelligence-virtual reality (AI-VR) intervention for the treatment of hot flashes in female breast or ovarian cancer patients. METHODS: Forty-two women with breast and/or ovarian cancer participated in the study. The mean age was 47 years (range: 25-60 years). Patients suffered from hot flashes at different frequencies. They used Bubble, a virtual reality (VR) mobile psychological intervention based on elements from both cognitive behavioral therapy and mindfulness-based stress reduction. The intervention took place in a VR environment, in a winter wonderland setting called Frosty. Patients were instructed to use Bubble at home twice a day (morning and evening) and when experiencing a hot flash. Participants were asked to use the application for 24 consecutive days. Before and after this 24-day period, patients completed self-report questionnaires assessing hot flashes, general

psychiatric distress, perceived stress, illness perception, sleep quality, and quality of life. RESULTS: Between pre- and post-intervention, participants reported a significant reduction in the daily frequency of hot flashes, stress, general psychiatric distress, several domains of QOL, and sleep difficulties, as well as an improvement in illness perception. In addition, they reported very high satisfaction with Bubble. Importantly, both age and baseline levels of psychopathology moderated the effect of Bubble on sleep difficulties. DISCUSSION: This study showed preliminary evidence for the potential of VR interventions in alleviating hot flashes and accompanying mental distress among those coping with breast and ovarian cancer. VR is a powerful therapeutic tool, able to address mind-body aspects in a direct, vivid way. More studies are needed in order to fully understand the potential of this unique intervention.

Hou, F., et al. (2016). "Yi Ai Fang, a traditional Chinese herbal formula, impacts the vasculogenic mimicry formation of human colorectal cancer through HIF-1alpha and epithelial mesenchymal transition." BMC Complement Altern Med **16**(1): 428.

BACKGROUND: Yi Ai Fang (YAF), a traditional Chinese medicine (TCM) formula, has been identified to have anticancer activity in our previously studies. The present study aimed to explore the potential mechanism of YAF suppression of VM on colorectal cancer (CRC) in vitro and in vivo. METHODS: Cell viability was measured by CCK-8 assay. HIF-1alpha, E-cd(E-cadherin), Claudin-4, and VIM (Vimentin) expressions level in vitro were evaluated by Western blot or RT-PCR. In addition, Human CRC HCT-116 cells were implanted in BALB/c nude mice; mice with xenografted tumors were randomly administrated vehicle (control), 8, 16, or 32 mg/mL YAF, or 1 mg/mL fluorouracil (5-FU). HIF-1alpha, E-cd, Claudin-4, and VIM expression in these tumors were determined by IHC. RESULTS: YAF effectively inhibited the growth and the formation of vasculogenic mimicry (VM) of CRC cells in a dose-dependent trend. YAF restrained the formation of vasculogenic mimicry(VM) through HIF-1alpha/EMT pathway in CRC. YAF suppressed VM was triggered by activation of E-cd and Claudin-4,which are characteristics of endothelial cells,and inhibition of HIF-1alpha and VIM in vitro. In vivo data showed that YAF remarkably inhibited growth of the xenografted tumors. The YAF-treated tumor samples were analyzed by IHC for levels of HIF-1alpha/EMT related proteins HIF-1alpha, E-cd, Claudin-4, and VIM. The results indicated that YAF significantly enhanced expression of E-cd and Claudin-4,but decreased expression of HIF-1alpha, VIM in a dose-dependent manner. CONCLUSIONS: In conclusion, this study provided the first direct evidence that YAF inhibited the formation of VM in human CRC, suggesting that YAF may be considered as a useful target for cancer therapy.

Hou, Y., et al. (2023). "Biopsy-free AI-aided precision MRI assessment in prediction of prostate cancer biochemical recurrence." Br J Cancer **129**(10): 1625-1633.

BACKGROUND: To investigate the predictive ability of high-throughput MRI with deep survival networks for biochemical recurrence (BCR) of prostate cancer (PCa) after prostatectomy. METHODS: Clinical-MRI and histopathologic data of 579 (train/test, 463/116) PCa patients were retrospectively collected. The deep survival network (iBCR-Net) is based on stepwise processing operations, which first built an MRI radiomics signature (RadS) for BCR, and predicted the T3 stage and lymph node metastasis (LN+) of tumour using two predefined AI models. Subsequently, clinical, imaging and histopathological variables were integrated into iBCR-Net for BCR prediction. RESULTS: RadS, derived from 2554 MRI features, was identified as an independent predictor of BCR. Two predefined AI models achieved an accuracy of 82.6% and 78.4% in staging T3 and LN+. The iBCR-Net, when expressed as a presurgical model by integrating RadS, AI-diagnosed T3 stage and PSA, can match a state-of-the-art histopathological model (C-index, 0.81 to 0.83 vs 0.79 to 0.81, $p > 0.05$); and has maximally 5.16-fold, 12.8-fold, and 2.09-fold ($p < 0.05$) benefit to conventional D'Amico score, the Cancer of the Prostate Risk Assessment (CAPRA) score and the CAPRA Postsurgical score. CONCLUSIONS: AI-aided iBCR-Net using high-throughput MRI can predict PCa BCR accurately and thus may provide an alternative to the conventional method for PCa risk stratification.

Huang, J. X., et al. (2024). "Elastography-based AI model can predict axillary status after neoadjuvant chemotherapy in breast cancer with nodal involvement: A prospective, multicenter, diagnostic study." Int J Surg.

OBJECTIVE: To develop a model for accurate prediction of axillary lymph node (LN) status after neoadjuvant chemotherapy (NAC) in breast cancer patients with nodal involvement. METHODS: Between October 2018 and February 2024, 671 breast cancer patients with biopsy-proven LN metastasis who received NAC followed by axillary LN dissection were enrolled in this prospective, multicenter study. Preoperative

ultrasound (US) images, including B-mode ultrasound (BUS) and shear wave elastography (SWE), were obtained. The included patients were randomly divided at a ratio of 8:2 into a training set and an independent test set, with five-fold cross-validation applied to training set. We first identified clinicopathological characteristics and conventional US features significantly associated with the axillary LN response and developed corresponding prediction models. We then constructed deep learning radiomics (DLR) models based on BUS and SWE data. Models performances were compared, and a combination model was developed using significant clinicopathological data and interpreted US features with the SWE-based DLR model. Discrimination, calibration and clinical utility of this model were analyzed using receiver operating characteristic curve, calibration curve and decision curve, respectively. RESULTS: Axillary pathologic complete response (pCR) was achieved in 52.41% of patients. In the test cohort, the clinicopathologic model had an accuracy of 71.30%, while radiologists' diagnoses ranged from 64.26% to 71.11%, indicating limited to moderate predictive ability for the axillary response to NAC. The SWE-based DLR model, with an accuracy of 80.81%, significantly outperformed the BUS-based DLR model, which scored 59.57%. The combination DLR model boasted an accuracy of 88.70% and a false-negative rate of 8.82%. It demonstrated strong discriminatory ability (AUC, 0.95), precise calibration (p value obtained by Hosmer-Lemeshow goodness-of-fit test, 0.68), and practical clinical utility (probability threshold, 2.5-97.5%). CONCLUSIONS: The combination SWE-based DLR model can predict the axillary status after NAC in patients with node-positive breast cancer, and thus, may inform clinical decision-making to help avoid unnecessary axillary LN dissection.

Huber, F. A., et al. (2024). "AI-based opportunistic quantitative image analysis of lung cancer screening CTs to reduce disparities in osteoporosis screening." Bone **186**: 117176.

Osteoporosis is underdiagnosed, especially in ethnic and racial minorities who are thought to be protected against bone loss, but often have worse outcomes after an osteoporotic fracture. We aimed to determine the prevalence of osteoporosis by opportunistic CT in patients who underwent lung cancer screening (LCS) using non-contrast CT in the Northeastern United States. Demographics including race and ethnicity were retrieved. We assessed trabecular bone and body composition using a fully-automated artificial intelligence algorithm. ROIs were placed at T12 vertebral body for attenuation measurements in Hounsfield Units (HU). Two validated thresholds were used to diagnose osteoporosis: high-sensitivity threshold (115-165 HU) and high specificity threshold (<115 HU). We performed descriptive statistics and ANOVA to compare differences across sex, race, ethnicity, and income class according to neighborhoods' mean household incomes. Forward stepwise regression modeling was used to determine body composition predictors of trabecular attenuation. We included 3708 patients (mean age 64 +/- 7 years, 54 % males) who underwent LCS, had available demographic information and an evaluable CT for trabecular attenuation analysis. Using the high sensitivity threshold, osteoporosis was more prevalent in females (74 % vs. 65 % in males, $p < 0.0001$) and Whites (72 % vs 49 % non-Whites, $p < 0.0001$). However, osteoporosis was present across all races (38 % Black, 55 % Asian, 56 % Hispanic) and affected all income classes (69 %, 69 %, and 91 % in low, medium, and high-income class, respectively). High visceral/subcutaneous fat-ratio, aortic calcification, and hepatic steatosis were associated with low trabecular attenuation ($p < 0.01$), whereas muscle mass was positively associated with trabecular attenuation ($p < 0.01$). In conclusion, osteoporosis is prevalent across all races, income classes and both sexes in patients undergoing LCS. Opportunistic CT using a fully-automated algorithm and uniform imaging protocol is able to detect osteoporosis and body composition without additional testing or radiation. Early identification of patients traditionally thought to be at low risk for bone loss will allow for initiating appropriate treatment to prevent future fragility fractures. CLINICALTRIALS.GOV IDENTIFIER: N/A.

Islam, R. and M. Tarique (2024). "Artificial Intelligence (AI) and Nuclear Features from the Fine Needle Aspirated (FNA) Tissue Samples to Recognize Breast Cancer." J Imaging **10**(8).

Breast cancer is one of the paramount causes of new cancer cases worldwide annually. It is a malignant neoplasm that develops in the breast cells. The early screening of this disease is essential to prevent its metastasis. A mammogram X-ray image is the most common screening tool practiced currently when this disease is suspected; all the breast lesions identified are not malignant. The invasive fine needle aspiration (FNA) of a breast mass sample is the secondary screening tool to clinically examine cancerous lesions. The visual image analysis of the stained aspirated sample imposes a challenge for the cytologist to identify the malignant cells accurately. The formulation of an artificial intelligence-based objective technique on top of the introspective assessment is essential to avoid misdiagnosis. This

paper addresses several artificial intelligence (AI)-based techniques to diagnose breast cancer from the nuclear features of FNA samples. The Wisconsin Breast Cancer dataset (WBCD) from the UCI machine learning repository is applied for this investigation. Significant statistical parameters are measured to evaluate the performance of the proposed techniques. The best detection accuracy of 98.10% is achieved with a two-layer feed-forward neural network (FFNN). Finally, the developed algorithm's performance is compared with some state-of-the-art works in the literature.

Islam, S., et al. (2024). "Leveraging AI and patient metadata to develop a novel risk score for skin cancer detection." Sci Rep **14**(1): 20842.

Melanoma of the skin is the 17th most common cancer worldwide. Early detection of suspicious skin lesions (melanoma) can increase 5-year survival rates by 20%. The 7-point checklist (7PCL) has been extensively used to suggest urgent referrals for patients with a possible melanoma. However, the 7PCL method only considers seven meta-features to calculate a risk score and is only relevant for patients with suspected melanoma. There are limited studies on the extensive use of patient metadata for the detection of all skin cancer subtypes. This study investigates artificial intelligence (AI) models that utilise patient metadata consisting of 23 attributes for suspicious skin lesion detection. We have identified a new set of most important risk factors, namely "C4C risk factors", which is not just for melanoma, but for all types of skin cancer. The performance of the C4C risk factors for suspicious skin lesion detection is compared to that of the 7PCL and the Williams risk factors that predict the lifetime risk of melanoma. Our proposed AI framework ensembles five machine learning models and identifies seven new skin cancer risk factors: lesion pink, lesion size, lesion colour, lesion inflamed, lesion shape, lesion age, and natural hair colour, which achieved a sensitivity of 80.46 +/- 2.50% and a specificity of 62.09 +/- 1.90% in detecting suspicious skin lesions when evaluated using the metadata of 53,601 skin lesions collected from different skin cancer diagnostic clinics across the UK, significantly outperforming the 7PCL-based method (sensitivity 68.09 +/- 2.10% , specificity 61.07 +/- 0.90%) and the Williams risk factors (sensitivity 66.32 +/- 1.90% , specificity 61.71 +/- 0.6%). Furthermore, through weighting the seven new risk factors we came up with a new risk score, namely "C4C risk score", which alone achieved a sensitivity of 76.09 +/- 1.20% and a specificity of 61.71 +/- 0.50% , significantly outperforming the 7PCL-based risk score (sensitivity 73.91 +/- 1.10% , specificity 49.49 +/- 0.50%) and the Williams risk score (sensitivity 60.68 +/- 1.30% , specificity 60.87 +/- 0.80%). Finally, fusing the C4C risk factors with the 7PCL and Williams risk factors achieved the best performance, with a sensitivity of 85.24 +/- 2.20% and a specificity of 61.12 +/- 0.90% . We believe that fusing these newly found risk factors and new risk score with image data will further boost the AI model performance for suspicious skin lesion detection. Hence, the new set of skin cancer risk factors has the potential to be used to modify current skin cancer referral guidelines for all skin cancer subtypes, including melanoma.

Islam, T., et al. (2024). "Predictive modeling for breast cancer classification in the context of Bangladeshi patients by use of machine learning approach with explainable AI." Sci Rep **14**(1): 8487.

Breast cancer has rapidly increased in prevalence in recent years, making it one of the leading causes of mortality worldwide. Among all cancers, it is by far the most common. Diagnosing this illness manually requires significant time and expertise. Since detecting breast cancer is a time-consuming process, preventing its further spread can be aided by creating machine-based forecasts. Machine learning and Explainable AI are crucial in classification as they not only provide accurate predictions but also offer insights into how the model arrives at its decisions, aiding in the understanding and trustworthiness of the classification results. In this study, we evaluate and compare the classification accuracy, precision, recall, and F1 scores of five different machine learning methods using a primary dataset (500 patients from Dhaka Medical College Hospital). Five different supervised machine learning techniques, including decision tree, random forest, logistic regression, naive bayes, and XGBoost, have been used to achieve optimal results on our dataset. Additionally, this study applied SHAP analysis to the XGBoost model to interpret the model's predictions and understand the impact of each feature on the model's output. We compared the accuracy with which several algorithms classified the data, as well as contrasted with other literature in this field. After final evaluation, this study found that XGBoost achieved the best model accuracy, which is 97%.

Ivanova, E., et al. (2023). "Empowering Renal Cancer Management with AI and Digital Pathology: Pathology, Diagnostics and Prognosis." Biomedicines **11**(11).

Renal cell carcinoma is a significant health burden worldwide, necessitating accurate and efficient diagnostic methods to guide treatment decisions. Traditional pathology practices have limitations, including interobserver variability and

time-consuming evaluations. In recent years, digital pathology tools emerged as a promising solution to enhance the diagnosis and management of renal cancer. This review aims to provide a comprehensive overview of the current state and potential of digital pathology in the context of renal cell carcinoma. Through advanced image analysis algorithms, artificial intelligence (AI) technologies facilitate quantification of cellular and molecular markers, leading to improved accuracy and reproducibility in renal cancer diagnosis. Digital pathology platforms empower remote collaboration between pathologists and help with the creation of comprehensive databases for further research and machine learning applications. The integration of digital pathology tools with other diagnostic modalities, such as radiology and genomics, enables a novel multimodal characterization of different types of renal cell carcinoma. With continuous advancements and refinement, AI technologies are expected to play an integral role in diagnostics and clinical decision-making, improving patient outcomes. In this article, we explored the digital pathology instruments available for clear cell, papillary and chromophobe renal cancers from pathologist and data analyst perspectives.

Jailin, C., et al. (2023). "AI-Based Cancer Detection Model for Contrast-Enhanced Mammography." Bioengineering (Basel) **10**(8).

BACKGROUND: The recent development of deep neural network models for the analysis of breast images has been a breakthrough in computer-aided diagnostics (CAD). Contrast-enhanced mammography (CEM) is a recent mammography modality providing anatomical and functional imaging of the breast. Despite the clinical benefits it could bring, only a few research studies have been conducted around deep-learning (DL) based CAD for CEM, especially because the access to large databases is still limited. This study presents the development and evaluation of a CEM-CAD for enhancing lesion detection and breast classification. MATERIALS & METHODS: A deep learning enhanced cancer detection model based on a YOLO architecture has been optimized and trained on a large CEM dataset of 1673 patients (7443 images) with biopsy-proven lesions from various hospitals and acquisition systems. The evaluation was conducted using metrics derived from the free receiver operating characteristic (FROC) for the lesion detection and the receiver operating characteristic (ROC) to evaluate the overall breast classification performance. The performances were evaluated for different types of image input and for each patient background parenchymal enhancement (BPE) level. RESULTS: The optimized model achieved an area under the curve (AUROC) of 0.964 for breast classification. Using both low-energy and recombined image as inputs for the DL model shows greater performance than using only the recombined image. For the lesion detection, the model was able to detect 90% of all cancers with a false positive (non-cancer) rate of 0.128 per image. This study demonstrates a high impact of BPE on classification and detection performance. CONCLUSION: The developed CEM CAD outperforms previously published papers and its performance is comparable to radiologist-reported classification and detection capability.

Jaklitsch, E., et al. (2023). "Clinical Utility of an AI-powered, Handheld Elastic Scattering Spectroscopy Device on the Diagnosis and Management of Skin Cancer by Primary Care Physicians." J Prim Care Community Health **14**: 21501319231205979.

BACKGROUND: Patients with lesions suspicious for skin cancer often present to primary care physicians (PCPs), who may have limited training in skin cancer diagnosis. OBJECTIVE: To measure the impact of an adjunctive handheld device for PCPs that employs elastic scattering spectroscopy (ESS) on the diagnosis and management of skin cancer. METHODS: Fifty-seven PCPs evaluated 50 clinical images of skin lesions (25 malignant and 25 benign), first without and then with knowledge of the handheld ESS device output, and in each case indicated if a lesion was likely to be benign or malignant. RESULTS: The diagnostic sensitivity of the PCPs with and without the use of the ESS device was 88% (95% CI, 84%-92%) and 67% (95% CI, 62%-72%), respectively ($P < .0001$). In contrast, no significant difference was observed in the diagnostic specificity. The management sensitivity of the physicians with and without the use of the ESS device was 94% (95% CI, 91%-96%) and 81% (95% CI, 77%-85%), respectively ($P = .0009$). Similarly, no significant difference was observed in the management specificity. CONCLUSION: The use of the ESS device may have the potential to help improve skin cancer diagnosis and confidence in management decision-making in a primary care setting.

Jaton, F. (2023). "Groundwork for AI: Enforcing a benchmark for neoantigen prediction in personalized cancer immunotherapy." Soc Stud Sci **53**(5): 787-810.

This article expands on recent studies of machine learning or artificial intelligence (AI) algorithms that crucially depend on benchmark datasets, often called 'ground truths.' These ground-truth datasets gather input-data and output-targets,

thereby establishing what can be retrieved computationally and evaluated statistically. I explore the case of the Tumor nEoantigen SeLection Alliance (TESLA), a consortium-based ground-truthing project in personalized cancer immunotherapy, where the 'truth' of the targets-immunogenic neoantigens-to be retrieved by the would-be AI algorithms depended on a broad technoscientific network whose setting up implied important organizational and material infrastructures. The study shows that instead of grounding an undisputable 'truth', the TESLA endeavor ended up establishing a contestable reference, the biology of neoantigens and how to measure their immunogenicity having slightly evolved alongside this four-year project. However, even if this controversy played down the scope of the TESLA ground truth, it did not discredit the whole undertaking. The magnitude of the technoscientific efforts that the TESLA project set into motion and the needs it ultimately succeeded in filling for the scientific and industrial community counterbalanced its metrological uncertainties, effectively instituting its contestable representation of 'true' neoantigens within the field of personalized cancer immunotherapy (at least temporarily). More generally, this case study indicates that the enforcement of ground truths, and what it leaves out, is a necessary condition to enable AI technologies in personalized medicine.

Javed, S., et al. (2022). "Risk prediction of pancreatic cancer using AI analysis of pancreatic subregions in computed tomography images." Front Oncol **12**: 1007990.

Early detection of Pancreatic Ductal Adenocarcinoma (PDAC) is complicated as PDAC remains asymptomatic until cancer advances to late stages when treatment is mostly ineffective. Stratifying the risk of developing PDAC can improve early detection as subsequent screening of high-risk individuals through specialized surveillance systems reduces the chance of misdiagnosis at the initial stage of cancer. Risk stratification is however challenging as PDAC lacks specific predictive biomarkers. Studies reported that the pancreas undergoes local morphological changes in response to underlying biological evolution associated with PDAC development. Accurate identification of these changes can help stratify the risk of PDAC. In this retrospective study, an extensive radiomic analysis of the precancerous pancreatic subregions was performed using abdominal Computed Tomography (CT) scans. The analysis was performed using 324 pancreatic subregions identified in 108 contrast-enhanced abdominal CT scans with equal proportion from healthy control, pre-diagnostic, and diagnostic groups. In a pairwise feature analysis, several textural features were found potentially predictive of PDAC. A machine learning classifier was then trained to perform risk prediction of PDAC by automatically classifying the CT scans into healthy control (low-risk) and pre-diagnostic (high-risk) classes and specifying the subregion(s) likely to develop a tumor. The proposed model was trained on CT scans from multiple phases. Whereas using 42 CT scans from the venous phase, model validation was performed which resulted in ~89.3% classification accuracy on average, with sensitivity and specificity reaching 86% and 93%, respectively, for predicting the development of PDAC (i.e., high-risk). To our knowledge, this is the first model that unveiled microlevel precancerous changes across pancreatic subregions and quantified the risk of developing PDAC. The model demonstrated improved prediction by 3.3% in comparison to the state-of-the-art method that considers the global (whole pancreas) features for PDAC prediction.

Ji, Y., et al. (2023). "Differences in Molecular Subtype Reference Standards Impact AI-based Breast Cancer Classification with Dynamic Contrast-enhanced MRI." Radiology **307**(1): e220984.

Background Breast cancer tumors can be identified as different luminal molecular subtypes depending on either immunohistochemical (IHC) staining or St Gallen criteria that includes Ki-67. Purpose To characterize molecular subtypes and understand the impact of disagreement among IHC and St Gallen molecular subtype reference standards on artificial intelligence classification of luminal A and luminal B tumors with use of radiomic features extracted from dynamic contrast-enhanced (DCE) MRI scans. Materials and Methods In this retrospective study, 28 radiomic features previously extracted from DCE-MRI scans of breast tumors imaged between February 2015 and October 2017 were examined in the following groups: (a) tumors classified as luminal A by both reference standards ("agreement"), (b) tumors classified as luminal A by IHC and luminal B by St Gallen ("disagreement"), and (c) tumors classified as luminal B by both ("agreement"). Luminal A or luminal B tumor classification with use of radiomic features was conducted with use of three sets: (a) IHC molecular subtyping, (b) St Gallen molecular subtyping, and (c) agreement tumors. The Kruskal-Wallis test was followed by the Mann-Whitney U test to determine pair-wise differences of radiomic features among agreement and disagreement tumors. Fivefold cross-validation with use of stepwise feature selection and linear discriminant analysis classified tumors in each set, with performance measured with use of area

under the receiver operating characteristic curve (AUC). Results A total of 877 breast cancer tumors from 872 women (mean age, 48 years [range, 19-75 years]) were analyzed. Six features (sphericity, irregularity, surface area to volume ratio, variance of radial gradient histogram, sum average, volume of most enhancing voxels) were different (P </= .001) among agreement and disagreement tumors. AUC (median, 0.74 [95% CI: 0.68, 0.80]) was higher than when using tumors subtyped by either reference standard (IHC, 0.66 [0.60, 0.71], P = .003; St Gallen, 0.62 [0.58, 0.67], P = .001). Conclusion Differences in reference standards can hinder artificial intelligence classification performance of luminal molecular subtypes with dynamic contrast-enhanced MRI. (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Bae in this issue.

Jiang, L., et al. (2024). "Effects of the "AI-TA" Mobile App With Intelligent Design on Psychological and Related Symptoms of Young Survivors of Breast Cancer: Randomized Controlled Trial." JMIR Mhealth Uhealth **12**: e50783.

BACKGROUND: Young women often face substantial psychological challenges in the initial years following cancer diagnosis, leading to a comparatively lower quality of life than older survivors. While mobile apps have emerged as potential interventions, their effectiveness remains inconclusive due to the diversity in intervention types and variation in follow-up periods. Furthermore, there is a particular dearth of evidence regarding the efficacy of these apps' intelligent features in addressing psychological distress with these apps. OBJECTIVE: This study aims to evaluate the effectiveness of a mobile app with intelligent design called "AI-TA" on cancer-related psychological health and ongoing symptoms with a randomized controlled design. METHODS: Women aged 18 to 45 years diagnosed with breast cancer were randomly assigned to the intervention or control group. The intervention was AI-TA, which included 2-way web-based follow-up every 2 weeks. Both intention-to-treat (ITT) and per-protocol (PP) analyses employed repeated measurement analysis of variance. The participants' background features, primary outcomes (psychological distress and frequency, self-efficacy, and social support), and secondary outcomes (quality of life) were measured using multiple instruments at 3 time points (baseline, 1-month intervention, and 3-month intervention). RESULTS: A total of 124 participants were randomly allocated to the control group (n=62, 50%) or intervention group (n=62, 50%). In total, 92.7% (115/124) of the participants completed the intervention. Significant improvements in psychological symptoms (Memorial Symptom Assessment Scale-Short Form) were observed in the ITT group from baseline to 1-month intervention relative to the control group (ITT vs control: 1.17 vs 1.23; P<.001), which persisted at 3-month follow-up (ITT vs control: 0.68 vs 0.91; P<.001). Both the ITT and PP groups exhibited greater improvements in self-efficacy (Cancer Behavior Inventory-Brief Version) than the control group at 1-month (ITT vs PP vs control: 82.83 vs 77.12 vs 65.35; P<.001) and 3-month intervention (ITT vs PP vs control: 92.83 vs 89.30 vs 85.65; P<.001). However, the change in social support (Social Support Rating Scale) did not increase significantly until 3-month intervention (ITT vs control: 50.09 vs 45.10; P=.002) (PP vs control: 49.78 vs 45.10; P<.001). All groups also experienced beneficial effects on quality of life (Functional Assessment of Cancer Therapy-Breast), which persisted at 3-month follow-up (P<.001). CONCLUSIONS: The intelligent mobile app AI-TA incorporating intelligent design shows promise for reducing psychological and cancer-related symptoms among young survivors of breast cancer. TRIAL REGISTRATION: Chinese Clinical Trial Registry ChiCTR2200058823; https://www.chictr.org.cn/showproj.html?proj=151195.

Jiang, Z., et al. (2024). "AI for interpreting screening mammograms: implications for missed cancer in double reading practices and challenging-to-locate lesions." Sci Rep **14**(1): 11893.

Although the value of adding AI as a surrogate second reader in various scenarios has been investigated, it is unknown whether implementing an AI tool within double reading practice would capture additional subtle cancers missed by both radiologists who independently assessed the mammograms. This paper assesses the effectiveness of two state-of-the-art Artificial Intelligence (AI) models in detecting retrospectively-identified missed cancers within a screening program employing double reading practices. The study also explores the agreement between AI and radiologists in locating the lesions, considering various levels of concordance among the radiologists in locating the lesions. The Globally-aware Multiple Instance Classifier (GMIC) and Global-Local Activation Maps (GLAM) models were fine-tuned for our dataset. We evaluated the sensitivity of both models on missed cancers retrospectively identified by a panel of three radiologists who reviewed prior examinations of 729 cancer cases detected in a screening program with double reading practice. Two of these experts annotated the lesions, and based on their concordance levels, cases were categorized as 'almost perfect,'

'substantial,' 'moderate,' and 'poor.' We employed Similarity or Histogram Intersection (SIM) and Kullback-Leibler Divergence (KLD) metrics to compare saliency maps of malignant cases from the AI model with annotations from radiologists in each category. In total, 24.82% of cancers were labeled as "missed." The performance of GMIC and GLAM on the missed cancer cases was 82.98% and 79.79%, respectively, while for the true screen-detected cancers, the performances were 89.54% and 87.25%, respectively (p-values for the difference in sensitivity < 0.05). As anticipated, SIM and KLD from saliency maps were best in 'almost perfect,' followed by 'substantial,' 'moderate,' and 'poor.' Both GMIC and GLAM (p-values < 0.05) exhibited greater sensitivity at higher concordance. Even in a screening program with independent double reading, adding AI could potentially identify missed cancers. However, the challenging-to-locate lesions for radiologists impose a similar challenge for AI.

Jiang, Z., et al. (2024). "Evaluating Recalibrating AI Models for Breast Cancer Diagnosis in a New Context: Insights from Transfer Learning, Image Enhancement and High-Quality Training Data Integration." Cancers (Basel) **16**(2).

This paper investigates the adaptability of four state-of-the-art artificial intelligence (AI) models to the Australian mammographic context through transfer learning, explores the impact of image enhancement on model performance and analyses the relationship between AI outputs and histopathological features for clinical relevance and accuracy assessment. A total of 1712 screening mammograms (n = 856 cancer cases and n = 856 matched normal cases) were used in this study. The 856 cases with cancer lesions were annotated by two expert radiologists and the level of concordance between their annotations was used to establish two sets: a 'high-concordances subset' with 99% agreement of cancer location and an 'entire dataset' with all cases included. The area under the receiver operating characteristic curve (AUC) was used to evaluate the performance of Globally aware Multiple Instance Classifier (GMIC), Global-Local Activation Maps (GLAM), I&H and End2End AI models, both in the pretrained and transfer learning modes, with and without applying the Contrast Limited Adaptive Histogram Equalization (CLAHE) algorithm. The four AI models with and without transfer learning in the high-concordance subset outperformed those in the entire dataset. Applying the CLAHE algorithm to mammograms improved the performance of the AI models. In the high-concordance subset with the transfer learning and CLAHE algorithm applied, the AUC of the GMIC model was highest (0.912), followed by the GLAM model (0.909), I&H (0.893) and End2End (0.875). There were significant differences ($p < 0.05$) in the performances of the four AI models between the high-concordance subset and the entire dataset. The AI models demonstrated significant differences in malignancy probability concerning different tumour size categories in mammograms. The performance of AI models was affected by several factors such as concordance classification, image enhancement and transfer learning. Mammograms with a strong concordance with radiologists' annotations, applying image enhancement and transfer learning could enhance the accuracy of AI models.

Jin, T., et al. (2022). "Multi-center verification of the influence of data ratio of training sets on test results of an AI system for detecting early gastric cancer based on the YOLO-v4 algorithm." Front Oncol **12**: 953090.

OBJECTIVE: Convolutional Neural Network(CNN) is increasingly being applied in the diagnosis of gastric cancer. However, the impact of proportion of internal data in the training set on test results has not been sufficiently studied. Here, we constructed an artificial intelligence (AI) system called EGC-YOLOV4 using the YOLO-v4 algorithm to explore the optimal ratio of training set with the power to diagnose early gastric cancer. DESIGN: A total of 22,0918 gastroscopic images from Yixing People's Hospital were collected. 7 training set models were established to identify 4 test sets. Respective sensitivity, specificity, Youden index, accuracy, and corresponding thresholds were tested, and ROC curves were plotted. RESULTS: 1. The EGC-YOLOV4 system completes all tests at an average reading speed of about 15 ms/sheet; 2. The AUC values in training set 1 model were 0.8325, 0.8307, 0.8706, and 0.8279, in training set 2 model were 0.8674, 0.8635, 0.9056, and 0.9249, in training set 3 model were 0.8544, 0.8881, 0.9072, and 0.9237, in training set 4 model were 0.8271, 0.9020, 0.9102, and 0.9316, in training set 5 model were 0.8249, 0.8484, 0.8796, and 0.8931, in training set 6 model were 0.8235, 0.8539, 0.9002, and 0.9051, in training set 7 model were 0.7581, 0.8082, 0.8803, and 0.8763. CONCLUSION: EGC-YOLOV4 can quickly and accurately identify the early gastric cancer lesions in gastroscopic images, and has good generalization.The proportion of positive and negative samples in the training set will affect the overall diagnostic performance of AI.In this study, the optimal ratio of positive samples to negative samples in the training set is 1:1~ 1:2.

Jinhua, L. I., et al. (2022). "Fuzheng Kang' ai

decoction inhibits cell proliferation, migration and invasion by modulating mir-21-5p/human phosphatase and tensin homology deleted on chromosome ten in lung cancer cells." J Tradit Chin Med **42**(3): 344-352.

OBJECTIVE: To elucidate the potential molecular mechanism by which Fuzheng Kang'ai decoction (, FZKA) inhibits proliferation, migration, and invasion of lung cancer cells. METHODS: Varying FZKA concentrations were used to manage lung cancer cells (A549 and PC9). We employed: cell counting kit-8 (CCK-8) and plate clone for-mation assays to examine the cell viability; flow cytometry (FCM) to analyze the cycle arrest; transwell and wound-healing assays to assess the cell invasion and migration, respectively. Further, a quantitative real-time polymerase chain reaction (qRT-PCR) assay was adopted to evaluate the miR-21-5p expression. For protein expression analysis, we employed the Western blot technique. Recombinant miR-21-5p overexpression adenovirus vector harboring GFP was constructed and transfected into A549 and PC9, after which we explored the effect of FZKA on miR-21-5p overexpression. RESULTS: Notably, treatment with FZKA inhibited viability, clone-formation ability, invasion, and migration of lung cancer cells. Mechanistically, FZKA markedly suppressed miR-21-5p expression but elevated the human phosphatase and tensin homology deleted on chromosome ten (PTEN) protein level in both A549 and PC9 cells. Over-expression of miR-21-5p lowered PTEN protein expression. Besides, overexpressed miR-21-5p levels with adenovirus antagonized FZKA-upregulated PTEN protein expression. CONCLUSION: The present study demonstrates how FZKA modulates cell biological behaviors, for instance, it impedes the proliferation by upregulating PTEN expression with miR-21-5p as the target. These findings unveil the potential novel molecular mechanisms from the microRNA aspect by which FZKA suppresses the growth of human lung cancer cells.

Kanan, M., et al. (2024). "AI-Driven Models for Diagnosing and Predicting Outcomes in Lung Cancer: A Systematic Review and Meta-Analysis." Cancers (Basel) **16**(3).

(1) Background: Lung cancer's high mortality due to late diagnosis highlights a need for early detection strategies. Artificial intelligence (AI) in healthcare, particularly for lung cancer, offers promise by analyzing medical data for early identification and personalized treatment. This systematic review evaluates AI's performance in early lung cancer detection, analyzing its techniques, strengths, limitations, and comparative edge over traditional methods. (2) Methods: This systematic review and meta-analysis followed the PRISMA guidelines rigorously, outlining a comprehensive protocol and employing tailored search strategies across diverse databases. Two reviewers independently screened studies based on predefined criteria, ensuring the selection of high-quality data relevant to AI's role in lung cancer detection. The extraction of key study details and performance metrics, followed by quality assessment, facilitated a robust analysis using R software (Version 4.3.0). The process, depicted via a PRISMA flow diagram, allowed for the meticulous evaluation and synthesis of the findings in this review. (3) Results: From 1024 records, 39 studies met the inclusion criteria, showcasing diverse AI model applications for lung cancer detection, emphasizing varying strengths among the studies. These findings underscore AI's potential for early lung cancer diagnosis but highlight the need for standardization amidst study variations. The results demonstrate promising pooled sensitivity and specificity of 0.87, signifying AI's accuracy in identifying true positives and negatives, despite the observed heterogeneity attributed to diverse study parameters. (4) Conclusions: AI demonstrates promise in early lung cancer detection, showing high accuracy levels in this systematic review. However, study variations underline the need for standardized protocols to fully leverage AI's potential in revolutionizing early diagnosis, ultimately benefiting patients and healthcare professionals. As the field progresses, validated AI models from large-scale perspective studies will greatly benefit clinical practice and patient care in the future.

Kapoor, D. U., et al. (2024). "AI illuminates paths in oral cancer: transformative insights, diagnostic precision, and personalized strategies." EXCLI J **23**: 1091-1116.

Oral cancer retains one of the lowest survival rates worldwide, despite recent therapeutic advancements signifying a tenacious challenge in healthcare. Artificial intelligence exhibits noteworthy potential in escalating diagnostic and treatment procedures, offering promising advancements in healthcare. This review entails the traditional imaging techniques for the oral cancer treatment. The role of artificial intelligence in prognosis of oral cancer including predictive modeling, identification of prognostic factors and risk stratification also discussed significantly in this review. The review also encompasses the utilization of artificial intelligence such as automated image analysis, computer-aided detection and diagnosis integration of machine learning algorithms for oral cancer diagnosis and treatment. The customizing treatment approaches

for oral cancer through artificial intelligence based personalized medicine is also part of this review. See also the graphical abstract(Fig. 1).

Kapuria, S., et al. (2024). "A Novel Dual Layer Cascade Reliability Framework for an Informed and Intuitive Clinician-AI Interaction In Diagnosis of Colorectal Cancer Polyps." IEEE J Biomed Health Inform **PP**.

We present a novel Cascade Reliability Framework (CRF) that integrates two independent cascade layers of reliability (i.e., variational temperature scaling and conformal prediction) with a pre-trained Machine Learning (ML) model in order to provide clinicians with a more reliable and tunable tool for early-stage diagnosis of Colorectal Cancer (CRC) polyps. The conformal prediction layer generates predictive sets that are guaranteed to contain the true polyp type with an adjustable error rate tuned by clinicians, while the confidence calibration generates meaningful confidence estimates for each predicted label. These two layers provide additional information and an error-tuning-ability for clinicians to assist them in making informed and intuitive decisions considering the outputs of the pre-trained ML model. Utilizing a novel vision-based tactile sensor and unique 3D-printed CRC polyp phantoms, we evaluated the trustworthiness of the proposed architecture and particularly dual outputs of four different types of CRF models, integrated with two different pre-trained ML models (i.e., ResNet18 and Dilated Residual Network) to highlight the model-agnostic feature of the architecture. To thoroughly assess the performance of the proposed approach, we used reliability diagrams and metrics such as accuracy, coverage, and average set size, while also addressing inter-class performance. Results demonstrate that the calibrated CRF models are well capable of handling non-ideal inputs with noise and blur. Moreover, using the conformal prediction with a user-defined error rate and various experiments, we show how clinicians can intuitively interact with a pre-trained ML model to make informed decisions and minimize the risk of CRC polyps misdiagnoses.

Karimzadeh, M., et al. (2024). "Deep generative AI models analyzing circulating orphan non-coding RNAs enable detection of early-stage lung cancer." Nat Commun **15**(1): 10090.

Liquid biopsies have the potential to revolutionize cancer care through non-invasive early detection of tumors. Developing a robust liquid biopsy test requires collecting high-dimensional data from a large number of blood samples across heterogeneous groups of patients. We propose that the generative capability of variational auto-encoders enables learning a robust and generalizable signature of blood-based biomarkers. In this study, we analyze orphan non-coding RNAs (oncRNAs) from serum samples of 1050 individuals diagnosed with non-small cell lung cancer (NSCLC) at various stages, as well as sex-, age-, and BMI-matched controls. We demonstrate that our multi-task generative AI model, Orion, surpasses commonly used methods in both overall performance and generalizability to held-out datasets. Orion achieves an overall sensitivity of 94% (95% CI: 87%-98%) at 87% (95% CI: 81%-93%) specificity for cancer detection across all stages, outperforming the sensitivity of other methods on held-out validation datasets by more than ~ 30%.

Katalinic, M., et al. (2024). "Generation of a Realistic Synthetic Laryngeal Cancer Cohort for AI Applications." Cancers (Basel) **16**(3).

BACKGROUND: Obtaining large amounts of real patient data involves great efforts and expenses, and processing this data is fraught with data protection concerns. Consequently, data sharing might not always be possible, particularly when large, open science datasets are needed, as for AI development. For such purposes, the generation of realistic synthetic data may be the solution. Our project aimed to generate realistic cancer data with the use case of laryngeal cancer. METHODS: We used the open-source software Synthea and programmed an additional module for development, treatment and follow-up for laryngeal cancer by using external, real-world (RW) evidence from guidelines and cancer registries from Germany. To generate an incidence-based cohort view, we randomly drew laryngeal cancer cases from the simulated population and deceased persons, stratified by the real-world age and sex distributions at diagnosis. RESULTS: A module with age- and stage-specific treatment and prognosis for laryngeal cancer was successfully implemented. The synthesized population reflects RW prevalence well, extracting a cohort of 50,000 laryngeal cancer patients. Descriptive data on stage-specific and 5-year overall survival were in accordance with published data. CONCLUSIONS: We developed a large cohort of realistic synthetic laryngeal cancer cases with Synthea. Such data can be shared and published open source without data protection issues.

Kenig, N., et al. (2024). "Is My Doctor Human? Acceptance of AI among Patients with Breast Cancer." Plast Reconstr Surg Glob Open **12**(10): e6257.

Artificial intelligence (AI) is becoming increasingly important in society, and medicine can

benefit from its advantages. What scenario can we envision when AI becomes as powerful and accurate as human physicians? How will the traditional patient-doctor relationship be affected by AI? Will patients come to trust and accept AI-assisted healthcare as much as their human counterparts? Our research team has been working on applications of AI in plastic surgery for more than 4 years. Between 2020 and 2024, AI algorithms were developed by the authors and applied on patients for symmetry evaluation after breast cancer surgery. Patients were aware of being evaluated with images for AI model training and assessment. Feedback was reported, and a survey was carried out among patients who underwent evaluation by our team. Among patients with breast cancer who underwent surgical reconstruction, 65% of patients reported very high levels of comfort with AI, given that it was mediated by a human doctor. Patients stated that nondoctor-mediated AI in medicine would greatly reduce trust. The influence of AI on the patient-doctor relationship is an important aspect that will greatly affect medicine. In this preliminary work, patients showed high levels of trust and comfort with the use of AI in healthcare, despite stating that they knew little about AI. Patients insisted that the mediation of a human doctor is key for acceptance. Currently, little is known about the acceptance of AI in medical roles among patients.

Kesiku, C. Y. and B. Garcia-Zapirain (2024). "AI-Enhanced Lung Cancer Prediction: A Hybrid Model's Precision Triumph." IEEE J Biomed Health Inform **PP**.

Lung cancer is considered one of the most dangerous cancers, with a 5-year survival rate, ranking the disease among the top three deadliest cancers globally. Effectively combating lung cancer requires early detection for timely targeted interventions. However, ensuring early detection poses a major challenge, giving rise to innovative approaches. The emergence of artificial intelligence offers revolutionary solutions for predicting cancer. While marking a significant healthcare shift, the imperative to enhance artificial intelligence models remains a focus, particularly in precision medicine. This study introduces a hybrid deep learning model, incorporating Convolutional Neural Networks (CNN) and Bidirectional Long Short-Term Memory Networks (BiLSTM), designed for lung cancer detection from patients' medical notes. Comparative analysis with the MIMIC IV dataset reveals the model's superiority, achieving an MCC of 96.2% with an Accuracy of 98.1%, and outperforming LSTM and BioBERT with an MCC of 93.5 %, an accuracy of 97.0% and MCC of 95.5 with an accuracy of 98.0% respectively. Another comprehensive comparison was conducted with state-of-the-art results using the Yelp Review Polarity dataset. Remarkably, our model significantly outperforms the compared models, showcasing its superior performance and potential impact in the field. This research signifies a significant stride toward precise and early lung cancer detection, emphasizing the ongoing necessity for Artificial Intelligence model refinement in precision medicine.

Kilintzis, V., et al. (2024). "Public data homogenization for AI model development in breast cancer." Eur Radiol Exp **8**(1): 42.

BACKGROUND: Developing trustworthy artificial intelligence (AI) models for clinical applications requires access to clinical and imaging data cohorts. Reusing of publicly available datasets has the potential to fill this gap. Specifically in the domain of breast cancer, a large archive of publicly accessible medical images along with the corresponding clinical data is available at The Cancer Imaging Archive (TCIA). However, existing datasets cannot be directly used as they are heterogeneous and cannot be effectively filtered for selecting specific image types required to develop AI models. This work focuses on the development of a homogenized dataset in the domain of breast cancer including clinical and imaging data. METHODS: Five datasets were acquired from the TCIA and were harmonized. For the clinical data harmonization, a common data model was developed and a repeatable, documented "extract-transform-load" process was defined and executed for their homogenization. Further, Digital Imaging and COmmunications in Medicine (DICOM) information was extracted from magnetic resonance imaging (MRI) data and made accessible and searchable. RESULTS: The resulting harmonized dataset includes information about 2,035 subjects with breast cancer. Further, a platform named RV-Cherry-Picker enables search over both the clinical and diagnostic imaging datasets, providing unified access, facilitating the downloading of all study imaging that correspond to specific series' characteristics (e.g., dynamic contrast-enhanced series), and reducing the burden of acquiring the appropriate set of images for the respective AI model scenario. CONCLUSIONS: RV-Cherry-Picker provides access to the largest, publicly available, homogenized, imaging/clinical dataset for breast cancer to develop AI models on top. RELEVANCE STATEMENT: We present a solution for creating merged public datasets supporting AI model development, using as an example the breast cancer domain and magnetic resonance imaging images. KEY POINTS: * The proposed platform allows

unified access to the largest, homogenized public imaging dataset for breast cancer. * A methodology for the semantically enriched homogenization of public clinical data is presented. * The platform is able to make a detailed selection of breast MRI data for the development of AI models.

Kim, J., et al. (2024). "Evaluation of the Diagnostic Efficacy of the AI-Based Software INF-M01 in Detecting Suspicious Areas of Bladder Cancer Using Cystoscopy Images." J Clin Med **13**(23).

Background/Objectives: We aimed to evaluate the accuracy of the artificial intelligence (AI)-based software INF-M01 in diagnosing suspected bladder tumors using cystoscopy images. Additionally, we aimed to assess the ability of INF-M01 to distinguish and mark suspected bladder cancer using whole cystoscopy images. Methods: A randomized retrospective clinical trial was conducted using a total of 5670 cystoscopic images provided by three institutions, comprising 1890 images each (486 bladder cancer images and 1404 normal images). The images were randomly distributed into five sets (A-E), each containing 1890 photographs. INF-M01 analyzed the images in set A to evaluate sensitivity, specificity, and accuracy. Sets B to E were analyzed by INF-M01 and four urologists, who marked the suspected bladder tumors. The Dice coefficient was used to compare the ability to differentiate bladder tumors. Results: For set A, the sensitivity, specificity, accuracy, and 95% confidence intervals were 0.973 (0.955-0.984), 0.921 (0.906-0.934), and 0.934 (0.922-0.945), respectively. The mean value of the Dice coefficient of AI was 0.889 (0.873-0.927), while that of clinicians was 0.941 (0.903-0.963), indicating that AI showed a reliable ability to distinguish bladder tumors from normal bladder tissue. AI demonstrated a sensitivity similar to that of urologists (0.971 (0.971-0.983) vs. 0.921 (0.777-0.995)), but a lower specificity (0.920 (0.882-0.962) vs. 0.991 (0.984-0.996)) compared to the urologists. Conclusions: INF-M01 demonstrated satisfactory accuracy in the diagnosis of bladder tumors. Additionally, it displayed an ability to distinguish and mark tumor regions from normal bladder tissue, similar to that of urologists. These results suggest that AI has promising diagnostic capabilities and clinical utility for urologists.

Kim, J. G., et al. (2024). "Impact of a Categorical AI System for Digital Breast Tomosynthesis on Breast Cancer Interpretation by Both General Radiologists and Breast Imaging Specialists." Radiol Artif Intell **6**(2): e230137.

Purpose To evaluate performance improvements of general radiologists and breast imaging specialists when interpreting a set of diverse digital breast tomosynthesis (DBT) examinations with the aid of a custom-built categorical artificial intelligence (AI) system. Materials and Methods A fully balanced multireader, multicase reader study was conducted to compare the performance of 18 radiologists (nine general radiologists and nine breast imaging specialists) reading 240 retrospectively collected screening DBT mammograms (mean patient age, 59.8 years +/- 11.3 [SD]; 100% women), acquired between August 2016 and March 2019, with and without the aid of a custom-built categorical AI system. The area under the receiver operating characteristic curve (AUC), sensitivity, and specificity across general radiologists and breast imaging specialists reading with versus without AI were assessed. Reader performance was also analyzed as a function of breast cancer characteristics and patient subgroups. Results Every radiologist demonstrated improved interpretation performance when reading with versus without AI, with an average AUC of 0.93 versus 0.87, demonstrating a difference in AUC of 0.06 (95% CI: 0.04, 0.08; P < .001). Improvement in AUC was observed for both general radiologists (difference of 0.08; P < .001) and breast imaging specialists (difference of 0.04; P < .001) and across all cancer characteristics (lesion type, lesion size, and pathology) and patient subgroups (race and ethnicity, age, and breast density) examined. Conclusion A categorical AI system helped improve overall radiologist interpretation performance of DBT screening mammograms for both general radiologists and breast imaging specialists and across various patient subgroups and breast cancer characteristics. Keywords: Computer-aided Diagnosis, Screening Mammography, Digital Breast Tomosynthesis, Breast Cancer, Screening, Convolutional Neural Network (CNN), Artificial Intelligence Supplemental material is available for this article. (c) RSNA, 2024.

Kim, K., et al. (2017). "C1QBP is upregulated in colon cancer and binds to apolipoprotein A-I." Exp Ther Med **13**(5): 2493-2500.

The present study aimed to investigate the expression of complement component 1, q subcomponent-binding protein (C1QBP) in colon cancer cells, and identify proteins that interact with C1QBP. Total proteins were extracted from both the tumor and normal tissues of 22 patients with colon cancer and analyzed using liquid chromatography-mass spectrometry (LC-MS) to identify proteins that were differentially-expressed in tumor tissues. C1QBP overexpression was induced in 293T cells using a pFLAG-CMV2 expression vector. Overexpressed FLAG-tagged C1QBP protein was

then immunoprecipitated using anti-FLAG antibodies and C1QBP-interacting proteins were screened using LC-MS analysis of the immunoprecipitates. The C1QBP-interacting proteins were confirmed using reverse-immunoprecipitation and the differential expression of C1QBP in tissues and cell lines was confirmed using western blot analysis. LC-MS analysis revealed that C1QBP exhibited a typical tumor expression pattern. Two immune-reactive signals (33 and 14 kDa) were detected in normal and tumor tissues from 19 patients. Furthermore, 14 kDa C1QBP protein was upregulated in the tumors of 15 patients. In total, 39 proteins were identified as candidate C1QBP-interacting proteins, and an interaction between C1QBP and apolipoprotein A-I was confirmed. The present study indicates that C1QBP is involved in colon cancer carcinogenesis, and that the mechanisms underlying the established anti-tumor properties of apolipoprotein A-I may include interacting with and inhibiting the activity of C1QBP.

Kiraly, A. P., et al. (2024). "Assistive AI in Lung Cancer Screening: A Retrospective Multinational Study in the United States and Japan." Radiol Artif Intell **6**(3): e230079.

Purpose To evaluate the impact of an artificial intelligence (AI) assistant for lung cancer screening on multinational clinical workflows. Materials and Methods An AI assistant for lung cancer screening was evaluated on two retrospective randomized multireader multicase studies where 627 (141 cancer-positive cases) low-dose chest CT cases were each read twice (with and without AI assistance) by experienced thoracic radiologists (six U.S.-based or six Japan-based radiologists), resulting in a total of 7524 interpretations. Positive cases were defined as those within 2 years before a pathology-confirmed lung cancer diagnosis. Negative cases were defined as those without any subsequent cancer diagnosis for at least 2 years and were enriched for a spectrum of diverse nodules. The studies measured the readers' level of suspicion (on a 0-100 scale), country-specific screening system scoring categories, and management recommendations. Evaluation metrics included the area under the receiver operating characteristic curve (AUC) for level of suspicion and sensitivity and specificity of recall recommendations. Results With AI assistance, the radiologists' AUC increased by 0.023 (0.70 to 0.72; P = .02) for the U.S. study and by 0.023 (0.93 to 0.96; P = .18) for the Japan study. Scoring system specificity for actionable findings increased 5.5% (57% to 63%; P < .001) for the U.S. study and 6.7% (23% to 30%; P < .001) for the Japan study. There was no evidence of a difference in corresponding sensitivity between unassisted and AI-assisted reads for the U.S. (67.3% to 67.5%; P = .88) and Japan (98% to 100%; P > .99) studies. Corresponding stand-alone AI AUC system performance was 0.75 (95% CI: 0.70, 0.81) and 0.88 (95% CI: 0.78, 0.97) for the U.S.- and Japan-based datasets, respectively. Conclusion The concurrent AI interface improved lung cancer screening specificity in both U.S.- and Japan-based reader studies, meriting further study in additional international screening environments. Keywords: Assistive Artificial Intelligence, Lung Cancer Screening, CT Supplemental material is available for this article. Published under a CC BY 4.0 license.

Kluckert, J., et al. (2024). "AI-based automated evaluation of image quality and protocol tailoring in patients undergoing MRI for suspected prostate cancer." Eur J Radiol **177**: 111581.

PURPOSE: To develop and validate an artificial intelligence (AI) application in a clinical setting to decide whether dynamic contrast-enhanced (DCE) sequences are necessary in multiparametric prostate MRI. METHODS: This study was approved by the institutional review board and requirement for study-specific informed consent was waived. A mobile app was developed to integrate AI-based image quality analysis into clinical workflow. An expert radiologist provided reference decisions. Diagnostic performance parameters (sensitivity and specificity) were calculated and inter-reader agreement was evaluated. RESULTS: Fully automated evaluation was possible in 87% of cases, with the application reaching a sensitivity of 80% and a specificity of 100% in selecting patients for multiparametric MRI. In 2% of patients, the application falsely decided on omitting DCE. With a technician reaching a sensitivity of 29% and specificity of 98%, and resident radiologists reaching sensitivity of 29% and specificity of 93%, the use of the application allowed a significant increase in sensitivity. CONCLUSION: The presented AI application accurately decides on a patient-specific MRI protocol based on image quality analysis, potentially allowing omission of DCE in the diagnostic workup of patients with suspected prostate cancer. This could streamline workflow and optimize time utilization of healthcare professionals.

Kneepkens, E., et al. (2022). "Clinical evaluation of two AI models for automated breast cancer plan generation." Radiat Oncol **17**(1): 25.

BACKGROUND: Artificial intelligence (AI) shows great potential to streamline the treatment planning process. However, its clinical adoption is slow due to the limited number of clinical evaluation studies and because often, the translation of the

predicted dose distribution to a deliverable plan is lacking. This study evaluates two different, deliverable AI plans in terms of their clinical acceptability based on quantitative parameters and qualitative evaluation by four radiation oncologists. METHODS: For 20 left-sided node-negative breast cancer patients, treated with a prescribed dose of 40.05 Gy, using tangential beam intensity modulated radiotherapy, two model-based treatment plans were evaluated against the corresponding manual plan. The two models used were an in-house developed U-net model and a vendor-developed contextual atlas regression forest model (cARF). Radiation oncologists evaluated the clinical acceptability of each blinded plan and ranked plans according to preference. Furthermore, a comparison with the manual plan was made based on dose volume histogram parameters, clinical evaluation criteria and preparation time. RESULTS: The U-net model resulted in a higher average and maximum dose to the PTV (median difference 0.37 Gy and 0.47 Gy respectively) and a slightly higher mean heart dose (MHD) (0.01 Gy). The cARF model led to higher average and maximum doses to the PTV (0.30 and 0.39 Gy respectively) and a slightly higher MHD (0.02 Gy) and mean lung dose (MLD, 0.04 Gy). The maximum MHD/MLD difference was </= 0.5 Gy for both AI plans. Regardless of these dose differences, 90-95% of the AI plans were considered clinically acceptable versus 90% of the manual plans. Preferences varied between the radiation oncologists. Plan preparation time was comparable between the U-net model and the manual plan (287 s vs 253 s) while the cARF model took longer (471 s). When only considering user interaction, plan generation time was 121 s for the cARF model and 137 s for the U-net model. CONCLUSIONS: Two AI models were used to generate deliverable plans for breast cancer patients, in a time-efficient manner, requiring minimal user interaction. Although the AI plans resulted in slightly higher doses overall, radiation oncologists considered 90-95% of the AI plans clinically acceptable.

Koch, H. W., et al. (2024). "How do AI markings on screening mammograms correspond to cancer location? An informed review of 270 breast cancer cases in BreastScreen Norway." Eur Radiol **34**(9): 6158-6167.

OBJECTIVES: To compare the location of AI markings on screening mammograms with cancer location on diagnostic mammograms, and to classify interval cancers with high AI score as false negative, minimal sign, or true negative. METHODS: In a retrospective study from 2022, we compared the performance of an AI system with independent double reading according to cancer detection. We found 93% (880/949) of the screen-detected cancers, and 40% (122/305) of the interval cancers to have the highest AI risk score (AI score of 10). In this study, four breast radiologists reviewed mammograms from 126 randomly selected screen-detected cancers and all 120 interval cancers with an AI score of 10. The location of the AI marking was stated as correct/not correct in craniocaudal and mediolateral oblique view. Interval cancers with an AI score of 10 were classified as false negative, minimal sign significant/non-specific, or true negative. RESULTS: All screen-detected cancers and 78% (93/120) of the interval cancers with an AI score of 10 were correctly located by the AI system. The AI markings matched in both views for 79% (100/126) of the screen-detected cancers and 22% (26/120) of the interval cancers. For interval cancers with an AI score of 10, 11% (13/120) were correctly located and classified as false negative, 10% (12/120) as minimal sign significant, 26% (31/120) as minimal sign non-specific, and 31% (37/120) as true negative. CONCLUSION: AI markings corresponded to cancer location for all screen-detected cancers and 78% of the interval cancers with high AI score, indicating a potential for reducing the number of interval cancers. However, it is uncertain whether interval cancers with subtle findings in only one view are actionable for recall in a true screening setting. CLINICAL RELEVANCE STATEMENT: In this study, AI markings corresponded to the location of the cancer in a high percentage of cases, indicating that the AI system accurately identifies the cancer location in mammograms with a high AI score. KEY POINTS: * All screen-detected and 78% of the interval cancers with high AI risk score (AI score of 10) had AI markings in one or two views corresponding to the location of the cancer on diagnostic images. * Among all 120 interval cancers with an AI score of 10, 21% (25/120) were classified as a false negative or minimal sign significant and had AI markings matching the cancer location, suggesting they may be visible on prior screening. * Most of the correctly located interval cancers matched only in one view, and the majority were classified as either true negative or minimal sign non-specific, indicating low potential for being detected earlier in a real screening setting.

Kohlberger, T., et al. (2019). "Whole-Slide Image Focus Quality: Automatic Assessment and Impact on AI Cancer Detection." J Pathol Inform **10**: 39.

BACKGROUND: Digital pathology enables remote access or consults and powerful image analysis algorithms. However, the slide digitization process can create artifacts such as out-of-focus

(OOF). OOF is often only detected on careful review, potentially causing rescanning, and workflow delays. Although scan time operator screening for whole-slide OOF is feasible, manual screening for OOF affecting only parts of a slide is impractical. METHODS: We developed a convolutional neural network (ConvFocus) to exhaustively localize and quantify the severity of OOF regions on digitized slides. ConvFocus was developed using our refined semi-synthetic OOF data generation process and evaluated using seven slides spanning three different tissue and three different stain types, each of which were digitized using two different whole-slide scanner models ConvFocus's predictions were compared with pathologist-annotated focus quality grades across 514 distinct regions representing 37,700 35 mum x 35 mum image patches, and 21 digitized "z-stack" WSIs that contain known OOF patterns. RESULTS: When compared to pathologist-graded focus quality, ConvFocus achieved Spearman rank coefficients of 0.81 and 0.94 on two scanners and reproduced the expected OOF patterns from z-stack scanning. We also evaluated the impact of OOF on the accuracy of a state-of-the-art metastatic breast cancer detector and saw a consistent decrease in performance with increasing OOF. CONCLUSIONS: Comprehensive whole-slide OOF categorization could enable rescans before pathologist review, potentially reducing the impact of digitization focus issues on the clinical workflow. We show that the algorithm trained on our semi-synthetic OOF data generalizes well to real OOF regions across tissue types, stains, and scanners. Finally, quantitative OOF maps can flag regions that might otherwise be misclassified by image analysis algorithms, preventing OOF-induced errors.

Kokuer, M., et al. (2004). "Hereditary non-polyposis colorectal cancer risk assessment based on AI analysis of pedigree data." Conf Proc IEEE Eng Med Biol Soc **2004**: 3229-3232.

Colorectal cancer (CRC) is one of the most common fatal cancers in developed countries and represents a significant public-health issue. About 3-5% of patients with CRC have hereditary non-polyposis colorectal cancer (HNPCC). Cancer morbidity and mortality can be reduced if early and intensive screening is pursued. But, despite advances in screening, population-wide genetic screening for HNPCC is not currently considered feasible due to its complexity and expense. If we can identify/assess the risk of a family having HNPCC, then only a fraction of the population will undergo intensive screening. This identification is currently performed by a genetic counsellor/physician who makes the decision based on some pre-defined criteria. The risk estimation by employing some mathematical methods, such as logistic regression, has also been reported. Our aim is to investigate the use of artificial intelligence techniques for genetic risk assessment. In this paper we summarize current knowledge on HNPCC and introduce the pedigree database used. Then we describe the system developed for HNPCC-risk assessment, which is based on analysing the pedigree data using self-organizing maps. The experimental evaluation shows good classification results.

Kolla, L., et al. (2021). "The case for AI-driven cancer clinical trials - The efficacy arm in silico." Biochim Biophys Acta Rev Cancer **1876**(1): 188572.

Pharmaceutical agents in oncology currently have high attrition rates from early to late phase clinical trials. Recent advances in computational methods, notably causal artificial intelligence, and availability of rich clinico-genomic databases have made it possible to simulate the efficacy of cancer drug protocols in diverse patient populations, which could inform and improve clinical trial design. Here, we review the current and potential use of in silico trials and causal AI to increase the efficacy and safety of traditional clinical trials. We conclude that in silico trials using causal AI approaches can simulate control and efficacy arms, inform patient recruitment and regimen titrations, and better enable subgroup analyses critical for precision medicine.

Kolokythas, A. (2022). "Can Artificial Intelligence (AI) assist in the diagnosis of oral mucosal lesions and/or oral cancer?" Oral Surg Oral Med Oral Pathol Oral Radiol **134**(4): 413-414.

Kondylakis, H., et al. (2022). "Data Ingestion for AI in Prostate Cancer." Stud Health Technol Inform **294**: 244-248.

Prostate cancer (PCa) is one of the most prevalent cancers in the male population. Current clinical practices lead to overdiagnosis and overtreatment necessitating more effective tools for improving diagnosis, thus the quality of life of patients. Recent advances in infrastructure, computing power and artificial intelligence enable the collection of tremendous amounts of clinical and imaging data that could assist towards this end. ProCAncer-I project aims to develop an AI platform integrating imaging data and models and hosting the largest collection of PCa (mp)MRI, anonymized image data worldwide. In this paper, we present an overview of the overall architecture focusing on the data ingestion part of the platform. We describe the workflow followed for uploading the data and the main repositories for storing imaging data, clinical

data and their corresponding metadata.

Kosvyra, A., et al. (2021). "Towards Data Integration for AI in Cancer Research()." Annu Int Conf IEEE Eng Med Biol Soc **2021**: 2054-2057.

Cancer research is increasing relying on data-driven methods and Artificial Intelligence (AI), to increase accuracy and efficiency in decision making. Such methods can solve a variety of clinically relevant problems in cancer diagnosis and treatment, provided that an adequate data availability is ensured. The generation of multicentric data repositories poses a series of integration and harmonization challenges. This work discusses the strategy, solutions and further issues identified along this procedure within the EU project INCISIVE that aims to generate an interoperable pan-European federated repository of medical images and an AI-based toolbox for medical imaging in cancer diagnosis and treatment.Clinical Relevance-Supporting the integration of medical imaging data and related clinical data into large interoperable repositories will enable the development, and validation, and wider adoption of AI-based methods in cancer diagnosis, prediction, treatment and follow-up.

Krakowski, I., et al. (2024). "Human-AI interaction in skin cancer diagnosis: a systematic review and meta-analysis." NPJ Digit Med **7**(1): 78.

The development of diagnostic tools for skin cancer based on artificial intelligence (AI) is increasing rapidly and will likely soon be widely implemented in clinical use. Even though the performance of these algorithms is promising in theory, there is limited evidence on the impact of AI assistance on human diagnostic decisions. Therefore, the aim of this systematic review and meta-analysis was to study the effect of AI assistance on the accuracy of skin cancer diagnosis. We searched PubMed, Embase, IEE Xplore, Scopus and conference proceedings for articles from 1/1/2017 to 11/8/2022. We included studies comparing the performance of clinicians diagnosing at least one skin cancer with and without deep learning-based AI assistance. Summary estimates of sensitivity and specificity of diagnostic accuracy with versus without AI assistance were computed using a bivariate random effects model. We identified 2983 studies, of which ten were eligible for meta-analysis. For clinicians without AI assistance, pooled sensitivity was 74.8% (95% CI 68.6-80.1) and specificity was 81.5% (95% CI 73.9-87.3). For AI-assisted clinicians, the overall sensitivity was 81.1% (95% CI 74.4-86.5) and specificity was 86.1% (95% CI 79.2-90.9). AI benefitted medical professionals of all experience levels in subgroup analyses, with the largest improvement among non-dermatologists. No publication bias was detected, and sensitivity analysis revealed that the findings were robust. AI in the hands of clinicians has the potential to improve diagnostic accuracy in skin cancer diagnosis. Given that most studies were conducted in experimental settings, we encourage future studies to further investigate these potential benefits in real-life settings.

Kranke, T., et al. (2023). "New AI-algorithms on smartphones to detect skin cancer in a clinical setting-A validation study." PLoS One **18**(2): e0280670.

BACKGROUND AND OBJECTIVES: The incidence of skin cancer is rising worldwide and there is medical need to optimize its early detection. This study was conducted to determine the diagnostic and risk-assessment accuracy of two new diagnosis-based neural networks (analyze and detect), which comply with the CE-criteria, in evaluating the malignant potential of various skin lesions on a smartphone. Of note, the intention of our study was to evaluate the performance of these medical products in a clinical setting for the first time. METHODS: This was a prospective, single-center clinical study at one tertiary referral center in Graz, Austria. Patients, who were either scheduled for preventive skin examination or removal of at least one skin lesion were eligible for participation. Patients were assessed by at least two dermatologists and by the integrated algorithms on different mobile phones. The lesions to be recorded were randomly selected by the dermatologists. The diagnosis of the algorithm was stated as correct if it matched the diagnosis of the two dermatologists or the histology (if available). The histology was the reference standard, however, if both clinicians considered a lesion as being benign no histology was performed and the dermatologists were stated as reference standard. RESULTS: A total of 238 patients with 1171 lesions (86 female; 36.13%) with an average age of 66.19 (SD = 17.05) was included. Sensitivity and specificity of the detect algorithm were 96.4% (CI 93.94-98.85) and 94.85% (CI 92.46-97.23); for the analyze algorithm a sensitivity of 95.35% (CI 93.45-97.25) and a specificity of 90.32% (CI 88.1-92.54) were achieved. DISCUSSION: The studied neural networks succeeded analyzing the risk of skin lesions with a high diagnostic accuracy showing that they are sufficient tools in calculating the probability of a skin lesion being malignant. In conjunction with the wide spread use of smartphones this new AI approach opens the opportunity for a higher early detection rate of skin cancer with consecutive lower epidemiological burden of metastatic cancer and

reducing health care costs. This neural network moreover facilitates the empowerment of patients, especially in regions with a low density of medical doctors. REGISTRATION: Approved and registered at the ethics committee of the Medical University of Graz, Austria (Approval number: 30-199 ex 17/18).

Krishnaswamy, D., et al. (2024). "Enrichment of lung cancer computed tomography collections with AI-derived annotations." Sci Data **11**(1): 25.

Public imaging datasets are critical for the development and evaluation of automated tools in cancer imaging. Unfortunately, many do not include annotations or image-derived features, complicating downstream analysis. Artificial intelligence-based annotation tools have been shown to achieve acceptable performance and can be used to automatically annotate large datasets. As part of the effort to enrich public data available within NCI Imaging Data Commons (IDC), here we introduce AI-generated annotations for two collections containing computed tomography images of the chest, NSCLC-Radiomics, and a subset of the National Lung Screening Trial. Using publicly available AI algorithms, we derived volumetric annotations of thoracic organs-at-risk, their corresponding radiomics features, and slice-level annotations of anatomical landmarks and regions. The resulting annotations are publicly available within IDC, where the DICOM format is used to harmonize the data and achieve FAIR (Findable, Accessible, Interoperable, Reusable) data principles. The annotations are accompanied by cloud-enabled notebooks demonstrating their use. This study reinforces the need for large, publicly accessible curated datasets and demonstrates how AI can aid in cancer imaging.

Kuhn, T. N., et al. (2024). "AI-driven Patient-Selection For Preoperative Portal Vein Embolization For Patients With Colorectal Cancer Liver Metastases." J Vasc Interv Radiol.

PURPOSE: To develop a machine-learning algorithm to improve hepatic resection selection for metastatic colorectal cancer patients by predicting post-PVE outcomes. MATERIAL & METHODS: This multicenter retrospective study (2000-2020) included 200 consecutive patients with CRC liver-metastases planned for PVE before surgery. Radiomic features and lab values were collected. Patient-specific eigenvalues for each liver shape were calculated using a statistical shape model approach. After semi-automatic segmentation and review by a board-certified radiologist, the data was split 70/30% for training and testing. Three machine learning algorithms predicting the total liver volume (TLV) after PVE, sufficient FLR%, and the kinetic growth rate % (KGR%) were trained with performance assessed using accuracy, sensitivty, specifity, AUC or RMSE. Significance between the internal and external test sets was assessed by the student's t-test. One institution was kept separate as an external testing set. RESULTS: A total of 114 (76m; 56y +/-12) and 37 (19m; 50y +/-11) patients met the inclusion criteria for the internal and external validation. Prediction accuracy (SD) and AUC (SD) for sufficient FLR% or liver growth potential (KGR%> 0%) were high in the internal testing set 0.91 (+/-0.01), 85.81% (+/-1.01%) or 0.66 (+/-0.03), 87.44% (+/-0.10%)). Similar results occurred on the external testing set 0.88 (+/-0.00), 79.66% (+/-0.60%) or 0.69 (+/-0.01), 72.06% (+/-0.30%)). TLV prediction showed a discrepancy of 12.56% (95% CI: +/-4.20%, p=0.86) internally and 13.57% (95% CI: +/-3.76%, p=0.91) externally. CONCLUSION: These machine learning-based models can help predict the FLR%, KGR%, and TLV as metrics for successful PVE.

Kulkarni, A., et al. (2024). "A Curated Cell Life Imaging Dataset of Immune-enriched Pancreatic Cancer Organoids with Pre-trained AI Models." Sci Data **11**(1): 820.

Tumor organoids are three-dimensional in vitro models which can recapitulate the complex mutational landscape and tissue architecture observed in cancer patients, providing a realistic model for testing novel therapies, including immunotherapies. A significant challenge in organoid research in oncology lies in developing efficient and reliable methods for segmenting organoid images, quantifying organoid growth, regression and response to treatments, as well as predicting the behavior of organoid systems. Up to now, a curated dataset of organoids co-cultured with immune cells is not available. To address this gap, we present a new public dataset, comprising both phase-contrast images of murine and patient-derived tumor organoids of one of the deadliest cancer types, the Pancreatic Ductal Adenocarcinoma, co-cultured with immune cells, and state-of-the-art algorithms for object detection and segmentation. Our dataset, OrganoIDNetData, encompassing 180 images with 33906 organoids, can be a potential common benchmark for different organoids segmentation protocols, moving beyond the current practice of training and testing these algorithms on isolated datasets.

Kumar, A., et al. (2024). "Personalized cancer vaccine design using AI-powered technologies." Front Immunol **15**: 1357217.

Immunotherapy has ushered in a new era of

cancer treatment, yet cancer remains a leading cause of global mortality. Among various therapeutic strategies, cancer vaccines have shown promise by activating the immune system to specifically target cancer cells. While current cancer vaccines are primarily prophylactic, advancements in targeting tumor-associated antigens (TAAs) and neoantigens have paved the way for therapeutic vaccines. The integration of artificial intelligence (AI) into cancer vaccine development is revolutionizing the field by enhancing various aspect of design and delivery. This review explores how AI facilitates precise epitope design, optimizes mRNA and DNA vaccine instructions, and enables personalized vaccine strategies by predicting patient responses. By utilizing AI technologies, researchers can navigate complex biological datasets and uncover novel therapeutic targets, thereby improving the precision and efficacy of cancer vaccines. Despite the promise of AI-powered cancer vaccines, significant challenges remain, such as tumor heterogeneity and genetic variability, which can limit the effectiveness of neoantigen prediction. Moreover, ethical and regulatory concerns surrounding data privacy and algorithmic bias must be addressed to ensure responsible AI deployment. The future of cancer vaccine development lies in the seamless integration of AI to create personalized immunotherapies that offer targeted and effective cancer treatments. This review underscores the importance of interdisciplinary collaboration and innovation in overcoming these challenges and advancing cancer vaccine development.

Kwon, H., et al. (2024). "Enhancing Breast Cancer Detection through Advanced AI-Driven Ultrasound Technology: A Comprehensive Evaluation of Vis-BUS." Diagnostics (Basel) **14**(17).

This study aims to enhance breast cancer detection accuracy through an AI-driven ultrasound tool, Vis-BUS, developed by Barreleye Inc., Seoul, South Korea. Vis-BUS incorporates Lesion Detection AI (LD-AI) and Lesion Analysis AI (LA-AI), along with a Cancer Probability Score (CPS), to differentiate between benign and malignant breast lesions. A retrospective analysis was conducted on 258 breast ultrasound examinations to evaluate Vis-BUS's performance. The primary methods included the application of LD-AI and LA-AI to b-mode ultrasound images and the generation of CPS for each lesion. Diagnostic accuracy was assessed using metrics such as the Area Under the Receiver Operating Characteristic curve (AUROC) and the Area Under the Precision-Recall curve (AUPRC). The study found that Vis-BUS achieved high diagnostic accuracy, with an AUROC of 0.964 and an AUPRC of 0.967, indicating its effectiveness in distinguishing between benign and malignant lesions. Logistic regression analysis identified that 'Fatty' lesion density had an extremely high odds ratio (OR) of 27.7781, suggesting potential convergence issues. The 'Unknown' density category had an OR of 0.3185, indicating a lower likelihood of correct classification. Medium and large lesion sizes were associated with lower likelihoods of correct classification, with ORs of 0.7891 and 0.8014, respectively. The presence of microcalcifications showed an OR of 1.360. Among Breast Imaging-Reporting and Data System categories, category C5 had a significantly higher OR of 10.173, reflecting a higher likelihood of correct classification. Vis-BUS significantly improves diagnostic precision and supports clinical decision-making in breast cancer screening. However, further refinement is needed in areas like lesion density characterization and calcification detection to optimize its performance.

Kwong, J. C. C., et al. (2024). "Predicting non-muscle invasive bladder cancer outcomes using artificial intelligence: a systematic review using APPRAISE-AI." NPJ Digit Med **7**(1): 98.

Accurate prediction of recurrence and progression in non-muscle invasive bladder cancer (NMIBC) is essential to inform management and eligibility for clinical trials. Despite substantial interest in developing artificial intelligence (AI) applications in NMIBC, their clinical readiness remains unclear. This systematic review aimed to critically appraise AI studies predicting NMIBC outcomes, and to identify common methodological and reporting pitfalls. MEDLINE, EMBASE, Web of Science, and Scopus were searched from inception to February 5th, 2024 for AI studies predicting NMIBC recurrence or progression. APPRAISE-AI was used to assess methodological and reporting quality of these studies. Performance between AI and non-AI approaches included within these studies were compared. A total of 15 studies (five on recurrence, four on progression, and six on both) were included. All studies were retrospective, with a median follow-up of 71 months (IQR 32-93) and median cohort size of 125 (IQR 93-309). Most studies were low quality, with only one classified as high quality. While AI models generally outperformed non-AI approaches with respect to accuracy, c-index, sensitivity, and specificity, this margin of benefit varied with study quality (median absolute performance difference was 10 for low, 22 for moderate, and 4 for high quality studies). Common pitfalls included dataset limitations, heterogeneous outcome definitions, methodological flaws, suboptimal model evaluation, and reproducibility issues. Recommendations to

address these challenges are proposed. These findings emphasise the need for collaborative efforts between urological and AI communities paired with rigorous methodologies to develop higher quality models, enabling AI to reach its potential in enhancing NMIBC care.

Laios, A., et al. (2022). "Stratification of Length of Stay Prediction following Surgical Cytoreduction in Advanced High-Grade Serous Ovarian Cancer Patients Using Artificial Intelligence; the Leeds L-AI-OS Score." Curr Oncol **29**(12): 9088-9104.

(1) Background: Length of stay (LOS) has been suggested as a marker of the effectiveness of short-term care. Artificial Intelligence (AI) technologies could help monitor hospital stays. We developed an AI-based novel predictive LOS score for advanced-stage high-grade serous ovarian cancer (HGSOC) patients following cytoreductive surgery and refined factors significantly affecting LOS. (2) Methods: Machine learning and deep learning methods using artificial neural networks (ANN) were used together with conventional logistic regression to predict continuous and binary LOS outcomes for HGSOC patients. The models were evaluated in a post-hoc internal validation set and a Graphical User Interface (GUI) was developed to demonstrate the clinical feasibility of sophisticated LOS predictions. (3) Results: For binary LOS predictions at differential time points, the accuracy ranged between 70-98%. Feature selection identified surgical complexity, pre-surgery albumin, blood loss, operative time, bowel resection with stoma formation, and severe postoperative complications (CD3-5) as independent LOS predictors. For the GUI numerical LOS score, the ANN model was a good estimator for the standard deviation of the LOS distribution by +/- two days. (4) Conclusions: We demonstrated the development and application of both quantitative and qualitative AI models to predict LOS in advanced-stage EOC patients following their cytoreduction. Accurate identification of potentially modifiable factors delaying hospital discharge can further inform services performing root cause analysis of LOS.

Laios, A., et al. (2023). "The Future of AI in Ovarian Cancer Research: The Large Language Models Perspective." Cancer Control **30**: 10732748231197915.

Conversational large language model (LLM)-based chatbots utilize neural networks to process natural language. By generating highly sophisticated outputs from contextual input text, they revolutionize the access to further learning, leading to the development of new skills and personalized interactions. Although they are not developed to provide healthcare, their potential to address biomedical issues is rather unexplored. Healthcare digitalization and documentation of electronic health records is now developing into a standard practice. Developing tools to facilitate clinical review of unstructured data such as LLMs can derive clinical meaningful insights for ovarian cancer, a heterogeneous but devastating disease. Compared to standard approaches, they can host capacity to condense results and optimize analysis time. To help accelerate research in biomedical language processing and improve the validity of scientific writing, task-specific and domain-specific language models may be required. In turn, we propose a bespoke, proprietary ovarian cancer-specific natural language using solely in-domain text, whereas transfer learning drifts away from the pretrained language models to fine-tune task-specific models for all possible downstream applications. This venture will be fueled by the abundance of unstructured text information in the electronic health records resulting in ovarian cancer research ultimately reaching its linguistic home.

Lancaster, H. L., et al. (2022). "Outstanding negative prediction performance of solid pulmonary nodule volume AI for ultra-LDCT baseline lung cancer screening risk stratification." Lung Cancer **165**: 133-140.

OBJECTIVE: To evaluate performance of AI as a standalone reader in ultra-low-dose CT lung cancer baseline screening, and compare it to that of experienced radiologists. METHODS: 283 participants who underwent a baseline ultra-LDCT scan in Moscow Lung Cancer Screening, between February 2017-2018, and had at least one solid lung nodule, were included. Volumetric nodule measurements were performed by five experienced blinded radiologists, and independently assessed using an AI lung cancer screening prototype (AVIEW LCS, v1.0.34, Coreline Soft, Co. ltd, Seoul, Korea) to automatically detect, measure, and classify solid nodules. Discrepancies were stratified into two groups: positive-misclassification (PM); nodule classified by the reader as a NELSON-plus /EUPS-indeterminate/positive nodule, which at the reference consensus read was < 100 mm(3), and negative-misclassification (NM); nodule classified as a NELSON-plus /EUPS-negative nodule, which at consensus read was >/= 100 mm(3). RESULTS: 1149 nodules with a solid-component were detected, of which 878 were classified as solid nodules. For the largest solid nodule per participant (n = 283); 61 [21.6 %; 53 PM, 8 NM] discrepancies were reported for AI as a standalone reader, compared to 43 [15.1 %; 22 PM, 21 NM], 36 [12.7 %; 25 PM, 11

NM], 29 [10.2 %; 25 PM, 4 NM], 28 [9.9 %; 6 PM, 22 NM], and 50 [17.7 %; 15 PM, 35 NM] discrepancies for readers 1, 2, 3, 4, and 5 respectively. CONCLUSION: Our results suggest that through the use of AI as an impartial reader in baseline lung cancer screening, negative-misclassification results could exceed that of four out of five experienced radiologists, and radiologists' workload could be drastically diminished by up to 86.7%.

Larsen, M., et al. (2023). "AI Risk Score on Screening Mammograms Preceding Breast Cancer Diagnosis." Radiology **309**(1): e230989.

Background Few studies have evaluated the role of artificial intelligence (AI) in prior screening mammography. Purpose To examine AI risk scores assigned to screening mammography in women who were later diagnosed with breast cancer. Materials and Methods Image data and screening information of examinations performed from January 2004 to December 2019 as part of BreastScreen Norway were used in this retrospective study. Prior screening examinations from women who were later diagnosed with cancer were assigned an AI risk score by a commercially available AI system (scores of 1-7, low risk of malignancy; 8-9, intermediate risk; and 10, high risk of malignancy). Mammographic features of the cancers based on the AI score were also assessed. The association between AI score and mammographic features was tested with a bivariate test. Results A total of 2787 prior screening examinations from 1602 women (mean age, 59 years +/- 5.1 [SD]) with screen-detected (n = 1016) or interval (n = 586) cancers showed an AI risk score of 10 for 389 (38.3%) and 231 (39.4%) cancers, respectively, on the mammograms in the screening round prior to diagnosis. Among the screen-detected cancers with AI scores available two screening rounds (4 years) before diagnosis, 23.0% (122 of 531) had a score of 10. Mammographic features were associated with AI score for invasive screen-detected cancers (P < .001). Density with calcifications was registered for 13.6% (43 of 317) of screen-detected cases with a score of 10 and 4.6% (15 of 322) for those with a score of 1-7. Conclusion More than one in three cases of screen-detected and interval cancers had the highest AI risk score at prior screening, suggesting that the use of AI in mammography screening may lead to earlier detection of breast cancers. (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Mehta in this issue.

Lauritzen, A. D., et al. (2024). "Early Indicators of the Impact of Using AI in Mammography Screening for Breast Cancer." Radiology **311**(3): e232479.

Background Retrospective studies have suggested that using artificial intelligence (AI) may decrease the workload of radiologists while preserving mammography screening performance. Purpose To compare workload and screening performance for two cohorts of women who underwent screening before and after AI system implementation. Materials and Methods This retrospective study included 50-69-year-old women who underwent biennial mammography screening in the Capital Region of Denmark. Before AI system implementation (October 1, 2020, to November 17, 2021), all screenings involved double reading. For screenings conducted after AI system implementation (November 18, 2021, to October 17, 2022), likely normal screenings (AI examination score </=5 before May 3, 2022, or </=7 on or after May 3, 2022) were single read by one of 19 senior full-time breast radiologists. The remaining screenings were read by two radiologists with AI-assisted decision support. Biopsy and surgical outcomes were retrieved between October 1, 2020, and April 15, 2023, ensuring at least 180 days of follow-up. Screening metrics were compared using the chi(2) test. Reading workload reduction was measured as saved screening reads. Results In total, 60 751 and 58 246 women were screened before and after AI system implementation, respectively (median age, 58 years [IQR, 54-64 years] for both cohorts), with a median screening interval before AI of 845 days (IQR, 820-878 days) and with AI of 993 days (IQR, 968-1013 days; P < .001). After AI system implementation, the recall rate decreased by 20.5% (3.09% before AI [1875 of 60 751] vs 2.46% with AI [1430 of 58 246]; P < .001), the cancer detection rate increased (0.70% [423 of 60 751] vs 0.82% [480 of 58 246]; P = .01), the false-positive rate decreased (2.39% [1452 of 60 751] vs 1.63% [950 of 58 246]; P < .001), the positive predictive value increased (22.6% [423 of 1875] vs 33.6% [480 of 1430]; P < .001), the rate of small cancers (</=1 cm) increased (36.6% [127 of 347] vs 44.9% [164 of 365]; P = .02), the rate of node-negative cancers was unchanged (76.7% [253 of 330] vs 77.8% [273 of 351]; P = .73), and the rate of invasive cancers decreased (84.9% [359 of 423] vs 79.6% [382 of 480]; P = .04). The reading workload was reduced by 33.5% (38 977 of 116 492 reads). Conclusion In a population-based mammography screening program, using AI reduced the overall workload of breast radiologists while improving screening performance. Published under a CC BY 4.0 license. Supplemental material is available for this article. See also the editorial by Lee and Friedewald in this issue.

Lauritzen, A. D., et al. (2023). "Assessing Breast

Cancer Risk by Combining AI for Lesion Detection and Mammographic Texture." Radiology **308**(2): e230227.

Background Recent mammography-based risk models can estimate short-term or long-term breast cancer risk, but whether risk assessment may improve by combining these models has not been evaluated. Purpose To determine whether breast cancer risk assessment improves when combining a diagnostic artificial intelligence (AI) system for lesion detection and a mammographic texture model. Materials and Methods This retrospective study included Danish women consecutively screened for breast cancer at mammography from November 2012 to December 2015 who had at least 5 years of follow-up data. Examinations were evaluated for short-term risk using a commercially available diagnostic AI system for lesion detection, which produced a score to indicate the probability of cancer. A mammographic texture model, trained on a separate data set, assessed textures associated with long-term cancer risk. Area under the receiver operating characteristic curve (AUC) analysis was used to evaluate both the individual and combined performance of the AI and texture models for the prediction of future cancers in women with a negative screening mammogram, including those with interval cancers diagnosed within 2 years of screening and long-term cancers diagnosed 2 years or more after screening. AUCs were compared using the DeLong test. Results The Danish screening cohort included 119 650 women (median age, 59 years [IQR, 53-64 years]), of whom 320 developed interval cancers and 1401 developed long-term cancers. The combination model achieved a higher AUC for interval and long-term cancers grouped together than either the diagnostic AI (AUC, 0.73 vs 0.70; P < .001) or the texture risk (AUC, 0.73 vs 0.66; P < .001) models. The 10% of women with the highest combined risk identified by the combination model accounted for 44.1% (141 of 320) of interval cancers and 33.7% (472 of 1401) of long-term cancers. Conclusion Combining a diagnostic AI system and mammographic texture model resulted in improved risk assessment for interval cancers and long-term cancers and enabled identification of women at high risk. (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Poynton and Slanetz in this issue.

Lazris, D., et al. (2024). "AI-Generated Content in Cancer Symptom Management: A Comparative Analysis Between ChatGPT and NCCN." J Pain Symptom Manage **68**(4): e303-e311.

BACKGROUND: Artificial intelligence-driven tools, like ChatGPT, are prevalent sources for online health information. Limited research has explored the congruity between AI-generated content and professional treatment guidelines. This study seeks to compare recommendations for cancer-related symptoms generated from ChatGPT with guidelines from the National Comprehensive Cancer Network (NCCN). INTERVENTION: We extracted treatment recommendations for nine symptoms from NCCN, separated into four full Supportive Care sections and five subsections of the Palliative Care webpage. We entered "How can I reduce my cancer-related [symptom]" into ChatGPT- 3.5 for these same symptoms and extracted its recommendations. A comparative content analysis focused on recommendations for medications, consultations, and non-pharmacological strategies. We compared word count and Flesch-Kincaid Grade Level (FKGL) readability for each NCCN and ChatGPT section. OUTCOMES: The mean percent agreement between NCCN and ChatGPT recommendations was 37.3% (range 16.7%-81.8%). NCCN offered more specific medication recommendations. ChatGPT did recommend medications in the constipation and diarrhea sections that were not recommended by NCCN. Significant differences in word count (P=0.03) and FKGL (P<0.01) were found for NCCN Supportive Care webpages, with ChatGPT having lower word count and reading level. In the NCCN Palliative Care webpage subsections, there was no significant difference in word count (P=0.076), but FKGL was significantly lower with ChatGPT (P<0.01). CONCLUSIONS/LESSONS LEARNED: While ChatGPT provides concise, accessible supportive care advice, discrepancies with guidelines raise concerns for patient-facing symptom management recommendations. Future research should consider how AI can be used in conjunction with evidence-based guidelines to support cancer patients' supportive care needs.

Leal, J. P., et al. (2022). "Automated lesion detection of breast cancer in [(18)F] FDG PET/CT using a novel AI-Based workflow." Front Oncol **12**: 1007874.

Applications based on artificial intelligence (AI) and deep learning (DL) are rapidly being developed to assist in the detection and characterization of lesions on medical images. In this study, we developed and examined an image-processing workflow that incorporates both traditional image processing with AI technology and utilizes a standards-based approach for disease identification and quantitation to segment and classify tissue within a whole-body [(18)F]FDG PET/CT study. METHODS: One hundred thirty baseline PET/CT studies from two multi-institutional preoperative clinical trials in early-stage breast cancer

were semi-automatically segmented using techniques based on PERCIST v1.0 thresholds and the individual segmentations classified as to tissue type by an experienced nuclear medicine physician. These classifications were then used to train a convolutional neural network (CNN) to automatically accomplish the same tasks. RESULTS: Our CNN-based workflow demonstrated Sensitivity at detecting disease (either primary lesion or lymphadenopathy) of 0.96 (95% CI [0.9, 1.0], 99% CI [0.87,1.00]), Specificity of 1.00 (95% CI [1.0,1.0], 99% CI [1.0,1.0]), DICE score of 0.94 (95% CI [0.89, 0.99], 99% CI [0.86, 1.00]), and Jaccard score of 0.89 (95% CI [0.80, 0.98], 99% CI [0.74, 1.00]). CONCLUSION: This pilot work has demonstrated the ability of AI-based workflow using DL-CNNs to specifically identify breast cancer tissue as determined by [(18)F]FDG avidity in a PET/CT study. The high sensitivity and specificity of the network supports the idea that AI can be trained to recognize specific tissue signatures, both normal and disease, in molecular imaging studies using radiopharmaceuticals. Future work will explore the applicability of these techniques to other disease types and alternative radiotracers, as well as explore the accuracy of fully automated and quantitative detection and response assessment.

Leatherdale, S. T. and J. Lee (2019). "Artificial intelligence (AI) and cancer prevention: the potential application of AI in cancer control programming needs to be explored in population laboratories such as COMPASS." Cancer Causes Control **30**(7): 671-675.

Understanding the risk factors that initiate cancer is essential for reducing the future cancer burden. Much of our current cancer control insight is from cohort studies and newer large-scale population laboratories designed to advance the science around precision oncology. Despite their promise for improving diagnosis and treatment outcomes, their current reductionist focus will likely have little impact shifting the cancer burden. However, it is possible that these big data assets can be adapted to have more impact on the future cancer burden through more focus on primary prevention efforts that incorporate artificial intelligence (AI) and machine learning (ML). ML automatically learns patterns and can devise complex models and algorithms that lend themselves to prediction in big data, revealing new unexpected relationships and pathways in a reliable and replicable fashion that otherwise would remain hidden given the complexities of big data. While AI has made big strides in several domains, the potential application in cancer prevention is lacking. As such, this commentary suggests that it may be time to consider the potential of AI within our existing cancer control population laboratories, and provides justification for why some small targeted investments to explore their impact on modelling existing real-time cancer prevention data may be a strategic cancer control opportunity.

Ledda, R. E., et al. (2024). "The added value of an AI-based body composition analysis in a lung cancer screening population: preliminary results." Nutr Metab Cardiovasc Dis.

BACKGROUND AND AIMS: Body composition has been linked with clinical and prognostic outcomes in patients with cancer and cardiovascular diseases. Body composition analysis in lung cancer screening (LCS) is very limited. This study aimed at assessing the association of subcutaneous fat volume (SFV) and subcutaneous fat density (SFD), measured on chest ultra-low dose computed tomography (ultra-LDCT) images by a fully automated artificial intelligence (AI)-based software, with clinical and anthropometric characteristics in a LCS population. METHODS AND RESULTS: Demographic, clinical, and dietary data were obtained from the written questionnaire completed by each participant at the first visit, when anthropometric measurements, blood sample collection and chest ultra-LDCT were performed. Images were analyzed for automated 3D segmentation of subcutaneous fat and muscle. The analysis included 938 volunteers (372 females); men with a smoking history of >/=40 pack-years had higher SFV ($p = 0.0009$), while former smokers had lower SFD ($p = 0.0019$). In female participants, SFV and SFD differed significantly according to age. SFV increased with rising BMI, waist circumference, waist-hip ratio, and CRP levels >/=2 mg/L ($p < 0.0001$), whereas SFD decreased with rising BMI, waist circumference, waist-hip ratio, and CRP levels >/=2 mg/L ($p < 0.001$) in both sexes. SFV was associated with glycemia and triglycerides levels ($p = 0.0067$ and $p=<0.0001$ in males, $p = 0.0074$ and $p < 0.0001$ in females, respectively), while SFD with triglycerides levels ($p < 0.0001$). CONCLUSION: We observed different associations of SFV and SFD with age and smoking history between men and women, whereas the association with anthropometric data, CRP, glycemia and triglycerides levels was similar in the two sexes.

Lee, J. W., et al. (2024). "Development of AI-generated medical responses using the ChatGPT for cancer patients." Comput Methods Programs Biomed **254**: 108302.

BACKGROUND AND OBJECTIVE: To

develop a healthcare chatbot service (AI-guided bot) that conducts real-time conversations using large language models to provide accurate health information to patients. METHODS: To provide accurate and specialized medical responses, we integrated several cancer practice guidelines. The size of the integrated meta-dataset was 1.17 million tokens. The integrated and classified metadata were extracted, transformed into text, segmented to specific character lengths, and vectorized using the embedding model. The AI-guide bot was implemented using Python 3.9. To enhance the scalability and incorporate the integrated dataset, we combined the AI-guide bot with OpenAI and the LangChain framework. To generate user-friendly conversations, a language model was developed based on Chat-Generative Pretrained Transformer (ChatGPT), an interactive conversational chatbot powered by GPT-3.5. The AI-guide bot was implemented using ChatGPT3.5 from Sep. 2023 to Jan. 2024. RESULTS: The AI-guide bot allowed users to select their desired cancer type and language for conversational interactions. The AI-guided bot was designed to expand its capabilities to encompass multiple major cancer types. The performance of the AI-guide bot responses was 90.98 +/- 4.02 (obtained by summing up the Likert scores). CONCLUSIONS: The AI-guide bot can provide medical information quickly and accurately to patients with cancer who are concerned about their health.

Lee, T. F., et al. (2024). "Utilizing radiomics and dosiomics with AI for precision prediction of radiation dermatitis in breast cancer patients." BMC Cancer **24**(1): 965.

PURPOSE: This study explores integrating clinical features with radiomic and dosiomic characteristics into AI models to enhance the prediction accuracy of radiation dermatitis (RD) in breast cancer patients undergoing volumetric modulated arc therapy (VMAT). MATERIALS AND METHODS: This study involved a retrospective analysis of 120 breast cancer patients treated with VMAT at Kaohsiung Veterans General Hospital from 2018 to 2023. Patient data included CT images, radiation doses, Dose-Volume Histogram (DVH) data, and clinical information. Using a Treatment Planning System (TPS), we segmented CT images into Regions of Interest (ROIs) to extract radiomic and dosiomic features, focusing on intensity, shape, texture, and dose distribution characteristics. Features significantly associated with the development of RD were identified using ANOVA and LASSO regression (p-value < 0.05). These features were then employed to train and evaluate Logistic Regression (LR) and Random Forest (RF) models, using tenfold cross-validation to ensure robust assessment of model efficacy. RESULTS: In this study, 102 out of 120 VMAT-treated breast cancer patients were included in the detailed analysis. Thirty-two percent of these patients developed Grade 2(+) RD. Age and BMI were identified as significant clinical predictors. Through feature selection, we narrowed down the vast pool of radiomic and dosiomic data to 689 features, distributed across 10 feature subsets for model construction. In the LR model, the J subset, comprising DVH, Radiomics, and Dosiomics features, demonstrated the highest predictive performance with an AUC of 0.82. The RF model showed that subset I, which includes clinical, radiomic, and dosiomic features, achieved the best predictive accuracy with an AUC of 0.83. These results emphasize that integrating radiomic and dosiomic features significantly enhances the prediction of Grade 2(+) RD. CONCLUSION: Integrating clinical, radiomic, and dosiomic characteristics into AI models significantly improves the prediction of Grade 2(+) RD risk in breast cancer patients post-VMAT. The RF model analysis demonstrates that a comprehensive feature set maximizes predictive efficacy, marking a promising step towards utilizing AI in radiation therapy risk assessment and enhancing patient care outcomes.

Leibig, C., et al. (2022). "Combining the strengths of radiologists and AI for breast cancer screening: a retrospective analysis." Lancet Digit Health **4**(7): e507-e519.

BACKGROUND: We propose a decision-referral approach for integrating artificial intelligence (AI) into the breast-cancer screening pathway, whereby the algorithm makes predictions on the basis of its quantification of uncertainty. Algorithmic assessments with high certainty are done automatically, whereas assessments with lower certainty are referred to the radiologist. This two-part AI system can triage normal mammography exams and provide post-hoc cancer detection to maintain a high degree of sensitivity. This study aimed to evaluate the performance of this AI system on sensitivity and specificity when used either as a standalone system or within a decision-referral approach, compared with the original radiologist decision. METHODS: We used a retrospective dataset consisting of 1 193 197 full-field, digital mammography studies carried out between Jan 1, 2007, and Dec 31, 2020, from eight screening sites participating in the German national breast-cancer screening programme. We derived an internal-test dataset from six screening sites (1670 screen-detected cancers and 19 997 normal mammography exams), and an external-test dataset of breast cancer screening

exams (2793 screen-detected cancers and 80 058 normal exams) from two additional screening sites to evaluate the performance of an AI algorithm on sensitivity and specificity when used either as a standalone system or within a decision-referral approach, compared with the original individual radiologist decision at the point-of-screen reading ahead of the consensus conference. Different configurations of the AI algorithm were evaluated. To account for the enrichment of the datasets caused by oversampling cancer cases, weights were applied to reflect the actual distribution of study types in the screening programme. Triaging performance was evaluated as the rate of exams correctly identified as normal. Sensitivity across clinically relevant subgroups, screening sites, and device manufacturers was compared between standalone AI, the radiologist, and decision referral. We present receiver operating characteristic (ROC) curves and area under the ROC (AUROC) to evaluate AI-system performance over its entire operating range. Comparison with radiologists and subgroup analysis was based on sensitivity and specificity at clinically relevant configurations. FINDINGS: The exemplary configuration of the AI system in standalone mode achieved a sensitivity of 84.2% (95% CI 82.4-85.8) and a specificity of 89.5% (89.0-89.9) on internal-test data, and a sensitivity of 84.6% (83.3-85.9) and a specificity of 91.3% (91.1-91.5) on external-test data, but was less accurate than the average unaided radiologist. By contrast, the simulated decision-referral approach significantly improved upon radiologist sensitivity by 2.6 percentage points and specificity by 1.0 percentage points, corresponding to a triaging performance at 63.0% on the external dataset; the AUROC was 0.982 (95% CI 0.978-0.986) on the subset of studies assessed by AI, surpassing radiologist performance. The decision-referral approach also yielded significant increases in sensitivity for a number of clinically relevant subgroups, including subgroups of small lesion sizes and invasive carcinomas. Sensitivity of the decision-referral approach was consistent across the eight included screening sites and three device manufacturers. INTERPRETATION: The decision-referral approach leverages the strengths of both the radiologist and AI, demonstrating improvements in sensitivity and specificity surpassing that of the individual radiologist and of the standalone AI system. This approach has the potential to improve the screening accuracy of radiologists, is adaptive to the requirements of screening, and could allow for the reduction of workload ahead of the consensus conference, without discarding the generalised knowledge of radiologists. FUNDING: Vara.

Levy, Y., et al. (2023). "The Fusion of Wide Field Optical Coherence Tomography and AI: Advancing Breast Cancer Surgical Margin Visualization." Life (Basel) **13**(12).

This study explores the integration of Wide Field Optical Coherence Tomography (WF-OCT) with an AI-driven clinical decision support system, with the goal of enhancing productivity and decision making in breast cancer surgery margin assessment. A computationally efficient convolutional neural network (CNN)-based binary classifier is developed using 585 WF-OCT margin scans from 151 subjects. The CNN model swiftly identifies suspicious areas within margins with an on-device inference time of approximately 10 ms for a 420 x 2400 image. In independent testing on 155 pathology-confirmed margins, including 31 positive margins from 29 patients, the classifier achieved an AUROC of 0.976, a sensitivity of 0.93, and a specificity of 0.98. At the margin level, the deep learning model accurately identified 96.8% of pathology-positive margins. These results highlight the clinical viability of AI-enhanced margin visualization using WF-OCT in breast cancer surgery and its potential to decrease reoperation rates due to residual tumors.

Li, A., et al. (2023). "Efficacy and safety of Xiao-ai-ping injection add-on therapy to chemotherapy in patients with non-small cell lung cancer: A systematic review and meta-analysis." Medicine (Baltimore) **102**(40): e35483.

BACKGROUND: Xiao-ai-ping injection (XAPI) combined with chemotherapy has potential efficacy and less side effects in the treatment of non-small cell lung cancer (NSCLC). At present, there are many clinical studies on XAPI combined with chemotherapy in the treatment of NSCLC, but the results are different. The purpose of this study was to evaluate the efficacy and safety of XAPI combined with chemotherapy in the treatment of NSCLC by meta-analysis system. METHODS: The databases to be searched include PubMed, Cochrane Library, Web of Science, Chinese National Knowledge Infrastructure, Chinese Biomedical Literature Database, Wanfang database, Chinese Scientific Journal Database, and so on. In addition, relevant journals and magazines will manually search in various fields as supplements. The search date is set from the establishment of the database until July 8, 2023. The 2 researchers will use Endnote X9 software for literature screening and data extraction and independently evaluate the quality. We then assessed the quality and risk of inclusion in the study and observed outcome indicators. RESULTS: A total of 28 trials were included in this study, 1947 patients with NSCLC (974 receiving XAPI combined

chemotherapy and 973 receiving chemotherapy alone). The results of meta-analysis showed that: Objective tumor response rate of NSCLC (P < .00001). Improvement in Karnofsky performance score of NSCLC (P < .00001). Quality of life score of NSCLC (P < .00001). The result of CD3 + (P < .00001). The result of CD4 + (P < .00001). The result of CD8 + (P < .00001). The result of CD4+/CD8 + (P = .0001). Leukopenia (P < .00001). Thrombocytopenia (P < .00001). Hemoglobin decrease (P < .00001). Liver function (P = .04). Nausea and vomiting (P < .00001). CONCLUSION: Our meta-analyses demonstrated that XAPI adjunct with chemotherapy can improve the patient quality of life, reduce adverse reactions, and enhanced immune function, the treatment is effective and high safety. Which suggests that it might be used for NSCLC. However, a large sample of randomized controlled trials are needed to further study the long-term efficacy of XAPI.

Li, B., et al. (2020). "Chinese Herbal Formulas Miao-Yi-Ai-Tang Inhibits the Proliferation and Migration of Lung Cancer Cells through Targeting beta-Catenin/AXIN and Presents Synergistic Effect with Cisplatin Suppressing Lung Cancer." Biomed Res Int **2020**: 2761850.

OBJECTIVE: Lung cancer is one of the major causes of cancer deaths worldwide, and the five-year survival still remains low despite the improvement of screening, prevention, and treatment methods. Chinese herbal medicines have been widely used for tumor prevention and treatment. Miao-Yi-Ai-Tang (Miao) is a novel herbal formulation and shows a potential anticancer effect. Materials and Methods. Human Small Cell Lung Cancer Cell was used for study in vitro. After treatments by Miao and Cisplatin (DDP), the invasion, migration, proliferation, and apoptosis of cells were detected by transwell, wound healing, CCK-8, and flow cytometry, respectively. The expression of beta-catenin, AXIN, and c-myc was detected by qRT-PCR and immunohistochemistry staining. Western blotting was applied for measuring the protein expression of beta-catenin, AXIN, and c-myc was detected by qRT-PCR and immunohistochemistry staining. Western blotting was applied for measuring the protein expression of. RESULTS: We found that Miao could inhibit invasion, migration, and proliferation and promote apoptosis of human lung cancer cells. Meanwhile, Miao and DDP presented synergy regulating the proliferation and apoptosis of lung cancer cells. The percentage of lung cancer cells in S and G2 stages was increased markedly by Miao. Besides, the expression of c-myc, AXIN, and beta-catenin, AXIN, and c-myc was detected by qRT-PCR and immunohistochemistry staining. Western blotting was applied for measuring the protein expression of. CONCLUSIONS: Chinese herbal formulas Miao could suppress lung cancer through targeting the beta-catenin/AXIN signaling pathway. Therefore, our findings may provide a novel strategy for the prevention and treatment of lung cancer.beta-catenin, AXIN, and c-myc was detected by qRT-PCR and immunohistochemistry staining. Western blotting was applied for measuring the protein expression of.

Li, C., et al. (2022). "Deep learning-based AI model for signet-ring cell carcinoma diagnosis and chemotherapy response prediction in gastric cancer." Med Phys **49**(3): 1535-1546.

PURPOSE: We aimed to develop a noninvasive artificial intelligence (AI) model to diagnose signet-ring cell carcinoma (SRCC) of gastric cancer (GC) and identify patients with SRCC who could benefit from postoperative chemotherapy based on preoperative contrast-enhanced computed tomography (CT). METHODS: A total of 855 GC patients with 855 single GCs were included, of which 249 patients were diagnosed as SRCC by histopathologic examinations. The AI model was generated with clinical, handcrafted radiomic, and deep learning features. Model diagnostic performance was measured by area under the receiver operating characteristic curve (AUC), sensitivity, and specificity, while predictive performance was measured by Kaplan-Meier curves. RESULTS: In the test cohort (n = 257), the AUC, sensitivity, and specificity of our AI model for diagnosing SRCC were 0.786 (95% CI: 0.721-0.845), 77.3%, and 69.2%, respectively. For the entire cohort, patients with AI-predicted high risk had a significantly shorter median OS compared with those with low risk (median overall survival [OS], 38.8 vs. 64.2 months, p = 0.009). Importantly, in pathologically confirmed advanced SRCC patients, AI-predicted high-risk status was indicative of a shorter overall survival (median overall survival [OS], 31.0 vs. 54.4 months, p = 0.036) and marked chemotherapy resistance, whereas AI-predicted low-risk status had substantial chemotherapy benefit (median OS [without vs. with chemotherapy], 26.0 vs. not reached, p = 0.013). CONCLUSIONS: The CT-based AI model demonstrated good performance for diagnosing SRCC, stratifying patient prognosis, and predicting chemotherapy responses. Advanced SRCC patients with AI-predicted low-risk status may benefit substantially from adjuvant chemotherapy.

Li, G., et al. (2024). "Transformer-based AI technology improves early ovarian cancer diagnosis using cfDNA methylation markers." Cell Rep Med

5(8): 101666.

Epithelial ovarian cancer (EOC) is the deadliest women's cancer and has a poor prognosis. Early detection is the key for improving survival (a 5-year survival rate in stage I/II is over 70% compared to that of 25% in stage III/IV) and can be achieved through methylation markers from circulating cell-free DNA (cfDNA) using a liquid biopsy. In this study, we first identify top 500 EOC markers differentiating EOC from healthy female controls from 3.3 million methylome-wide CpG sites and validated them in 1,800 independent cfDNA samples. We then utilize a pretrained AI transformer system called MethylBERT to develop an EOC diagnostic model which achieves 80% sensitivity and 95% specificity in early-stage EOC diagnosis. We next develop a simple digital droplet PCR (ddPCR) assay which archives good performance, facilitating early EOC detection.

Li, H., et al. (2000). "[Effect of chang'ai kangfu decoction on immunity in postoperational patients with large intestine cancer]." Zhongguo Zhong Xi Yi Jie He Za Zhi **20**(8): 580-582.

OBJECTIVE: To explore the effect of Chinese drug Chang'ai Kangfu decoction (CAKF) on immunity in post-operational patients with large intestine cancer (LIC). METHODS: Forty-eight patients with LIC in Dukes' B, C stage after operation were randomly assigned to 3 groups, the CAKF group (16 cases), chemotherapy group (17 cases) and combination therapy (CAKF plus chemotherapy) group (15 cases). 5-FU and mitomycin C were given to the chemotherapy group. The dynamic changes of T-lymphocyte subsets, NK cells and immunoglobulins were investigated. RESULTS: Before operation, the CD3+, CD4+, CD4+/CD8+ and the activity of NK cells in LIC patients were lower, but CD8+ was higher than that of normal level ($P < 0.01$), which indicated that cellular immunity in LIC was in immunosuppressive state, they all further reduced 1 week after operation, particularly CD3+ cell counts, but CD3+, CD4+ and the activity of NK cells normalized 1 month after operation in CAKF group, and 2 months were needed to normalize in combination therapy group. Both groups recovered to a certain extent in comparing with before treatment, but the chemotherapy group recovered slower. The similar results appeared in humoral immunity. CONCLUSION: CAKF could obviously increase the immunity in LIC patients after operation.

Li, L., et al. (2017). "Traditional Chinese medicine, Fuzheng Kang-Ai decoction, inhibits metastasis of lung cancer cells through the STAT3/MMP9 pathway." Mol Med Rep **16**(3): 2461-2468.

Lung cancer is a leading cause of cancer-associated mortality worldwide, including in developing countries such as China. Traditional Chinese medicine may provide a novel insight for the treatment of patients with lung cancer. The present study aimed to uncover the mechanism by which the Chinese herbal medicine, Fuzheng Kang-Ai (FZKA), functions on lung cancer cell metastasis. The results demonstrated that treatment with FZKA markedly inhibited cell viability, migration and invasion of lung cancer cells, as determined by cell viability and Transwell assays. Notably, the activity and expression of matrix metalloproteinase 9 (MMP9) was significantly inhibited by FZKA treatment on lung cancer cells, as determined by an MMP9 activity assay and western blot analysis. Furthermore, FZKA markedly inhibited epithelial-mesenchymal transition (EMT) of lung cancer cells by inhibiting the expression of the mesenchymal markers N-cadherin and vimentin. In addition, activation of the oncoprotein signal transducer and activator of transcription 3 (STAT3) was suppressed following treatment with FZKA. Conversely, overexpression of STAT3 was able to rescue MMP9 activity following FZKA treatment. The present study indicated that FZKA may inhibit lung cancer metastasis via the STAT3/MMP9 pathway and EMT, suggesting that FZKA may serve as a novel promising therapeutic strategy for the treatment of patients with late stage lung cancer.

Li, L., et al. (2021). "[Corrigendum] Traditional Chinese medicine, Fuzheng Kang-Ai decoction, inhibits metastasis of lung cancer cells through the STAT3/MMP9 pathway." Mol Med Rep **24**(2).

Following the publication of the above article, an interested reader drew to the authors' attention that various of the data panels shown for the cell migration assay experiments in Figs. 2B and 3 appeared to show overlapping regions, such that they were not generated from discretely performed experiments.The authors have re-examined their original data, and realize that the figures in question were assembled incorrectly. In addition, the authors have also realized that certain of the western blotting data panels in Figs. 5 and 6 had likewise been assembled incorrectly. The corrected versions of Figs. 2, 3, 5 and 6 are shown on the next two pages. All these corrections were approved by all authors. The authors regret that these errors were included in the paper, and are grateful to the Editor of Molecular Medicine Reports for allowing them the opportunity to publish this corrigendum. They also wish to emphasize that the errors made during the compilation of the figures did not substantially alter any of the major conclusions reported in the study,

and apologize to the readership for any inconvenience caused. [the original article was published in Molecular Medicine Reports 16: 2461-2468, 2017; DOI: 10.3892/mmr.2017.6905].

Li, L., et al. (2016). "Chinese herbal medicine Fuzheng Kang-Ai decoction sensitized the effect of gefitinib on inhibition of human lung cancer cells through inactivating PI3-K/Akt -mediated suppressing MUC1 expression." J Ethnopharmacol **194**: 918-929.

ETHNOPHARMACOLOGICAL RELEVANCE: Chinese herbal medicine (CHM) Fuzheng Kang-Ai (FZKA for short) decoction has been used as adjuvant treatment strategies in lung cancer patients for decades. However, the molecular mechanism underlying the therapeutic potential especially in sensitizing the effect of EGFR-TKI gefitinib has not been well elucidated. MATERIALS AND METHODS: Cell viability was detected by MTT assay. Cell cycle distribution was detected by flow cytometry. Western blot were used to examine phosphorylation and protein levels of Akt, p65, p50 and MUC1. The mRNA level of MUC1 was measured by qRT-PCR. Transient transfection experiments were used to overexpression of Akt, p65 and MUC1. Tumor xenograft and bioluminescent imaging experiments were carried out to confirm the in vitro findings. RESULTS: Cell viability was inhibited by FZKA treatment and showed more significant when treated with FZKA and gefitinib in combine in lung cancer cells. FZKA induced the cell arrest at G0/G1 phase. Mechanistically, we showed that the phosphorylation of Akt, protein expressions of p65 and MUC1 were suppressed by FZKA and even more responses were observed in the FZKA and gefitinib combining. Overexpressed Akt overcame the effect of FZKA on p65 protein, and exogenously expressed p65 resisted the inhibitory effect of MUC1 protein expression by FZKA. On the contrary, while overexpressed MUC1 had no effect on p65 expression, it feedback increased phosphorylation of Akt, and more importantly, reversed the cell growth inhibition affected by FZKA. In line with the above, our results confirmed the synergistic effects of FZKA and gefitinib combination on tumor growth, the phosphorylation of Akt, and protein expression of p65 and MUC1 in vivo. CONCLUSION: This study shows that FZKA decoction inhibits the growth of NSCLC cells through Akt-mediated inhibition of p65, followed by reducing the expression of MUC1. More importantly, there is a synergistic effect of FZKA decoction and gefitinib combination with greater suppression. The positive feedback regulatory loop of MUC1 to Akt signaling pathway further added the important role of MUC1 in mediating the overall responses of FZKA decoction in this process. The in vitro and in vivo study provides an additional and a novel mechanism by which the FZKA decoction enhances the growth inhibition of gefitinib in gefitinib-resistant NSCLC cells.

Li, S., et al. (2023). "AI-predicted mpMRI image features for the prediction of clinically significant prostate cancer." Int Urol Nephrol **55**(11): 2703-2715.

PURPOSE: To evaluate the feasibility of using mpMRI image features predicted by AI algorithms in the prediction of clinically significant prostate cancer (csPCa). MATERIALS AND METHODS: This study analyzed patients who underwent prostate mpMRI and radical prostatectomy (RP) at the Affiliated Hospital of Jiaxing University between November 2017 and December 2022. The clinical data collected included age, serum prostate-specific antigen (PSA), and biopsy pathology. The reference standard was the prostatectomy pathology, and a Gleason Score (GS) of 3 + 3 = 6 was considered non-clinically significant prostate cancer (non-csPCa), while a GS >/= 3 + 4 was considered csPCa. A pre-trained AI algorithm was used to extract the lesion on mpMRI, and the image features of the lesion and the prostate gland were analyzed. Two logistic regression models were developed to predict csPCa: an MR model and a combined model. The MR model used age, PSA, PSA density (PSAD), and the AI-predicted MR image features as predictor variables. The combined model used biopsy pathology and the aforementioned variables as predictor variables. The model's effectiveness was evaluated by comparing it to biopsy pathology using the area under the curve (AUC) of receiver operation characteristic (ROC) analysis. RESULTS: A total of 315 eligible patients were enrolled with an average age of 70.8 +/- 5.9. Based on RP pathology, 18 had non-csPCa, and 297 had csPCa. PSA, PSAD, biopsy pathology, and ADC value of the prostate outside the lesion (ADC(prostate)) varied significantly across different ISUP grade groups of RP pathology ($P < 0.001$). Other clinical variables and image features did not vary significantly across different ISUP grade groups ($P > 0.05$). The MR model included PSAD, the ratio of ADC value between the lesion and the prostate outside the lesion (ADC(lesion/prostate)), the signal intensity ratio of DWI between the lesion and the prostate outside the lesion (DWI(lesion/prostate)), and the ratio of DWI(lesion/prostate) to ADC(lesion/prostate). The combined model included biopsy pathology, ADC(lesion/prostate), mean signal intensity of the lesion on DWI (DWI(lesion)), DWI signal intensity of the prostate outside the lesion (DWI(prostate)), and signal intensity ratio of DWI

between the lesion and the prostate outside the lesion (DWI(lesion/prostate)). The AUC of the MR model (0.830, 95% CI 0.743, 0.916) was not significantly different from that of biopsy pathology (0.820, 95% CI 0.728, 0.912, P = 0.884). The AUC of the combined model (0.915, 95% CI 0.849, 0.980) was higher than that of the biopsy pathology (P = 0.042) and MR model (P = 0.031). CONCLUSION: The aggressiveness of prostate cancer can be effectively predicted using AI-extracted image features from mpMRI images, similar to biopsy pathology. The prediction accuracy was improved by combining the AI-extracted mpMRI image features with biopsy pathology, surpassing the performance of biopsy pathology alone.

Li, W., et al. (2013). "Xiao-Ai-Ping, a TCM Injection, Enhances the Antigrowth Effects of Cisplatin on Lewis Lung Cancer Cells through Promoting the Infiltration and Function of CD8(+) T Lymphocytes." Evid Based Complement Alternat Med **2013**: 879512.

Objectives. To investigate how Xiao-Ai-Ping injection, a traditional Chinese medicine and an ancillary drug in tumor treatment, enhances the antitumor effects of cisplatin on Lewis lung cancer (LLC) cells. Methods. LLC-bearing mice were daily intraperitoneally injected with various doses of cisplatin, Xiao-Ai-Ping, or cisplatin plus Xiao-Ai-Ping, respectively. Body weight and tumor volumes were measured every three days. Results. Combination of Xiao-Ai-Ping and cisplatin yielded significantly better antigrowth and proapoptotic effects on LLC xenografts than sole drug treatment did. In addition, we found that Xiao-Ai-Ping triggered the infiltration of CD8(+) T cells, a group of cytotoxic T cells, to LLC xenografts. Furthermore, the mRNA levels of interferon- gamma (ifn- gamma), perforin-1 (prf-1), and granzyme B (gzmb) in CD8(+) T cells were significantly increased after combination treatment of Xiao-Ai-Ping and cisplatin. In vitro studies showed that Xiao-Ai-Ping markedly upregulated the mRNA levels of ifn- gamma , prf-1, and gzmb in CD8(+) T cells in a concentration-dependent manner, suggesting that Xiao-Ai-Ping augments the function of CD8(+) T cells. Conclusions. Xiao-Ai-Ping promotes the infiltration and function of CD8(+) T cells and thus enhances the antigrowth effects of cisplatin on LLC xenografts, which provides new evidence for the combination of Xiao-Ai-Ping and cisplatin in clinic in China.

Li, Z., et al. (2021). "Preliminary study of AI-assisted diagnosis using FDG-PET/CT for axillary lymph node metastasis in patients with breast cancer." EJNMMI Res **11**(1): 10.

BACKGROUND: To improve the diagnostic accuracy of axillary lymph node (LN) metastasis in breast cancer patients using 2-[(18)F]FDG-PET/CT, we constructed an artificial intelligence (AI)-assisted diagnosis system that uses deep-learning technologies. MATERIALS AND METHODS: Two clinicians and the new AI system retrospectively analyzed and diagnosed 414 axillae of 407 patients with biopsy-proven breast cancer who had undergone 2-[(18)F]FDG-PET/CT before a mastectomy or breast-conserving surgery with a sentinel lymph node (LN) biopsy and/or axillary LN dissection. We designed and trained a deep 3D convolutional neural network (CNN) as the AI model. The diagnoses from the clinicians were blended with the diagnoses from the AI model to improve the diagnostic accuracy. RESULTS: Although the AI model did not outperform the clinicians, the diagnostic accuracies of the clinicians were considerably improved by collaborating with the AI model: the two clinicians' sensitivities of 59.8% and 57.4% increased to 68.6% and 64.2%, respectively, whereas the clinicians' specificities of 99.0% and 99.5% remained unchanged. CONCLUSIONS: It is expected that AI using deep-learning technologies will be useful in diagnosing axillary LN metastasis using 2-[(18)F]FDG-PET/CT. Even if the diagnostic performance of AI is not better than that of clinicians, taking AI diagnoses into consideration may positively impact the overall diagnostic accuracy.

Li, Z., et al. (2024). "AI identifies potent inducers of breast cancer stem cell differentiation based on adversarial learning from gene expression data." Brief Bioinform **25**(3).

Cancer stem cells (CSCs) are a subpopulation of cancer cells within tumors that exhibit stem-like properties and represent a potentially effective therapeutic target toward long-term remission by means of differentiation induction. By leveraging an artificial intelligence approach solely based on transcriptomics data, this study scored a large library of small molecules based on their predicted ability to induce differentiation in stem-like cells. In particular, a deep neural network model was trained using publicly available single-cell RNA-Seq data obtained from untreated human-induced pluripotent stem cells at various differentiation stages and subsequently utilized to screen drug-induced gene expression profiles from the Library of Integrated Network-based Cellular Signatures (LINCS) database. The challenge of adapting such different data domains was tackled by devising an adversarial learning approach that was able to effectively identify and remove domain-specific bias during the training phase. Experimental validation in MDA-MB-231 and MCF7 cells

demonstrated the efficacy of five out of six tested molecules among those scored highest by the model. In particular, the efficacy of triptolide, OTS-167, quinacrine, granisetron and A-443654 offer a potential avenue for targeted therapies against breast CSCs.

Lian, W., et al. (2024). "Let it shine: Autofluorescence of Papanicolaou-stain improves AI-based cytological oral cancer detection." Comput Biol Med **185**: 109498.

BACKGROUND AND OBJECTIVES: Oral cancer is a global health challenge. The disease can be successfully treated if detected early, but the survival rate drops significantly for late stage cases. There is a growing interest in a shift from the current standard of invasive and time-consuming tissue sampling and histological examination, towards non-invasive brush biopsies and cytological examination, facilitating continued risk group monitoring. For cost effective and accurate cytological analysis there is a great need for reliable computer-assisted data-driven approaches. However, infeasibility of accurate cell-level annotation hinders model performance, and limits evaluation and interpretation of the results. This study aims to improve AI-based oral cancer detection by introducing additional information through multimodal imaging and deep multimodal information fusion. METHODS: We combine brightfield and fluorescence whole slide microscopy imaging to analyze Papanicolaou-stained liquid-based cytology slides of brush biopsies collected from both healthy and cancer patients. Given the challenge of detailed cytological annotations, we utilize a weakly supervised deep learning approach only relying on patient-level labels. We evaluate various multimodal information fusion strategies, including early, late, and three recent intermediate fusion methods. RESULTS: Our experiments demonstrate that: (i) there is substantial diagnostic information to gain from fluorescence imaging of Papanicolaou-stained cytological samples, (ii) multimodal information fusion improves classification performance and cancer detection accuracy, compared to single-modality approaches. Intermediate fusion emerges as the leading method among the studied approaches. Specifically, the Co-Attention Fusion Network (CAFNet) model achieves impressive results, with an F1 score of 83.34% and an accuracy of 91.79% at cell level, surpassing human performance on the task. Additional tests highlight the importance of accurate image registration to maximize the benefits of the multimodal analysis. CONCLUSION: This study advances the field of cytopathology by integrating deep learning methods, multimodal imaging and information fusion to enhance non-invasive early detection of oral cancer. Our approach not only improves diagnostic accuracy, but also allows an efficient, yet uncomplicated, clinical workflow. The developed pipeline has potential applications in other cytological analysis settings. We provide a validated open-source analysis framework and share a unique multimodal oral cancer dataset to support further research and innovation.

Liao, M., et al. (2021). "Autophagy Blockade by Ai Du Qing Formula Promotes Chemosensitivity of Breast Cancer Stem Cells Via GRP78/beta-Catenin/ABCG2 Axis." Front Pharmacol **12**: 659297.

Accumulating evidence suggests that the root of drug chemoresistance in breast cancer is tightly associated with subpopulations of cancer stem cells (CSCs), whose activation is largely dependent on taxol-promoting autophagy. Our pilot study identified GRP78 as a specific marker for chemoresistance potential of breast CSCs by regulating Wnt/beta-catenin signaling. Ai Du Qing (ADQ) is a traditional Chinese medicine formula that has been utilized in the treatment cancer, particularly during the consolidation phase. In the present study, we investigated the regulatory effects and molecular mechanisms of ADQ in promoting autophagy-related breast cancer chemosensitivity. ADQ with taxol decreasing the cell proliferation and colony formation of breast cancer cells, which was accompanied by suppressed breast CSC ratio, limited self-renewal capability, as well as attenuated multi-differentiation. Furthermore, autophagy in ADQ-treated breast CSCs was blocked by taxol via regulation of beta-catenin/ABCG2 signaling. We also validated that autophagy suppression and chemosensitizing activity of this formula was GRP78-dependent. In addition, GRP78 overexpression promoted autophagy-inducing chemoresistance in breast cancer cells by stabilizing beta-catenin, while ADQ treatment downregulated GRP78, activated the Akt/GSK3beta-mediated proteasome degradation of beta-catenin via ubiquitination activation, and consequently attenuated the chemoresistance-promoted effect of GRP78. In addition, both mouse breast cancer xenograft and zebrafish xenotransplantation models demonstrated that ADQ inhibited mammary tumor growth, and the breast CSC subpopulation showed obscure adverse effects. Collectively, this study not only reveals the chemosensitizating mechanism of ADQ in breast CSCs, but also highlights the importance of GRP78 in mediating autophagy-promoting drug resistance via beta-catenin/ABCG2 signaling.

Liu, G., et al. (2023). "The added value of AI-based

computer-aided diagnosis in classification of cancer at prostate MRI." Eur Radiol **33**(7): 5118-5130.

OBJECTIVES: To develop an artificial intelligence (AI) model for prostate segmentation and prostate cancer (PCa) detection, and explore the added value of AI-based computer-aided diagnosis (CAD) compared to conventional PI-RADS assessment. METHODS: A retrospective study was performed on multi-centers and included patients who underwent prostate biopsies and multiparametric MRI. A convolutional-neural-network-based AI model was trained and validated; the reliability of different CAD methods (concurrent read and AI-first read) were tested in an internal/external cohort. The diagnostic performance, consistency and efficiency of radiologists and AI-based CAD were compared. RESULTS: The training/validation/internal test sets included 650 (400/100/150) cases from one center; the external test included 100 cases (25/25/50) from three centers. For diagnosis accuracy, AI-based CAD methods showed no significant differences and were equivalent to the radiologists in the internal test (127/150 vs. 130/150 vs. 125/150 for reader 1; 127/150 vs.132/150 vs. 131/150 for reader 2; all $p > 0.05$), whereas in the external test, concurrent-read methods were superior/equal to AI-first read (87/100 vs. 71/100, $p < 0.001$, for reader 2; 79/100 vs. 69/100, $p = 0.076$, for reader 1) and better than/equal to radiologists (79/100 vs. 72/100, $p = 0.039$, for reader 1; 87/100 vs. 86/100, $p = 1.000$, for reader 2). Moreover, AI-first read/concurrent read improved consistency in both internal test (kappa = 1.000, 0.830) and external test (kappa = 0.958, 0.713) compared to radiologists (kappa = 0.747, 0.600); AI-first read method (8.54 s/7.66 s) was faster than readers (92.72 s/89.54 s) and concurrent-read method (29.15 s/28.92 s), respectively. CONCLUSION: AI-based CAD could improve the consistency and efficiency for accurate diagnosis; the concurrent-read method could enhance the diagnostic capabilities of an inexperienced radiologist in unfamiliar situations. KEY POINTS: * For prostate cancer segmentation, the performance of multi-small Vnet displays optimal compared to small Vnet and Vnet (DSC(msvnet) vs. DSC(svnet), $p = 0.021$; DSC(msvnet) vs. DSC(vnet), $p < 0.001$). * For prostate gland segmentation, the mean/median DSCs for fine and coarse segmentation were 0.91/0.91 and 0.88/0.89, respectively. Fine segmentation displays superior performance compared to coarse (DSC(coarse) vs. DSC(fine), $p < 0.001$). * For PCa diagnosis, AI-based CAD methods improve consistency in internal (kappa = 1.000; 0.830) and external (kappa = 0.958; 0.713) tests compared to radiologists (kappa = 0.747; 0.600); the AI-first read (8.54 s/7.66 s) was faster than the readers (92.72 s/89.54 s) and the concurrent-read method (29.15 s/28.92 s).

Liu, L., et al. (2021). "Design and Analysis Methods for Trials with AI-Based Diagnostic Devices for Breast Cancer." J Pers Med **11**(11).

Imaging is important in cancer diagnostics. It takes a long period of medical training and clinical experience for radiologists to be able to accurately interpret diagnostic images. With the advance of big data analysis, machine learning and AI-based devices are currently under development and taking a role in imaging diagnostics. If an AI-based imaging device can read the image as accurately as experienced radiologists, it may be able to help radiologists increase the accuracy of their reading and manage their workloads. In this paper, we consider two potential study objectives of a clinical trial to evaluate an AI-based device for breast cancer diagnosis by comparing its concordance with human radiologists. We propose statistical design and analysis methods for each study objective. Extensive numerical studies are conducted to show that the proposed statistical testing methods control the type I error rate accurately and the design methods provide required sample sizes with statistical powers close to pre-specified nominal levels. The proposed methods were successfully used to design and analyze a real device trial.

Liu, Q., et al. (2024). "AI based diagnostics product design for osteosarcoma cells microscopy imaging of bone cancer patients using CA-MobileNet V3." J Bone Oncol **49**: 100644.

OBJECTIVE: The incidence of osteosarcoma (OS) is low, but primary malignant bone tumors rank third among the causes of death in cancer patients under the age of 20. Currently, analysis of cellular structure and tumor morphology through microscopic images remains one of the main diagnostic methods for osteosarcoma. However, this completely manual approach is tedious, time-consuming, and difficult to diagnose accurately due to the similarities in certain characteristics of malignant and benign tumors. METHODS: Leveraging the potential of artificial intelligence (AI) in assessing and classifying images, this study explored a modified CA-MobileNet V3 model that was embedded into innovative microscope products to enhance the microscope's feature extraction capabilities and help reduce misclassification during diagnosis. RESULTS: The intelligent recognition model method introduced in this paper has significant advantages in retrieval and classification of osteosarcoma cells and other cell types. Compared with models such as ShuffleNet V2, EfficientNet V2, Mobilenet V3 (without transfer learning), TL-

MobileNet V3 (with transfer learning), etc., the model size is only 5.33 MB, is a lightweight model, and the accuracy of the improved model reached 98.69 %. In addition, the artificial intelligence microscope (AIM) with integrated design based on this model can also help improve diagnostic efficiency. CONCLUSION: The innovative method of the CA-MobileNet V3 automatic classification model based on deep learning provides an efficient and reliable solution for the pathological diagnosis of osteosarcoma. This study contributes to medical image analysis and provides doctors with an accurate and valuable tool for microscopic diagnosis. It also promotes the advancement of artificial intelligence in medical imaging technology.

Liu, S., et al. (2008). "[Effects of Ru'ai Shuhou Recipe on 5-year recurrence rate after mastectomy in breast cancer]." Zhong Xi Yi Jie He Xue Bao **6**(10): 1000-1004.

OBJECTIVE: To observe the effects of Ru'ai Shuhou Recipe (RSR), a compound traditional Chinese herbal medicine, on 5-year recurrence rate after mastectomy in breast cancer. METHODS: A total of 300 patients with breast cancer were divided into two groups: treatment group and control group. The patients in the treatment group were treated with Western medicine and RSR, and the patients in the control group were treated only with Western medicine (the same as the treatment group). In the two groups, the 5-year recurrence rates after mastectomy in breast cancer were investigated. RESULTS: Thirty-four breast cancer patients were lost to five-year follow-up during the course of investigation, and 266 breast cancer patients went through the evaluation. The 5-year recurrence rate after mastectomy in the treatment group was significantly lower than that in the control group ($P<0.05$). The recurrence rate after mastectomy was influenced by positive lymph node, primary breast tumor size, clinical stage, and patients' health status. There was significant difference in the 5-year recurrence rates between the two groups ($P<0.05$) under the following conditions, such as the positive lymph nodes more than four, the primary breast tumor larger than two centimeters, and in the clinical stage II and III, estrogen receptor (ER)-positive/progesterone receptor (PR)-positive and ER-negative/PR-negative. The recurrence rate was not associated with the operation method and age distribution. CONCLUSION: RSR can reduce the 5-year recurrence rate after mastectomy in breast cancer.

Liu, Y., et al. (2024). "Pioneering noninvasive colorectal cancer detection with an AI-enhanced breath volatilomics platform." Theranostics **14**(11): 4240-4255.

Background: The sensitivity and specificity of current breath biomarkers are often inadequate for effective cancer screening, particularly in colorectal cancer (CRC). While a few exhaled biomarkers in CRC exhibit high specificity, they lack the requisite sensitivity for early-stage detection, thereby limiting improvements in patient survival rates. Methods: In this study, we developed an advanced Mass Spectrometry-based volatilomics platform, complemented by an enhanced breath sampler. The platform integrates artificial intelligence (AI)-assisted algorithms to detect multiple volatile organic compounds (VOCs) biomarkers in human breath. Subsequently, we applied this platform to analyze 364 clinical CRC and normal exhaled samples. Results: The diagnostic signatures, including 2-methyl, octane, and butyric acid, generated by the platform effectively discriminated CRC patients from normal controls with high sensitivity (89.7%), specificity (86.8%), and accuracy (AUC = 0.91). Furthermore, the metastatic signature correctly identified over 50% of metastatic patients who tested negative for carcinoembryonic antigen (CEA). Fecal validation indicated that elevated breath biomarkers correlated with an inflammatory response guided by Bacteroides fragilis in CRC. Conclusion: This study introduces a sophisticated AI-aided Mass Spectrometry-based platform capable of identifying novel and feasible breath biomarkers for early-stage CRC detection. The promising results position the platform as an efficient noninvasive screening test for clinical applications, offering potential advancements in early detection and improved survival rates for CRC patients.

Liu, Y., et al. (2024). "Use of an AI Score Combining Cancer Signs, Masking, and Risk to Select Patients for Supplemental Breast Cancer Screening." Radiology **311**(1): e232535.

Background Mammographic density measurements are used to identify patients who should undergo supplemental imaging for breast cancer detection, but artificial intelligence (AI) image analysis may be more effective. Purpose To assess whether AISmartDensity-an AI-based score integrating cancer signs, masking, and risk-surpasses measurements of mammographic density in identifying patients for supplemental breast imaging after a negative screening mammogram. Materials and Methods This retrospective study included randomly selected individuals who underwent screening mammography at Karolinska University Hospital between January 2008 and December 2015. The models in AISmartDensity were trained and

validated using nonoverlapping data. The ability of AISmartDensity to identify future cancer in patients with a negative screening mammogram was evaluated and compared with that of mammographic density models. Sensitivity and positive predictive value (PPV) were calculated for the top 8% of scores, mimicking the proportion of patients in the Breast Imaging Reporting and Data System "extremely dense" category. Model performance was evaluated using area under the receiver operating characteristic curve (AUC) and was compared using the DeLong test. Results The study population included 65 325 examinations (median patient age, 53 years [IQR, 47-62 years])-64 870 examinations in healthy patients and 455 examinations in patients with breast cancer diagnosed within 3 years of a negative screening mammogram. The AUC for detecting subsequent cancers was 0.72 and 0.61 ($P < .001$) for AISmartDensity and the best-performing density model (age-adjusted dense area), respectively. For examinations with scores in the top 8%, AISmartDensity identified 152 of 455 (33%) future cancers with a PPV of 2.91%, whereas the best-performing density model (age-adjusted dense area) identified 57 of 455 (13%) future cancers with a PPV of 1.09% ($P < .001$). AISmartDensity identified 32% (41 of 130) and 34% (111 of 325) of interval and next-round screen-detected cancers, whereas the best-performing density model (dense area) identified 16% (21 of 130) and 9% (30 of 325), respectively. Conclusion AISmartDensity, integrating cancer signs, masking, and risk, outperformed traditional density models in identifying patients for supplemental imaging after a negative screening mammogram. (c) RSNA, 2024 Supplemental material is available for this article. See also the editorial by Kim and Chang in this issue.

Liu, Y., et al. (2023). "AI-Powered Segmentation of Invasive Carcinoma Regions in Breast Cancer Immunohistochemical Whole-Slide Images." Cancers (Basel) **16**(1).

AIMS: The automation of quantitative evaluation for breast immunohistochemistry (IHC) plays a crucial role in reducing the workload of pathologists and enhancing the objectivity of diagnoses. However, current methods face challenges in achieving fully automated immunohistochemistry quantification due to the complexity of segmenting the tumor area into distinct ductal carcinoma in situ (DCIS) and invasive carcinoma (IC) regions. Moreover, the quantitative analysis of immunohistochemistry requires a specific focus on invasive carcinoma regions. METHODS AND RESULTS: In this study, we propose an innovative approach to automatically identify invasive carcinoma regions in breast cancer immunohistochemistry whole-slide images (WSIs). Our method leverages a neural network that combines multi-scale morphological features with boundary features, enabling precise segmentation of invasive carcinoma regions without the need for additional H&E and P63 staining slides. In addition, we introduced an advanced semi-supervised learning algorithm, allowing efficient training of the model using unlabeled data. To evaluate the effectiveness of our approach, we constructed a dataset consisting of 618 IHC-stained WSIs from 170 cases, including four types of staining (ER, PR, HER2, and Ki-67). Notably, the model demonstrated an impressive intersection over union (IoU) score exceeding 80% on the test set. Furthermore, to ascertain the practical utility of our model in IHC quantitative evaluation, we constructed a fully automated Ki-67 scoring system based on the model's predictions. Comparative experiments convincingly demonstrated that our system exhibited high consistency with the scores given by experienced pathologists. CONCLUSIONS: Our developed model excels in accurately distinguishing between DCIS and invasive carcinoma regions in breast cancer immunohistochemistry WSIs. This method paves the way for a clinically available, fully automated immunohistochemistry quantitative scoring system.

Lobanova, O. A., et al. (2024). "Artificial intelligence (AI) for tumor microenvironment (TME) and tumor budding (TB) identification in colorectal cancer (CRC) patients: A systematic review." J Pathol Inform **15**: 100353.

Evaluation of the parameters such as tumor microenvironment (TME) and tumor budding (TB) is one of the most important steps in colorectal cancer (CRC) diagnosis and cancer development prognosis. In recent years, artificial intelligence (AI) has been successfully used to solve such problems. In this paper, we summarize the latest data on the use of artificial intelligence to predict tumor microenvironment and tumor budding in histological scans of patients with colorectal cancer. We performed a systematic literature search using 2 databases (Medline and Scopus) with the following search terms: ("tumor microenvironment" OR "tumor budding") AND ("colorectal cancer" OR CRC) AND ("artificial intelligence" OR "machine learning " OR "deep learning"). During the analysis, we gathered from the articles performance scores such as sensitivity, specificity, and accuracy of identifying TME and TB using artificial intelligence. The systematic review showed that machine learning and deep learning successfully cope with the prediction of these parameters. The highest accuracy values in TB

and TME prediction were 97.7% and 97.3%, respectively. This review led us to the conclusion that AI platforms can already be used as diagnostic aids, which will greatly facilitate the work of pathologists in detection and estimation of TB and TME as instruments and second-opinion services. A key limitation in writing this systematic review was the heterogeneous use of performance metrics for machine learning models by different authors, as well as relatively small datasets used in some studies.

Logothetis, C. J., et al. (1994). "The clinical and biological study of androgen independent prostate cancer (AI PCa)." Semin Oncol **21**(5): 620-629.

Lombardo, R., et al. (2024). "Quality of information and appropriateness of Open AI outputs for prostate cancer." Prostate Cancer Prostatic Dis.

Chat-GPT, a natural language processing (NLP) tool created by Open-AI, can potentially be used as a quick source for obtaining information related to prostate cancer. This study aims to analyze the quality and appropriateness of Chat-GPT's responses to inquiries related to prostate cancer compared to those of the European Urology Association's (EAU) 2023 prostate cancer guidelines. Overall, 195 questions were prepared according to the recommendations gathered in the prostate cancer section of the EAU 2023 Guideline. All questions were systematically presented to Chat-GPT's August 3 Version, and two expert urologists independently assessed and assigned scores ranging from 1 to 4 to each response (1: completely correct, 2: correct but inadequate, 3: a mix of correct and misleading information, and 4: completely incorrect). Sub-analysis per chapter and per grade of recommendation were performed. Overall, 195 recommendations were evaluated. Overall, 50/195 (26%) were completely correct, 51/195 (26%) correct but inadequate, 47/195 (24%) a mix of correct and misleading and 47/195 (24%) incorrect. When looking at different chapters Open AI was particularly accurate in answering questions on follow-up and QoL. Worst performance was recorded for the diagnosis and treatment chapters with respectively 19% and 30% of the answers completely incorrect. When looking at the strength of recommendation, no differences in terms of accuracy were recorded when comparing weak and strong recommendations ($p > 0,05$). Chat-GPT has a poor accuracy when answering questions on the PCa EAU guidelines recommendations. Future studies should assess its performance after adequate training.

Lorkowski, S. W., et al. (2024). "The practical utility of AI-assisted molecular profiling in the diagnosis and management of cancer of unknown primary: an updated review." Virchows Arch **484**(2): 369-375.

Cancer of unknown primary (CUP) presents a complex diagnostic challenge, characterized by metastatic tumors of unknown tissue origin and a dismal prognosis. This review delves into the emerging significance of artificial intelligence (AI) and machine learning (ML) in transforming the landscape of CUP diagnosis, classification, and treatment. ML approaches, trained on extensive molecular profiling data, have shown promise in accurately predicting tissue of origin. Genomic profiling, encompassing driver mutations and copy number variations, plays a pivotal role in CUP diagnosis by providing insights into tumor type-specific oncogenic alterations. Mutational signatures (MS), reflecting somatic mutation patterns, offer further insights into CUP diagnosis. Known MS with established etiology, such as ultraviolet (UV) light-induced DNA damage and tobacco exposure, have been identified in cases of dedifferentiated/transdifferentiated melanoma and carcinoma. Deep learning models that integrate gene expression data and DNA methylation patterns offer insights into tissue lineage and tumor classification. In digital pathology, machine learning algorithms analyze whole-slide images to aid in CUP classification. Finally, precision oncology, guided by molecular profiling, offers targeted therapies independent of primary tissue identification. Clinical trials assigning CUP patients to molecularly guided therapies, including targetable alterations and tumor mutation burden as an immunotherapy biomarker, have resulted in improved overall survival in a subset of patients. In conclusion, AI- and ML-driven approaches are revolutionizing CUP management by enhancing diagnostic accuracy. Precision oncology utilizing enhanced molecular profiling facilitates the identification of targeted therapies that transcend the need to identify the tissue of origin, ultimately improving patient outcomes.

Lu, S., et al. (1999). "Molecular mechanisms of androgen-independent growth of human prostate cancer LNCaP-AI cells." Endocrinology **140**(11): 5054-5059.

The goal of this study is to investigate the molecular mechanisms of androgen-independent growth in prostate cancer. We have established an androgen-independent prostatic carcinoma LNCaP-AI (defined as a LNCaP cell line that is capable of growing in charcoal-stripped serum) from the androgen-dependent LNCaP-FGC cells. In contrast to the androgen-independent PC-3 human prostate cancer cells, LNCaP-AI cells still express a similar level of androgen receptor as their parental cells and

are sensitive to androgen stimulation. Compared with the parental LNCaP-FGC cells, LNCaP-AI cells are more resistant to apoptosis induced by 12-O-tetradecanoylphorbol-13-acetate and express a much higher level of antiapoptotic gene bcl-2 and cyclin-dependent kinase inhibitor p21, which may confer an enhanced antiapoptosis phenotype. On the other hand, expression of cyclin-dependent kinase inhibitor p16 is significantly reduced in the LNCaP-AI cells, implying the release of an inhibitory effect of p16 on cell cycle progression. Taken together, our results suggest that multiple factors contribute to the development of androgen-independent growth of prostatic carcinoma cells, including enhancement of cell antiapoptosis function, release of cell cycle inhibition, and stimulation of cell proliferation by alternative signaling pathways.

Lu, W., et al. (2024). "AI-based intra-tumor heterogeneity score of Ki67 expression as a prognostic marker for early-stage ER+/HER2- breast cancer." J Pathol Clin Res **10**(1): e346.

Early-stage estrogen receptor positive and human epidermal growth factor receptor negative (ER+/HER2-) luminal breast cancer (BC) is quite heterogeneous and accounts for about 70% of all BCs. Ki67 is a proliferation marker that has a significant prognostic value in luminal BC despite the challenges in its assessment. There is increasing evidence that spatial colocalization, which measures the evenness of different types of cells, is clinically important in several types of cancer. However, reproducible quantification of intra-tumor spatial heterogeneity remains largely unexplored. We propose an automated pipeline for prognostication of luminal BC based on the analysis of spatial distribution of Ki67 expression in tumor cells using a large well-characterized cohort (n = 2,081). The proposed Ki67 colocalization (Ki67CL) score can stratify ER+/HER2- BC patients with high significance in terms of BC-specific survival ($p < 0.00001$) and distant metastasis-free survival ($p = 0.0048$). Ki67CL score is shown to be highly significant compared with the standard Ki67 index. In addition, we show that the proposed Ki67CL score can help identify luminal BC patients who can potentially benefit from adjuvant chemotherapy.

Lv, T., et al. (2024). "AI-powered interpretable imaging phenotypes noninvasively characterize tumor microenvironment associated with diverse molecular signatures and survival in breast cancer." Comput Methods Programs Biomed **243**: 107857.

BACKGROUND AND OBJECTIVES: Tumor microenvironment (TME) is a determining factor in decision-making and personalized treatment for breast cancer, which is highly intra-tumor heterogeneous (ITH). However, the noninvasive imaging phenotypes of TME are poorly understood, even invasive genotypes have been largely known in breast cancer. METHODS: Here, we develop an artificial intelligence (AI)-driven approach for noninvasively characterizing TME by integrating the predictive power of deep learning with the explainability of human-interpretable imaging phenotypes (IMPs) derived from 4D dynamic imaging (DCE-MRI) of 342 breast tumors linked to genomic and clinical data, which connect cancer phenotypes to genotypes. An unsupervised dual-attention deep graph clustering model (DGCLM) is developed to divide bulk tumor into multiple spatially segregated and phenotypically consistent subclusters. The IMPs ranging from spatial heterogeneity to kinetic heterogeneity are leveraged to capture architecture, interaction, and proximity between intratumoral subclusters. RESULTS: We demonstrate that our IMPs correlate with well-known markers of TME and also can predict distinct molecular signatures, including expression of hormone receptor, epithelial growth factor receptor and immune checkpoint proteins, with the performance of accuracy, reliability and transparency superior to recent state-of-the-art radiomics and 'black-box' deep learning methods. Moreover, prognostic value is confirmed by survival analysis accounting for IMPs. CONCLUSIONS: Our approach provides an interpretable, quantitative, and comprehensive perspective to characterize TME in a noninvasive and clinically relevant manner.

Lynch, M. (2024). "Beyond the Algorithm: Ethical Challenges in AI-Driven Skin Cancer Diagnosis." Br J Dermatol.

Magalhaes, C., et al. (2019). "The role of AI classifiers in skin cancer images." Skin Res Technol **25**(5): 750-757.

BACKGROUND: The use of different imaging modalities to assist in skin cancer diagnosis is a common practice in clinical scenarios. Different features representative of the lesion under evaluation can be retrieved from image analysis and processing. However, the integration and understanding of these additional parameters can be a challenging task for physicians, so artificial intelligence (AI) methods can be implemented to assist in this process. This bibliographic research was performed with the goal of assessing the current applications of AI algorithms as an assistive tool in skin cancer diagnosis, based on information retrieved from different imaging modalities. MATERIALS AND METHODS: The bibliography databases ISI Web of Science, PubMed

and Scopus were used for the literature search, with the combination of keywords: skin cancer, skin neoplasm, imaging and classification methods. RESULTS: The search resulted in 526 publications, which underwent a screening process, considering the established eligibility criteria. After screening, only 65 were qualified for revision. CONCLUSION: Different imaging modalities have already been coupled with AI methods, particularly dermoscopy for melanoma recognition. Learners based on support vector machines seem to be the preferred option. Future work should focus on image analysis, processing stages and image fusion assuring the best possible classification outcome.

Mammas, C. S., et al. (2022). "Remote AI Supported E-Multidisciplinary Oncology Conference in Breast Cancer as a Technology and Method to Optimize Outcomes in the Peripheries." Stud Health Technol Inform **289**: 309-312.

AIM: Feasibility-reliability control of Telemedicine Systems (TS) integrated with Multimedia Systems (MS) and Artificial intelligence (AI) for remote e-Multidisciplinary Oncology Conference in Breast Cancer. MATERIAL AND METHODS: Forty (n1=40) patients suffering from breast surgical oncology malignant (n2=32) and non-malignant (n3=8) diseases classified to seven categories: Nipple Discharge, Dominant Breast Mass, Occult Breast Lesion, Early Breast Carcinoma, Advanced Breast Carcinoma, Recurrent Breast Carcinoma) and treated clinically with the standard diagnostic (Mammography, US, MRI, Cytology, Pathology, BRCA1/2 Mutation Predisposition and Breast Cancer Risk Analysis) surgical, auxiliary therapeutic methods. Then clinical decisions compared to those proposed remotely by the virtual AI supported e-Oncology Conference for each patient. RESULTS: In four (n4=4) out of forty patients (TS, MS and AI) supported decision making and surgical treatment proposal including postoperative Radiotherapy proposal was not as clear as expected. Non-output answer for non-malignant breast pathologies (n3=8) was accurately indicated by (MS and AI). Mean accuracy of (TS, MS and AI) for: 1.Surgical Operative Planning including Rad=94.1%, 2.Chem=96.8%, 3.Horm=96.7% [In 95%, (Confidence interval: 85-99%)]. CONCLUSION: High feasibility-reliability of the virtual AI supported e-Multidisciplinary Oncology Conference for remote decision making and surgical planning and for optimum outcomes in Breast Cancer treatment makes it a clinical necessity especially for the periphery of Hellas.

Mamounas, E. P., et al. (2006). "NSABP B-42: a clinical trial to determine the efficacy of five years of letrozole compared with placebo in patients completing five years of hormonal therapy consisting of an aromatase inhibitor (AI) or tamoxifen followed by an AI in prolonging disease-free survival in postmenopausal women with hormone receptor-positive breast cancer." Clin Breast Cancer **7**(5): 416-421.

Maouche, I., et al. (2023). "An Explainable AI Approach for Breast Cancer Metastasis Prediction Based on Clinicopathological Data." IEEE Trans Biomed Eng **70**(12): 3321-3329.

OBJECTIVE: Breast Cancer is the most prevalent cancer and the first cause of cancer deaths among women worldwide. In 90% of the cases, mortality is related to distant metastasis. Computer-aided prognosis systems using machine learning models have been widely used to predict breast cancer metastasis. Despite that, these systems still face several challenges. First, the models are generally biased toward the majority class due to datasets unbalance. Second, their increased complexity is associated with decreased interpretability which causes clinicians to distrust their prognosis. METHODS: To tackle these issues, we have proposed an explainable approach for predicting breast cancer metastasis using clinicopathological data. Our approach is based on cost-sensitive CatBoost classifier and utilises LIME explainer to provide patient-level explanations. RESULTS: We used a public dataset of 716 breast cancer patients to assess our approach. The results demonstrate the superiority of cost-sensitive CatBoost in precision (76.5%), recall (79.5%), and f1-score (77%) over classical and boosting models. The LIME explainer was used to quantify the impact of patient and treatment characteristics on breast cancer metastasis, revealing that they have different impacts ranging from high impact like the non-use of adjuvant chemotherapy, and moderate impact including carcinoma with medullary features histological type, to low impact like oral contraception use. The code is available at https://github.com/IkramMaouche/CS-CatBoost
Conclusion: Our approach serves as a first step toward introducing more efficient and explainable computer-aided prognosis systems for breast cancer metastasis prediction. SIGNIFICANCE: This approach could help clinicians understand the factors behind metastasis and assist them in proposing more patient-specific therapeutic decisions.

Marchi, F., et al. (2024). "Exploring the landscape of AI-assisted decision-making in head and neck cancer treatment: a comparative analysis of NCCN

guidelines and ChatGPT responses." Eur Arch Otorhinolaryngol **281**(4): 2123-2136.

PURPOSE: Recent breakthroughs in natural language processing and machine learning, exemplified by ChatGPT, have spurred a paradigm shift in healthcare. Released by OpenAI in November 2022, ChatGPT rapidly gained global attention. Trained on massive text datasets, this large language model holds immense potential to revolutionize healthcare. However, existing literature often overlooks the need for rigorous validation and real-world applicability. METHODS: This head-to-head comparative study assesses ChatGPT's capabilities in providing therapeutic recommendations for head and neck cancers. Simulating every NCCN Guidelines scenarios. ChatGPT is queried on primary treatments, adjuvant treatment, and follow-up, with responses compared to the NCCN Guidelines. Performance metrics, including sensitivity, specificity, and F1 score, are employed for assessment. RESULTS: The study includes 68 hypothetical cases and 204 clinical scenarios. ChatGPT exhibits promising capabilities in addressing NCCN-related queries, achieving high sensitivity and overall accuracy across primary treatment, adjuvant treatment, and follow-up. The study's metrics showcase robustness in providing relevant suggestions. However, a few inaccuracies are noted, especially in primary treatment scenarios. CONCLUSION: Our study highlights the proficiency of ChatGPT in providing treatment suggestions. The model's alignment with the NCCN Guidelines sets the stage for a nuanced exploration of AI's evolving role in oncological decision support. However, challenges related to the interpretability of AI in clinical decision-making and the importance of clinicians understanding the underlying principles of AI models remain unexplored. As AI continues to advance, collaborative efforts between models and medical experts are deemed essential for unlocking new frontiers in personalized cancer care.

Marcinkiewicz, A. M., et al. (2024). "AI for Multistructure Incidental Findings and Mortality Prediction at Chest CT in Lung Cancer Screening." Radiology **312**(3): e240541.

Background Incidental extrapulmonary findings are commonly detected on chest CT scans and can be clinically important. Purpose To integrate artificial intelligence (AI)-based segmentation for multiple structures, coronary artery calcium (CAC), and epicardial adipose tissue with automated feature extraction methods and machine learning to detect extrapulmonary abnormalities and predict all-cause mortality (ACM) in a large multicenter cohort. Materials and Methods In this post hoc analysis, baseline chest CT scans in patients enrolled in the National Lung Screening Trial (NLST) from August 2002 to September 2007 were included from 33 participating sites. Per scan, 32 structures were segmented with a multistructure model. For each structure, 15 clinically interpretable radiomic features were quantified. Four general codes describing abnormalities reported by NLST radiologists were applied to identify extrapulmonary significant incidental findings on the CT scans. Death at 2-year and 10-year follow-up and the presence of extrapulmonary significant incidental findings were predicted with ensemble AI models, and individualized structure risk scores were evaluated. Area under the receiver operating characteristic curve (AUC) analysis was used to evaluate the performance of the models for prediction of ACM and extrapulmonary significant incidental findings. The Pearson chi(2) test and Kruskal-Wallis rank sum test were used for statistical analyses. Results A total of 24 401 participants (median age, 61 years [IQR, 57-65 years]; 14 468 male) were included. In 3880 of 24 401 participants (16%), 4283 extrapulmonary significant incidental findings were reported. During the 10-year follow-up, 3389 of 24 401 participants (14%) died. CAC had the highest feature importance for predicting the three study end points. The 10-year ACM model demonstrated the best AUC performance (0.72; per-year mortality of 2.6% above and 0.8% below the risk threshold), followed by 2-year ACM (0.71; per-year mortality of 1.13% above and 0.3% below the risk threshold) and prediction of extrapulmonary significant incidental findings (0.70; probability of occurrence of 25.4% above and 9.6% below the threshold). Conclusion A fully automated AI model indicated extrapulmonary structures at risk on chest CT scans and predicted ACM with explanations. ClinicalTrials.gov Identifier: NCT00047385 (c) RSNA, 2024 Supplemental material is available for this article. See also the editorial by Yanagawa and Hata in this issue.

Marinovich, M. L., et al. (2023). "Artificial intelligence (AI) for breast cancer screening: BreastScreen population-based cohort study of cancer detection." EBioMedicine **90**: 104498.

BACKGROUND: Artificial intelligence (AI) has been proposed to reduce false-positive screens, increase cancer detection rates (CDRs), and address resourcing challenges faced by breast screening programs. We compared the accuracy of AI versus radiologists in real-world population breast cancer screening, and estimated potential impacts on CDR, recall and workload for simulated AI-radiologist reading. METHODS: External validation of a commercially-available AI algorithm in a retrospective cohort of 108,970 consecutive

mammograms from a population-based screening program, with ascertained outcomes (including interval cancers by registry linkage). Area under the ROC curve (AUC), sensitivity and specificity for AI were compared with radiologists who interpreted the screens in practice. CDR and recall were estimated for simulated AI-radiologist reading (with arbitration) and compared with program metrics. FINDINGS: The AUC for AI was 0.83 compared with 0.93 for radiologists. At a prospective threshold, sensitivity for AI (0.67; 95% CI: 0.64-0.70) was comparable to radiologists (0.68; 95% CI: 0.66-0.71) with lower specificity (0.81 [95% CI: 0.81-0.81] versus 0.97 [95% CI: 0.97-0.97]). Recall rate for AI-radiologist reading (3.14%) was significantly lower than for the BSWA program (3.38%) (-0.25%; 95% CI: -0.31 to -0.18; P < 0.001). CDR was also lower (6.37 versus 6.97 per 1000) (-0.61; 95% CI: -0.77 to -0.44; P < 0.001); however, AI detected interval cancers that were not found by radiologists (0.72 per 1000; 95% CI: 0.57-0.90). AI-radiologist reading increased arbitration but decreased overall screen-reading volume by 41.4% (95% CI: 41.2-41.6). INTERPRETATION: Replacement of one radiologist by AI (with arbitration) resulted in lower recall and overall screen-reading volume. There was a small reduction in CDR for AI-radiologist reading. AI detected interval cases that were not identified by radiologists, suggesting potentially higher CDR if radiologists were unblinded to AI findings. These results indicate AI's potential role as a screen-reader of mammograms, but prospective trials are required to determine whether CDR could improve if AI detection was actioned in double-reading with arbitration. FUNDING: National Breast Cancer Foundation (NBCF), National Health and Medical Research Council (NHMRC).

Marinovich, M. L., et al. (2022). "Artificial intelligence (AI) to enhance breast cancer screening: protocol for population-based cohort study of cancer detection." BMJ Open **12**(1): e054005.

INTRODUCTION: Arti fi cial intelligence (AI) algorithms for interpreting mammograms have the potential to improve the effectiveness of population breast cancer screening programmes if they can detect cancers, including interval cancers, without contributing substantially to overdiagnosis. Studies suggesting that AI has comparable or greater accuracy than radiologists commonly employ 'enriched' datasets in which cancer prevalence is higher than in population screening. Routine screening outcome metrics (cancer detection and recall rates) cannot be estimated from these datasets, and accuracy estimates may be subject to spectrum bias which limits generalisabilty to real-world screening. We aim to address these limitations by comparing the accuracy of AI and radiologists in a cohort of consecutive of women attending a real-world population breast cancer screening programme. METHODS AND ANALYSIS: A retrospective, consecutive cohort of digital mammography screens from 109 000 distinct women was assembled from BreastScreen WA (BSWA), Western Australia's biennial population screening programme, from November 2016 to December 2017. The cohort includes 761 screen-detected and 235 interval cancers. Descriptive characteristics and results of radiologist double-reading will be extracted from BSWA outcomes data collection. Mammograms will be reinterpreted by a commercial AI algorithm (DeepHealth). AI accuracy will be compared with that of radiologist single-reading based on the di ff erence in the area under the receiver operating characteristic curve. Cancer detection and recall rates for combined AI-radiologist reading will be estimated by pairing the first radiologist read per screen with the AI algorithm, and compared with estimates for radiologist double-reading. ETHICS AND DISSEMINATION: This study has ethical approval from the Women and Newborn Health Service Ethics Committee (EC00350) and the Curtin University Human Research Ethics Committee (HRE2020-0316). Findings will be published in peer-reviewed journals and presented at national and international conferences. Results will also be disseminated to stakeholders in Australian breast cancer screening programmes and policy makers in population screening.

Markopoulos, C. J. (2010). "Minimizing early relapse and maximizing treatment outcomes in hormone-sensitive postmenopausal breast cancer: efficacy review of AI trials." Cancer Metastasis Rev **29**(4): 581-594.

Breast cancer is one of the leading causes of cancer-related deaths in women. Regardless of prognosis, all women with breast cancer are at risk for early recurrence. Nearly 50% of early recurrences occur within 5 years of surgery, and they peak at 2 years after surgery in women treated with adjuvant tamoxifen. Most early recurrences are distant metastases, which strongly correlate with increased mortality. Treatments that mitigate the risk of early distant metastases (DM) are, therefore, likely to improve overall survival in women with early breast cancer (EBC). Aromatase inhibitors (AIs)--anastrozole, letrozole, and exemestane-have been investigated as alternatives to tamoxifen for adjuvant treatment of hormone receptor-positive (HR+) EBC in postmenopausal women (PMW). AIs are better at minimizing risk of early relapse compared with

tamoxifen. However, it is not clear if preferential use of AIs over tamoxifen will benefit all PMW with HR+ EBC. The ability to subtype HR+ breast cancer on the basis of biomarkers predictive of response to AIs and tamoxifen would likely be key to determining the most beneficial hormonal treatment within patient subpopulations, but this process requires thorough investigation. Until then, adjuvant therapies that provide the greatest reduction in risk of DM should be considered for all PMW with HR+ EBC. This article reviews the clinical trials of AI adjuvant therapies for hormone-sensitive breast cancer, particularly in the context of how they compare with tamoxifen in minimizing the risk of relapse, occurrence of DM, and breast cancer-related deaths.

Marsden, H., et al. (2023). "Effectiveness of an image analyzing AI-based Digital Health Technology to identify Non-Melanoma Skin Cancer and other skin lesions: results of the DERM-003 study." Front Med (Lausanne) **10**: 1288521.

INTRODUCTION: Identification of skin cancer by an Artificial Intelligence (AI)-based Digital Health Technology could help improve the triage and management of suspicious skin lesions. METHODS: The DERM-003 study (NCT04116983) was a prospective, multi-center, single-arm, masked study that aimed to demonstrate the effectiveness of an AI as a Medical Device (AIaMD) to identify Squamous Cell Carcinoma (SCC), Basal Cell Carcinoma (BCC), pre-malignant and benign lesions from dermoscopic images of suspicious skin lesions. Suspicious skin lesions that were suitable for photography were photographed with 3 smartphone cameras (iPhone 6S, iPhone 11, Samsung 10) with a DL1 dermoscopic lens attachment. Dermatologists provided clinical diagnoses and histopathology results were obtained for biopsied lesions. Each image was assessed by the AIaMD and the output compared to the ground truth diagnosis. RESULTS: 572 patients (49.5% female, mean age 68.5 years, 96.9% Fitzpatrick skin types I-III) were recruited from 4 UK NHS Trusts, providing images of 611 suspicious lesions. 395 (64.6%) lesions were biopsied; 47 (11%) were diagnosed as SCC and 184 (44%) as BCC. The AIaMD AUROC on images taken by iPhone 6S was 0.88 (95% CI: 0.83-0.93) for SCC and 0.87 (95% CI: 0.84-0.91) for BCC. For Samsung 10 the AUROCs were 0.85 (95% CI: 0.79-0.90) and 0.87 (95% CI, 0.83-0.90), and for the iPhone 11 they were 0.88 (95% CI, 0.84-0.93) and 0.89 (95% CI, 0.86-0.92) for SCC and BCC, respectively. Using pre-determined diagnostic thresholds on images taken on the iPhone 6S the AIaMD achieved a sensitivity and specificity of 98% (95% CI, 88-100%) and 38% (95% CI, 33-44%) for SCC; and 94% (95% CI, 90-97%) and 28% (95 CI, 21-35%) for BCC. All 16 lesions diagnosed as melanoma in the study were correctly classified by the AIaMD. DISCUSSION: The AIaMD has the potential to support the timely diagnosis of malignant and premalignant skin lesions.

Masone, M. C. (2023). "Using AI to assist pathologists in bladder cancer metastases detection." Nat Rev Urol **20**(5): 262.

Massarweh, S., et al. (2014). "A phase II study of combined fulvestrant and everolimus in patients with metastatic estrogen receptor (ER)-positive breast cancer after aromatase inhibitor (AI) failure." Breast Cancer Res Treat **143**(2): 325-332.

Fulvestrant, which degrades ER, is used after AI failure in metastatic breast cancer but resistance develops quickly. We hypothesized that using everolimus to inhibit mTOR, a key signaling pathway in endocrine resistance, may delay fulvestrant resistance in patients and thus improve its efficacy. We conducted a phase II trial of combined fulvestrant and everolimus in postmenopausal women with disease progression or relapse after an AI. Primary endpoint was time to progression (TTP) and secondary endpoints included objective response rate, clinical benefit rate (CBR), safety, and biomarker correlates. Tumor blocks were collected and biopsy of accessible tumor was done for future biomarker analysis. Of 33 patients enrolled two were ruled ineligible after enrollment and were excluded from study analysis, for a total of 31 evaluable patients. Median age was 54 years (range 45-85). Prior therapy included tamoxifen (81 %), chemotherapy (71 %), with 26 % of patients having received 3 or more endocrine agents. Median TTP was 7.4 months (95 % CI 1.9-12.1) with an objective response rate of 13 % and CBR of 49 %. Of particular note, 32 % of patients exhibited de novo resistance to study treatment with disease progression as their best response. Most common adverse events (AEs) were elevated AST (87 %) and ALT (77 %), anemia (74 %), hyperglycemia (71 %), and hypercholesterolemia (68 %). Prominent clinical toxicities were mucositis (58 %), weight loss (48 %), and rash (42 %). Most AEs were grade 1 or 2 and largely reversible with infrequent need for everolimus dose reduction. To conclude, everolimus plus fulvestrant is effective after AI failure in heavily pretreated metastatic ER-positive breast cancer and has manageable toxicity. Further study of this combination is warranted in randomized studies. Since not all patients experience benefit, and in view of potential toxicities, biomarker examination is critical to help select patients most likely to benefit

from this strategy in future studies.

Masud, S. F., et al. (2024). "U.S. payer budget impact of using an AI-augmented cancer risk discrimination digital histopathology platform to identify high-risk of recurrence in women with early-stage invasive breast cancer." J Med Econ **27**(1): 972-981.

AIMS: Use of gene expression signatures to predict adjuvant chemotherapy benefit in women with early-stage breast cancer is increasing. However, high cost, limited access, and eligibility for these tests results in the adoption of less precise assessment approaches. This study evaluates the cost impact of PreciseDx Breast (PDxBr), an AI-augmented histopathology platform that assesses the 6-year risk of recurrence in early-stage invasive breast cancer patients to help improve informed use of adjuvant chemotherapy. MATERIALS AND METHODS: A decision-tree Markov model was developed to compare the costs of treatment guided by standard of care (SOC) risk assessment (i.e. clinical diagnostic workup with or without Oncotype DX) versus PDxBr with SOC in a hypothetical cohort of U.S. women with early-stage invasive breast cancer. A commercial payer perspective compares costs of testing, adjuvant therapy, recurrence, adverse events, surveillance, and end-of-life care. RESULTS: PDxBr use in prognostic evaluation resulted in savings of $4 million (M) in year one compared to current SOC in 1 M females members. Over 6-years, savings increased to $12.5 M. The per-treated patient costs in year one amounted to $19.5 thousand (K) for SOC and $16.9K for PDxBr. LIMITATIONS: For simplicity, recurrence was not specified. We performed scenario analyses to account for variations in rates for local, regional, and distant recurrence. Second, a recurrent patient incurs the total cost of treated recurrence in the first year and goes back to remission or death. Third, CDK4/6i treatment is only incorporated in the recurrence costs but not in the first line of treatment for early-stage breast cancer due to limited data. CONCLUSIONS: Sensitivity analyses demonstrated robust overall savings to changes in all variables in the model. The use of PDxBr to assess breast cancer recurrence risk has the potential to fill gaps in care and reduce costs when gene expression signatures are not available.

Mazidi, M., et al. (2020). "Apolipoprotein B/Apolipoprotein A-I Ratio Is a Better Predictor of Cancer Mortality Compared with C-Reactive Protein: Results from Two Multi-Ethnic US Populations." J Clin Med **9**(1).

BACKGROUND: There is a lack of evidence regarding the link between apolipoproteins and cancer mortality. By using two nationally representative samples of US adults, we prospectively evaluated the associations between apolipoprotein B (apoB) levels and apoB/apoA-I ratio with cancer mortality. We also examined the role of C-reactive protein (CRP) in these associations. MATERIALS AND METHODS: Adults aged >/=20 years, enrolled in the 3rd National Health and Nutrition Examination Survey (NHANES III, 1988-1994) and continuous NHANES (2005-2010), and followed up to 31 December 2011, were included in the analysis. Multiple Cox regressions were applied to evaluate the associations between the variables of interest and cancer mortality. RESULTS: Overall, 7695 participants were included (mean age: 49.2 years; 50.4% men, median follow-up: 19.1 years). In the fully adjusted model, participants in the highest quartile (Q4) of apoB/apoA-I had a significantly greater risk for cancer mortality (hazard ratio (HR): 1.40; 95% confidence interval (CI): 1.25-1.93) compared with those in the first quartile (Q1). In the same model, a positive and significant association between apoB levels and cancer mortality was observed for individuals in Q3 (HR: 1.12; 95% CI: 1.09-1.16) and Q4 (HR: 1.17; 95% CI: 1.09-1.25) compared with those in Q1. When CRP levels were added in the analysis, the apoB/apoA-I ratio, but not apoB levels, remained significantly related to cancer mortality (Q4 = HR: 1.17; 95% CI: 1.09-1.25). In contrast, CRP levels were not able to predict cancer death after correction for apoB/apoA-I ratio. CONCLUSIONS: In a large representative sample of the US adult population, the apoB/apoA-I ratio and apoB levels significantly predicted cancer mortality, independently of several cardiometabolic risk factors. The predictive value of apoB/apoA-I, but not apoB levels, remained significant after taking into account CRP, whereas CRP was not associated with cancer mortality after adjustment for apoB/apoA-I ratio. If further evidence supports our findings, apoA-I and apoB measurements could be considered in general healthcare policies.

McKinney, S. M., et al. (2020). "International evaluation of an AI system for breast cancer screening." Nature **577**(7788): 89-94.

Screening mammography aims to identify breast cancer at earlier stages of the disease, when treatment can be more successful(1). Despite the existence of screening programmes worldwide, the interpretation of mammograms is affected by high rates of false positives and false negatives(2). Here we present an artificial intelligence (AI) system that is capable of surpassing human experts in breast cancer prediction. To assess its performance in the clinical setting, we curated a large representative dataset from the UK and a large enriched dataset

from the USA. We show an absolute reduction of 5.7% and 1.2% (USA and UK) in false positives and 9.4% and 2.7% in false negatives. We provide evidence of the ability of the system to generalize from the UK to the USA. In an independent study of six radiologists, the AI system outperformed all of the human readers: the area under the receiver operating characteristic curve (AUC-ROC) for the AI system was greater than the AUC-ROC for the average radiologist by an absolute margin of 11.5%. We ran a simulation in which the AI system participated in the double-reading process that is used in the UK, and found that the AI system maintained non-inferior performance and reduced the workload of the second reader by 88%. This robust assessment of the AI system paves the way for clinical trials to improve the accuracy and efficiency of breast cancer screening.

McNaughton, M., et al. (2016). "Proteasomal degradation of sphingosine kinase 1 and inhibition of dihydroceramide desaturase by the sphingosine kinase inhibitors, SKi or ABC294640, induces growth arrest in androgen-independent LNCaP-AI prostate cancer cells." Oncotarget **7**(13): 16663-16675.

Sphingosine kinases (two isoforms termed SK1 and SK2) catalyse the formation of the bioactive lipid sphingosine 1-phosphate. We demonstrate here that the SK2 inhibitor, ABC294640 (3-(4-chlorophenyl)-adamantane-1-carboxylic acid (pyridin-4-ylmethyl)amide) or the SK1/SK2 inhibitor, SKi (2-(p-hydroxyanilino)-4-(p-chlorophenyl)thiazole)) induce the proteasomal degradation of SK1a (Mr = 42 kDa) and inhibit DNA synthesis in androgen-independent LNCaP-AI prostate cancer cells. These effects are recapitulated by the dihydroceramide desaturase (Des1) inhibitor, fenretinide. Moreover, SKi or ABC294640 reduce Des1 activity in Jurkat cells and ABC294640 induces the proteasomal degradation of Des1 (Mr = 38 kDa) in LNCaP-AI prostate cancer cells. Furthermore, SKi or ABC294640 or fenretinide increase the expression of the senescence markers, p53 and p21 in LNCaP-AI prostate cancer cells. The siRNA knockdown of SK1 or SK2 failed to increase p53 and p21 expression, but the former did reduce DNA synthesis in LNCaP-AI prostate cancer cells. Moreover, N-acetylcysteine (reactive oxygen species scavenger) blocked the SK inhibitor-induced increase in p21 and p53 expression but had no effect on the proteasomal degradation of SK1a. In addition, siRNA knockdown of Des1 increased p53 expression while a combination of Des1/SK1 siRNA increased the expression of p21. Therefore, Des1 and SK1 participate in regulating LNCaP-AI prostate cancer cell growth and this involves p53/p21-dependent and -independent pathways. Therefore, we propose targeting androgen-independent prostate cancer cells with compounds that affect Des1/SK1 to modulate both de novo and sphingolipid rheostat pathways in order to induce growth arrest.

Medina-Echeverz, J., et al. (2015). "Overexpression of apolipoprotein A-I fused to an anti-transforming growth factor beta peptide modulates the tumorigenicity and immunogenicity of mouse colon cancer cells." Cancer Immunol Immunother **64**(6): 717-725.

Transforming growth factor beta (TGF-beta) promotes tumor growth, invasion and metastasis in established tumors. In this study, we analyzed the effect of overexpressing an anti-TGF-beta peptide fused to apolipoprotein A-I (ApoA-I) as a scaffold molecule. We generated and characterized stable MC38 colon carcinoma clones expressing ApoA-I fused to the anti-TGF-beta peptide P144 and ApoA-I as control cells. We evaluated in vitro the gene expression profile, cell cycle and anchorage-independent growth. The in vivo tumorigenic potential and immunogenicity were analyzed inoculating the MC38 clones into C57BL/6 mice, recombination-activating gene 1 knockout mice or mice deficient in NK cells either subcutaneously or intrasplenically to generate hepatic metastases. While overexpression of ApoA-I had no effect on the parameters analyzed, ApoA-I fused to P144 markedly diminished the tumorigenic capacity and metastatic potential of MC38 in vitro and in vivo, thus generating a highly immunogenic cell line. MC38 cells transfected with ApoA-I fused to P144 triggered memory T cell responses able to eliminate the parental cell line upon re-challenge. In summary, expression of ApoA-I fused to P144 is a novel strategy to modulate TGF-beta in tumor cells. These results highlight the potential of TGF-beta as a target in the development of new antitumor treatments.

Melarkode, N., et al. (2023). "AI-Powered Diagnosis of Skin Cancer: A Contemporary Review, Open Challenges and Future Research Directions." Cancers (Basel) **15**(4).

Skin cancer continues to remain one of the major healthcare issues across the globe. If diagnosed early, skin cancer can be treated successfully. While early diagnosis is paramount for an effective cure for cancer, the current process requires the involvement of skin cancer specialists, which makes it an expensive procedure and not easily available and affordable in developing countries. This dearth of skin cancer specialists has given rise to the need to develop automated diagnosis systems. In this context, Artificial Intelligence (AI)-based methods have been

proposed. These systems can assist in the early detection of skin cancer and can consequently lower its morbidity, and, in turn, alleviate the mortality rate associated with it. Machine learning and deep learning are branches of AI that deal with statistical modeling and inference, which progressively learn from data fed into them to predict desired objectives and characteristics. This survey focuses on Machine Learning and Deep Learning techniques deployed in the field of skin cancer diagnosis, while maintaining a balance between both techniques. A comparison is made to widely used datasets and prevalent review papers, discussing automated skin cancer diagnosis. The study also discusses the insights and lessons yielded by the prior works. The survey culminates with future direction and scope, which will subsequently help in addressing the challenges faced within automated skin cancer diagnosis.

Mendes, J., et al. (2022). "AI in Breast Cancer Imaging: A Survey of Different Applications." J Imaging **8**(9).

Breast cancer was the most diagnosed cancer in 2020. Several thousand women continue to die from this disease. A better and earlier diagnosis may be of great importance to improving prognosis, and that is where Artificial Intelligence (AI) could play a major role. This paper surveys different applications of AI in Breast Imaging. First, traditional Machine Learning and Deep Learning methods that can detect the presence of a lesion and classify it into benign/malignant-which could be important to diminish reading time and improve accuracy-are analyzed. Following that, researches in the field of breast cancer risk prediction using mammograms-which may be able to allow screening programs customization both on periodicity and modality-are reviewed. The subsequent section analyzes different applications of augmentation techniques that allow to surpass the lack of labeled data. Finally, still concerning the absence of big datasets with labeled data, the last section studies Self-Supervised learning, where AI models are able to learn a representation of the input by themselves. This review gives a general view of what AI can give in the field of Breast Imaging, discussing not only its potential but also the challenges that still have to be overcome.

Menon, T., et al. (2023). "Targeted therapies in non-small cell lung cancer and the potential role of AI interventions in cancer treatment." Biotechnol Appl Biochem **70**(1): 344-356.

Non-small cell lung cancer is the most prevalent lung cancer, and almost three-fourths of patients are diagnosed in the advanced stage directly. In this stage, chemotherapy gives only a 15% 5-year survival rate. As people have varied symptoms and reactions to a specific cancer type, treatment for the tumor is likely to fall short, complicating cancer therapy. Immunotherapy is a breakthrough treatment involving drugs targeting novel immune checkpoint inhibitors like CTLA-4 and PD-1/PD-L1, along with combination therapies. In addition, the utility of engineered CAR-T and CAR-NK cells can be an effective strategy to promote the immune response against tumors. The concept of personalized cancer vaccines with the discovery of neoantigens loaded on dendritic cell vectors can also be an effective approach to cure cancer. Advances in genetic engineering tools like CRISPR/Cas9-mediated gene editing of T cells to enhance their effector function is another ray of hope. This review aims to provide an overview of recent developments in cancer immunotherapy, which can be used in first- and second-line treatments in the clinical space. Further, the intervention of artificial intelligence to detect cancer tumors at an initial stage with the help of machine learning techniques is also explored.

Mheidly, N. (2024). "Unleashing the power of AI: Assessing the reliability of ChatGPT in disseminating breast cancer awareness." J Educ Health Promot **13**: 172.

ChatGPT is a large language model that can initiate conversations with humans and respond to their questions. Due to its access to vast amounts of text data, it has the potential to offer health information. This study will explore the ability of ChatGPT to disseminate health information on breast cancer to draw predictions on its acceptance and utilization as a portal for breast cancer awareness. Through the Technology Acceptance Model that focuses on two main aspects, the ease of use and the usefulness, a qualitative comparative analysis was conducted to assess breast cancer information retrieved from ChatGPT and the Centers for Disease Control and Prevention (CDC) website. Common queries that patients with breast cancer and the public often ask were used for assessment. A checklist of the essential elements covered by each question was created. Four themes (definition, prevention, diagnostics, and therapeutics) were used for the coding process and truth tables were created to compare answers. Results showed that the design of ChatGPT renders it an easy platform to initiate conversation and obtain clarifications and explanations for ideas and questions instantaneously. ChatGPT provides adequate and correct information on breast cancer compared to the CDC website, collects information from multiple authentic resources, and provides better access to information. Nevertheless, ChatGPT lacks accountability, and the

nature of its responses changes over time. Overall, ChatGPT is a promising medium for the dissemination of health information on breast cancer and an important tool for raising awareness and improving public health knowledge on the disease.

Mikdadi, D., et al. (2022). "Applications of artificial intelligence (AI) in ovarian cancer, pancreatic cancer, and image biomarker discovery." Cancer Biomark **33**(2): 173-184.

BACKGROUND: Artificial intelligence (AI), including machine learning (ML) and deep learning, has the potential to revolutionize biomedical research. Defined as the ability to "mimic" human intelligence by machines executing trained algorithms, AI methods are deployed for biomarker discovery. OBJECTIVE: We detail the advancements and challenges in the use of AI for biomarker discovery in ovarian and pancreatic cancer. We also provide an overview of associated regulatory and ethical considerations. METHODS: We conducted a literature review using PubMed and Google Scholar to survey the published findings on the use of AI in ovarian cancer, pancreatic cancer, and cancer biomarkers. RESULTS: Most AI models associated with ovarian and pancreatic cancer have yet to be applied in clinical settings, and imaging data in many studies are not publicly available. Low disease prevalence and asymptomatic disease limits data availability required for AI models. The FDA has yet to qualify imaging biomarkers as effective diagnostic tools for these cancers. CONCLUSIONS: Challenges associated with data availability, quality, bias, as well as AI transparency and explainability, will likely persist. Explainable and trustworthy AI efforts will need to continue so that the research community can better understand and construct effective models for biomarker discovery in rare cancers.

Minami, S., et al. (2022). "Diagnosis of Depth of Submucosal Invasion in Colorectal Cancer with AI Using Deep Learning." Cancers (Basel) **14**(21).

The submucosal invasion depth predicts prognosis in early colorectal cancer. Although colorectal cancer with shallow submucosal invasion can be treated via endoscopic resection, colorectal cancer with deep submucosal invasion requires surgical colectomy. However, accurately diagnosing the depth of submucosal invasion via endoscopy is difficult. We developed a tool to diagnose the depth of submucosal invasion in early colorectal cancer using artificial intelligence. We reviewed data from 196 patients who had undergone a preoperative colonoscopy at the Osaka University Hospital and Osaka International Cancer Institute between 2011 and 2018 and were diagnosed pathologically as having shallow submucosal invasion or deep submucosal invasion colorectal cancer. A convolutional neural network for predicting invasion depth was constructed using 706 images from 91 patients between 2011 and 2015 as the training dataset. The diagnostic accuracy of the constructed convolutional neural network was evaluated using 394 images from 49 patients between 2016 and 2017 as the validation dataset. We also prospectively tested the tool from 56 patients in 2018 with suspected early-stage colorectal cancer. The sensitivity, specificity, accuracy, and area under the curve of the convolutional neural network for diagnosing deep submucosal invasion colorectal cancer were 87.2% (258/296), 35.7% (35/98), 74.4% (293/394), and 0.758, respectively. The positive predictive value was 84.4% (356/422) and the sensitivity was 75.7% (356/470) in the test set. The diagnostic accuracy of the constructed convolutional neural network seemed to be as high as that of a skilled endoscopist. Thus, endoscopic image recognition by deep learning may be able to predict the submucosal invasion depth in early-stage colorectal cancer in clinical practice.

Moreira, P., et al. (2023). "AI-Based Isotherm Prediction for Focal Cryoablation of Prostate Cancer." Acad Radiol **30 Suppl 1**(Suppl 1): S14-S20.

RATIONALE AND OBJECTIVES: Focal therapies have emerged as minimally invasive alternatives for patients with localized low-risk prostate cancer (PCa) and those with postradiation recurrence. Among the available focal treatment methods for PCa, cryoablation offers several technical advantages, including the visibility of the boundaries of frozen tissue on the intraprocedural images, access to anterior lesions, and the proven ability to treat postradiation recurrence. However, predicting the final volume of the frozen tissue is challenging as it depends on several patient-specific factors, such as proximity to heat sources and thermal properties of the prostatic tissue. MATERIALS AND METHODS: This paper presents a convolutional neural network model based on 3D-Unet to predict the frozen isotherm boundaries (iceball) resultant from a given a cryo-needle placement. Intraprocedural magnetic resonance images acquired during 38 cases of focal cryoablation of PCa were retrospectively used to train and validate the model. The model accuracy was assessed and compared against a vendor-provided geometrical model, which is used as a guideline in routine procedures. RESULTS: The mean Dice Similarity Coefficient using the proposed model was 0.79+/-0.08 (mean+SD) vs 0.72+/-0.06 using the geometrical model (P<.001). CONCLUSION: The model provided an accurate iceball boundary prediction in

less than 0.4second and has proven its feasibility to be implemented in an intraprocedural planning algorithm.

Mori, Y., et al. (2020). "How Far Will Clinical Application of AI Applications Advance for Colorectal Cancer Diagnosis?" J Anus Rectum Colon **4**(2): 47-50.

Integrating artificial intelligence (AI) applications into colonoscopy practice is being accelerated as deep learning technologies emerge. In this field, most of the preceding research has focused on polyp detection and characterization, which can mitigate inherent human errors accompanying colonoscopy procedures. On the other hand, more challenging research areas are currently capturing attention: the automated prediction of invasive cancers. Colorectal cancers (CRCs) harbor potential lymph node metastasis when they invade deeply into submucosal layers, which should be resected surgically rather than endoscopically. However, pretreatment discrimination of deeply invasive submucosal CRCs is considered difficult, according to previous prospective studies (e.g., <70% sensitivity), leading to an increased number of unnecessary surgeries for large adenomas or slightly invasive submucosal CRCs. AI is now expected to overcome this challenging hurdle because it is considered to provide better performance in predicting invasive cancer than non-expert endoscopists. In this review, we introduce five relevant publications in this area. Unfortunately, progress in this research area is in a very preliminary phase, compared to that of automated polyp detection and characterization, because of the lack of number of invasive CRCs used for machine learning. However, this issue will be overcome with more target images and cases. The research field of AI for invasive CRCs is just starting but could be a game changer of patient care in the near future, given rapidly growing technologies, and research will gradually increase.

Moser, E. C. and G. Narayan (2020). "Improving breast cancer care coordination and symptom management by using AI driven predictive toolkits." Breast **50**: 25-29.

Integrated breast cancer care is complex, marked by multiple hand-offs between primary care and specialists over an extensive period of time. Communication is essential for treatment compliance, lowering error and complication risk, as well as handling co-morbidity. The director role of care, however, becomes often unclear, and patients remain lost across departments. Digital tools can add significant value to care communication but need clarity about the directives to perform in the care team. In effective breast cancer care, multidisciplinary team meetings can drive care planning, create directives and structured data collection. Subsequently, nurse navigators can take the director's role and become a pivotal determinant for patient care continuity. In the complexity of care, automated AI driven planning can facilitate their tasks, however, human intervention stays needed for psychosocial support and tackling unexpected urgency. Care allocation of patients across centres, is often still done by hand and phone demanding time due to overbooked agenda's and discontinuous system solutions limited by privacy rules and moreover, competition among providers. Collection of complete outcome information is limited to specific collaborative networks today. With data continuity over time, AI tools can facilitate both care allocation and risk prediction which may unveil non-compliance due to local scarce resources, distance and costs. Applied research is needed to bring AI modelling into clinical practice and drive well-coordinated, patient-centric cancer care in the complex web of modern healthcare today.

Mota, A. M., et al. (2024). "Breast Cancer Molecular Subtype Prediction: A Mammography-Based AI Approach." Biomedicines **12**(6).

Breast cancer remains a leading cause of mortality among women, with molecular subtypes significantly influencing prognosis and treatment strategies. Currently, identifying the molecular subtype of cancer requires a biopsy-a specialized, expensive, and time-consuming procedure, often yielding to results that must be supported with additional biopsies due to technique errors or tumor heterogeneity. This study introduces a novel approach for predicting breast cancer molecular subtypes using mammography images and advanced artificial intelligence (AI) methodologies. Using the OPTIMAM imaging database, 1397 images from 660 patients were selected. The pretrained deep learning model ResNet-101 was employed to classify tumors into five subtypes: Luminal A, Luminal B1, Luminal B2, HER2, and Triple Negative. Various classification strategies were studied: binary classifications (one vs. all others, specific combinations) and multi-class classification (evaluating all subtypes simultaneously). To address imbalanced data, strategies like oversampling, undersampling, and data augmentation were explored. Performance was evaluated using accuracy and area under the receiver operating characteristic curve (AUC). Binary classification results showed a maximum average accuracy and AUC of 79.02% and 64.69%, respectively, while multi-class classification

achieved an average AUC of 60.62% with oversampling and data augmentation. The most notable binary classification was HER2 vs. non-HER2, with an accuracy of 89.79% and an AUC of 73.31%. Binary classification for specific combinations of subtypes revealed an accuracy of 76.42% for HER2 vs. Luminal A and an AUC of 73.04% for HER2 vs. Luminal B1. These findings highlight the potential of mammography-based AI for non-invasive breast cancer subtype prediction, offering a promising alternative to biopsies and paving the way for personalized treatment plans.

Moulson, R., et al. (2024). "Real-World Treatment Patterns and Clinical Outcomes among Patients Receiving CDK4/6 Inhibitors for Metastatic Breast Cancer in a Canadian Setting Using AI-Extracted Data." Curr Oncol **31**(4): 2172-2184.

Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) are widely used in patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2 negative (HER2-) advanced/metastatic breast cancer (ABC/MBC) in first line (1L), but little is known about their real-world use and clinical outcomes long-term, in Canada. This study used Pentavere's previously validated artificial intelligence (AI) to extract real-world data on the treatment patterns and outcomes of patients receiving CDK4/6i+endocrine therapy (ET) for HR+/HER2- ABC/MBC at Sinai Health in Toronto, Canada. Between 1 January 2016 and 1 July 2021, 48 patients were diagnosed with HR+/HER2- ABC/MBC and received CDK4/6i + ET. A total of 38 out of 48 patients received CDK4/6i + ET in 1L, of which 34 of the 38 (89.5%) received palbociclib + ET. In 2L, 12 of the 21 (57.1%) patients received CDK4/6i + ET, of which 58.3% received abemaciclib. In 3L, most patients received chemotherapy (10/12, 83.3%). For the patients receiving CDK4/6i in 1L, the median (95% CI) time to the next treatment was 42.3 (41.2, NA) months. The median (95% CI) time to chemotherapy was 46.5 (41.4, NA) months. The two-year overall survival (95% CI) was 97.4% (92.4, 100.0), and the median (range) follow-up was 28.7 (3.4-67.6) months. Despite the limitations inherent in real-world studies and a limited number of patients, these AI-extracted data complement previous studies, demonstrating the effectiveness of CDK4/6i + ET in the Canadian real-world 1L, with most patients receiving palbociclib as CDK4/6i in 1L.

Moynihan, A., et al. (2024). "Technical and functional design considerations for a real-world interpretable AI solution for NIR perfusion analysis (including cancer)." Eur J Surg Oncol **50**(12): 108273.

Near infrared (NIR) analysis of tissue perfusion via indocyanine green fluorescence assessment is performed clinically during surgery for a range of indications. Its usefulness can potentially be further enhanced through the application of interpretable artificial intelligence (AI) methods to improve dynamic interpretation accuracy in these and also open new applications. While its main use currently is for perfusion assessment as a tissue health check prior to performing an anastomosis, there is increasing interest in using fluorophores for cancer detection during surgical interventions with most research being based on the paradigm of static imaging for fluorophore uptake hours after preoperative dosing. Although some image boosting and relative estimation of fluorescence signals is already inbuilt into commercial NIR systems, fuller implementation of AI methods can enable actionable predictions especially when applied during the dynamic, early inflow-outflow phase that occurs seconds to minutes after ICG (or indeed other fluorophore) administration. Already research has shown that such methods can accurately differentiate cancer from benign tissue in the operating theatre in real time in principle based on their differential signalling and could be useful for tissue perfusion classification more generally. This can be achieved through the generation of fluorescence intensity curves from an intra-operative NIR video stream. These curves are processed to adjust for image disturbances and curve features known to be influential in tissue characterisation are extracted. Existing machine learning based classifiers can then use these features to classify the tissue in question according to prior training sets. The use of this interpretable methodology enables accurate classification algorithms to be built with modest training sets in comparison to those required for deep learning modelling in addition to achieving compliance with medical device regulations. Integration of the multiple algorithms required to achieve this classification into a desktop application or medical device could make the use of this method accessible and useful to (as well as useable by) surgeons without prior training in computer technology. This document details some technical and functional design considerations underlying such a novel recommender system to advance the foundational concept and methodology as software as medical device for in situ cancer characterisation with relevance more broadly also to other tissue perfusion applications.

Mukherjee, D., et al. (2024). "Transforming Cancer Care: The Impact of AI-Driven Strategies." Curr Cancer Drug Targets.

AI is a critical component in healthcare,

especially in the application of precision medicine where patients' characteristics, including genetic makeup, determine the treatment options that should be implemented. AI sorts big data, predicting people's reactions to specific treatments, the right combinations of drugs, and possible side effects, therefore increasing the efficiency of the treatment process and decreasing negative outcomes. This article briefly presents the ethical issues and concerns that might arise due to the integration of AI in society, such as the privacy of data, the issues of bias in the algorithms, and the issues of interpretability of the AI systems. Nevertheless, there is no doubt that AI can bring qualitative changes in cancer care based on its potential to enhance patient prognosis and reduce health care costs, as well as become a defining feature of the standard of care.

Murcia Pienkowski, V., et al. (2024). "Harnessing the power of AI in precision medicine: NGS-based therapeutic insights for colorectal cancer cohort." Front Oncol **14**: 1407465.

PURPOSE: Developing innovative precision and personalized cancer therapeutics is essential to enhance cancer survivability, particularly for prevalent cancer types such as colorectal cancer. This study aims to demonstrate various approaches for discovering new targets for precision therapies using artificial intelligence (AI) on a Polish cohort of colorectal cancer patients. METHODS: We analyzed 71 patients with histopathologically confirmed advanced resectional colorectal adenocarcinoma. Whole exome sequencing was performed on tumor and peripheral blood samples, while RNA sequencing (RNAseq) was conducted on tumor samples. We employed three approaches to identify potential targets for personalized and precision therapies. First, using our in-house neoantigen calling pipeline, ARDentify, combined with an AI-based model trained on immunopeptidomics mass spectrometry data (ARDisplay), we identified neoepitopes in the cohort. Second, based on recurrent mutations found in our patient cohort, we selected corresponding cancer cell lines and utilized knock-out gene dependency scores to identify synthetic lethality genes. Third, an AI-based model trained on cancer cell line data was employed to identify cell lines with genomic profiles similar to selected patients. Copy number variants and recurrent single nucleotide variants in these cell lines, along with gene dependency data, were used to find personalized synthetic lethality pairs. RESULTS: We identified approximately 8,700 unique neoepitopes, but none were shared by more than two patients, indicating limited potential for shared neoantigenic targets across our cohort. Additionally, we identified three synthetic lethality pairs: the well-known APC-CTNNB1 and BRAF-DUSP4 pairs, along with the recently described APC-TCF7L2 pair, which could be significant for patients with APC and BRAF variants. Furthermore, by leveraging the identification of similar cancer cell lines, we uncovered a potential gene pair, VPS4A and VPS4B, with therapeutic implications. CONCLUSION: Our study highlights three distinct approaches for identifying potential therapeutic targets in cancer patients. Each approach yielded valuable insights into our cohort, underscoring the relevance and utility of these methodologies in the development of precision and personalized cancer therapies. Importantly, we developed a novel AI model that aligns tumors with representative cell lines using RNAseq and methylation data. This model enables us to identify cell lines closely resembling patient tumors, facilitating accurate selection of models needed for in vitro validation.

Murugesan, G. K., et al. (2024). "AI-Generated Annotations Dataset for Diverse Cancer Radiology Collections in NCI Image Data Commons." Sci Data **11**(1): 1165.

The National Cancer Institute (NCI) Image Data Commons (IDC) offers publicly available cancer radiology collections for cloud computing, crucial for developing advanced imaging tools and algorithms. Despite their potential, these collections are minimally annotated; only 4% of DICOM studies in collections considered in the project had existing segmentation annotations. This project increases the quantity of segmentations in various IDC collections. We produced high-quality, AI-generated imaging annotations dataset of tissues, organs, and/or cancers for 11 distinct IDC image collections. These collections contain images from a variety of modalities, including computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). The collections cover various body parts, such as the chest, breast, kidneys, prostate, and liver. A portion of the AI annotations were reviewed and corrected by a radiologist to assess the performance of the AI models. Both the AI's and the radiologist's annotations were encoded in conformance to the Digital Imaging and Communications in Medicine (DICOM) standard, allowing for seamless integration into the IDC collections as third-party analysis collections. All the models, images and annotations are publicly accessible.

Muthamilselvan, S., et al. (2023). "Microfluidics for Profiling miRNA Biomarker Panels in AI-Assisted Cancer Diagnosis and Prognosis." Technol Cancer

Res Treat **22**: 15330338231185284.

Early detection of cancers and their precise subtyping are essential to patient stratification and effective cancer management. Data-driven identification of expression biomarkers coupled with microfluidics-based detection shows promise to revolutionize cancer diagnosis and prognosis. MicroRNAs play key roles in cancers and afford detection in tissue and liquid biopsies. In this review, we focus on the microfluidics-based detection of miRNA biomarkers in AI-based models for early-stage cancer subtyping and prognosis. We describe various subclasses of miRNA biomarkers that could be useful in machine-based predictive modeling of cancer staging and progression. Strategies for optimizing the feature space of miRNA biomarkers are necessary to obtain a robust signature panel. This is followed by a discussion of the issues in model construction and validation towards producing Software-as-Medical-Devices (SaMDs). Microfluidic devices could facilitate the multiplexed detection of miRNA biomarker panels, and an overview of the different strategies for designing such microfluidic systems is presented here, with an outline of the detection principles used and the corresponding performance measures. Microfluidics-based profiling of miRNAs coupled with SaMD represent high-performance point-of-care solutions that would aid clinical decision-making and pave the way for accessible precision personalized medicine.

Mynhier, M., et al. (2021). "Core services that power AI-driven transformation in cancer research and care." Biochim Biophys Acta Rev Cancer **1876**(1): 188535.

This review captures some key lessons learned in the course of helping some of America's leading healthcare AI innovators achieve scale and sustained impact in complex research and care delivery ecosystems. AI innovators may find it useful to access core services to form effective collaborations, find and manage the right data and technology, incentivize and regulate partnerships, demonstrate they can improve lives, and create self-sustaining networks by redistributing realized value.

Na, K. J., et al. (2024). "Clinical Utility of a CT-based AI Prognostic Model for Segmentectomy in Non-Small Cell Lung Cancer." Radiology **311**(1): e231793.

Background Currently, no tool exists for risk stratification in patients undergoing segmentectomy for non-small cell lung cancer (NSCLC). Purpose To develop and validate a deep learning (DL) prognostic model using preoperative CT scans and clinical and radiologic information for risk stratification in patients with clinical stage IA NSCLC undergoing segmentectomy. Materials and Methods In this single-center retrospective study, transfer learning of a pretrained model was performed for survival prediction in patients with clinical stage IA NSCLC who underwent lobectomy from January 2008 to March 2017. The internal set was divided into training, validation, and testing sets based on the assignments from the pretraining set. The model was tested on an independent test set of patients with clinical stage IA NSCLC who underwent segmentectomy from January 2010 to December 2017. Its prognostic performance was analyzed using the time-dependent area under the receiver operating characteristic curve (AUC), sensitivity, and specificity for freedom from recurrence (FFR) at 2 and 4 years and lung cancer-specific survival and overall survival at 4 and 6 years. The model sensitivity and specificity were compared with those of the Japan Clinical Oncology Group (JCOG) eligibility criteria for sublobar resection. Results The pretraining set included 1756 patients. Transfer learning was performed in an internal set of 730 patients (median age, 63 years [IQR, 56-70 years]; 366 male), and the segmentectomy test set included 222 patients (median age, 65 years [IQR, 58-71 years]; 114 male). The model performance for 2-year FFR was as follows: AUC, 0.86 (95% CI: 0.76, 0.96); sensitivity, 87.4% (7.17 of 8.21 patients; 95% CI: 59.4, 100); and specificity, 66.7% (136 of 204 patients; 95% CI: 60.2, 72.8). The model showed higher sensitivity for FFR than the JCOG criteria (87.4% vs 37.6% [3.08 of 8.21 patients], P = .02), with similar specificity. Conclusion The CT-based DL model identified patients at high risk among those with clinical stage IA NSCLC who underwent segmentectomy, outperforming the JCOG criteria. (c) RSNA, 2024 Supplemental material is available for this article.

Naghavi, M., et al. (2023). "Opportunistic AI-enabled automated bone mineral density measurements in lung cancer screening and coronary calcium scoring CT scans are equivalent." Eur J Radiol Open **10**: 100492.

RATIONALE AND OBJECTIVES: We previously reported a novel manual method for measuring bone mineral density (BMD) in coronary artery calcium (CAC) scans and validated our method against Dual X-Ray Absorptiometry (DEXA). Furthermore, we have developed and validated an artificial intelligence (AI) based automated BMD (AutoBMD) measurement as an opportunistic add-on to CAC scans that recently received FDA approval. In this report, we present evidence of equivalency between AutoBMD measurements in cardiac vs lung

CT scans. MATERIALS AND METHODS: AI models were trained using 132 cases with 7649 (3 mm) slices for CAC, and 37 cases with 21918 (0.5 mm) slices for lung scans. To validate AutoBMD against manual measurements, we used 6776 cases of BMD measured manually on CAC scans in the Multi-Ethnic Study of Atherosclerosis (MESA). We then used 165 additional cases from Harbor UCLA Lundquist Institute to compare AutoBMD in patients who underwent both cardiac and lung scans on the same day. RESULTS: Mean+/-SD for age was 69 +/- 9.4 years with 52.4% male. AutoBMD in lung and cardiac scans, and manual BMD in cardiac scans were 153.7 +/- 43.9, 155.1 +/- 44.4, and 163.6 +/- 45.3 g/cm(3), respectively (p = 0.09). Bland-Altman agreement analysis between AutoBMD lung and cardiac scans resulted in 1.37 g/cm(3) mean differences. Pearson correlation coefficient between lung and cardiac AutoBMD was R(2) = 0.95 (p < 0.0001). CONCLUSION: Opportunistic BMD measurement using AutoBMD in CAC and lung cancer screening scans is promising and yields similar results. No extra radiation plus the high prevalence of asymptomatic osteoporosis makes AutoBMD an ideal screening tool for osteopenia and osteoporosis in CT scans done for other reasons.

Naik, H. R., et al. (2023). "Synchronous Bilateral Breast Cancer: A Case Report Piloting and Evaluating the Implementation of the AI-Powered Large Language Model (LLM) ChatGPT." Cureus **15**(4): e37587.

Primary breast carcinoma is the most common cancer type in women, and although bilateral synchronous breast cancers (s-BBC) remain quite rare, the reported incidence may increase with the adoption of more sensitive imaging modalities. Here, we present a case of histomorphological and clinically distinct s-BBC, together with a discussion of clinical management decisions, prognosis, and treatment standards and how these relate to outcomes vis-a-vis more established standards in unifocal breast carcinoma. The case report also constitutes a pilot and formal evaluation of a large language model (LLM) of ChatGPT as a tool to aid in generating a single patient case report.

Nauman, A. (2024). "Revolutionizing pancreatic cancer management: AI-enhanced vascular burden index assessment with CT imaging." Eur J Surg Oncol **50**(11): 108577.

Ng, A. Y., et al. (2023). "Prospective implementation of AI-assisted screen reading to improve early detection of breast cancer." Nat Med **29**(12): 3044-3049.

Artificial intelligence (AI) has the potential to improve breast cancer screening; however, prospective evidence of the safe implementation of AI into real clinical practice is limited. A commercially available AI system was implemented as an additional reader to standard double reading to flag cases for further arbitration review among screened women. Performance was assessed prospectively in three phases: a single-center pilot rollout, a wider multicenter pilot rollout and a full live rollout. The results showed that, compared to double reading, implementing the AI-assisted additional-reader process could achieve 0.7-1.6 additional cancer detection per 1,000 cases, with 0.16-0.30% additional recalls, 0-0.23% unnecessary recalls and a 0.1-1.9% increase in positive predictive value (PPV) after 7-11% additional human reads of AI-flagged cases (equating to 4-6% additional overall reading workload). The majority of cancerous cases detected by the AI-assisted additional-reader process were invasive (83.3%) and small-sized (</=10 mm, 47.0%). This evaluation suggests that using AI as an additional reader can improve the early detection of breast cancer with relevant prognostic features, with minimal to no unnecessary recalls. Although the AI-assisted additional-reader workflow requires additional reads, the higher PPV suggests that it can increase screening effectiveness.

Nicholson, N., et al. (2023). "Ontology-Based AI Design Patterns and Constraints in Cancer Registry Data Validation." Cancers (Basel) **15**(24).

Data validation in cancer registration is a critical operation but is resource-intensive and has traditionally depended on proprietary software. Ontology-based AI is a novel approach utilising machine reasoning based on axioms formally described in description logic. This is a different approach from deep learning AI techniques but not exclusive of them. The advantage of the ontology approach lies in its ability to address a number of challenges concurrently. The disadvantages relate to computational costs, which increase with language expressivity and the size of data sets, and class containment restrictions imposed by description logics. Both these aspects would benefit from the availability of design patterns, which is the motivation behind this study. We modelled the European cancer registry data validation rules in description logic using a number of design patterns and showed the viability of the approach. Reasoning speeds are a limiting factor for large cancer registry data sets comprising many hundreds of thousands of records, but these can be offset to a certain extent by developing the ontology in a modular way. Data validation is also a highly parallelisable process.

Important potential future work in this domain would be to identify and optimise reusable design patterns, paying particular attention to avoiding any unintended reasoning efficiency hotspots.

Normanno, N., et al. (1998). "Apolipoprotein A-I reverse transcriptase-polymerase chain reaction analysis for detection of hematogenous colon cancer dissemination." Int J Oncol **13**(3): 443-447.

Detection of systemic tumor dissemination in colon carcinoma patients might be important for selection of appropriate treatment modalities. It has been previously shown that Apolipoprotein A-I (Apo A-I) is expressed in human intestinal epithelial cells, and in some human colon carcinoma cell lines. We examined the expression of Apo A-I mRNA in 14 human primary colon carcinomas by Northern blot and/or reverse transcriptase-polymerase chain reaction (RT-PCR) analysis. An Apo A-I specific transcript was found in up to 70% of the colon carcinomas. We developed an RT-PCR assay for Apo A-I transcripts, to identify circulating carcinoma cells in the peripheral blood of colon cancer patients. The Apo A-I RT-PCR assay was optimized using limiting dilution of an Apo A-I positive cancer cell line mixed with peripheral blood from healthy donor. In this system, up to 10 colon carcinoma cells were detected in 5 ml of peripheral blood. We examined Apo A-I mRNA expression in peripheral blood samples from 4 healthy donors, 20 colon carcinoma patients, and 11 individuals with tumor disease other than colon cancer. No Apo A-I mRNA was detected in the healthy donors and in the patients without colon cancer. Two out of 10 patients with metastatic colon carcinoma were positive by this assay, whereas Apo A-I mRNA was not found in any of the blood samples from the 10 radically resected colon carcinoma patients. These data suggest that Apo A-I RT-PCR assay is a highly specific and sensitive assay, although a low number of advanced colon carcinoma patients was found to be positive.

Nowak, M., et al. (2024). "Single-cell AI-based detection and prognostic and predictive value of DNA mismatch repair deficiency in colorectal cancer." Cell Rep Med **5**(9): 101727.

Testing for DNA mismatch repair deficiency (MMRd) is recommended for all colorectal cancers (CRCs). Automating this would enable precision medicine, particularly if providing information on etiology not captured by deep learning (DL) methods. We present AIMMeR, an AI-based method for determination of mismatch repair (MMR) protein expression at a single-cell level in routine pathology samples. AIMMeR shows an area under the receiver-operator curve (AUROC) of 0.98, and specificity of >/=75% at 98% sensitivity against pathologist ground truth in stage II/III in two trial cohorts, with positive predictive value of >/=98% for the commonest pattern of somatic MMRd. Lower agreement with microsatellite instability (MSI) testing (AUROC 0.86) reflects discordance between MMR and MSI PCR rather than AIMMeR misclassification. Analysis of the SCOT trial confirms MMRd prognostic value in oxaliplatin-treated patients; while MMRd does not predict differential benefit of chemotherapy duration, it correlates with difference in relapse by regimen (P(Interaction) = 0.04). AIMMeR may help reduce pathologist workload and streamline diagnostics in CRC.

Oberije, C. J. G., et al. (2023). "Comparing Prognostic Factors of Cancers Identified by Artificial Intelligence (AI) and Human Readers in Breast Cancer Screening." Cancers (Basel) **15**(12).

Invasiveness status, histological grade, lymph node stage, and tumour size are important prognostic factors for breast cancer survival. This evaluation aims to compare these features for cancers detected by AI and human readers using digital mammography. Women diagnosed with breast cancer between 2009 and 2019 from three UK double-reading sites were included in this retrospective cohort evaluation. Differences in prognostic features of cancers detected by AI and the first human reader (R1) were assessed using chi-square tests, with significance at $p < 0.05$. From 1718 screen-detected cancers (SDCs) and 293 interval cancers (ICs), AI flagged 85.9% and 31.7%, respectively. R1 detected 90.8% of SDCs and 7.2% of ICs. Of the screen-detected cancers detected by the AI, 82.5% had an invasive component, compared to 81.1% for R1 (p-0.374). For the ICs, this was 91.5% and 93.8% for AI and R1, respectively ($p = 0.829$). For the invasive tumours, no differences were found for histological grade, tumour size, or lymph node stage. The AI detected more ICs. In summary, no differences in prognostic factors were found comparing SDC and ICs identified by AI or human readers. These findings support a potential role for AI in the double-reading workflow.

Oerther, B., et al. (2023). "Prediction of upgrade to clinically significant prostate cancer in patients under active surveillance: Performance of a fully automated AI-algorithm for lesion detection and classification." Prostate **83**(9): 871-878.

BACKGROUND: Multiparametric MRI (mpMRI) improves the detection of aggressive prostate cancer (PCa) subtypes. As cases of active surveillance (AS) increase and tumor progression

triggers definitive treatment, we evaluated whether an AI-driven algorithm can detect clinically significant PCa (csPCa) in patients under AS. METHODS: Consecutive patients under AS who received mpMRI (PI-RADSv2.1 protocol) and subsequent MR-guided ultrasound fusion (targeted and extensive systematic) biopsy between 2017 and 2020 were retrospectively analyzed. Diagnostic performance of an automated clinically certified AI-driven algorithm was evaluated on both lesion and patient level regarding the detection of csPCa. RESULTS: Analysis of 56 patients resulted in 93 target lesions. Patient level sensitivity and specificity of the AI algorithm was 92.5%/31% for the detection of ISUP >/= 1 and 96.4%/25% for the detection of ISUP >/= 2, respectively. The only case of csPCa missed by the AI harbored only 1/47 Gleason 7a core (systematic biopsy; previous and subsequent biopsies rendered non-csPCa). CONCLUSIONS: AI-augmented lesion detection and PI-RADS scoring is a robust tool to detect progression to csPCa in patients under AS. Integration in the clinical workflow can serve as reassurance for the reader and streamline reporting, hence improve efficiency and diagnostic confidence.

Oh, J., et al. (2023). "OView-AI Supporter for Classifying Pneumonia, Pneumothorax, Tuberculosis, Lung Cancer Chest X-ray Images Using Multi-Stage Superpixels Classification." Diagnostics (Basel) **13**(9).

The deep learning approach has recently attracted much attention for its outstanding performance to assist in clinical diagnostic tasks, notably in computer-aided solutions. Computer-aided solutions are being developed using chest radiography to identify lung diseases. A chest X-ray image is one of the most often utilized diagnostic imaging modalities in computer-aided solutions since it produces non-invasive standard-of-care data. However, the accurate identification of a specific illness in chest X-ray images still poses a challenge due to their high inter-class similarities and low intra-class variant abnormalities, especially given the complex nature of radiographs and the complex anatomy of the chest. In this paper, we proposed a deep-learning-based solution to classify four lung diseases (pneumonia, pneumothorax, tuberculosis, and lung cancer) and healthy lungs using chest X-ray images. In order to achieve a high performance, the EfficientNet B7 model with the pre-trained weights of ImageNet trained by Noisy Student was used as a backbone model, followed by our proposed fine-tuned layers and hyperparameters. Our study achieved an average test accuracy of 97.42%, sensitivity of 95.93%, and specificity of 99.05%. Additionally, our findings were utilized as diagnostic supporting software in OView-AI system (computer-aided application). We conducted 910 clinical trials and achieved an AUC confidence interval (95% CI) of the diagnostic results in the OView-AI system of 97.01%, sensitivity of 95.68%, and specificity of 99.34%.

Oh, Y., et al. (2023). "Multi-Scale Hybrid Vision Transformer for Learning Gastric Histology: AI-Based Decision Support System for Gastric Cancer Treatment." IEEE J Biomed Health Inform **27**(8): 4143-4153.

Gastric endoscopic screening is an effective way to decide appropriate gastric cancer treatment at an early stage, reducing gastric cancer-associated mortality rate. Although artificial intelligence has brought a great promise to assist pathologist to screen digitalized endoscopic biopsies, existing artificial intelligence systems are limited to be utilized in planning gastric cancer treatment. We propose a practical artificial intelligence-based decision support system that enables five subclassifications of gastric cancer pathology, which can be directly matched to general gastric cancer treatment guidance. The proposed framework is designed to efficiently differentiate multi-classes of gastric cancer through multiscale self-attention mechanism using 2-stage hybrid vision transformer networks, by mimicking the way how human pathologists understand histology. The proposed system demonstrates its reliable diagnostic performance by achieving class-average sensitivity of above 0.85 for multicentric cohort tests. Moreover, the proposed system demonstrates its great generalization capability on gastrointestinal track organ cancer by achieving the best class-average sensitivity among contemporary networks. Furthermore, in the observational study, artificial intelligence-assisted pathologists show significantly improved diagnostic sensitivity within saved screening time compared to human pathologists. Our results demonstrate that the proposed artificial intelligence system has a great potential for providing presumptive pathologic opinion and supporting decision of appropriate gastric cancer treatment in practical clinical settings.

Olawade, D. B., et al. (2024). "AI-Guided Cancer Therapy for Patients with Coexisting Migraines." Cancers (Basel) **16**(21).

Background: Cancer remains a leading cause of death worldwide. Progress in its effective treatment has been hampered by challenges in personalized therapy, particularly in patients with comorbid conditions. The integration of artificial intelligence (AI) into patient profiling offers a promising approach to enhancing individualized

anticancer therapy. Objective: This narrative review explores the role of AI in refining anticancer therapy through personalized profiling, with a specific focus on cancer patients with comorbid migraine. Methods: A comprehensive literature search was conducted across multiple databases, including PubMed, Scopus, and Google Scholar. Studies were selected based on their relevance to AI applications in oncology and migraine management, with a focus on personalized medicine and predictive modeling. Key themes were synthesized to provide an overview of recent developments, challenges, and emerging directions. Results: AI technologies, such as machine learning (ML), deep learning (DL), and natural language processing (NLP), have become instrumental in the discovery of genetic and molecular biomarkers of cancer and migraine. These technologies also enable predictive analytics for assessing the impact of migraine on cancer therapy in comorbid cases, predicting outcomes and provide clinical decision support systems (CDSS) for real-time treatment adjustments. Conclusions: AI holds significant potential to improve the precision and effectiveness of the management and therapy of cancer patients with comorbid migraine. Nevertheless, challenges remain over data integration, clinical validation, and ethical consideration, which must be addressed to appreciate the full potential for the approach outlined herein.

Oner, M. U., et al. (2022). "An AI-assisted tool for efficient prostate cancer diagnosis in low-grade and low-volume cases." Patterns (N Y) **3**(12): 100642.

Pathologists diagnose prostate cancer by core needle biopsy. In low-grade and low-volume cases, they look for a few malignant glands out of hundreds within a core. They may miss a few malignant glands, resulting in repeat biopsies or missed therapeutic opportunities. This study developed a multi-resolution deep-learning pipeline to assist pathologists in detecting malignant glands in core needle biopsies of low-grade and low-volume cases. Analyzing a gland at multiple resolutions, our model exploited morphology and neighborhood information, which were crucial in prostate gland classification. We developed and tested our pipeline on the slides of a local cohort of 99 patients in Singapore. Besides, we made the images publicly available, becoming the first digital histopathology dataset of patients of Asian ancestry with prostatic carcinoma. Our multi-resolution classification model achieved an area under the receiver operating characteristic curve (AUROC) value of 0.992 (95% confidence interval [CI]: 0.985-0.997) in the external validation study, showing the generalizability of our multi-resolution approach.

Ortiz, B. L., et al. (2024). "Data Preprocessing Techniques for AI and Machine Learning Readiness: Scoping Review of Wearable Sensor Data in Cancer Care." JMIR Mhealth Uhealth **12**: e59587.

BACKGROUND: Wearable sensors are increasingly being explored in health care, including in cancer care, for their potential in continuously monitoring patients. Despite their growing adoption, significant challenges remain in the quality and consistency of data collected from wearable sensors. Moreover, preprocessing pipelines to clean, transform, normalize, and standardize raw data have not yet been fully optimized. OBJECTIVE: This study aims to conduct a scoping review of preprocessing techniques used on raw wearable sensor data in cancer care, specifically focusing on methods implemented to ensure their readiness for artificial intelligence and machine learning (AI/ML) applications. We sought to understand the current landscape of approaches for handling issues, such as noise, missing values, normalization or standardization, and transformation, as well as techniques for extracting meaningful features from raw sensor outputs and converting them into usable formats for subsequent AI/ML analysis. METHODS: We systematically searched IEEE Xplore, PubMed, Embase, and Scopus to identify potentially relevant studies for this review. The eligibility criteria included (1) mobile health and wearable sensor studies in cancer, (2) written and published in English, (3) published between January 2018 and December 2023, (4) full text available rather than abstracts, and (5) original studies published in peer-reviewed journals or conferences. RESULTS: The initial search yielded 2147 articles, of which 20 (0.93%) met the inclusion criteria. Three major categories of preprocessing techniques were identified: data transformation (used in 12/20, 60% of selected studies), data normalization and standardization (used in 8/20, 40% of the selected studies), and data cleaning (used in 8/20, 40% of the selected studies). Transformation methods aimed to convert raw data into more informative formats for analysis, such as by segmenting sensor streams or extracting statistical features. Normalization and standardization techniques usually normalize the range of features to improve comparability and model convergence. Cleaning methods focused on enhancing data reliability by handling artifacts like missing values, outliers, and inconsistencies. CONCLUSIONS: While wearable sensors are gaining traction in cancer care, realizing their full potential hinges on the ability to reliably translate raw outputs into high-quality data suitable for AI/ML applications. This review found that researchers are using various preprocessing

techniques to address this challenge, but there remains a lack of standardized best practices. Our findings suggest a pressing need to develop and adopt uniform data quality and preprocessing workflows of wearable sensor data that can support the breadth of cancer research and varied patient populations. Given the diverse preprocessing techniques identified in the literature, there is an urgency for a framework that can guide researchers and clinicians in preparing wearable sensor data for AI/ML applications. For the scoping review as well as our research, we propose a general framework for preprocessing wearable sensor data, designed to be adaptable across different disease settings, moving beyond cancer care.

Osorio, P., et al. (2024). "Latent Diffusion Models with Image-Derived Annotations for Enhanced AI-Assisted Cancer Diagnosis in Histopathology." Diagnostics (Basel) **14**(13).

Artificial Intelligence (AI)-based image analysis has immense potential to support diagnostic histopathology, including cancer diagnostics. However, developing supervised AI methods requires large-scale annotated datasets. A potentially powerful solution is to augment training data with synthetic data. Latent diffusion models, which can generate high-quality, diverse synthetic images, are promising. However, the most common implementations rely on detailed textual descriptions, which are not generally available in this domain. This work proposes a method that constructs structured textual prompts from automatically extracted image features. We experiment with the PCam dataset, composed of tissue patches only loosely annotated as healthy or cancerous. We show that including image-derived features in the prompt, as opposed to only healthy and cancerous labels, improves the Frechet Inception Distance (FID) by 88.6. We also show that pathologists find it challenging to detect synthetic images, with a median sensitivity/specificity of 0.55/0.55. Finally, we show that synthetic data effectively train AI models.

Ostrowska, M., et al. (2024). "To trust or not to trust: evaluating the reliability and safety of AI responses to laryngeal cancer queries." Eur Arch Otorhinolaryngol **281**(11): 6069-6081.

PURPOSE: As online health information-seeking surges, concerns mount over the quality and safety of accessible content, potentially leading to patient harm through misinformation. On one hand, the emergence of Artificial Intelligence (AI) in healthcare could prevent it; on the other hand, questions raise regarding the quality and safety of the medical information provided. As laryngeal cancer is a prevalent head and neck malignancy, this study aims to evaluate the utility and safety of three large language models (LLMs) as sources of patient information about laryngeal cancer. METHODS: A cross-sectional study was conducted using three LLMs (ChatGPT 3.5, ChatGPT 4.0, and Bard). A questionnaire comprising 36 inquiries about laryngeal cancer was categorised into diagnosis (11 questions), treatment (9 questions), novelties and upcoming treatments (4 questions), controversies (8 questions), and sources of information (4 questions). The population of reviewers consisted of 3 groups, including ENT specialists, junior physicians, and non-medicals, who graded the responses. Each physician evaluated each question twice for each model, while non-medicals only once. Everyone was blinded to the model type, and the question order was shuffled. Outcome evaluations were based on a safety score (1-3) and a Global Quality Score (GQS, 1-5). Results were compared between LLMs. The study included iterative assessments and statistical validations. RESULTS: Analysis revealed that ChatGPT 3.5 scored highest in both safety (mean: 2.70) and GQS (mean: 3.95). ChatGPT 4.0 and Bard had lower safety scores of 2.56 and 2.42, respectively, with corresponding quality scores of 3.65 and 3.38. Inter-rater reliability was consistent, with less than 3% discrepancy. About 4.2% of responses fell into the lowest safety category (1), particularly in the novelty category. Non-medical reviewers' quality assessments correlated moderately ($r = 0.67$) with response length. CONCLUSIONS: LLMs can be valuable resources for patients seeking information on laryngeal cancer. ChatGPT 3.5 provided the most reliable and safe responses among the models evaluated.

Ouattara, T. A., et al. (2024). "Development of an AI Platform for Advanced Breast Cancer Management." Stud Health Technol Inform **321**: 215-219.

This article explores the transition from a traditional histopathological examination system to an innovative platform using artificial intelligence (AI) for breast cancer detection from histopathological images in Burkina Faso. The existing system is analyzed in detail, highlighting the steps of querying, sample preparation, analysis by the pathologist, and validation by the physician. From this analysis, the needs and challenges are identified, emphasizing the opportunities for AI to improve the efficiency and accuracy of the diagnosis. The design of the AI platform is then presented, including data collection, AI model development, and its integration into existing processes. Finally, the expected results and implications for improving healthcare in Burkina Faso are discussed, highlighting the potential benefits and challenges to overcome for the successful adoption of this promising technology.

Ouyang, B., et al. (2024). "AI-powered omics-based drug pair discovery for pyroptosis therapy targeting triple-negative breast cancer." Nat Commun **15**(1): 7560.

Due to low success rates and long cycles of traditional drug development, the clinical tendency is to apply omics techniques to reveal patient-level disease characteristics and individualized responses to treatment. However, the heterogeneous form of data and uneven distribution of targets make drug discovery and precision medicine a non-trivial task. This study takes pyroptosis therapy for triple-negative breast cancer (TNBC) as a paradigm and uses data mining of a large TNBC cohort and drug databases to establish a biofactor-regulated neural network for rapidly screening and optimizing compound pyroptosis drug pairs. Subsequently, biomimetic nanococrystals are prepared using the preferred combination of mitoxantrone and gambogic acid for rational drug delivery. The unique mechanism of obtained nanococrystals regulating pyroptosis genes through ribosomal stress and triggering pyroptosis cascade immune effects are revealed in TNBC models. In this work, a target omics-based intelligent compound drug discovery framework explores an innovative drug development paradigm, which repurposes existing drugs and enables precise treatment of refractory diseases.

Ozaki, Y., et al. (2024). "Integrating Omics Data and AI for Cancer Diagnosis and Prognosis." Cancers (Basel) **16**(13).

Cancer is one of the leading causes of death, making timely diagnosis and prognosis very important. Utilization of AI (artificial intelligence) enables providers to organize and process patient data in a way that can lead to better overall outcomes. This review paper aims to look at the varying uses of AI for diagnosis and prognosis and clinical utility. PubMed and EBSCO databases were utilized for finding publications from 1 January 2020 to 22 December 2023. Articles were collected using key search terms such as "artificial intelligence" and "machine learning." Included in the collection were studies of the application of AI in determining cancer diagnosis and prognosis using multi-omics data, radiomics, pathomics, and clinical and laboratory data. The resulting 89 studies were categorized into eight sections based on the type of data utilized and then further subdivided into two subsections focusing on cancer diagnosis and prognosis, respectively. Eight studies integrated more than one form of omics, namely genomics, transcriptomics, epigenomics, and proteomics. Incorporating AI into cancer diagnosis and prognosis alongside omics and clinical data represents a significant advancement. Given the considerable potential of AI in this domain, ongoing prospective studies are essential to enhance algorithm interpretability and to ensure safe clinical integration.

Ozyoruk, K. B., et al. (2024). "AI-ADC: Channel and Spatial Attention-Based Contrastive Learning to Generate ADC Maps from T2W MRI for Prostate Cancer Detection." J Pers Med **14**(10).

BACKGROUND/OBJECTIVES: Apparent Diffusion Coefficient (ADC) maps in prostate MRI can reveal tumor characteristics, but their accuracy can be compromised by artifacts related with patient motion or rectal gas associated distortions. To address these challenges, we propose a novel approach that utilizes a Generative Adversarial Network to synthesize ADC maps from T2-weighted magnetic resonance images (T2W MRI). METHODS: By leveraging contrastive learning, our model accurately maps axial T2W MRI to ADC maps within the cropped region of the prostate organ boundary, capturing subtle variations and intricate structural details by learning similar and dissimilar pairs from two imaging modalities. We trained our model on a comprehensive dataset of unpaired T2-weighted images and ADC maps from 506 patients. In evaluating our model, named AI-ADC, we compared it against three state-of-the-art methods: CycleGAN, CUT, and StyTr2. RESULTS: Our model demonstrated a higher mean Structural Similarity Index (SSIM) of 0.863 on a test dataset of 3240 2D MRI slices from 195 patients, compared to values of 0.855, 0.797, and 0.824 for CycleGAN, CUT, and StyTr2, respectively. Similarly, our model achieved a significantly lower Frechet Inception Distance (FID) value of 31.992, compared to values of 43.458, 179.983, and 58.784 for the other three models, indicating its superior performance in generating ADC maps. Furthermore, we evaluated our model on 147 patients from the publicly available ProstateX dataset, where it demonstrated a higher SSIM of 0.647 and a lower FID of 113.876 compared to the other three models. CONCLUSIONS: These results highlight the efficacy of our proposed model in generating ADC maps from T2W MRI, showcasing its potential for enhancing clinical diagnostics and radiological workflows.

Pacurari, A. C., et al. (2023). "Diagnostic Accuracy of Machine Learning AI Architectures in Detection and Classification of Lung Cancer: A Systematic Review." Diagnostics (Basel) **13**(13).

The application of artificial intelligence (AI) in diagnostic imaging has gained significant interest in recent years, particularly in lung cancer detection. This systematic review aims to assess the accuracy of

machine learning (ML) AI algorithms in lung cancer detection, identify the ML architectures currently in use, and evaluate the clinical relevance of these diagnostic imaging methods. A systematic search of PubMed, Web of Science, Cochrane, and Scopus databases was conducted in February 2023, encompassing the literature published up until December 2022. The review included nine studies, comprising five case-control studies, three retrospective cohort studies, and one prospective cohort study. Various ML architectures were analyzed, including artificial neural network (ANN), entropy degradation method (EDM), probabilistic neural network (PNN), support vector machine (SVM), partially observable Markov decision process (POMDP), and random forest neural network (RFNN). The ML architectures demonstrated promising results in detecting and classifying lung cancer across different lesion types. The sensitivity of the ML algorithms ranged from 0.81 to 0.99, while the specificity varied from 0.46 to 1.00. The accuracy of the ML algorithms ranged from 77.8% to 100%. The AI architectures were successful in differentiating between malignant and benign lesions and detecting small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). This systematic review highlights the potential of ML AI architectures in the detection and classification of lung cancer, with varying levels of diagnostic accuracy. Further studies are needed to optimize and validate these AI algorithms, as well as to determine their clinical relevance and applicability in routine practice.

Pan, Y., et al. (2022). "The apolipoprotein B and apolipoprotein A-I Ratio serves as a strong prognostic factor for the overall survival of patients with colorectal cancer." Front Oncol **12**: 1089688.

BACKGROUND: The lipid metabolism status of patients with colorectal cancer (CRC) has not been understood comprehensively. The present study investigated the characteristics of lipid metabolism parameters in CRC patients with or without metastases and identified the independent prognostic factors of long-term prognosis. METHODS: The clinicopathological data of 231 CRC patients along with 259 formalin-fixed paraffin-embedded samples with or without liver or lung metastasis were retrieved and stained for apolipoprotein B (apoB) via immunohistochemistry (IHC) in our center. The correlation and multivariable analysis between blood circulating apolipoprotein A-I (apoA1), apoB and overall survival (OS) were analyzed. RESULTS: In the multivariable analysis, apoA1, apoB and apolipoprotein B and apolipoprotein A-I (apoB/A) ratio, were identified as independent prognostic factors for OS. Moreover, the apoB/A ratio showed a significantly negative association with OS time (R=-0.187, P=0.004). CRC patients with low apoB/A ratio had better 1-, 3- and 5-year OS rates than those who had high apoB/A ratio (87.1%, 54.3%, and 37.1% vs. 92.5%, 72.0%, and 59.5%, respectively, P=0.001). On histological level, similar expression intensity of apoB between primary CRC and liver metastases indicated better prognostic outcomes than those with different expression levels (100%, 83.3%, and 77.8% vs. 100%, 66.7%, and 33.3%, respectively; P=0.033). Higher level of apoB in the primary CRC interprets into increased incidence of liver metastases. However, the apoB expression levels in the CRC tumor were not parallel to the circulating lipid metabolism parameters. CONCLUSIONS: The apoB/A ratio was a reliable independent prognostic factor for predicting the long-term OS of CRC patients. Moreover, the IHC of the primary CRC and metastatic lesions verified the metastatic potential of apoB through a different aspect. Lipid metabolism status for cancer progression reported in the present study possessed potentially prognostic value, but bench-scale studies are needed for their future clinical applications.

Parimbelli, E., et al. (2021). "A review of AI and Data Science support for cancer management." Artif Intell Med **117**: 102111.

INTRODUCTION: Thanks to improvement of care, cancer has become a chronic condition. But due to the toxicity of treatment, the importance of supporting the quality of life (QoL) of cancer patients increases. Monitoring and managing QoL relies on data collected by the patient in his/her home environment, its integration, and its analysis, which supports personalization of cancer management recommendations. We review the state-of-the-art of computerized systems that employ AI and Data Science methods to monitor the health status and provide support to cancer patients managed at home. OBJECTIVE: Our main objective is to analyze the literature to identify open research challenges that a novel decision support system for cancer patients and clinicians will need to address, point to potential solutions, and provide a list of established best-practices to adopt. METHODS: We designed a review study, in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, analyzing studies retrieved from PubMed related to monitoring cancer patients in their home environments via sensors and self-reporting: what data is collected, what are the techniques used to collect data, semantically integrate it, infer the patient's state from it and deliver

coaching/behavior change interventions. RESULTS: Starting from an initial corpus of 819 unique articles, a total of 180 papers were considered in the full-text analysis and 109 were finally included in the review. Our findings are organized and presented in four main sub-topics consisting of data collection, data integration, predictive modeling and patient coaching. CONCLUSION: Development of modern decision support systems for cancer needs to utilize best practices like the use of validated electronic questionnaires for quality-of-life assessment, adoption of appropriate information modeling standards supplemented by terminologies/ontologies, adherence to FAIR data principles, external validation, stratification of patients in subgroups for better predictive modeling, and adoption of formal behavior change theories. Open research challenges include supporting emotional and social dimensions of well-being, including PROs in predictive modeling, and providing better customization of behavioral interventions for the specific population of cancer patients.

Park, E. K., et al. (2024). "Impact of AI for Digital Breast Tomosynthesis on Breast Cancer Detection and Interpretation Time." Radiol Artif Intell **6**(3): e230318.

Purpose To develop an artificial intelligence (AI) model for the diagnosis of breast cancer on digital breast tomosynthesis (DBT) images and to investigate whether it could improve diagnostic accuracy and reduce radiologist reading time. Materials and Methods A deep learning AI algorithm was developed and validated for DBT with retrospectively collected examinations (January 2010 to December 2021) from 14 institutions in the United States and South Korea. A multicenter reader study was performed to compare the performance of 15 radiologists (seven breast specialists, eight general radiologists) in interpreting DBT examinations in 258 women (mean age, 56 years +/- 13.41 [SD]), including 65 cancer cases, with and without the use of AI. Area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and reading time were evaluated. Results The AUC for stand-alone AI performance was 0.93 (95% CI: 0.92, 0.94). With AI, radiologists' AUC improved from 0.90 (95% CI: 0.86, 0.93) to 0.92 (95% CI: 0.88, 0.96) (P = .003) in the reader study. AI showed higher specificity (89.64% [95% CI: 85.34%, 93.94%]) than radiologists (77.34% [95% CI: 75.82%, 78.87%]) (P < .001). When reading with AI, radiologists' sensitivity increased from 85.44% (95% CI: 83.22%, 87.65%) to 87.69% (95% CI: 85.63%, 89.75%) (P = .04), with no evidence of a difference in specificity. Reading time decreased from 54.41 seconds (95% CI: 52.56, 56.27) without AI to 48.52 seconds (95% CI: 46.79, 50.25) with AI (P < .001). Interreader agreement measured by Fleiss kappa increased from 0.59 to 0.62. Conclusion The AI model showed better diagnostic accuracy than radiologists in breast cancer detection, as well as reduced reading times. The concurrent use of AI in DBT interpretation could improve both accuracy and efficiency. Keywords: Breast, Computer-Aided Diagnosis (CAD), Tomosynthesis, Artificial Intelligence, Digital Breast Tomosynthesis, Breast Cancer, Computer-Aided Detection, Screening Supplemental material is available for this article. (c) RSNA, 2024 See also the commentary by Bae in this issue.

Park, J., et al. (2021). "Dr. Answer AI for Prostate Cancer: Predicting Biochemical Recurrence Following Radical Prostatectomy." Technol Cancer Res Treat **20**: 15330338211024660.

OBJECTIVES: To develop a model to predict biochemical recurrence (BCR) after radical prostatectomy (RP), using artificial intelligence (AI) techniques. PATIENTS AND METHODS: This study collected data from 7,128 patients with prostate cancer (PCa) who received RP at 3 tertiary hospitals. After preprocessing, we used the data of 6,755 cases to generate the BCR prediction model. There were 16 input variables with BCR as the outcome variable. We used a random forest to develop the model. Several sampling techniques were used to address class imbalances. RESULTS: We achieved good performance using a random forest with synthetic minority oversampling technique (SMOTE) using Tomek links, edited nearest neighbors (ENN), and random oversampling: accuracy = 96.59%, recall = 95.49%, precision = 97.66%, F1 score = 96.59%, and ROC AUC = 98.83%. CONCLUSION: We developed a BCR prediction model for RP. The Dr. Answer AI project, which was developed based on our BCR prediction model, helps physicians and patients to make treatment decisions in the clinical follow-up process as a clinical decision support system.

Parums, D. V. (2024). "Editorial: Artificial Intelligence (AI), Digital Image Analysis, and the Future of Cancer Diagnosis and Prognosis." Med Sci Monit **30**: e947038.

On October 8 2024, the Royal Swedish Academy of Sciences announced the 2024 Nobel Prize in Physics was awarded to Hopfield and Hinton for their foundation research on machine learning with artificial neural networks, which resulted in the current applications for artificial intelligence (AI). Digital diagnostic histopathology combines image

capture with image analysis and uses digital tools to collect, analyze, and share diagnostic information. An increase in chronic diseases, diagnostic departmental workloads, and diagnostic tests to support targeted therapy in cancer patients have driven the use and development of image analysis systems, and several medical device companies have recently developed whole-slide scanning devices. In April 2017, the US Food and Drug Administration (FDA) permitted marketing authorization for the first whole slide imaging (WSI) system. During 2024, large-scale studies from several cancer centers have shown the potential for diagnostic reporting for real-world data and whole-slide modeling to develop validated diagnostic AI algorithms. This editorial discusses why recent advances and applications in AI and digital image analysis may have an important future role in cancer diagnosis and prognosis.

Parvaiz, A., et al. (2024). "From Pixels to Prognosis: A Survey on AI-Driven Cancer Patient Survival Prediction Using Digital Histology Images." J Imaging Inform Med **37**(4): 1728-1751.

Survival analysis is an integral part of medical statistics that is extensively utilized to establish prognostic indices for mortality or disease recurrence, assess treatment efficacy, and tailor effective treatment plans. The identification of prognostic biomarkers capable of predicting patient survival is a primary objective in the field of cancer research. With the recent integration of digital histology images into routine clinical practice, a plethora of Artificial Intelligence (AI)-based methods for digital pathology has emerged in scholarly literature, facilitating patient survival prediction. These methods have demonstrated remarkable proficiency in analyzing and interpreting whole slide images, yielding results comparable to those of expert pathologists. The complexity of AI-driven techniques is magnified by the distinctive characteristics of digital histology images, including their gigapixel size and diverse tissue appearances. Consequently, advanced patch-based methods are employed to effectively extract features that correlate with patient survival. These computational methods significantly enhance survival prediction accuracy and augment prognostic capabilities in cancer patients. The review discusses the methodologies employed in the literature, their performance metrics, ongoing challenges, and potential solutions for future advancements. This paper explains survival analysis and feature extraction methods for analyzing cancer patients. It also compiles essential acronyms related to cancer precision medicine. Furthermore, it is noteworthy that this is the inaugural review paper in the field. The target audience for this interdisciplinary review comprises AI practitioners, medical statisticians, and progressive oncologists who are enthusiastic about translating AI-driven solutions into clinical practice. We expect this comprehensive review article to guide future research directions in the field of cancer research.

Pattilachan, T. M., et al. (2024). "Diagnosis to dissection: AI's role in early detection and surgical intervention for gastric cancer." J Robot Surg **18**(1): 259.

Gastric cancer remains a formidable health challenge worldwide; early detection and effective surgical intervention are critical for improving patient outcomes. This comprehensive review explores the evolving landscape of gastric cancer management, emphasizing the significant contributions of artificial intelligence (AI) in revolutionizing both diagnostic and therapeutic approaches. Despite advancements in the medical field, the subtle nature of early gastric cancer symptoms often leads to late-stage diagnoses, where survival rates are notably decreased. Historically, the treatment of gastric cancer has transitioned from palliative care to surgical resection, evolving further with the introduction of minimally invasive surgical (MIS) techniques. In the current era, AI has emerged as a transformative force, enhancing the precision of early gastric cancer detection through sophisticated image analysis, and supporting surgical decision-making with predictive modeling and real-time preop-, intraop-, and postoperative guidance. However, the deployment of AI in healthcare raises significant ethical, legal, and practical challenges, including the necessity for ongoing professional education and the development of standardized protocols to ensure patient safety and the effective use of AI technologies. Future directions point toward a synergistic integration of AI with clinical best practices, promising a new era of personalized, efficient, and safer gastric cancer management.

Peng, M., et al. (2017). "Apolipoprotein A-I mimetic peptide 4F suppresses tumor-associated macrophages and pancreatic cancer progression." Oncotarget **8**(59): 99693-99706.

Pancreatic cancer is an aggressive malignancy that is unresponsive to conventional radiation and chemotherapy. Therefore, development of novel immune therapeutic strategies is urgently needed. L-4F, an Apolipoprotein A-I (ApoA-I) mimetic peptide, is engineered to mimic the anti-inflammatory and anti-oxidative functionalities of ApoA-I. In this work, H7 cells were orthotopically implanted in C57BL/6 mice and treated with L-4F. Then, pancreatic cancer progression and the inflammatory microenvironment were investigated in

vivo. The cytotoxicity of L-4F toward H7 cells was assessed in vitro. Furthermore, we investigated the effects of L-4F on macrophage polarization by analyzing the polarization and genes of mouse bone marrow-derived macrophages in vitro. The results show that L-4F substantially reduced the tumorigenicity of H7 cells. L-4F inhibited inflammation by reducing the accumulation of inflammatory cells, such as IL-17A-, IL-4-, GM-CSF-, IL-1beta-, and IL-6-producing cells and Th1 and Th17. Notably, L-4F also decreased the percentage of macrophages in tumor tissues, especially M2 macrophages (CD11b(+)F4/80(+)CD206(+)), which was also confirmed in vitro. Additionally, the expression of the M2 marker genes Arg1, MRC1, and CCL22 and the inflammatory genes IL-6, iNOS, and IL-12 was decreased by L-4F, indicating that L-4F prevents M2 type macrophage polarization. However, L-4F could not directly attenuate H7 cell invasion or proliferation and did not induce apoptosis. In addition, L-4F potently down-regulated STAT3, JNK and ERK signaling pathways but not affects the phosphorylation of p38 in RAW 264.7 cells. These results suggest that L-4F exhibits an effective therapeutic effect on pancreatic cancer progression by inhibiting tumor-associated macrophages and inflammation.

Peng, M., et al. (2020). "Apolipoprotein A-I Mimetic Peptide L-4F Suppresses Granulocytic-Myeloid-Derived Suppressor Cells in Mouse Pancreatic Cancer." Front Pharmacol **11**: 576.

L-4F is an apolipoprotein A-I (ApoA-I) mimetic peptide, it was engineered to imitate the anti-inflammatory and anti-oxidative activity of ApoA-I. In this paper, H7 cell was used to construct a mouse model of pancreatic cancer in situ, and the mice were treated with L-4F. Then, the development of pancreatic cancer and myeloid-derived suppressor cells (MDSCs) infiltration were investigated in vivo. After L-4F treatment, the differentiation, proliferation and apoptosis of MDSCs were detected in vitro. Moreover, we test its effects on the immunosuppressive function of MDSCs ex vivo. The results show that L-4F significantly reduced the tumorigenicity of H7 cells. L-4F suppressed granulocytic myeloid-derived suppressor cells (PMN-MDSCs) differentiation and inhibited the accumulation of PMN-MDSCs in the mouse spleen and tumor tissue. L-4F weakened the immunosuppressive function of MDSCs, resulting in decreased production of ROS and H(2)O(2) by MDSCs, and increased T cell proliferation, interferon gamma and tumor necrosis factor beta secretion, and CD3(+)CD4(+) T and CD3(+)CD8(+) T cell infiltration into the mouse spleen and pancreatic cancer tissue. Furthermore, L-4F significantly down regulated the STAT3 signaling pathway in PMN-MDSCs. These results indicated that L-4F exerts an effective anti-tumor and immunomodulatory effect in pancreatic cancer by inhibiting PMN-MDSCs.

Peng, W., et al. (2024). "Evaluating AI in medicine: a comparative analysis of expert and ChatGPT responses to colorectal cancer questions." Sci Rep **14**(1): 2840.

Colorectal cancer (CRC) is a global health challenge, and patient education plays a crucial role in its early detection and treatment. Despite progress in AI technology, as exemplified by transformer-like models such as ChatGPT, there remains a lack of in-depth understanding of their efficacy for medical purposes. We aimed to assess the proficiency of ChatGPT in the field of popular science, specifically in answering questions related to CRC diagnosis and treatment, using the book "Colorectal Cancer: Your Questions Answered" as a reference. In general, 131 valid questions from the book were manually input into ChatGPT. Responses were evaluated by clinical physicians in the relevant fields based on comprehensiveness and accuracy of information, and scores were standardized for comparison. Not surprisingly, ChatGPT showed high reproducibility in its responses, with high uniformity in comprehensiveness, accuracy, and final scores. However, the mean scores of ChatGPT's responses were significantly lower than the benchmarks, indicating it has not reached an expert level of competence in CRC. While it could provide accurate information, it lacked in comprehensiveness. Notably, ChatGPT performed well in domains of radiation therapy, interventional therapy, stoma care, venous care, and pain control, almost rivaling the benchmarks, but fell short in basic information, surgery, and internal medicine domains. While ChatGPT demonstrated promise in specific domains, its general efficiency in providing CRC information falls short of expert standards, indicating the need for further advancements and improvements in AI technology for patient education in healthcare.

Pereira, T., et al. (2020). "Comprehensive Perspective for Lung Cancer Characterisation Based on AI Solutions Using CT Images." J Clin Med **10**(1).

Lung cancer is still the leading cause of cancer death in the world. For this reason, novel approaches for early and more accurate diagnosis are needed. Computer-aided decision (CAD) can be an interesting option for a noninvasive tumour characterisation based on thoracic computed tomography (CT) image analysis. Until now,

radiomics have been focused on tumour features analysis, and have not considered the information on other lung structures that can have relevant features for tumour genotype classification, especially for epidermal growth factor receptor (EGFR), which is the mutation with the most successful targeted therapies. With this perspective paper, we aim to explore a comprehensive analysis of the need to combine the information from tumours with other lung structures for the next generation of CADs, which could create a high impact on targeted therapies and personalised medicine. The forthcoming artificial intelligence (AI)-based approaches for lung cancer assessment should be able to make a holistic analysis, capturing information from pathological processes involved in cancer development. The powerful and interpretable AI models allow us to identify novel biomarkers of cancer development, contributing to new insights about the pathological processes, and making a more accurate diagnosis to help in the treatment plan selection.

Pesapane, F., et al. (2023). "Women's perceptions and attitudes to the use of AI in breast cancer screening: a survey in a cancer referral centre." Br J Radiol **96**(1141): 20220569.

OBJECTIVE: Although breast cancer screening can benefit from Artificial Intelligence (AI), it is still unknown whether, to which extent or under which conditions, the use of AI is going to be accepted by the general population. The aim of our study is to evaluate what the females who are eligible for breast cancer screening know about AI and how they perceive such innovation. METHODS: We used a prospective survey consisting of a 11-multiple-choice questionnaire evaluating statistical associations with Chi-Square-test or Fisher-exact-test. Multinomial-logistic-regression was performed on items with more than two response categories. Odds ratio (OR) with 95% CI were computed to estimate the probability of a specific response according to patient's characteristics. RESULTS: In the 800 analysed questionnaires, 51% of respondents confirmed to have knowledge of AI. Of these, 88% expressed a positive opinion about its use in medicine. Non-Italian respondents were associated with the belief of having a deep awareness about AI more often than Italian respondents (OR = 1.91;95% CI[1.10-3.33]). Higher education level was associated with better opinions on the use of AI in medicine (OR = 4.69;95% CI[1.36-16.12]). According to 94% of respondents, the radiologists should always produce their own report on mammograms, whilst 77% agreed that AI should be used as a second reader. Most respondents (52%) considered that both the software developer and the radiologist should be held accountable for AI errors. CONCLUSIONS: Most of the females undergoing screening in our Institute approve the introduction of AI, although only as a support to radiologist, and not in substitution thereof. Yet, accountability in case of AI errors is still unsolved. advances in knowledge:This survey may be considered as a pilot-study for the development of large-scale studies to understand females's demands and concerns about AI applications in breast cancer screening.

Pun, F. W., et al. (2023). "A comprehensive AI-driven analysis of large-scale omic datasets reveals novel dual-purpose targets for the treatment of cancer and aging." Aging Cell **22**(12): e14017.

As aging and tumorigenesis are tightly interconnected biological processes, targeting their common underlying driving pathways may induce dual-purpose anti-aging and anti-cancer effects. Our transcriptomic analyses of 16,740 healthy samples demonstrated tissue-specific age-associated gene expression, with most tumor suppressor genes downregulated during aging. Furthermore, a large-scale pan-cancer analysis of 11 solid tumor types (11,303 cases and 4431 control samples) revealed that many cellular processes, such as protein localization, DNA replication, DNA repair, cell cycle, and RNA metabolism, were upregulated in cancer but downregulated in healthy aging tissues, whereas pathways regulating cellular senescence were upregulated in both aging and cancer. Common cancer targets were identified by the AI-driven target discovery platform-PandaOmics. Age-associated cancer targets were selected and further classified into four groups based on their reported roles in lifespan. Among the 51 identified age-associated cancer targets with anti-aging experimental evidence, 22 were proposed as dual-purpose targets for anti-aging and anti-cancer treatment with the same therapeutic direction. Among age-associated cancer targets without known lifespan-regulating activity, 23 genes were selected based on predicted dual-purpose properties. Knockdown of histone demethylase KDM1A, one of these unexplored candidates, significantly extended lifespan in Caenorhabditis elegans. Given KDM1A's anti-cancer activities reported in both preclinical and clinical studies, our findings propose KDM1A as a promising dual-purpose target. This is the first study utilizing an innovative AI-driven approach to identify dual-purpose target candidates for anti-aging and anti-cancer treatment, supporting the value of AI-assisted target identification for drug discovery.

Qiu, X., et al. (2024). "Advances in AI for Protein

Structure Prediction: Implications for Cancer Drug Discovery and Development." Biomolecules **14**(3).

Recent advancements in AI-driven technologies, particularly in protein structure prediction, are significantly reshaping the landscape of drug discovery and development. This review focuses on the question of how these technological breakthroughs, exemplified by AlphaFold2, are revolutionizing our understanding of protein structure and function changes underlying cancer and improve our approaches to counter them. By enhancing the precision and speed at which drug targets are identified and drug candidates can be designed and optimized, these technologies are streamlining the entire drug development process. We explore the use of AlphaFold2 in cancer drug development, scrutinizing its efficacy, limitations, and potential challenges. We also compare AlphaFold2 with other algorithms like ESMFold, explaining the diverse methodologies employed in this field and the practical effects of these differences for the application of specific algorithms. Additionally, we discuss the broader applications of these technologies, including the prediction of protein complex structures and the generative AI-driven design of novel proteins.

Quan, Q., et al. (2017). "Impact of Serum Apolipoprotein A-I on Prognosis and Bevacizumab Efficacy in Patients with Metastatic Colorectal Cancer: a Propensity Score-Matched Analysis." Transl Oncol **10**(2): 288-294.

PURPOSE: We aimed to investigate the role of apolipoprotein A-I (ApoA-I) as a predictor of prognosis and treatment efficacy of bevacizumab in patients with metastatic colorectal cancer (mCRC) treated with first-line chemotherapy with or without bevacizumab. METHODS: We conducted a retrospective study on consecutive patients who were diagnosed with mCRC at Sun Yat-sen University Cancer Center. According to their pretreatment ApoA-I level, patients were divided into low- and high-ApoA-I groups. Propensity score-matched method was performed to balance baseline characteristics between two groups. Based on whether they accepted bevacizumab as a first-line therapy, patients were further divided into the chemo + bevacizumab group and the chemo group. Overall survival (OS) and progression-free survival (PFS) were assessed with Kaplan-Meier method, log-rank test, and Cox regression. RESULTS: The optimal cutoff value for the ApoA-I level was determined to be 1.105 g/l. In the propensity-matched cohort of 508 patients, low ApoA-I was significantly associated with inferior OS (P<.001) and PFS (P<.001) than high ApoA-I. Multivariate analysis showed that ApoA-I level was an independent prognostic maker of OS (P<.001) and PFS (P=.001). PFS (P<.001) in either the high- or low-ApoA-I groups could be extended significantly after the administration of bevacizumab, and patients with a high ApoA-I level also had a better OS in the chemo + bevacizumab group than the chemo group (P=.049). CONCLUSIONS: Patients with a low ApoA-I level have poor prognoses, and they did not display an OS benefit from bevacizumab.

Rahsepar, A. A., et al. (2023). "How AI Responds to Common Lung Cancer Questions: ChatGPT vs Google Bard." Radiology **307**(5): e230922.

Background The recent release of large language models (LLMs) for public use, such as ChatGPT and Google Bard, has opened up a multitude of potential benefits as well as challenges. Purpose To evaluate and compare the accuracy and consistency of responses generated by publicly available ChatGPT-3.5 and Google Bard to non-expert questions related to lung cancer prevention, screening, and terminology commonly used in radiology reports based on the recommendation of Lung Imaging Reporting and Data System (Lung-RADS) v2022 from American College of Radiology and Fleischner society. Materials and Methods Forty of the exact same questions were created and presented to ChatGPT-3.5 and Google Bard experimental version as well as Bing and Google search engines by three different authors of this paper. Each answer was reviewed by two radiologists for accuracy. Responses were scored as correct, partially correct, incorrect, or unanswered. Consistency was also evaluated among the answers. Here, consistency was defined as the agreement between the three answers provided by ChatGPT-3.5, Google Bard experimental version, Bing, and Google search engines regardless of whether the concept conveyed was correct or incorrect. The accuracy among different tools were evaluated using Stata. Results ChatGPT-3.5 answered 120 questions with 85 (70.8%) correct, 14 (11.7%) partially correct, and 21 (17.5%) incorrect. Google Bard did not answer 23 (19.1%) questions. Among the 97 questions answered by Google Bard, 62 (51.7%) were correct, 11 (9.2%) were partially correct, and 24 (20%) were incorrect. Bing answered 120 questions with 74 (61.7%) correct, 13 (10.8%) partially correct, and 33 (27.5%) incorrect. Google search engine answered 120 questions with 66 (55%) correct, 27 (22.5%) partially correct, and 27 (22.5%) incorrect. The ChatGPT-3.5 is more likely to provide correct or partially answer than Google Bard, approximately by 1.5 folds (OR = 1.55, P = 0.004). ChatGPT-3.5 and Google search engine were more likely to be consistent than Google Bard by approximately 7 and 29 folds (OR = 6.65, P

= 0.002 for ChatGPT and OR = 28.83, P = 0.002 for Google search engine, respectively). Conclusion Although ChatGPT-3.5 had a higher accuracy in comparison with the other tools, neither ChatGPT nor Google Bard, Bing and Google search engines answered all questions correctly and with 100% consistency.

Raya-Povedano, J. L., et al. (2021). "AI-based Strategies to Reduce Workload in Breast Cancer Screening with Mammography and Tomosynthesis: A Retrospective Evaluation." Radiology **300**(1): 57-65.

Background The workflow of breast cancer screening programs could be improved given the high workload and the high number of false-positive and false-negative assessments. Purpose To evaluate if using an artificial intelligence (AI) system could reduce workload without reducing cancer detection in breast cancer screening with digital mammography (DM) or digital breast tomosynthesis (DBT). Materials and Methods Consecutive screening-paired and independently read DM and DBT images acquired from January 2015 to December 2016 were retrospectively collected from the Cordoba Tomosynthesis Screening Trial. The original reading settings were single or double reading of DM or DBT images. An AI system computed a cancer risk score for DM and DBT examinations independently. Each original setting was compared with a simulated autonomous AI triaging strategy (the least suspicious examinations for AI are not human-read; the rest are read in the same setting as the original, and examinations not recalled by radiologists but graded as very suspicious by AI are recalled) in terms of workload, sensitivity, and recall rate. The McNemar test with Bonferroni correction was used for statistical analysis. Results A total of 15 987 DM and DBT examinations (which included 98 screening-detected and 15 interval cancers) from 15 986 women (mean age +/- standard deviation, 58 years +/- 6) were evaluated. In comparison with double reading of DBT images (568 hours needed, 92 of 113 cancers detected, 706 recalls in 15 987 examinations), AI with DBT would result in 72.5% less workload (P < .001, 156 hours needed), noninferior sensitivity (95 of 113 cancers detected, P = .38), and 16.7% lower recall rate (P < .001, 588 recalls in 15 987 examinations). Similar results were obtained for AI with DM. In comparison with the original double reading of DM images (222 hours needed, 76 of 113 cancers detected, 807 recalls in 15 987 examinations), AI with DBT would result in 29.7% less workload (P < .001), 25.0% higher sensitivity (P < .001), and 27.1% lower recall rate (P < .001). Conclusion Digital mammography and digital breast tomosynthesis screening strategies based on artificial intelligence systems could reduce workload up to 70%. Published under a CC BY 4.0 license.

Rentiya, Z. S., et al. (2024). "Revolutionizing Breast Cancer Detection With Artificial Intelligence (AI) in Radiology and Radiation Oncology: A Systematic Review." Cureus **16**(4): e57619.

The number one cause of cancer in women worldwide is breast cancer. Over the last three decades, the use of traditional screen-film mammography has increased, but in recent years, digital mammography and 3D tomosynthesis have become standard procedures for breast cancer screening. With the advancement of technology, the interpretation of images using automated algorithms has become a subject of interest. Initially, computer-aided detection (CAD) was introduced; however, it did not show any long-term benefit in clinical practice. With recent advances in artificial intelligence (AI) methods, these technologies are showing promising potential for more accurate and efficient automated breast cancer detection and treatment. While AI promises widespread integration in breast cancer detection and treatment, challenges such as data quality, regulatory, ethical implications, and algorithm validation are crucial. Addressing these is essential for fully realizing AI's potential in enhancing early diagnosis and improving patient outcomes in breast cancer management. In this review article, we aim to provide an overview of the latest developments and applications of AI in breast cancer screening and treatment. While the existing literature primarily consists of retrospective studies, ongoing and future prospective research is poised to offer deeper insights. Artificial intelligence is on the verge of widespread integration into breast cancer detection and treatment, holding the potential to enhance early diagnosis and improve patient outcomes.

Resch, D., et al. (2024). "AI-enhanced Mammography With Digital Breast Tomosynthesis for Breast Cancer Detection: Clinical Value and Comparison With Human Performance." Radiol Imaging Cancer **6**(4): e230149.

Purpose To compare two deep learning-based commercially available artificial intelligence (AI) systems for mammography with digital breast tomosynthesis (DBT) and benchmark them against the performance of radiologists. Materials and Methods This retrospective study included consecutive asymptomatic patients who underwent mammography with DBT (2019-2020). Two AI systems (Transpara 1.7.0 and ProFound AI 3.0) were used to evaluate the DBT examinations. The systems

were compared using receiver operating characteristic (ROC) analysis to calculate the area under the ROC curve (AUC) for detecting malignancy overall and within subgroups based on mammographic breast density. Breast Imaging Reporting and Data System results obtained from standard-of-care human double-reading were compared against AI results with use of the DeLong test. Results Of 419 female patients (median age, 60 years [IQR, 52-70 years]) included, 58 had histologically proven breast cancer. The AUC was 0.86 (95% CI: 0.85, 0.91), 0.93 (95% CI: 0.90, 0.95), and 0.98 (95% CI: 0.96, 0.99) for Transpara, ProFound AI, and human double-reading, respectively. For Transpara, a rule-out criterion of score 7 or lower yielded 100% (95% CI: 94.2, 100.0) sensitivity and 60.9% (95% CI: 55.7, 66.0) specificity. The rule-in criterion of higher than score 9 yielded 96.6% sensitivity (95% CI: 88.1, 99.6) and 78.1% specificity (95% CI: 73.8, 82.5). For ProFound AI, a rule-out criterion of lower than score 51 yielded 100% sensitivity (95% CI: 93.8, 100) and 67.0% specificity (95% CI: 62.2, 72.1). The rule-in criterion of higher than score 69 yielded 93.1% (95% CI: 83.3, 98.1) sensitivity and 82.0% (95% CI: 77.9, 86.1) specificity. Conclusion Both AI systems showed high performance in breast cancer detection but lower performance compared with human double-reading. Keywords: Mammography, Breast, Oncology, Artificial Intelligence, Deep Learning, Digital Breast Tomosynthesis (c) RSNA, 2024.

Rho, M. J., et al. (2022). "Dr. Answer AI for prostate cancer: Intention to use, expected effects, performance, and concerns of urologists." Prostate Int **10**(1): 38-44.

OBJECTIVES: To efficiently implement artificial intelligence (AI) software for medical applications, it is crucial to understand the acceptance, expected effects, expected performance, and concerns of software users. In this study, we examine the acceptance and expectation of the Dr. Answer AI software for prostate cancer. METHODS: We conducted an online survey for urologists from August 13 to September 18, 2020. The target software is an AI-based clinical software called Dr. Answer AI software, used for prostate cancer diagnosis. We collected data from 86 urologists and conducted a basic statistical and multiple regression analysis using the R package. RESULTS: The compatibility was significantly associated with the intention to use the Dr. Answer AI software. The expected average accuracy for the software ranges from 86.91% to 87.51%, and the urologists perceived that the cloud method is suitable to introduce the software. The most desirable function of the software for the specialists is predicting the occurrence of extracapsular extension, seminal vesicle invasion, and lymph node metastasis after radical prostatectomy. Finally, the primary concerns involved the cost, compatibility with existing systems, and obtaining accurate information from the software. CONCLUSIONS: Our results present an understanding of the acceptance, expected effects, expected performance, and concerns of software users. The results provide a guide to help AI software be properly developed and implemented in medical applications.

Rho, M. J., et al. (2020). "Dr. Answer AI for prostate cancer: Clinical outcome prediction model and service." PLoS One **15**(8): e0236553.

OBJECTIVES: The importance of clinical outcome prediction models using artificial intelligence (AI) is being emphasized owing to the increasing necessity of developing a clinical decision support system (CDSS) employing AI. Therefore, in this study, we proposed a "Dr. Answer" AI software based on the clinical outcome prediction model for prostate cancer treated with radical prostatectomy. METHODS: The Dr. Answer AI was developed based on a clinical outcome prediction model, with a user-friendly interface. We used 7,128 clinical data of prostate cancer treated with radical prostatectomy from three hospitals. An outcome prediction model was developed to calculate the probability of occurrence of 1) tumor, node, and metastasis (TNM) staging, 2) extracapsular extension, 3) seminal vesicle invasion, and 4) lymph node metastasis. Random forest and k-nearest neighbors algorithms were used, and the proposed system was compared with previous algorithms. RESULTS: Random forest exhibited good performance for TNM staging (recall value: 76.98%), while k-nearest neighbors exhibited good performance for extracapsular extension, seminal vesicle invasion, and lymph node metastasis (80.24%, 98.67%, and 95.45%, respectively). The Dr. Answer AI software consisted of three primary service structures: 1) patient information, 2) clinical outcome prediction, and outcomes according to the National Comprehensive Cancer Network guideline. CONCLUSION: The proposed clinical outcome prediction model could function as an effective CDSS, supporting the decisions of the physicians, while enabling the patients to understand their treatment outcomes. The Dr. Answer AI software for prostate cancer helps the doctors to explain the treatment outcomes to the patients, allowing the patients to be more confident about their treatment plans.

Rigamonti, A., et al. (2024). "Integrating AI-Powered

Digital Pathology and Imaging Mass Cytometry Identifies Key Classifiers of Tumor Cells, Stroma, and Immune Cells in Non-Small Cell Lung Cancer." Cancer Res **84**(7): 1165-1177.

Artificial intelligence (AI)-powered approaches are becoming increasingly used as histopathologic tools to extract subvisual features and improve diagnostic workflows. On the other hand, hi-plex approaches are widely adopted to analyze the immune ecosystem in tumor specimens. Here, we aimed at combining AI-aided histopathology and imaging mass cytometry (IMC) to analyze the ecosystem of non-small cell lung cancer (NSCLC). An AI-based approach was used on hematoxylin and eosin (H&E) sections from 158 NSCLC specimens to accurately identify tumor cells, both adenocarcinoma and squamous carcinoma cells, and to generate a classifier of tumor cell spatial clustering. Consecutive tissue sections were stained with metal-labeled antibodies and processed through the IMC workflow, allowing quantitative detection of 24 markers related to tumor cells, tissue architecture, CD45+ myeloid and lymphoid cells, and immune activation. IMC identified 11 macrophage clusters that mainly localized in the stroma, except for S100A8+ cells, which infiltrated tumor nests. T cells were preferentially localized in peritumor areas or in tumor nests, the latter being associated with better prognosis, and they were more abundant in highly clustered tumors. Integrated tumor and immune classifiers were validated as prognostic on whole slides. In conclusion, integration of AI-powered H&E and multiparametric IMC allows investigation of spatial patterns and reveals tissue relevant features with clinical relevance. SIGNIFICANCE: Leveraging artificial intelligence-powered H&E analysis integrated with hi-plex imaging mass cytometry provides insights into the tumor ecosystem and can translate tumor features into classifiers to predict prognosis, genotype, and therapy response.

Rinderknecht, E., et al. (2024). "Modification and Validation of the System Causability Scale Using AI-Based Therapeutic Recommendations for Urological Cancer Patients: A Basis for the Development of a Prospective Comparative Study." Curr Oncol **31**(11): 7061-7073.

The integration of artificial intelligence, particularly Large Language Models (LLMs), has the potential to significantly enhance therapeutic decision-making in clinical oncology. Initial studies across various disciplines have demonstrated that LLM-based treatment recommendations can rival those of multidisciplinary tumor boards (MTBs); however, such data are currently lacking for urological cancers. This preparatory study establishes a robust methodological foundation for the forthcoming CONCORDIA trial, including the validation of the System Causability Scale (SCS) and its modified version (mSCS), as well as the selection of LLMs for urological cancer treatment recommendations based on recommendations from ChatGPT-4 and an MTB for 40 urological cancer scenarios. Both scales demonstrated strong validity, reliability (all aggregated Cohen's K > 0.74), and internal consistency (all Cronbach's Alpha > 0.9), with the mSCS showing superior reliability, internal consistency, and clinical applicability ($p < 0.01$). Two Delphi processes were used to define the LLMs to be tested in the CONCORDIA study (ChatGPT-4 and Claude 3.5 Sonnet) and to establish the acceptable non-inferiority margin for LLM recommendations compared to MTB recommendations. The forthcoming ethics-approved and registered CONCORDIA non-inferiority trial will require 110 urological cancer scenarios, with an mSCS difference threshold of 0.15, a Bonferroni corrected alpha of 0.025, and a beta of 0.1. Blinded mSCS assessments of MTB recommendations will then be compared to those of the LLMs. In summary, this work establishes the necessary prerequisites prior to initiating the CONCORDIA study and validates a modified score with high applicability and reliability for this and future trials.

Rodriguez-Rodriguez, A. M., et al. (2024). "AI-Enhanced evaluation of YouTube content on post-surgical incontinence following pelvic cancer treatment." SSM Popul Health **26**: 101677.

BACKGROUND: Several pelvic area cancers exhibit high incidence rates, and their surgical treatment can result in adverse effects such as urinary and fecal incontinence, significantly impacting patients' quality of life. Post-surgery incontinence is a significant concern, with prevalence rates ranging from 25 to 45% for urinary incontinence and 9-68% for fecal incontinence. Cancer survivors are increasingly turning to YouTube as a platform to connect with others, yet caution is warranted as misinformation is prevalent. OBJECTIVE: This study aims to evaluate the information quality in YouTube videos about post-surgical incontinence after pelvic area cancer surgery. METHODS: A YouTube search for "Incontinence after cancer surgery" yielded 108 videos, which were subsequently analyzed. To evaluate these videos, several quality assessment tools were utilized, including DISCERN, GQS, JAMA, PEMAT, and MQ-VET. Statistical analyses, such as descriptive statistics and intercorrelation tests, were employed to assess various video attributes, including characteristics, popularity, educational value, quality,

and reliability. Also, artificial intelligence techniques like PCA, t-SNE, and UMAP were used for data analysis. HeatMap and Hierarchical Clustering Dendrogram techniques validated the Machine Learning results. RESULTS: The quality scales presented a high level of correlation one with each other ($p < 0.01$) and the Artificial Intelligence-based techniques presented clear clustering representations of the dataset samples, which were reinforced by the Heat Map and Hierarchical Clustering Dendrogram. CONCLUSIONS: YouTube videos on "Incontinence after Cancer Surgery" present a "High" quality across multiple scales. The use of AI tools, like PCA, t-SNE, and UMAP, is highlighted for clustering large health datasets, improving data visualization, pattern recognition, and complex healthcare analysis.

Roest, C., et al. (2023). "AI-assisted biparametric MRI surveillance of prostate cancer: feasibility study." Eur Radiol **33**(1): 89-96.

OBJECTIVES: To evaluate the feasibility of automatic longitudinal analysis of consecutive biparametric MRI (bpMRI) scans to detect clinically significant (cs) prostate cancer (PCa). METHODS: This retrospective study included a multi-center dataset of 1513 patients who underwent bpMRI (T2 + DWI) between 2014 and 2020, of whom 73 patients underwent at least two consecutive bpMRI scans and repeat biopsies. A deep learning PCa detection model was developed to produce a heatmap of all PIRADS >/= 2 lesions across prior and current studies. The heatmaps for each patient's prior and current examination were used to extract differential volumetric and likelihood features reflecting explainable changes between examinations. A machine learning classifier was trained to predict from these features csPCa (ISUP > 1) at the current examination according to biopsy. A classifier trained on the current study only was developed for comparison. An extended classifier was developed to incorporate clinical parameters (PSA, PSA density, and age). The cross-validated diagnostic accuracies were compared using ROC analysis. The diagnostic performance of the best model was compared to the radiologist scores. RESULTS: The model including prior and current study (AUC 0.81, CI: 0.69, 0.91) resulted in a higher ($p = 0.04$) diagnostic accuracy than the current only model (AUC 0.73, CI: 0.61, 0.84). Adding clinical variables further improved diagnostic performance (AUC 0.86, CI: 0.77, 0.93). The diagnostic performance of the surveillance AI model was significantly better ($p = 0.02$) than of radiologists (AUC 0.69, CI: 0.54, 0.81). CONCLUSIONS: Our proposed AI-assisted surveillance of prostate MRI can pick up explainable, diagnostically relevant changes with promising diagnostic accuracy. KEY POINTS: * Sequential prostate MRI scans can be automatically evaluated using a hybrid deep learning and machine learning approach. * The diagnostic accuracy of our csPCa detection AI model improved by including clinical parameters.

Roest, C., et al. (2024). "Multimodal AI Combining Clinical and Imaging Inputs Improves Prostate Cancer Detection." Invest Radiol **59**(12): 854-860.

OBJECTIVES: Deep learning (DL) studies for the detection of clinically significant prostate cancer (csPCa) on magnetic resonance imaging (MRI) often overlook potentially relevant clinical parameters such as prostate-specific antigen, prostate volume, and age. This study explored the integration of clinical parameters and MRI-based DL to enhance diagnostic accuracy for csPCa on MRI. MATERIALS AND METHODS: We retrospectively analyzed 932 biparametric prostate MRI examinations performed for suspected csPCa (ISUP >/=2) at 2 institutions. Each MRI scan was automatically analyzed by a previously developed DL model to detect and segment csPCa lesions. Three sets of features were extracted: DL lesion suspicion levels, clinical parameters (prostate-specific antigen, prostate volume, age), and MRI-based lesion volumes for all DL-detected lesions. Six multimodal artificial intelligence (AI) classifiers were trained for each combination of feature sets, employing both early (feature-level) and late (decision-level) information fusion methods. The diagnostic performance of each model was tested internally on 20% of center 1 data and externally on center 2 data (n = 529). Receiver operating characteristic comparisons determined the optimal feature combination and information fusion method and assessed the benefit of multimodal versus unimodal analysis. The optimal model performance was compared with a radiologist using PI-RADS. RESULTS: Internally, the multimodal AI integrating DL suspicion levels with clinical features via early fusion achieved the highest performance. Externally, it surpassed baselines using clinical parameters (0.77 vs 0.67 area under the curve [AUC], $P < 0.001$) and DL suspicion levels alone (AUC: 0.77 vs 0.70, $P = 0.006$). Early fusion outperformed late fusion in external data (0.77 vs 0.73 AUC, $P = 0.005$). No significant performance gaps were observed between multimodal AI and radiologist assessments (internal: 0.87 vs 0.88 AUC; external: 0.77 vs 0.75 AUC, both $P > 0.05$). CONCLUSIONS: Multimodal AI (combining DL suspicion levels and clinical parameters) outperforms clinical and MRI-only AI for csPCa detection. Early information fusion enhanced AI robustness in our multicenter setting.

Incorporating lesion volumes did not enhance diagnostic efficacy.

Roggia, M., et al. (2024). "Discovering Dually Active Anti-cancer Compounds with a Hybrid AI-structure-based Approach." J Chem Inf Model **64**(21): 8299-8309.

Cancer's persistent growth often relies on its ability to maintain telomere length and tolerate the accumulation of DNA damage. This study explores a computational approach to identify compounds that can simultaneously target both G-quadruplex (G4) structures and poly(ADP-ribose) polymerase (PARP)1 enzyme, offering a potential multipronged attack on cancer cells. We employed a hybrid virtual screening (VS) protocol, combining the power of machine learning with traditional structure-based methods. PyRMD, our AI-powered tool, was first used to analyze vast chemical libraries and to identify potential PARP1 inhibitors based on known bioactivity data. Subsequently, a structure-based VS approach selected compounds from these identified inhibitors for their G4 stabilization potential. This two-step process yielded 50 promising candidates, which were then experimentally validated for their ability to inhibit PARP1 and stabilize G4 structures. Ultimately, four lead compounds emerged as promising candidates with the desired dual activity and demonstrated antiproliferative effects against specific cancer cell lines. This study highlights the potential of combining Artificial Intelligence and structure-based methods for the discovery of multitarget anticancer compounds, offering a valuable approach for future drug development efforts.

Romeo, V., et al. (2022). "AI-enhanced simultaneous multiparametric (18)F-FDG PET/MRI for accurate breast cancer diagnosis." Eur J Nucl Med Mol Imaging **49**(2): 596-608.

PURPOSE: To assess whether a radiomics and machine learning (ML) model combining quantitative parameters and radiomics features extracted from simultaneous multiparametric (18)F-FDG PET/MRI can discriminate between benign and malignant breast lesions. METHODS: A population of 102 patients with 120 breast lesions (101 malignant and 19 benign) detected on ultrasound and/or mammography was prospectively enrolled. All patients underwent hybrid (18)F-FDG PET/MRI for diagnostic purposes. Quantitative parameters were extracted from DCE (MTT, VD, PF), DW (mean ADC of breast lesions and contralateral breast parenchyma), PET (SUVmax, SUVmean, and SUVminimum of breast lesions, as well as SUVmean of the contralateral breast parenchyma), and T2-weighted images. Radiomics features were extracted from DCE, T2-weighted, ADC, and PET images. Different diagnostic models were developed using a fine Gaussian support vector machine algorithm which explored different combinations of quantitative parameters and radiomics features to obtain the highest accuracy in discriminating between benign and malignant breast lesions using fivefold cross-validation. The performance of the best radiomics and ML model was compared with that of expert reader review using McNemar's test. RESULTS: Eight radiomics models were developed. The integrated model combining MTT and ADC with radiomics features extracted from PET and ADC images obtained the highest accuracy for breast cancer diagnosis (AUC 0.983), although its accuracy was not significantly higher than that of expert reader review (AUC 0.868) ($p = 0.508$). CONCLUSION: A radiomics and ML model combining quantitative parameters and radiomics features extracted from simultaneous multiparametric (18)F-FDG PET/MRI images can accurately discriminate between benign and malignant breast lesions.

Romeo, V., et al. (2023). "AI-Enhanced PET and MR Imaging for Patients with Breast Cancer." PET Clin **18**(4): 567-575.

New challenges are currently faced by clinical and surgical oncologists in the management of patients with breast cancer, mainly related to the need for molecular and prognostic data. Recent technological advances in diagnostic imaging and informatics have led to the introduction of functional imaging modalities, such as hybrid PET/MR imaging, and artificial intelligence (AI) software, aimed at the extraction of quantitative radiomics data, which may reflect tumor biology and behavior. In this article, the most recent applications of radiomics and AI to PET/MR imaging are described to address the new needs of clinical and surgical oncology.

Romine, P. E., et al. (2021). "(18)F-fluorodeoxyglucose (FDG) PET or (18)F-fluorothymidine (FLT) PET to assess early response to aromatase inhibitors (AI) in women with ER+ operable breast cancer in a window-of-opportunity study." Breast Cancer Res **23**(1): 88.

PURPOSE: This study evaluated the ability of (18)F-Fluorodeoxyglucose (FDG) and (18)F-Fluorothymidine (FLT) imaging with positron emission tomography (PET) to measure early response to endocrine therapy from baseline to just prior to surgical resection in estrogen receptor positive (ER+) breast tumors. METHODS: In two separate studies, women with early stage ER+ breast cancer underwent either paired FDG-PET (n = 22) or

FLT-PET (n = 27) scans prior to endocrine therapy and again in the pre-operative setting. Tissue samples for Ki-67 were taken for all patients both prior to treatment and at the time of surgery. RESULTS: FDG maximum standardized uptake value (SUVmax) declined in 19 of 22 lesions (mean 17% (range -45 to 28%)). FLT SUVmax declined in 24 of 27 lesions (mean 26% (range -77 to 7%)). The Ki-67 index declined in both studies, from pre-therapy (mean 23% (range 1 to 73%)) to surgery [mean 8% (range < 1 to 41%)]. Pre- and post-therapy PET measures showed strong rank-order agreement with Ki-67 percentages for both tracers; however, the percent change in FDG or FLT SUVmax did not demonstrate a strong correlation with Ki-67 index change or Ki-67 at time of surgery. CONCLUSIONS: A window-of-opportunity approach using PET imaging to assess early response of breast cancer therapy is feasible. FDG and FLT-PET imaging following a short course of neoadjuvant endocrine therapy demonstrated measurable changes in SUVmax in early stage ER+ positive breast cancers. The percentage change in FDG and FLT-PET uptake did not correlate with changes in Ki-67; post-therapy SUVmax for both tracers was significantly associated with post-therapy Ki-67, an established predictor of endocrine therapy response.

Rynazal, R., et al. (2023). "Leveraging explainable AI for gut microbiome-based colorectal cancer classification." Genome Biol **24**(1): 21.

Studies have shown a link between colorectal cancer (CRC) and gut microbiome compositions. In these studies, machine learning is used to infer CRC biomarkers using global explanation methods. While these methods allow the identification of bacteria generally correlated with CRC, they fail to recognize species that are only influential for some individuals. In this study, we investigate the potential of Shapley Additive Explanations (SHAP) for a more personalized CRC biomarker identification. Analyses of five independent datasets show that this method can even separate CRC subjects into subgroups with distinct CRC probabilities and bacterial biomarkers.

Saikali, S., et al. (2025). "Development and Assessment of an AI-based Machine Learning Model for Predicting Urinary Continence and Erectile Function Recovery after Robotic-Assisted Radical Prostatectomy: Insights from a Prostate Cancer Referral Center." Comput Methods Programs Biomed **259**: 108522.

INTRODUCTION: Prostate cancer remains a significant health concern, with radical prostatectomy being a common treatment approach. However, predicting postoperative functional outcomes, particularly urinary continence and erectile function, poses challenges. Emerging artificial intelligence (AI) technologies offer promise in predictive modeling. This study aimed to develop and validate AI-based models to predict continence and potency following nerve-sparing robotic radical prostatectomy (RARP). METHODS: A cohort of 8,524 patients undergoing RARP was analyzed. Preoperative variables were collected, and two separate machine-learning Artificial Neural Network (ANN) models were trained to predict continence and potency at 12 months post- surgery. Model performance was assessed using area under the curve (AUC) values, with comparisons made to other machine learning algorithms. Feature importance analysis was conducted to identify key predictors. RESULTS: The ANN models demonstrated AUCs of 0.74 for potency and 0.68 for continence prediction, outperforming other algorithms. Feature importance analysis identified variables such as age, comorbidities, and preoperative scores as significant predictors for both outcomes. CONCLUSION: AI-based models show potential in predicting postoperative functional outcomes following RARP. Continued efforts in optimizing models and exploring additional factors are needed to improve predictive accuracy and clinical applicability. Multi-center studies and larger datasets will further contribute to enhancing the value of AI in clinical decision-making for prostate cancer treatment.

Saillard, C., et al. (2023). "Validation of MSIntuit as an AI-based pre-screening tool for MSI detection from colorectal cancer histology slides." Nat Commun **14**(1): 6695.

Mismatch Repair Deficiency (dMMR)/Microsatellite Instability (MSI) is a key biomarker in colorectal cancer (CRC). Universal screening of CRC patients for MSI status is now recommended, but contributes to increased workload for pathologists and delayed therapeutic decisions. Deep learning has the potential to ease dMMR/MSI testing and accelerate oncologist decision making in clinical practice, yet no comprehensive validation of a clinically approved tool has been conducted. We developed MSIntuit, a clinically approved artificial intelligence (AI) based pre-screening tool for MSI detection from haematoxylin-eosin (H&E) stained slides. After training on samples from The Cancer Genome Atlas (TCGA), a blind validation is performed on an independent dataset of 600 consecutive CRC patients. Inter-scanner reliability is studied by digitising each slide using two different scanners. MSIntuit yields a sensitivity of 0.96-0.98, a specificity of 0.47-0.46, and an excellent inter-

scanner agreement (Cohen's kappa: 0.82). By reaching high sensitivity comparable to gold standard methods while ruling out almost half of the non-MSI population, we show that MSIntuit can effectively serve as a pre-screening tool to alleviate MSI testing burden in clinical practice.

Sakashita, S., et al. (2023). "Requirement of image standardization for AI-based macroscopic diagnosis for surgical specimens of gastric cancer." J Cancer Res Clin Oncol **149**(9): 6467-6477.

PURPOSE: The pathological diagnosis of surgically resected gastric cancer involves both a macroscopic diagnosis by gross observation and a microscopic diagnosis by microscopy. Macroscopic diagnosis determines the location and stage of the disease and the involvement of other organs and surgical margin. Lesion recognition is, thus, an important diagnostic step that requires a skilled pathologist. Nonetheless, artificial intelligence (AI) technologies could allow even inexperienced doctors and laboratory technicians to examine surgically resected specimens without the need for pathologists. However, organ imaging conditions vary across hospitals, and an AI algorithm created in one setting may not work properly in another. Thus, we identified and standardized factors affecting the quality of pathological macroscopic images, which could further affect lesion identification using AI. METHODS: We examined necessary image standardization for developing cancer detection AI for surgically resected gastric cancer by changing the following imaging conditions: focus, resolution, brightness, and contrast. RESULTS: Regarding focus, brightness, and contrast, the farther away the test data were from the training macro-image, the less likely the inference was to be correct. Little change was observed for resolution, even with differing conditions for the training and test data. Regarding focus, brightness, and contrast, there were conditions appropriate for AI. Contrast, in particular, was far from the conditions appropriate for humans. CONCLUSION: Standardizing focus, brightness, and contrast is important in the development of AI methodologies for lesion detection in surgically resected gastric cancer. This standardization is essential for AI to be implemented across hospitals.

Saleh, G. A., et al. (2023). "Impact of Imaging Biomarkers and AI on Breast Cancer Management: A Brief Review." Cancers (Basel) **15**(21).

Breast cancer stands out as the most frequently identified malignancy, ranking as the fifth leading cause of global cancer-related deaths. The American College of Radiology (ACR) introduced the Breast Imaging Reporting and Data System (BI-RADS) as a standard terminology facilitating communication between radiologists and clinicians; however, an update is now imperative to encompass the latest imaging modalities developed subsequent to the 5th edition of BI-RADS. Within this review article, we provide a concise history of BI-RADS, delve into advanced mammography techniques, ultrasonography (US), magnetic resonance imaging (MRI), PET/CT images, and microwave breast imaging, and subsequently furnish comprehensive, updated insights into Molecular Breast Imaging (MBI), diagnostic imaging biomarkers, and the assessment of treatment responses. This endeavor aims to enhance radiologists' proficiency in catering to the personalized needs of breast cancer patients. Lastly, we explore the augmented benefits of artificial intelligence (AI), machine learning (ML), and deep learning (DL) applications in segmenting, detecting, and diagnosing breast cancer, as well as the early prediction of the response of tumors to neoadjuvant chemotherapy (NAC). By assimilating state-of-the-art computer algorithms capable of deciphering intricate imaging data and aiding radiologists in rendering precise and effective diagnoses, AI has profoundly revolutionized the landscape of breast cancer radiology. Its vast potential holds the promise of bolstering radiologists' capabilities and ameliorating patient outcomes in the realm of breast cancer management.

Salim, M., et al. (2024). "AI-based selection of individuals for supplemental MRI in population-based breast cancer screening: the randomized ScreenTrustMRI trial." Nat Med **30**(9): 2623-2630.

Screening mammography reduces breast cancer mortality, but studies analyzing interval cancers diagnosed after negative screens have shown that many cancers are missed. Supplemental screening using magnetic resonance imaging (MRI) can reduce the number of missed cancers. However, as qualified MRI staff are lacking, the equipment is expensive to purchase and cost-effectiveness for screening may not be convincing, the utilization of MRI is currently limited. An effective method for triaging individuals to supplemental MRI screening is therefore needed. We conducted a randomized clinical trial, ScreenTrustMRI, using a recently developed artificial intelligence (AI) tool to score each mammogram. We offered trial participation to individuals with a negative screening mammogram and a high AI score (top 6.9%). Upon agreeing to participate, individuals were assigned randomly to one of two groups: those receiving supplemental MRI and those not receiving MRI. The primary endpoint of ScreenTrustMRI is advanced breast cancer defined as either interval cancer, invasive component larger

than 15 mm or lymph node positive cancer, based on a 27-month follow-up time from the initial screening. Secondary endpoints, prespecified in the study protocol to be reported before the primary outcome, include cancer detected by supplemental MRI, which is the focus of the current paper. Compared with traditional breast density measures used in a previous clinical trial, the current AI method was nearly four times more efficient in terms of cancers detected per 1,000 MRI examinations (64 versus 16.5). Most additional cancers detected were invasive and several were multifocal, suggesting that their detection was timely. Altogether, our results show that using an AI-based score to select a small proportion (6.9%) of individuals for supplemental MRI after negative mammography detects many missed cancers, making the cost per cancer detected comparable with screening mammography. ClinicalTrials.gov registration: NCT04832594 .

Salmon, R. J., et al. (2006). "Estrogen receptors evolution in neoadjuvant aromatase inhibitor (AI) therapy for breast cancer in elderly women: stability of hormonal receptor expression during treatment." Am J Clin Oncol **29**(4): 385-388.

In France, 20% of breast cancers occur in women over the age of 70 and 10% in women over the age of 80. As these women are not included in screening programs, breast cancer is often diagnosed later, at the stage of a large tumor. PURPOSE: To analyze clinical response, possibilities of conservative treatment and course of hormonal receptors in patients receiving neoadjuvant aromatase inhibitor (AI) therapy for at least 6 months. PATIENTS AND METHODS: There were 75 patients, with a mean age of 75 +/- 8 years (range, 58-91 years) received AI for 6 months after the diagnosis of invasive breast cancer with positive hormonal receptors. Clinical and radiologic tumor reduction, the number of conservative treatments and the course of estrogens receptor-labeled cells were determined for each patient. RESULTS: All but 1 of these patients obtained clinical reduction of their tumor. Of these, 86% patients received conservative treatment. In the majority of patients, estrogen receptor (ER) level did not vary between the initial assay and analysis of the operative specimen. DISCUSSION AND CONCLUSION: Aromatase inhibitors are effective as neoadjuvant therapy in ER positive elderly patients with large tumors, as is tamoxifen. Changes in hormone receptor expression during treatment do not predict clinical response. In our experience, neoadjuvant AI therapy should be administered for at least 6 months to optimize clinical response before deciding upon surgery. Discrepancy observed in the literature could be explained by the duration of the treatment.

Sandeman, K., et al. (2022). "AI Model for Prostate Biopsies Predicts Cancer Survival." Diagnostics (Basel) **12**(5).

An artificial intelligence (AI) algorithm for prostate cancer detection and grading was developed for clinical diagnostics on biopsies. The study cohort included 4221 scanned slides from 872 biopsy sessions at the HUS Helsinki University Hospital during 2016-2017 and a subcohort of 126 patients treated by robot-assisted radical prostatectomy (RALP) during 2016-2019. In the validation cohort (n = 391), the model detected cancer with a sensitivity of 98% and specificity of 98% (weighted kappa 0.96 compared with the pathologist's diagnosis). Algorithm-based detection of the grade area recapitulated the pathologist's grade group. The area of AI-detected cancer was associated with extra-prostatic extension (G5 OR: 48.52; 95% CI 1.11-8.33), seminal vesicle invasion (cribriform G4 OR: 2.46; 95% CI 0.15-1.7; G5 OR: 5.58; 95% CI 0.45-3.42), and lymph node involvement (cribriform G4 OR: 2.66; 95% CI 0.2-1.8; G5 OR: 4.09; 95% CI 0.22-3). Algorithm-detected grade group 3-5 prostate cancer depicted increased risk for biochemical recurrence compared with grade groups 1-2 (HR: 5.91; 95% CI 1.96-17.83). This study showed that a deep learning model not only can find and grade prostate cancer on biopsies comparably with pathologists but also can predict adverse staging and probability for recurrence after surgical treatment.

Santeramo, R., et al. (2024). "Are better AI algorithms for breast cancer detection also better at predicting risk? A paired case-control study." Breast Cancer Res **26**(1): 25.

BACKGROUND: There is increasing evidence that artificial intelligence (AI) breast cancer risk evaluation tools using digital mammograms are highly informative for 1-6 years following a negative screening examination. We hypothesized that algorithms that have previously been shown to work well for cancer detection will also work well for risk assessment and that performance of algorithms for detection and risk assessment is correlated. METHODS: To evaluate our hypothesis, we designed a case-control study using paired mammograms at diagnosis and at the previous screening visit. The study included n = 3386 women from the OPTIMAM registry, that includes mammograms from women diagnosed with breast cancer in the English breast screening program 2010-2019. Cases were diagnosed with invasive breast cancer or ductal carcinoma in situ at screening and were selected if they had a mammogram available at

the screening examination that led to detection, and a paired mammogram at their previous screening visit 3y prior to detection when no cancer was detected. Controls without cancer were matched 1:1 to cases based on age (year), screening site, and mammography machine type. Risk assessment was conducted using a deep-learning model designed for breast cancer risk assessment (Mirai), and three open-source deep-learning algorithms designed for breast cancer detection. Discrimination was assessed using a matched area under the curve (AUC) statistic. RESULTS: Overall performance using the paired mammograms followed the same order by algorithm for risk assessment (AUC range 0.59-0.67) and detection (AUC 0.81-0.89), with Mirai performing best for both. There was also a correlation in performance for risk and detection within algorithms by cancer size, with much greater accuracy for large cancers (30 mm+, detection AUC: 0.88-0.92; risk AUC: 0.64-0.74) than smaller cancers (0 to < 10 mm, detection AUC: 0.73-0.86, risk AUC: 0.54-0.64). Mirai was relatively strong for risk assessment of smaller cancers (0 to < 10 mm, risk, Mirai AUC: 0.64 (95% CI 0.57 to 0.70); other algorithms AUC 0.54-0.56). CONCLUSIONS: Improvements in risk assessment could stem from enhancing cancer detection capabilities of smaller cancers. Other state-of-the-art AI detection algorithms with high performance for smaller cancers might achieve relatively high performance for risk assessment.

Sathyakumar, K., et al. (2020). "Automated Lung Cancer Detection Using Artificial Intelligence (AI) Deep Convolutional Neural Networks: A Narrative Literature Review." Cureus **12**(8): e10017.

Lung cancer is the number one cause of cancer-related deaths in the United States as well as worldwide. Radiologists and physicians experience heavy daily workloads, thus are at high risk for burn-out. To alleviate this burden, this narrative literature review compares the performance of four different artificial intelligence (AI) models in lung nodule cancer detection, as well as their performance to physicians/radiologists reading accuracy. A total of 648 articles were selected by two experienced physicians with over 10 years of experience in the fields of pulmonary critical care, and hospital medicine. The data bases used to search and select the articles are PubMed/MEDLINE, EMBASE, Cochrane library, Google Scholar, Web of science, IEEEXplore, and DBLP. The articles selected range from the years between 2008 and 2019. Four out of 648 articles were selected using the following inclusion criteria: 1) 18-65 years old, 2) CT chest scans, 2) lung nodule, 3) lung cancer, 3) deep learning, 4) ensemble and 5) classic methods. The exclusion criteria used in this narrative review include: 1) age greater than 65 years old, 2) positron emission tomography (PET) hybrid scans, 3) chest X-ray (CXR) and 4) genomics. The model performance outcomes metrics are measured and evaluated in sensitivity, specificity, accuracy, receiver operator characteristic (ROC) curve, and the area under the curve (AUC). This hybrid deep-learning model is a state-of-the-art architecture, with high-performance accuracy and low false-positive results. Future studies, comparing each model accuracy at depth is key. Automated physician-assist systems as this model in this review article help preserve a quality doctor-patient relationship.

Sato, A., et al. (2024). "Preliminary Screening for Hereditary Breast and Ovarian Cancer Using an AI Chatbot as a Genetic Counselor: Clinical Study." J Med Internet Res **26**: e48914.

BACKGROUND: Hereditary breast and ovarian cancer (HBOC) is a major type of hereditary cancer. Establishing effective screening to identify high-risk individuals for HBOC remains a challenge. We developed a prototype of a chatbot system that uses artificial intelligence (AI) for preliminary HBOC screening to determine whether individuals meet the National Comprehensive Cancer Network BRCA1/2 testing criteria. OBJECTIVE: This study's objective was to validate the feasibility of this chatbot in a clinical setting by using it on a patient population that visited a hospital. METHODS: We validated the medical accuracy of the chatbot system by performing a test on patients who consecutively visited the Kanagawa Cancer Center. The participants completed a preoperation questionnaire to understand their background, including information technology literacy. After the operation, qualitative interviews were conducted to collect data on the usability and acceptability of the system and examine points needing improvement. RESULTS: A total of 11 participants were enrolled between October and December 2020. All of the participants were women, and among them, 10 (91%) had cancer. According to the questionnaire, 6 (54%) participants had never heard of a chatbot, while 7 (64%) had never used one. All participants were able to complete the chatbot operation, and the average time required for the operation was 18.0 (SD 5.44) minutes. The determinations by the chatbot of whether the participants met the BRCA1/2 testing criteria based on their medical and family history were consistent with those by certified genetic counselors (CGCs). We compared the medical histories obtained from the participants by the CGCs with those by the chatbot. Of the 11 participants, 3 (27%) entered information different from that obtained by the CGCs. These

discrepancies were caused by the participant's omissions or communication errors with the chatbot. Regarding the family histories, the chatbot provided new information for 3 (27%) of the 11 participants and complemented information for the family members of 5 (45%) participants not interviewed by the CGCs. The chatbot could not obtain some information on the family history of 6 (54%) participants due to several reasons, such as being outside of the scope of the chatbot's interview questions, the participant's omissions, and communication errors with the chatbot. Interview data were classified into the following: (1) features, (2) appearance, (3) usability and preferences, (4) concerns, (5) benefits, and (6) implementation. Favorable comments on implementation feasibility and comments on improvements were also obtained. CONCLUSIONS: This study demonstrated that the preliminary screening system for HBOC using an AI chatbot was feasible for real patients.

Saurabh, R., et al. (2020). "Prediction of survival rate and effect of drugs on cancer patients with somatic mutations of genes: An AI-based approach." Chem Biol Drug Des **96**(3): 1005-1019.

The causal role of somatic mutation and its interrelationship with gene expression profile during tumor development has already been observed, which plays a major role to decide the cancer grades and overall survival. Accurate and robust prediction of tumor grades and patients' overall survival are important for prognosis, risk factors identification and betterment of the treatment strategy, especially for highly lethal tumors, like gliomas. Here, with the help of more accurate and widely used machine learning-based approaches, we propose an integrative computational pipeline that incorporates somatic mutations and gene expression profile for survival and grade prediction of glioma patients and simultaneously relates it to the drugs to be administered. This study gives us a clear understanding that the same drug is not effective for the treatment of same grade of cancer if the gene mutations are different. The alteration in a specific gene plays a very important role in tumor progression and should also be considered for the selection of appropriate drugs. This proposed framework includes all the necessary factors required for enhancement of therapeutic designs and could be useful for clinicians in determining an accurate and personalized treatment strategy for individual patients suffering from different life threatening diseases.

Sekaran, K., et al. (2023). "Unraveling the Dysbiosis of Vaginal Microbiome to Understand Cervical Cancer Disease Etiology-An Explainable AI Approach." Genes (Basel) **14**(4).

Microbial Dysbiosis is associated with the etiology and pathogenesis of diseases. The studies on the vaginal microbiome in cervical cancer are essential to discern the cause and effect of the condition. The present study characterizes the microbial pathogenesis involved in developing cervical cancer. Relative species abundance assessment identified Firmicutes, Actinobacteria, and Proteobacteria dominating the phylum level. A significant increase in Lactobacillus iners and Prevotella timonensis at the species level revealed its pathogenic influence on cervical cancer progression. The diversity, richness, and dominance analysis divulges a substantial decline in cervical cancer compared to control samples. The beta diversity index proves the homogeneity in the subgroups' microbial composition. The association between enriched Lactobacillus iners at the species level, Lactobacillus, Pseudomonas, and Enterococcus genera with cervical cancer is identified by Linear discriminant analysis Effect Size (LEfSe) prediction. The functional enrichment corroborates the microbial disease association with pathogenic infections such as aerobic vaginitis, bacterial vaginosis, and chlamydia. The dataset is trained and validated with repeated k-fold cross-validation technique using a random forest algorithm to determine the discriminative pattern from the samples. SHapley Additive exPlanations (SHAP), a game theoretic approach, is employed to analyze the results predicted by the model. Interestingly, SHAP identified that the increase in Ralstonia has a higher probability of predicting the sample as cervical cancer. New evidential microbiomes identified in the experiment confirm the presence of pathogenic microbiomes in cervical cancer vaginal samples and their mutuality with microbial imbalance.

Shahadat, N., et al. (2024). "Lung and Colon Cancer Detection Using a Deep AI Model." Cancers (Basel) **16**(22).

Lung and colon cancers are among the leading causes of cancer-related mortality worldwide. Early and accurate detection of these cancers is crucial for effective treatment and improved patient outcomes. False or incorrect detection is harmful. Accurately detecting cancer in a patient's tissue is crucial to their effective treatment. While analyzing tissue samples is complicated and time-consuming, deep learning techniques have made it possible to complete this process more efficiently and accurately. As a result, researchers can study more patients in a shorter amount of time and at a lower cost. Much research has been conducted to investigate deep learning models that require great computational

ability and resources. However, none of these have had a 100% accurate detection rate for these life-threatening malignancies. Misclassified or falsely detecting cancer can have very harmful consequences. This research proposes a new lightweight, parameter-efficient, and mobile-embedded deep learning model based on a 1D convolutional neural network with squeeze-and-excitation layers for efficient lung and colon cancer detection. This proposed model diagnoses and classifies lung squamous cell carcinomas and adenocarcinoma of the lung and colon from digital pathology images. Extensive experiment demonstrates that our proposed model achieves 100% accuracy for detecting lung, colon, and lung and colon cancers from the histopathological (LC25000) lung and colon datasets, which is considered the best accuracy for around 0.35 million trainable parameters and around 6.4 million flops. Compared with the existing results, our proposed architecture shows state-of-the-art performance in lung, colon, and lung and colon cancer detection.

Shakil, R., et al. (2024). "A precise machine learning model: Detecting cervical cancer using feature selection and explainable AI." J Pathol Inform **15**: 100398.

Cervical cancer is a cancer that remains a significant global health challenge all over the world. Due to improper screening in the early stages, and healthcare disparities, a large number of women are suffering from this disease, and the mortality rate increases day by day. Hence, in these studies, we presented a precise approach utilizing six different machine learning models (decision tree, logistic regression, naive bayes, random forest, k nearest neighbors, support vector machine), which can predict the early stage of cervical cancer by analysing 36 risk factor attributes of 858 individuals. In addition, two data balancing techniques-Synthetic Minority Oversampling Technique and Adaptive Synthetic Sampling-were used to mitigate the data imbalance issues. Furthermore, Chi-square and Least Absolute Shrinkage and Selection Operator are two distinct feature selection processes that have been applied to evaluate the feature rank, which are mostly correlated to identify the particular disease, and also integrate an explainable artificial intelligence technique, namely Shapley Additive Explanations, for clarifying the model outcome. The applied machine learning model outcome is evaluated by performance evaluation matrices, namely accuracy, sensitivity, specificity, precision, f1-score, false-positive rate and false-negative rate, and area under the Receiver operating characteristic curve score. The decision tree outperformed in Chi-square feature selection with outstanding accuracy with 97.60%, 98.73% sensitivity, 80% specificity, and 98.73% precision, respectively. During the data imbalance, DT performed 97% accuracy, 99.35% sensitivity, 69.23% specificity, and 97.45% precision. This research is focused on developing diagnostic frameworks with automated tools to improve the detection and management of cervical cancer, as well as on helping healthcare professionals deliver more efficient and personalized care to their patients.

Shamir, S. B., et al. (2024). "New Frontiers in Breast Cancer Imaging: The Rise of AI." Bioengineering (Basel) **11**(5).

Artificial intelligence (AI) has been implemented in multiple fields of medicine to assist in the diagnosis and treatment of patients. AI implementation in radiology, more specifically for breast imaging, has advanced considerably. Breast cancer is one of the most important causes of cancer mortality among women, and there has been increased attention towards creating more efficacious methods for breast cancer detection utilizing AI to improve radiologist accuracy and efficiency to meet the increasing demand of our patients. AI can be applied to imaging studies to improve image quality, increase interpretation accuracy, and improve time efficiency and cost efficiency. AI applied to mammography, ultrasound, and MRI allows for improved cancer detection and diagnosis while decreasing intra- and interobserver variability. The synergistic effect between a radiologist and AI has the potential to improve patient care in underserved populations with the intention of providing quality and equitable care for all. Additionally, AI has allowed for improved risk stratification. Further, AI application can have treatment implications as well by identifying upstage risk of ductal carcinoma in situ (DCIS) to invasive carcinoma and by better predicting individualized patient response to neoadjuvant chemotherapy. AI has potential for advancement in pre-operative 3-dimensional models of the breast as well as improved viability of reconstructive grafts.

Shang, Z., et al. (2018). "Preoperative serum apolipoprotein A-I levels predict long-term survival in non-muscle-invasive bladder cancer patients." Cancer Manag Res **10**: 1177-1190.

INTRODUCTION: The aim of this study was to elucidate the association between apolipoprotein A-I (Apo A-I) and overall survival (OS) as well as cancer-specific survival (CSS) in non-muscle-invasive bladder cancer (NMIBC) patients undergoing transurethral resection of bladder tumor (TURBT). PATIENTS AND METHODS: We

retrospectively collected data of 470 eligible patients diagnosed with NMIBC and who received TURBT between January 2004 and December 2011. Pretreatment blood indexes were examined. The association of Apo A-I with clinicopathological characteristics was further analyzed by dichotomizing our sample into those with Apo A-I </= 1.19 g/L (low Apo A-I group) and those with Apo A-I > 1.19 g/L (high Apo A-I group). OS and CSS were estimated by Kaplan-Meier analysis and the log-rank test was used to compare differences between groups. Univariate and multivariate Cox regression analyses were plotted to assess the prognostic value of Apo A-I in NMIBC patients. In addition, subgroup analyses were performed according to the risk classification of the International Bladder Cancer Group. RESULTS: In the overall population, patients in the high Apo A-I group had greater 5-year OS and 5-year CSS rates as compared to those in the low Apo A-I group. Kaplan-Meier survival analysis revealed that higher albumin, Apo A-I, and hemoglobin levels were associated with greater OS and CSS while elevated neutrophil-lymphocyte ratio was associated with worse OS and CSS in the overall and high-risk population rather than low- and intermediate-risk population. Furthermore, Apo A-I was shown to be an independent predictor in the overall population (for OS, hazard ratio [HR], 0.364, 95% confidence interval [CI], 0.221-0.598, p < 0.001; for CSS, HR, 0.328, 95% CI, 0.185-0.583, p < 0.001) and high-risk patients (for OS, HR, 0.232, 95% CI 0.121-0.443, p < 0.001; for CSS, HR, 0.269, 95% CI, 0.133-0.541, p < 0.001). CONCLUSION: These results suggest that Apo A-I level could potentially serve as a useful prognostic indicator for therapeutic decision making in NMIBC patients.

Shao, Z. X., et al. (2001). "[Clinical study on treatment of middle-advanced stage liver cancer by combined treatment of hepatic artery chemoembolization with gan'ai no. I and no. II]." Zhongguo Zhong Xi Yi Jie He Za Zhi **21**(3): 168-170.

OBJECTIVE: To observe the clinical effect of combined treatment of hepatic artery chemoembolization (HACE) and Chinese herbal medicine (CHM) in treating middle-advanced stage liver cancer. METHODS: Sixty patients with middle-advanced stage liver cancer were randomly divided into two groups. The 30 patients in Group A were treated with combined HACE and Chinese herbal medicine (Gan'ai No. I and No. II) and the other 30 in Group B were treated with HACE alone. All patients were followed up for over 3 years. RESULTS: The 0.5-, 1- and 2-year survival rate in Group A was 76.7%, 56.7% and 30.0% respectively, and those in Group B was 50.0%, 33.3% and 16.7% respectively. The 1- and 2-year recurrence rate in Group A was 43.3%, 66.7% and that in Group B was 66.7%, 90.0% respectively. Moreover, Group A was significantly superior to Group B in tumor shrinking, AFP decreasing and blood leucocyte reducing (P < 0.01), as well as in improving clinical symptoms. CONCLUSION: The combined treatment has obvious effect in treating middle-advanced stage liver cancer.

Sharma, A., et al. (2024). "Validation of an AI-based solution for breast cancer risk stratification using routine digital histopathology images." Breast Cancer Res **26**(1): 123.

BACKGROUND: Stratipath Breast is a CE-IVD marked artificial intelligence-based solution for prognostic risk stratification of breast cancer patients into high- and low-risk groups, using haematoxylin and eosin (H&E)-stained histopathology whole slide images (WSIs). In this validation study, we assessed the prognostic performance of Stratipath Breast in two independent breast cancer cohorts. METHODS: This retrospective multi-site validation study included 2719 patients with primary breast cancer from two Swedish hospitals. The Stratipath Breast tool was applied to stratify patients based on digitised WSIs of the diagnostic H&E-stained tissue sections from surgically resected tumours. The prognostic performance was evaluated using time-to-event analysis by multivariable Cox Proportional Hazards analysis with progression-free survival (PFS) as the primary endpoint. RESULTS: In the clinically relevant oestrogen receptor (ER)-positive/human epidermal growth factor receptor 2 (HER2)-negative patient subgroup, the estimated hazard ratio (HR) associated with PFS between low- and high-risk groups was 2.76 (95% CI: 1.63-4.66, p-value < 0.001) after adjusting for established risk factors. In the ER+/HER2- Nottingham histological grade (NHG) 2 subgroup, the HR was 2.20 (95% CI: 1.22-3.98, p-value = 0.009) between low- and high-risk groups. CONCLUSION: The results indicate an independent prognostic value of Stratipath Breast among all breast cancer patients, as well as in the clinically relevant ER+/HER2- subgroup and the NHG2/ER+/HER2- subgroup. Improved risk stratification of intermediate-risk ER+/HER2- breast cancers provides information relevant for treatment decisions of adjuvant chemotherapy and has the potential to reduce both under- and overtreatment. Image-based risk stratification provides the added benefit of short lead times and substantially lower cost compared to molecular diagnostics and therefore has the potential to reach broader patient groups.

Sharma, N. K. and S. C. Sarode (2024). "Evolving

Artificial Intelligence (AI) at the Crossroads: Potentiating Productive vs. Declining Disruptive Cancer Research." Cancers (Basel) **16**(21).

Artificial intelligence (AI), encompassing several tools and platforms such as artificial "general" intelligence (AGI) and generative artificial intelligence (GenAI), has facilitated cancer research, enhancing productivity in terms of research publications and translational value for cancer patients. AGI tools, such as ChatGPT, assist preclinical and clinical scientists in identifying tumor heterogeneity, predicting therapy outcomes, and streamlining research publications. However, this perspective review also explores the potential of AI's influence on cancer research with regard to its impact on disruptive sciences and discoveries by preclinical and clinical scientists. The increasing reliance on AI tools may compromise biological intelligence, disrupting abstraction, creativity, and critical thinking. This could contribute to the declining trend of disruptive sciences, hindering landmark discoveries and innovations. This perspective review narrates the role of different forms of AI in the potentiation of productive cancer research and the potential disruption of disruptive sciences due to AI's influence.

Sharpless, N. E. and A. R. Kerlavage (2021). "The potential of AI in cancer care and research." Biochim Biophys Acta Rev Cancer **1876**(1): 188573.

Current applications of artificial intelligence (AI), machine learning, and deep learning in cancer research and clinical care are highly diverse-from aiding radiologists in reading medical images to predicting oncoprotein folding and dynamics. The list of available AI-based tools is growing rapidly and will only continue to expand. With the immense potential for AI to advance cancer research and clinical care, the National Cancer Institute (NCI) has a responsibility to consider and support the development and evaluation of such technologies. NCI's current involvement in AI research spans the spectrum of development, implementation, and assessment. That includes generating large, publicly available, curated datasets; shifting the culture of data sharing; training the next generation of scientists in both AI and cancer sciences; fostering interdisciplinary collaborations; investing in research to improve AI methods and models that are designed specifically for cancer; widening access to computing power; procuring computer architecture for future developments; and assuring AI research and technologies follow ethical principles. In addition to a broad overview of AI applications in cancer research and care, and NCI's ongoing AI-based activities, this Perspective outlines NCI's four priority areas for future investment of cancer-focused AI development.

Sheen, A. R. and H. W. U. Saqib (2024). ""Harnessing AI for treatment optimization: Neoadjuvant chemotherapy in gastroesophageal cancer"." Eur J Surg Oncol **50**(4): 108228.

Shehata, M., et al. (2023). "Role of AI and Radiomic Markers in Early Diagnosis of Renal Cancer and Clinical Outcome Prediction: A Brief Review." Cancers (Basel) **15**(10).

Globally, renal cancer (RC) is the 10th most common cancer among men and women. The new era of artificial intelligence (AI) and radiomics have allowed the development of AI-based computer-aided diagnostic/prediction (AI-based CAD/CAP) systems, which have shown promise for the diagnosis of RC (i.e., subtyping, grading, and staging) and prediction of clinical outcomes at an early stage. This will absolutely help reduce diagnosis time, enhance diagnostic abilities, reduce invasiveness, and provide guidance for appropriate management procedures to avoid the burden of unresponsive treatment plans. This survey mainly has three primary aims. The first aim is to highlight the most recent technical diagnostic studies developed in the last decade, with their findings and limitations, that have taken the advantages of AI and radiomic markers derived from either computed tomography (CT) or magnetic resonance (MR) images to develop AI-based CAD systems for accurate diagnosis of renal tumors at an early stage. The second aim is to highlight the few studies that have utilized AI and radiomic markers, with their findings and limitations, to predict patients' clinical outcome/treatment response, including possible recurrence after treatment, overall survival, and progression-free survival in patients with renal tumors. The promising findings of the aforementioned studies motivated us to highlight the optimal AI-based radiomic makers that are correlated with the diagnosis of renal tumors and prediction/assessment of patients' clinical outcomes. Finally, we conclude with a discussion and possible future avenues for improving diagnostic and treatment prediction performance.

Shen, B., et al. (2023). "Development of multiple AI pipelines that predict neoadjuvant chemotherapy response of breast cancer using H&E-stained tissues." J Pathol Clin Res **9**(3): 182-194.

In recent years, the treatment of breast cancer has advanced dramatically and neoadjuvant chemotherapy (NAC) has become a common treatment method, especially for locally advanced breast cancer. However, other than the subtype of breast cancer, no clear factor indicating sensitivity to

NAC has been identified. In this study, we attempted to use artificial intelligence (AI) to predict the effect of preoperative chemotherapy from hematoxylin and eosin images of pathological tissue obtained from needle biopsies prior to chemotherapy. Application of AI to pathological images typically uses a single machine-learning model such as support vector machines (SVMs) or deep convolutional neural networks (CNNs). However, cancer tissues are extremely diverse and learning with a realistic number of cases limits the prediction accuracy of a single model. In this study, we propose a novel pipeline system that uses three independent models each focusing on different characteristics of cancer atypia. Our system uses a CNN model to learn structural atypia from image patches and SVM and random forest models to learn nuclear atypia from fine-grained nuclear features extracted by image analysis methods. It was able to predict the NAC response with 95.15% accuracy on a test set of 103 unseen cases. We believe that this AI pipeline system will contribute to the adoption of personalized medicine in NAC therapy for breast cancer.

Shi, H., et al. (2018). "Decreased pretherapy serum apolipoprotein A-I is associated with extent of metastasis and poor prognosis of non-small-cell lung cancer." Onco Targets Ther **11**: 6995-7003.

BACKGROUND: Apolipoprotein A-I (ApoA-I), which recently attracted great attention as an important protein related to the increasing risk of various cancers, is a factor closely related to metabolic diseases such as ardiovascular diseases and atherosclerosis. However, the diagnostic and prognostic value of pretherapy serum ApoA-I levels in non-small-cell lung cancer (NSCLC) patients is still not very clear. METHODS: In 325 NSCLC patients and 312 healthy controls, pretherapy serum ApoA-I was measured by turbidimetric immunoassay. The association of serum ApoA-I levels with the clinicopathologic characteristics and clinical outcomes of NSCLC patients was analyzed. Receiver-operating characteristic (ROC) curve analysis and univariate and multivariate Cox regression analyses were used to assess the diagnostic and prognostic significance of serum ApoA-I levels. RESULTS: Serum ApoA-I levels were obviously decreased in NSCLC patients compared with healthy controls (1.22+/-0.27 vs 1.46+/-0.22 g/L, P<0.0001). Pretherapy serum ApoA-I levels were significantly decreased in the NSCLC patients with increased pretherapy C-reactive protein levels (P=0.046), lower albumin serum level (P=0.040), advanced TNM stage (P=0.004), poorer Eastern Cooperative Oncology Group PS: performance status scores (P=0.007), and more than two sites of distant metastasis (P<0.0001). ROC curve showed the optimal cut-off for ApoA-I was 1.26 g/L (Area under ROC curve=0.69, 95% CI=0.54-0.65) with a specificity of 0.75 and a sensitivity of 0.59. The whole cohort was divided into two groups: low ApoA-I levels group (ApoA-I </=1.26 g/L) consisted of 193 (59.4%) patients and high ApoA-I levels group (ApoA-I >1.26 g/L) consisted of 132 (40.6%) patients. The median survival time of low and high ApoA-I levels patients were 16.45 and 20.90 months, respectively, which indicated a statistically significant difference (chi (2)=0.609, P<0.0001) between the two groups. The multivariate analysis results showed that CRP levels (HR=1.273, P=0.038), ApoA-I levels (HR=0.761, P=0.030), Eastern Cooperative Oncology Group performance status (HR=1.486, P=0.016), and extent of metastasis (HR=1.394, P=0.009) were significant independent predictors of favorable overall survival. CONCLUSION: A decreased level of pretherapy ApoA-I was associated with a worse survival in patients with NSCLC. Serum ApoA-I measurement before initial treatment may be a novel and routine biomarker to evaluate for metastasis and predict prognosis for NSCLC patients in daily clinical practice.

Shin, H., et al. (2023). "Single test-based diagnosis of multiple cancer types using Exosome-SERS-AI for early stage cancers." Nat Commun **14**(1): 1644.

Early cancer detection has significant clinical value, but there remains no single method that can comprehensively identify multiple types of early-stage cancer. Here, we report the diagnostic accuracy of simultaneous detection of 6 types of early-stage cancers (lung, breast, colon, liver, pancreas, and stomach) by analyzing surface-enhanced Raman spectroscopy profiles of exosomes using artificial intelligence in a retrospective study design. It includes classification models that recognize signal patterns of plasma exosomes to identify both their presence and tissues of origin. Using 520 test samples, our system identified cancer presence with an area under the curve value of 0.970. Moreover, the system classified the tumor organ type of 278 early-stage cancer patients with a mean area under the curve of 0.945. The final integrated decision model showed a sensitivity of 90.2% at a specificity of 94.4% while predicting the tumor organ of 72% of positive patients. Since our method utilizes a non-specific analysis of Raman signatures, its diagnostic scope could potentially be expanded to include other diseases.

Shukla, P. K., et al. (2022). "AI-DRIVEN Novel Approach for Liver Cancer Screening and Prediction Using Cascaded Fully Convolutional Neural

Network." J Healthc Eng **2022**: 4277436.

In experimental analysis and computer-aided design sustain scheme, segmentation of cell liver and hepatic lesions by an automated method is a significant step for studying the biomarkers characteristics in experimental analysis and computer-aided design sustain scheme. Patient to patient, the change in lesion type is dependent on the size, imaging equipment (such as the setting dissimilarity approach), and timing of the lesion, all of which are different. With practical approaches, it is difficult to determine the stages of liver cancer based on the segmentation of lesion patterns. Based on the training accuracy rate, the present algorithm confronts a number of obstacles in some domains. The suggested work proposes a system for automatically detecting liver tumours and lesions in magnetic resonance imaging of the abdomen pictures by using 3D affine invariant and shape parameterization approaches, as well as the results of this study. This point-to-point parameterization addresses the frequent issues associated with concave surfaces by establishing a standard model level for the organ's surface throughout the modelling process. Initially, the geodesic active contour analysis approach is used to separate the liver area from the rest of the body. The proposal is as follows: It is possible to minimise the error rate during the training operations, which are carried out using Cascaded Fully Convolutional Neural Networks (CFCNs) using the input of the segmented tumour area. Liver segmentation may help to reduce the error rate during the training procedures. The stage analysis of the data sets, which are comprised of training and testing pictures, is used to get the findings and validate their validity. The accuracy attained by the Cascaded Fully Convolutional Neural Network (CFCN) for the liver tumour analysis is 94.21 percent, with a calculation time of less than 90 seconds per volume for the liver tumour analysis. The results of the trials show that the total accuracy rate of the training and testing procedure is 93.85 percent in the various volumes of 3DIRCAD datasets tested.

Silverwood, S., et al. (2024). "The Promise and Challenges of AI Integration in Ovarian Cancer Screenings." Reprod Sci **31**(9): 2637-2640.

PURPOSE: Ovarian cancer is oftendiagnosed late due to vague symptoms, leading to poor survival rate. Improved screening tests could mitigate this issue. This narrative review examines the potential and challenges of integrating artificial intelligence (A.I.) into ovarian cancer screenings, with a focus on improving early detection, diagnosis, and personalized risk assessment. METHOD: A comprehensive review of existing literature was conducted, analyzing studies and discussions within the scientific community. RESULTS: A.I. shows promise in significantly improving the ovarian cancer screening processes, increasing accuracy, efficiency, and resource allocation. However, data quality and bias issues pose considerable challenges, potentially leading to healthcare disparities. CONCLUSIONS: Integrating A.I. into ovarian cancer screenings offers potential benefits but comes with significant challenges. By promoting diverse data collection, engaging with underrepresented groups, and ensuring ethical data use, A.I. can be harnessed for more accurate and equitable ovarian cancer diagnoses.

Singh, A., et al. (2024). "Research trends on AI in breast cancer diagnosis, and treatment over two decades." Discov Oncol **15**(1): 772.

OBJECTIVE: Recently, the integration of Artificial Intelligence (AI) has significantly enhanced the diagnostic accuracy in breast cancer screening. This study aims to deliver an extensive review of the advancements in AI for breast cancer diagnosis and prognosis through a bibliometric analysis. METHODOLOGY: Therefore, this study gathered pertinent peer-reviewed research articles from the Scopus database, spanning the years 2000 to 2024. These articles were subsequently subjected to quantitative analysis and visualization through the Bibliometrix R package. Ultimately, potential areas for future research challenges were pinpointed. RESULTS: This study analyzes the development of Artificial Intelligence (AI) research for breast cancer diagnosis and prognosis from 2000 to 2024, based on 2678 publications sourced from Scopus. A sharp rise in global publication trends is observed between 2018 and 2023, with 2023 producing 456 papers, indicating intensified academic focus. Leading contributors include ZHENG B, with 36 publications, and institutions like RADBOUD UNIVERSITY MEDICAL CENTER and the IEO EUROPEAN INSTITUTE OF ONCOLOGY IRCCS. The USA leads both in publications (473) and total citations (18,530), followed by India with 289 papers. Co-occurrence analysis shows that "mammography" (3171 occurrences) and "artificial intelligence" (1691 occurrences) are among the most frequent keywords, reflecting core themes. Co-citation network analysis identifies foundational works by authors like Lecun Y. and Simonyan K. in advancing AI applications in breast cancer. Institutional and country-level collaboration analysis reveals the USA's significant partnerships with China, the UK, and Canada, driving the global research agenda in this field. CONCLUSION: In conclusion, this bibliometric review underscores the growing influence of AI, particularly deep learning, in breast cancer diagnosis

and treatment research from 2000 to 2024. The United States leads the field in publications and collaborations, with India, Spain, and the Netherlands also making significant contributions. Key institutions and journals have driven advancements, with AI applications focusing on improving diagnostic imaging and early detection. However, challenges like data limitations, regulatory hurdles, and unequal global collaboration persist, requiring further interdisciplinary efforts to enhance AI integration in clinical practice.

Singh, S., et al. (2024). "AI screening and molecular dynamic simulation-driven identification of novel inhibitors of TGFssR1 for pancreatic cancer therapy." Comput Biol Chem **113**: 108262.

Pancreatic cancer, with a 5-year survival rate below 10 %, is one of the deadliest malignancies. The TGF-ss pathway plays a crucial role in this disease, making it a key target for therapeutic intervention. Clinical trials targeting TGF-beta have faced challenges of toxicity and limited efficacy, highlighting the need for more potent small molecule inhibitors. We selected TGFssR1 as the drug target to inhibit TGF-ss signaling in pancreatic cancer. A multi-faceted approach was employed, commencing with AI-driven screening techniques to rapidly identify potential TGFssR1 inhibitors from vast compound libraries, including the ZINC and ChEMBL databases. AI-screened compounds were further validated through structure-based high-throughput virtual screening (HTVS) to evaluate their binding affinity to TGFssR1. In addition to this, a dedicated library of anticancer compounds (65,000 compounds) and protein kinase inhibitors (36,324 compounds) were also used for HTVS. Subsequently, pharmacokinetic profiling narrowed the selection to 40 hit compounds. Five hit compounds were chosen based on binding affinity, non-bonded interactions, stereochemistry, and pharmacokinetic profiles for molecular dynamics (MD) simulations. Trajectory analysis showed that residues HIS283, ASP351, LYS232, SER280, ILE211, and LYS213 within TGFssR1's active site are crucial for ligand binding through hydrogen bonds and hydrophobic interactions. Principal component analysis (PCA) and Dynamic cross-correlation matrix (DCCM) analysis were used to evaluate the receptor's dynamic response to the hit compounds. The simulation data revealed that compounds 1, 2, 3, 4, and 5 formed stable complexes with TGFssR1. Notably, post-MDS MM-GBSA analysis showed that compounds 4 and 5 exhibited exceptionally strong binding energies of -81.0 kcal/mol and -85.5 kcal/mol, respectively. The comprehensive computational analysis confirms compounds 4 and 5 as promising TGFssR1 hits with potential therapeutic applications in development of new treatments for pancreatic cancer.

Singh, Y., et al. (2024). "Generative AI in oncological imaging: Revolutionizing cancer detection and diagnosis." Oncotarget **15**: 607-608.

Generative AI is revolutionizing oncological imaging, enhancing cancer detection and diagnosis. This editorial explores its impact on expanding datasets, improving image quality, and enabling predictive oncology. We discuss ethical considerations and introduce a unique perspective on personalized cancer screening using AI-generated digital twins. This approach could optimize screening protocols, improve early detection, and tailor treatment plans. While challenges remain, generative AI in oncological imaging offers unprecedented opportunities to advance cancer care and improve patient outcomes.

Singh, Y., et al. (2024). "Beyond the hype: Navigating bias in AI-driven cancer detection." Oncotarget **15**: 764-766.

Singha, M., et al. (2023). "Unlocking the Potential of Kinase Targets in Cancer: Insights from CancerOmicsNet, an AI-Driven Approach to Drug Response Prediction in Cancer." Cancers (Basel) **15**(16).

Deregulated protein kinases are crucial in promoting cancer cell proliferation and driving malignant cell signaling. Although these kinases are essential targets for cancer therapy due to their involvement in cell development and proliferation, only a small part of the human kinome has been targeted by drugs. A comprehensive scoring system is needed to evaluate and prioritize clinically relevant kinases. We recently developed CancerOmicsNet, an artificial intelligence model employing graph-based algorithms to predict the cancer cell response to treatment with kinase inhibitors. The performance of this approach has been evaluated in large-scale benchmarking calculations, followed by the experimental validation of selected predictions against several cancer types. To shed light on the decision-making process of CancerOmicsNet and to better understand the role of each kinase in the model, we employed a customized saliency map with adjustable channel weights. The saliency map, functioning as an explainable AI tool, allows for the analysis of input contributions to the output of a trained deep-learning model and facilitates the identification of essential kinases involved in tumor progression. The comprehensive survey of biomedical literature for essential kinases selected by CancerOmicsNet demonstrated that it could help

pinpoint potential druggable targets for further investigation in diverse cancer types.

Song, Q., et al. (2020). "Protocol for a systematic review and meta-analysis of Kang-ai injection for patients with oesophageal cancer." Medicine (Baltimore) **99**(36): e22148.

BACKGROUND: Oesophageal cancer (OC) is the sixth leading cause of cancer death worldwide. Despite the improvement of therapeutic methods in recent years, the prognosis of OC remains unsatisfactory. Kang-ai injection, a kind of traditional Chinese herbal medicine, has been widely applied as a promising adjunctive drug for OC. In this study, we aimed to summarize the efficacy and safety of Kang-ai injection for patients with advanced OC through the meta-analysis, in order to provide scientific reference for the design of future clinical trials. METHODS: Relevant randomized controlled trials and high-quality prospective cohort studies were searched from PubMed, Web of Science, Medline, Cochrane Library, Google Scholar, Excerpt Medica Database, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, China Scientific Journal Database and Wanfang Database. Papers in English or Chinese published from their inception to August 2020 will be included without any restrictions.Study selection and data extraction will be performed independently by 2 investigators. The clinical outcomes including overall response rate, disease control rate, overall survival, disease-free survival, quality of life, immune function and adverse events, were systematically evaluated. Stata 14.0 and Review Manager 5.3 were used for data synthesis, subgroup analysis, sensitivity analysis, meta regression, and risk of bias assessment. RESULTS: The results of this study will be published in a peer-reviewed journal, or presented the findings at a relevant conference. CONCLUSION: Our study will draw an objective conclusion of the effects of Kang-ai injection combined with conventional treatment for advanced OC and provide a helpful evidence for clinicians to formulate the best postoperative adjuvant treatment strategy for OC patients. INPLASY REGISTRATION NUMBER: INPLASY202080019.

Soria-Utrilla, V., et al. (2024). "AI-Assisted Body Composition Assessment Using CT Imaging in Colorectal Cancer Patients: Predictive Capacity for Sarcopenia and Malnutrition Diagnosis." Nutrients **16**(12).

(1) Background: The assessment of muscle mass is crucial in the nutritional evaluation of patients with colorectal cancer (CRC), as decreased muscle mass is linked to increased complications and poorer prognosis. This study aims to evaluate the utility of AI-assisted L3 CT for assessing body composition and determining low muscle mass using both the Global Leadership Initiative on Malnutrition (GLIM) criteria for malnutrition and the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria for sarcopenia in CRC patients prior to surgery. Additionally, we aim to establish cutoff points for muscle mass in men and women and propose their application in these diagnostic frameworks. (2) Methods: This retrospective observational study included CRC patients assessed by the Endocrinology and Nutrition services of the Regional University Hospitals of Malaga, Virgen de la Victoria of Malaga, and Vall d'Hebron of Barcelona from October 2018 to July 2023. A morphofunctional assessment, including anthropometry, bioimpedance analysis (BIA), and handgrip strength, was conducted to apply the GLIM criteria for malnutrition and the EWGSOP2 criteria for sarcopenia. Body composition evaluation was performed through AI-assisted analysis of CT images at the L3 level. ROC analysis was used to determine the predictive capacity of variables derived from the CT analysis regarding the diagnosis of low muscle mass and to describe cutoff points. (3) Results: A total of 586 patients were enrolled, with a mean age of 68.4 +/- 10.2 years. Using the GLIM criteria, 245 patients (41.8%) were diagnosed with malnutrition. Applying the EWGSOP2 criteria, 56 patients (9.6%) were diagnosed with sarcopenia. ROC curve analysis for the skeletal muscle index (SMI) showed a strong discriminative capacity of muscle area to detect low fat-free mass index (FFMI) (AUC = 0.82, 95% CI 0.77-0.87, $p < 0.001$). The identified SMI cutoff for diagnosing low FFMI was 32.75 cm(2)/m(2) (Sn 77%, Sp 64.3%; AUC = 0.79, 95% CI 0.70-0.87, $p < 0.001$) in women, and 39.9 cm(2)/m(2) (Sn 77%, Sp 72.7%; AUC = 0.85, 95% CI 0.80-0.90, $p < 0.001$) in men. Additionally, skeletal muscle area (SMA) showed good discriminative capacity for detecting low appendicular skeletal muscle mass (ASMM) (AUC = 0.71, 95% CI 0.65-0.76, $p < 0.001$). The identified SMA cutoff points for diagnosing low ASMM were 83.2 cm(2) (Sn 76.7%, Sp 55.3%; AUC = 0.77, 95% CI 0.69-0.84, $p < 0.001$) in women and 112.6 cm(2) (Sn 82.3%, Sp 58.6%; AUC = 0.79, 95% CI 0.74-0.85, $p < 0.001$) in men. (4) Conclusions: AI-assisted body composition assessment using CT is a valuable tool in the morphofunctional evaluation of patients with colorectal cancer prior to surgery. CT provides quantitative data on muscle mass for the application of the GLIM criteria for malnutrition and the EWGSOP2 criteria for sarcopenia, with specific cutoff points established for diagnostic use.

Spratt, D. E. (2022). "The use of AI to identify predictive, pathology-based biomarkers in men with prostate cancer." Clin Adv Hematol Oncol **20**(11): 659-661.

Stower, H. (2020). "AI for breast-cancer screening." Nat Med **26**(2): 163.

Su, F., et al. (2010). "Apolipoprotein A-I (apoA-I) and apoA-I mimetic peptides inhibit tumor development in a mouse model of ovarian cancer." Proc Natl Acad Sci U S A **107**(46): 19997-20002.

We examined whether reduced levels of Apolipoprotein A-I (apoA-I) in ovarian cancer patients are causal in ovarian cancer in a mouse model. Mice expressing a human apoA-I transgene had (i) increased survival ($P < 0.0001$) and (ii) decreased tumor development ($P < 0.01$), when compared with littermates, following injection of mouse ovarian epithelial papillary serous adenocarcinoma cells (ID-8 cells). ApoA-I mimetic peptides reduced viability and proliferation of ID8 cells and cis-platinum-resistant human ovarian cancer cells, and decreased ID-8 cell-mediated tumor burden in C57BL/6J mice when administered subcutaneously or orally. Serum levels of lysophosphatidic acid, a well-characterized modulator of tumor cell proliferation, were significantly reduced (>50% compared with control mice, $P < 0.05$) in mice that received apoA-I mimetic peptides (administered either subcutaneously or orally), suggesting that binding and removal of lysophosphatidic acid is a potential mechanism for the inhibition of tumor development by apoA-I mimetic peptides, which may serve as a previously unexplored class of anticancer agents.

Talens, J. B., et al. (2023). "Prostate cancer detection using e-nose and AI for high probability assessment." BMC Med Inform Decis Mak **23**(1): 205.

This research aims to develop a diagnostic tool that can quickly and accurately detect prostate cancer using electronic nose technology and a neural network trained on a dataset of urine samples from patients diagnosed with both prostate cancer and benign prostatic hyperplasia, which incorporates a unique data redundancy method. By analyzing signals from these samples, we were able to significantly reduce the number of unnecessary biopsies and improve the classification method, resulting in a recall rate of 91% for detecting prostate cancer. The goal is to make this technology widely available for use in primary care centers, to allow for rapid and non-invasive diagnoses.

Tan, B. K. J., et al. (2021). "Personalised, Rational, Efficacy-Driven Cancer Drug Dosing via an Artificial Intelligence SystEm (PRECISE): A Protocol for the PRECISE CURATE.AI Pilot Clinical Trial." Front Digit Health **3**: 635524.

Introduction: Oncologists have traditionally administered the maximum tolerated doses of drugs in chemotherapy. However, these toxicity-guided doses may lead to suboptimal efficacy. CURATE.AI is an indication-agnostic, mechanism-independent and efficacy-driven personalised dosing platform that may offer a more optimal solution. While CURATE.AI has already been applied in a variety of clinical settings, there are no prior randomised controlled trials (RCTs) on CURATE.AI-guided chemotherapy dosing for solid tumours. Therefore, we aim to assess the technical and logistical feasibility of a future RCT for CURATE.AI-guided solid tumour chemotherapy dosing. We will also collect exploratory data on efficacy and toxicity, which will inform RCT power calculations. Methods and analysis: This is an open-label, single-arm, two-centre, prospective pilot clinical trial, recruiting adults with metastatic solid tumours and raised baseline tumour marker levels who are planned for palliative-intent, capecitabine-based chemotherapy. As CURATE.AI is a small data platform, it will guide drug dosing for each participant based only on their own tumour marker levels and drug doses as input data. The primary outcome is the proportion of participants in whom CURATE.AI is successfully applied to provide efficacy-driven personalised dosing, as judged based on predefined considerations. Secondary outcomes include the timeliness of dose recommendations, participant and physician adherence to CURATE.AI-recommended doses, and the proportion of clinically significant dose changes. We aim to initially enrol 10 participants from two hospitals in Singapore, perform an interim analysis, and consider either cohort expansion or an RCT. Recruitment began in August 2020. This pilot clinical trial will provide key data for a future RCT of CURATE.AI-guided personalised dosing for precision oncology. Ethics and dissemination: The National Healthcare Group (NHG) Domain Specific Review Board has granted ethical approval for this study (DSRB 2020/00334). We will distribute our findings at scientific conferences and publish them in peer-reviewed journals. Trial registration number: NCT04522284.

Tan, E., et al. (2024). "Bridging AI development with clinical relevance-A scoping review of skin cancer models since CLEAR Derm. Where to next?" Australas J Dermatol **65**(3): e56-e58.

Tan, Y., et al. (2024). "AI models predicting breast

cancer distant metastasis using LightGBM with clinical blood markers and ultrasound maximum diameter." Sci Rep **14**(1): 15561.

Breast cancer metastasis significantly impacts women's health globally. This study aimed to construct predictive models using clinical blood markers and ultrasound data to predict distant metastasis in breast cancer patients, ensuring clinical applicability, cost-effectiveness, relative non-invasiveness, and accessibility of these models. Analysis was conducted on data from 416 patients across two centers, focusing on clinical blood markers (tumor markers, liver and kidney function indicators, blood lipid markers, cardiovascular biomarkers) and maximum lesion diameter from ultrasound. Feature reduction was performed using Spearman correlation and LASSO regression. Two models were built using LightGBM: a clinical model (using clinical blood markers) and a combined model (incorporating clinical blood markers and ultrasound features), validated in training, internal test, and external validation (test1) cohorts. Feature importance analysis was conducted for both models, followed by univariate and multivariate regression analyses of these features. The AUC values of the clinical model in the training, internal test, and external validation (test1) cohorts were 0.950, 0.795, and 0.883, respectively. The combined model showed AUC values of 0.955, 0.835, and 0.918 in the training, internal test, and external validation (test1) cohorts, respectively. Clinical utility curve analysis indicated the combined model's superior net benefit in identifying breast cancer with distant metastasis across all cohorts. This suggests the combined model's superior discriminatory ability and strong generalization performance. Creatine kinase isoenzyme (CK-MB), CEA, CA153, albumin, creatine kinase, and maximum lesion diameter from ultrasound played significant roles in model prediction. CA153, CK-MB, lipoprotein (a), and maximum lesion diameter from ultrasound positively correlated with breast cancer distant metastasis, while indirect bilirubin and magnesium ions showed negative correlations. This study successfully utilized clinical blood markers and ultrasound data to develop AI models for predicting distant metastasis in breast cancer. The combined model, incorporating clinical blood markers and ultrasound features, exhibited higher accuracy, suggesting its potential clinical utility in predicting and identifying breast cancer distant metastasis. These findings highlight the potential prospects of developing cost-effective and accessible predictive tools in clinical oncology.

Tanabe, K., et al. (2020). "Comprehensive Serum Glycopeptide Spectra Analysis Combined with Artificial Intelligence (CSGSA-AI) to Diagnose Early-Stage Ovarian Cancer." Cancers (Basel) **12**(9).

Ovarian cancer is a leading cause of deaths among gynecological cancers, and a method to detect early-stage epithelial ovarian cancer (EOC) is urgently needed. We aimed to develop an artificial intelligence (AI)-based comprehensive serum glycopeptide spectra analysis (CSGSA-AI) method in combination with convolutional neural network (CNN) to detect aberrant glycans in serum samples of patients with EOC. We converted serum glycopeptide expression patterns into two-dimensional (2D) barcodes to let CNN learn and distinguish between EOC and non-EOC. CNN was trained using 60% samples and validated using 40% samples. We observed that principal component analysis-based alignment of glycopeptides to generate 2D barcodes significantly increased the diagnostic accuracy (88%) of the method. When CNN was trained with 2D barcodes colored on the basis of serum levels of CA125 and HE4, a diagnostic accuracy of 95% was achieved. We believe that this simple and low-cost method will increase the detection of EOC.

Tang, F. H., et al. (2023). "Radiomics-Clinical AI Model with Probability Weighted Strategy for Prognosis Prediction in Non-Small Cell Lung Cancer." Biomedicines **11**(8).

In this study, we propose a radiomics clinical probability-weighted model for the prediction of prognosis for non-small cell lung cancer (NSCLC). The model combines radiomics features extracted from radiotherapy (RT) planning images with clinical factors such as age, gender, histology, and tumor stage. CT images with radiotherapy structures of 422 NSCLC patients were retrieved from The Cancer Imaging Archive (TCIA). Radiomic features were extracted from gross tumor volumes (GTVs). Five machine learning algorithms, namely decision trees (DT), random forests (RF), extreme boost (EB), support vector machine (SVM) and generalized linear model (GLM) were optimized by a voted ensemble machine learning (VEML) model. A probabilistic weighted approach is used to incorporate the uncertainty associated with both radiomic and clinical features and to generate a probabilistic risk score for each patient. The performance of the model is evaluated using a receiver operating characteristic (ROC). The Radiomic model, clinical factor model, and combined radiomic clinical probability-weighted model demonstrated good performance in predicting NSCLC survival with AUC of 0.941, 0.856 and 0.949, respectively. The combined radiomics clinical probability-weighted enhanced model achieved significantly better performance than the radiomic model in 1-year survival prediction (chi-square test, p

< 0.05). The proposed model has the potential to improve NSCLC prognosis and facilitate personalized treatment decisions.

Tapper, W., et al. (2024). "The Application of Radiomics and AI to Molecular Imaging for Prostate Cancer." J Pers Med **14**(3).

Molecular imaging is a key tool in the diagnosis and treatment of prostate cancer (PCa). Magnetic Resonance (MR) plays a major role in this respect with nuclear medicine imaging, particularly, Prostate-Specific Membrane Antigen-based, (PSMA-based) positron emission tomography with computed tomography (PET/CT) also playing a major role of rapidly increasing importance. Another key technology finding growing application across medicine and specifically in molecular imaging is the use of machine learning (ML) and artificial intelligence (AI). Several authoritative reviews are available of the role of MR-based molecular imaging with a sparsity of reviews of the role of PET/CT. This review will focus on the use of AI for molecular imaging for PCa. It will aim to achieve two goals: firstly, to give the reader an introduction to the AI technologies available, and secondly, to provide an overview of AI applied to PET/CT in PCa. The clinical applications include diagnosis, staging, target volume definition for treatment planning, outcome prediction and outcome monitoring. ML and AL techniques discussed include radiomics, convolutional neural networks (CNN), generative adversarial networks (GAN) and training methods: supervised, unsupervised and semi-supervised learning.

Tavolara, T. E., et al. (2024). "An AI Model (LORIS) to Predict Immune Checkpoint Blockade Response in Cancer: A Clinical Data Science Perspective." Clin Chem.

Temple, S. W. P. and C. G. Rowbottom (2024). "Gross failure rates and failure modes for a commercial AI-based auto-segmentation algorithm in head and neck cancer patients." J Appl Clin Med Phys **25**(6): e14273.

PURPOSE: Artificial intelligence (AI) based commercial software can be used to automatically delineate organs at risk (OAR), with potential for efficiency savings in the radiotherapy treatment planning pathway, and reduction of inter- and intra-observer variability. There has been little research investigating gross failure rates and failure modes of such systems. METHOD: 50 head and neck (H&N) patient data sets with "gold standard" contours were compared to AI-generated contours to produce expected mean and standard deviation values for the Dice Similarity Coefficient (DSC), for four common H&N OARs (brainstem, mandible, left and right parotid). An AI-based commercial system was applied to 500 H&N patients. AI-generated contours were compared to manual contours, outlined by an expert human, and a gross failure was set at three standard deviations below the expected mean DSC. Failures were inspected to assess reason for failure of the AI-based system with failures relating to suboptimal manual contouring censored. True failures were classified into 4 sub-types (setup position, anatomy, image artefacts and unknown). RESULTS: There were 24 true failures of the AI-based commercial software, a gross failure rate of 1.2%. Fifteen failures were due to patient anatomy, four were due to dental image artefacts, three were due to patient position and two were unknown. True failure rates by OAR were 0.4% (brainstem), 2.2% (mandible), 1.4% (left parotid) and 0.8% (right parotid). CONCLUSION: True failures of the AI-based system were predominantly associated with a non-standard element within the CT scan. It is likely that these non-standard elements were the reason for the gross failure, and suggests that patient datasets used to train the AI model did not contain sufficient heterogeneity of data. Regardless of the reasons for failure, the true failure rate for the AI-based system in the H&N region for the OARs investigated was low (approximately 1%).

Thavanesan, N., et al. (2024). "Insights from explainable AI in oesophageal cancer team decisions." Comput Biol Med **180**: 108978.

BACKGROUND: Clinician-led quality control into oncological decision-making is crucial for optimising patient care. Explainable artificial intelligence (XAI) techniques provide data-driven approaches to unravel how clinical variables influence this decision-making. We applied global XAI techniques to examine the impact of key clinical decision-drivers when mapped by a machine learning (ML) model, on the likelihood of receiving different oesophageal cancer (OC) treatment modalities by the multidisciplinary team (MDT). METHODS: Retrospective analysis of 893 OC patients managed between 2010 and 2022 at our tertiary unit, used a random forests (RF) classifier to predict four possible treatment pathways as determined by the MDT: neoadjuvant chemotherapy followed by surgery (NACT + S), neoadjuvant chemoradiotherapy followed by surgery (NACRT + S), surgery-alone, and palliative management. Variable importance and partial dependence (PD) analyses then examined the influence of targeted high-ranking clinical variables within the ML model on treatment decisions as a surrogate model of the MDT decision-making

dynamic. RESULTS: Amongst guideline-variables known to determine treatments, such as Tumour-Node-Metastasis (TNM) staging, age also proved highly important to the RF model (16.1 % of total importance) on variable importance analysis. PD subsequently revealed that predicted probabilities for all treatment modalities change significantly after 75 years ($p < 0.001$). Likelihood of surgery-alone and palliative therapies increased for patients aged 75-85yrs but lowered for NACT/NACRT. Performance status divided patients into two clusters which influenced all predicted outcomes in conjunction with age. CONCLUSION: XAI techniques delineate the relationship between clinical factors and OC treatment decisions. These techniques identify advanced age as heavily influencing decisions based on our model with a greater role in patients with specific tumour characteristics. This study methodology provides the means for exploring conscious/subconscious bias and interrogating inconsistencies in team-based decision-making within the era of AI-driven decision support.

Thimansson, E., et al. (2024). "A pilot study of AI-assisted reading of prostate MRI in Organized Prostate Cancer Testing." Acta Oncol **63**: 816-821.

OBJECTIVES: To evaluate the feasibility of AI-assisted reading of prostate magnetic resonance imaging (MRI) in Organized Prostate cancer Testing (OPT). METHODS: Retrospective cohort study including 57 men with elevated prostate-specific antigen (PSA) levels >/=3 microg/L that performed bi-parametric MRI in OPT. The results of a CE-marked deep learning (DL) algorithm for prostate MRI lesion detection were compared with assessments performed by on-site radiologists and reference radiologists. Per patient PI-RADS (Prostate Imaging-Reporting and Data System)/Likert scores were cross-tabulated and compared with biopsy outcomes, if performed. Positive MRI was defined as PI-RADS/Likert >/=4. Reader variability was assessed with weighted kappa scores. RESULTS: The number of positive MRIs was 13 (23%), 8 (14%), and 29 (51%) for the local radiologists, expert consensus, and DL, respectively. Kappa scores were moderate for local radiologists versus expert consensus 0.55 (95% confidence interval [CI]: 0.37-0.74), slight for local radiologists versus DL 0.12 (95% CI: -0.07 to 0.32), and slight for expert consensus versus DL 0.17 (95% CI: -0.01 to 0.35). Out of 10 cases with biopsy proven prostate cancer with Gleason >/=3+4 the DL scored 7 as Likert >/=4. INTERPRETATION: The Dl-algorithm showed low agreement with both local and expert radiologists. Training and validation of DL-algorithms in specific screening cohorts is essential before introduction in organized testing.

Thomas, J., et al. (2023). "Advancing Colorectal Cancer Screening: A Comprehensive Systematic Review of Artificial Intelligence (AI)-Assisted Versus Routine Colonoscopy." Cureus **15**(9): e45278.

Colorectal cancer (CRC) is a rapidly escalating public health concern, which underlines the significance of its early detection and the need for the refinement of current screening methods. In this systematic review, we aimed to analyze the potential advantages and limitations of artificial intelligence (AI)-based computer-aided detection (CADe) systems as compared to routine colonoscopy. This review begins by shedding light on the global prevalence and mortality rates of CRC, highlighting the urgent need for effective screening techniques and early detection of this cancer type. It addresses the problems associated with undetected adenomas and polyps and the subsequent risk of interval CRC following colonoscopy. The incorporation of AI into diagnostics has been studied, specifically the use of CADe systems which are powered by deep learning. The review summarizes the findings from 13 randomized controlled trials (RCTs) (2019-2023), evaluating the impact of CADe on polyp and adenoma detection. The findings from the studies consistently show that CADe is superior to conventional colonoscopy procedures in terms of adenoma detection rate (ADR) and polyp detection rate (PDR), particularly with regard to small and flat lesions which are easily overlooked. The review acknowledges certain limitations of the included studies, such as potential performance bias and geographic limitations. The review ultimately concludes that AI-assisted colonoscopy can reduce missed lesion rates and improve CRC diagnosis. Collaboration between experts and clinicians is key for successful implementation. In summary, this review analyzes recent RCTs on AI-assisted colonoscopy for polyp and adenoma detection. It describes the likely benefits, limitations, and future implications of AI in enhancing colonoscopy procedures and lowering the incidence of CRC. More double-blinded trials and studies among diverse populations from different countries must be conducted to substantiate and expand upon the findings of this review.

Tian, M., et al. (2024). "DeepRisk network: an AI-based tool for digital pathology signature and treatment responsiveness of gastric cancer using whole-slide images." J Transl Med **22**(1): 182.

BACKGROUND: Digital histopathology provides valuable information for clinical decision-making. We hypothesized that a deep risk network

(DeepRisk) based on digital pathology signature (DPS) derived from whole-slide images could improve the prognostic value of the tumor, node, and metastasis (TNM) staging system and offer chemotherapeutic benefits for gastric cancer (GC). METHODS: DeepRisk is a multi-scale, attention-based learning model developed on 1120 GCs in the Zhongshan dataset and validated with two external datasets. Then, we assessed its association with prognosis and treatment response. The multi-omics analysis and multiplex Immunohistochemistry were conducted to evaluate the potential pathogenesis and spatial immune contexture underlying DPS. RESULTS: Multivariate analysis indicated that the DPS was an independent prognosticator with a better C-index (0.84 for overall survival and 0.71 for disease-free survival). Patients with low-DPS after neoadjuvant chemotherapy responded favorably to treatment. Spatial analysis indicated that exhausted immune clusters and increased infiltration of CD11b(+)CD11c(+) immune cells were present at the invasive margin of high-DPS group. Multi-omics data from the Cancer Genome Atlas-Stomach adenocarcinoma (TCGA-STAD) hint at the relevance of DPS to myeloid derived suppressor cells infiltration and immune suppression. CONCLUSION: DeepRisk network is a reliable tool that enhances prognostic value of TNM staging and aid in precise treatment, providing insights into the underlying pathogenic mechanisms.

Tian, Y. L., et al. (2022). "Mechanism of Fuzheng Kang'ai Formula Regulating Tumor Microenvironment in Non-Small Cell Lung Cancer." Chin J Integr Med **28**(5): 425-433.

OBJECTIVE: To study the mechanism of Chinese herbal medicine Fuzheng Kang'ai Formula (, FZKA) on tumor microenvironment (TME). METHODS: CIBERSORTx was used for analysis of TME. Traditional Chinese Medicine Systems Pharmacology and Analysis Platform was applied to identify compounds-targets network and the Cancer Genome Atlas (TCGA) was employed to identify the differential expression genes (DEGs) between tumor and paracancerous tissues in lung adenocarcinoma (LUAD) from TCGA-LUAD. Additionally, DEGs with prognosis in LUAD was calculated by univariable and multivariate Cox regression. The core targets of FZKA were analyzed in lung adenocarcinoma TME. Protein-protein interaction database was employed to predict down-stream of target. Quantitative reverse transcription polymerase chain reaction was employed for biological experiment in A549, H1299 and PC9 cell lines. RESULTS: The active and resting mast cells were significantly associated with prognosis of LUAD ($P<0.05$). Of the targets, CCNA2 as an important target of FZKA (hazard ratio=1.41, 95% confidential interval: 1.01-2.01, $P<0.05$) was a prognostic target and significantly associated with mast cells. CCNA2 was positively correlated with mast cell activation and negatively correlated with mast cell resting state. BCL1L2, ACTL6A and ITGAV were down-stream of CCNA2, which were validated by qRT-PCR in A549 cell. CONCLUSION: FZKA could directly bind to CCNA2 and inhibit tumor growth by regulating CCNA2 downstream genes and TME of NSCLC closely related to CCNA2.

Togher, D., et al. (2024). "Evolution of radiology staff perspectives during artificial intelligence (AI) implementation for expedited lung cancer triage." Clin Radiol.

AIMS: To investigate radiology staff perceptions of an AI tool for chest radiography triage, flagging findings suspicious for lung cancer to expedite same-day CT chest examination studies. MATERIALS AND METHODS: Surveys were distributed to all radiology staff at three time points: at pre-implementation, one month and also seven months post-implementation of artificial intelligence (AI). Survey questions captured feedback on AI use and patient impact. RESULTS: Survey response rates at the three time periods were 23.1% (45/195), 14.9% (29/195) and 27.2% (53/195), respectively. Most respondents initially anticipated AI to be time-saving for the department and patient (50.8%), but this shifted to faster follow-up care for patients after AI implementation (51.7%). From the free text comments, early apprehension about job role changes evolved into frustration regarding technical integration challenges after implementation. This later transitioned to a more balanced view of recognised patient benefits versus minor ongoing logistical issues by the late post-implementation stage. There was majority disagreement across all survey periods that AI could be considered to be used autonomously (53.3-72.5%), yet acceptance grew for personal AI usage if staff were to be patients themselves (from 31.1% pre-implementation to 47.2% post-implementation). CONCLUSION: Successful AI integration in radiology demands active staff engagement, addressing concerns to transform initial mixed excitement and resistance into constructive adaptation. Continual feedback is vital for refining AI deployment strategies, ensuring its beneficial and sustainable incorporation into clinical care pathways.

Tragardh, E., et al. (2022). "Freely Available, Fully Automated AI-Based Analysis of Primary Tumour and Metastases of Prostate Cancer in Whole-Body [(18)F]-PSMA-1007 PET-CT." Diagnostics (Basel)

12(9).

Here, we aimed to develop and validate a fully automated artificial intelligence (AI)-based method for the detection and quantification of suspected prostate tumour/local recurrence, lymph node metastases, and bone metastases from [(18)F]PSMA-1007 positron emission tomography-computed tomography (PET-CT) images. Images from 660 patients were included. Segmentations by one expert reader were ground truth. A convolutional neural network (CNN) was developed and trained on a training set, and the performance was tested on a separate test set of 120 patients. The AI method was compared with manual segmentations performed by several nuclear medicine physicians. Assessment of tumour burden (total lesion volume (TLV) and total lesion uptake (TLU)) was performed. The sensitivity of the AI method was, on average, 79% for detecting prostate tumour/recurrence, 79% for lymph node metastases, and 62% for bone metastases. On average, nuclear medicine physicians' corresponding sensitivities were 78%, 78%, and 59%, respectively. The correlations of TLV and TLU between AI and nuclear medicine physicians were all statistically significant and ranged from R = 0.53 to R = 0.83. In conclusion, the development of an AI-based method for prostate cancer detection with sensitivity on par with nuclear medicine physicians was possible. The developed AI tool is freely available for researchers.

Trebeschi, S., et al. (2021). "Development of a Prognostic AI-Monitor for Metastatic Urothelial Cancer Patients Receiving Immunotherapy." Front Oncol **11**: 637804.

Background: Immune checkpoint inhibitor efficacy in advanced cancer patients remains difficult to predict. Imaging is the only technique available that can non-invasively provide whole body information of a patient's response to treatment. We hypothesize that quantitative whole-body prognostic information can be extracted by leveraging artificial intelligence (AI) for treatment monitoring, superior and complementary to the current response evaluation methods. Methods: To test this, a cohort of 74 stage-IV urothelial cancer patients (37 in the discovery set, 37 in the independent test, 1087 CTs), who received anti-PD1 or anti-PDL1 were retrospectively collected. We designed an AI system [named prognostic AI-monitor (PAM)] able to identify morphological changes in chest and abdominal CT scans acquired during follow-up, and link them to survival. Results: Our findings showed significant performance of PAM in the independent test set to predict 1-year overall survival from the date of image acquisition, with an average area under the curve (AUC) of 0.73 ($p < 0.001$) for abdominal imaging, and 0.67 AUC ($p < 0.001$) for chest imaging. Subanalysis revealed higher accuracy of abdominal imaging around and in the first 6 months of treatment, reaching an AUC of 0.82 ($p < 0.001$). Similar accuracy was found by chest imaging, 5-11 months after start of treatment. Univariate comparison with current monitoring methods (laboratory results and radiological assessments) revealed higher or similar prognostic performance. In multivariate analysis, PAM remained significant against all other methods ($p < 0.001$), suggesting its complementary value in current clinical settings. Conclusions: Our study demonstrates that a comprehensive AI-based method such as PAM, can provide prognostic information in advanced urothelial cancer patients receiving immunotherapy, leveraging morphological changes not only in tumor lesions, but also tumor spread, and side-effects. Further investigations should focus beyond anatomical imaging. Prospective studies are warranted to test and validate our findings.

Tripathi, A., et al. (2025). "Oncointerpreter.ai enables interactive, personalized summarization of cancer diagnostics data." J Am Med Inform Assoc **32**(1): 129-138.

OBJECTIVES: Cancer diagnosis comes as a shock to many patients, and many of them feel unprepared to handle the complexity of the life-changing event, understand technicalities of the diagnostic reports, and fully engage with the clinical team regarding the personalized clinical decision-making. MATERIALS AND METHODS: We develop Oncointerpreter.ai an interactive resource to offer personalized summarization of clinical cancer genomic and pathological data, and frame questions or address queries about therapeutic opportunities in near-real time via a graphical interface. It is built on the Mistral-7B and Llama-2 7B large language models trained on a local database trained using a large, curated corpus. RESULTS: We showcase its utility with case studies, where Oncointerpreter.ai extracted key clinical and molecular attributes from deidentified pathology and clinical genomics reports, summarized their contextual significance and answered queries on pertinent treatment options. Oncointerpreter also provided personalized summary of currently active clinical trials that match the patients' disease status, their selection criteria, and geographic locations. Benchmarking and comparative assessment indicated that the model responses were generally consistent, and hallucination, ie, factually incorrect or nonsensical response was rare; treatment- and outcome related queries led to context-aware responses, and response time correlated with verbosity. DISCUSSION: The choice of model and domain-specific training also affected the response

quality. CONCLUSION: Oncointerpreter.ai can aid the existing clinical care with interactive, individualized summarization of diagnostics data to promote informed dialogs with the patients with new cancer diagnoses. AVAILABILITY: https://github.com/Siris2314/Oncointerpreter.

Tripathi, S., et al. (2024). "From Machine Learning to Patient Outcomes: A Comprehensive Review of AI in Pancreatic Cancer." Diagnostics (Basel) **14**(2).

Pancreatic cancer is a highly aggressive and difficult-to-detect cancer with a poor prognosis. Late diagnosis is common due to a lack of early symptoms, specific markers, and the challenging location of the pancreas. Imaging technologies have improved diagnosis, but there is still room for improvement in standardizing guidelines. Biopsies and histopathological analysis are challenging due to tumor heterogeneity. Artificial Intelligence (AI) revolutionizes healthcare by improving diagnosis, treatment, and patient care. AI algorithms can analyze medical images with precision, aiding in early disease detection. AI also plays a role in personalized medicine by analyzing patient data to tailor treatment plans. It streamlines administrative tasks, such as medical coding and documentation, and provides patient assistance through AI chatbots. However, challenges include data privacy, security, and ethical considerations. This review article focuses on the potential of AI in transforming pancreatic cancer care, offering improved diagnostics, personalized treatments, and operational efficiency, leading to better patient outcomes.

Trump, D. L. (2013). "Commentary on "Cabozantinib in patients with advanced prostate cancer: results of a phase II randomized discontinuation trial." Smith DC, Smith MR, Sweeney C, Elfiky AA, Logothetis C, Corn PG, Vogelzang NJ, Small EJ, Harzstark AL, Gordon MS, Vaishampayan UN, Haas NB, Spira AI, Lara PN Jr, Lin CC, Srinivas S, Sella A, SchoffskiSchoffski P, Scheffold C, Weitzman AL, Hussain M, University of Michigan, Ann Arbor, MI. J Clin Oncol 2013;31(4):412-9. doi: 10.1200/JCO.2012.45.0494. Epub 2012 Nov 19." Urol Oncol **31**(8): 1848.

PURPOSE: Cabozantinib (XL184) is an orally bioavailable tyrosine kinase inhibitor with activity against MET and vascular endothelial growth factor receptor 2. We evaluated the activity of cabozantinib in patients with castration-resistant prostate cancer (CRPC) in a phase II randomized discontinuation trial with an expansion cohort. PATIENTS AND METHODS: Patients received 100mg of cabozantinib daily. Those with stable disease per RECIST at 12 weeks were randomly assigned to cabozantinib or placebo. Primary end points were objective response rate at 12 weeks and progression-free survival (PFS) after random assignment. RESULTS: One hundred seventy-one men with CRPC were enrolled. Random assignment was halted early based on the observed activity of cabozantinib. Seventy-two percent of patients had regression in soft tissue lesions, whereas 68% of evaluable patients had improvement on bone scan, including complete resolution in 12%. The objective response rate at 12 weeks was 5%, with stable disease in 75% of patients. Thirty-one patients with stable disease at week 12 were randomly assigned. Median PFS was 23.9 weeks (95% CI, 10.7 to 62.4 weeks) with cabozantinib and 5.9 weeks (95% CI, 5.4 to 6.6 weeks) with placebo (hazard ratio, 0.12; P<.001). Serum total alkaline phosphatase and plasma cross-linked C-terminal telopeptide of type I collagen were reduced by >/= 50% in 57% of evaluable patients. On retrospective review, bone pain improved in 67% of evaluable patients, with a decrease in narcotic use in 56%. The most common grade 3 adverse events were fatigue (16%), hypertension (12%), and hand-foot syndrome (8%). CONCLUSION: Cabozantinib has clinical activity in men with CRPC, including reduction of soft tissue lesions, improvement in PFS, resolution of bone scans, and reductions in bone turnover markers, pain, and narcotic use.

Tsvetkov, P. O., et al. (2021). "An AI-Powered Blood Test to Detect Cancer Using NanoDSF." Cancers (Basel) **13**(6).

Glioblastoma is the most frequent and aggressive primary brain tumor. Its diagnosis is based on resection or biopsy that could be especially difficult and dangerous in the case of deep location or patient comorbidities. Monitoring disease evolution and progression also requires repeated biopsies that are often not feasible. Therefore, there is an urgent need to develop biomarkers to diagnose and follow glioblastoma evolution in a minimally invasive way. In the present study, we described a novel cancer detection method based on plasma denaturation profiles obtained by a non-conventional use of differential scanning fluorimetry. Using blood samples from 84 glioma patients and 63 healthy controls, we showed that their denaturation profiles can be automatically distinguished with the help of machine learning algorithms with 92% accuracy. Proposed high throughput workflow can be applied to any type of cancer and could become a powerful pan-cancer diagnostic and monitoring tool requiring only a simple blood test.

Tu, Z., et al. (2024). "Helicobacter pylori-targeted

AI-driven vaccines: a paradigm shift in gastric cancer prevention." Front Immunol **15**: 1500921.

Helicobacter pylori (H. pylori), a globally prevalent pathogen Group I carcinogen, presents a formidable challenge in gastric cancer prevention due to its increasing antimicrobial resistance and strain diversity. This comprehensive review critically analyzes the limitations of conventional antibiotic-based therapies and explores cutting-edge approaches to combat H. pylori infections and associated gastric carcinogenesis. We emphasize the pressing need for innovative therapeutic strategies, with a particular focus on precision medicine and tailored vaccine development. Despite promising advancements in enhancing host immunity, current Helicobacter pylori vaccine clinical trials have yet to achieve long-term efficacy or gain approval regulatory approval. We propose a paradigm-shifting approach leveraging artificial intelligence (AI) to design precision-targeted, multiepitope vaccines tailored to multiple H. pylori subtypes. This AI-driven strategy has the potential to revolutionize antigen selection and optimize vaccine efficacy, addressing the critical need for personalized interventions in H. pylori eradication efforts. By leveraging AI in vaccine design, we propose a revolutionary approach to precision therapy that could significantly reduce H. pylori -associated gastric cancer burden.

Turkbey, B. and M. A. Haider (2022). "Artificial Intelligence for Automated Cancer Detection on Prostate MRI: Opportunities and Ongoing Challenges, From the AJR Special Series on AI Applications." AJR Am J Roentgenol **219**(2): 188-194.

Use of prostate MRI has increased greatly in the past decade, primarily in directing targeted prostate biopsy. However, prostate MRI interpretation remains prone to interreader variation. Artificial intelligence (AI) has the potential to standardize detection of lesions on MRI that are suspicious for prostate cancer (PCa). The purpose of this review is to explore the current status of AI for the automated detection of PCa on MRI. Recent literature describing promising results regarding AI models for PCa detection on MRI is highlighted. Numerous limitations of the existing literature are also described, including biases in model validation, heterogeneity in reporting of performance metrics, and lack of sufficient evidence of clinical translation. Challenges related to AI ethics and data governance are also discussed. An outlook is provided for AI in lesion detection on prostate MRI in the coming years, emphasizing current research needs. Future investigations, incorporating large-scale diverse multiinstitutional training and testing datasets, are anticipated to enable the development of more robust AI models for PCa detection on MRI, though prospective clinical trials will ultimately be required to establish benefit of AI in patient management.

Uprety, D., et al. (2023). "ChatGPT-A promising generative AI tool and its implications for cancer care." Cancer **129**(15): 2284-2289.

Since its launch, ChatGPT has taken the internet by storm and has the potential to be used broadly in the health care system, particularly in a setting such as medical oncology. ChatGPT is well suited to review and extract key content from records of patients with cancer, interpret next-generation sequencing reports, and offer a list of potential clinical trial options.

van Capelleveen, J. C., et al. (2017). "Association of High-Density Lipoprotein-Cholesterol Versus Apolipoprotein A-I With Risk of Coronary Heart Disease: The European Prospective Investigation Into Cancer-Norfolk Prospective Population Study, the Atherosclerosis Risk in Communities Study, and the Women's Health Study." J Am Heart Assoc **6**(8).

BACKGROUND: The contribution of apolipoprotein A-I (apoA-I) to coronary heart disease (CHD) risk stratification over and above high-density lipoprotein cholesterol (HDL-C) is unclear. We studied the associations between plasma levels of HDL-C and apoA-I, either alone or combined, with risk of CHD events and cardiovascular risk factors among apparently healthy men and women. METHODS AND RESULTS: HDL-C and apoA-I levels were measured among 17 661 participants of the EPIC (European Prospective Investigation into Cancer)-Norfolk prospective population study. Hazard ratios for CHD events and distributions of risk factors were calculated by quartiles of HDL-C and apoA-I. Results were validated using data from the ARIC (Atherosclerosis Risk in Communities) and WHS (Women's Health Study) cohorts, comprising 15 494 and 27 552 individuals, respectively. In EPIC-Norfolk, both HDL-C and apoA-I quartiles were strongly and inversely associated with CHD risk. Within HDL-C quartiles, higher apoA-I levels were not associated with lower CHD risk; in fact, CHD risk was higher within some HDL-C quartiles. ApoA-I levels were associated with higher levels of CHD risk factors: higher body mass index, HbA1c, non-HDL-C, triglycerides, apolipoprotein B, systolic blood pressure, and C-reactive protein, within fixed HDL-C quartiles. In contrast, HDL-C levels were consistently inversely associated with overall CHD risk and CHD risk factors within apoA-I quartiles ($P<0.001$). These findings were validated in the ARIC and WHS cohorts. CONCLUSIONS: Our findings demonstrate that apoA-I levels do not offer

predictive information over and above HDL-C. In fact, within some HDL-C quartiles, higher apoA-I levels were associated with higher risk of CHD events, possibly because of the unexpected higher prevalence of cardiovascular risk factors in association with higher apoA-I levels. CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT00000479.

Van Hemelrijck, M., et al. (2011). "Low levels of apolipoprotein A-I and HDL are associated with risk of prostate cancer in the Swedish AMORIS study." Cancer Causes Control **22**(7): 1011-1019.

BACKGROUND: A detailed analysis of lipid profiles, using apolipoproteins, has not yet been conducted for prostate cancer (PCa). Since several etiological pathways have been proposed for PCa and lipids, we aimed to study this in a large Swedish cohort with 1,469 primary prostate cancers. METHODS: A cohort (n = 69,735) of all men aged 35 years or older, whose levels of triglycerides (TG) (mmol/L), total cholesterol (mmol/L), glucose (mmol/L), LDL (mmol/L), HDL (mmol/L), apoB (g/L), and apoA-I (g/L) were measured at baseline, was selected from the Apolipoprotein MOrtality RISk (AMORIS) database. About 2,008 men developed PCa. Multivariate Cox proportional hazard models were used to analyze associations between lipid components and PCa. RESULTS: ApoA-I and HDL were inversely associated with PCa risk (e.g., HR for HDL: 0.93 (95% CI: 0.81-1.07), 0.88 (0.76-1.01), 0.81 (0.70-0.94), for second, third, and fourth quartiles compared with the first quartile; with p for trend: 0.004; HR for apoA-I: 1.00 (0.88-1.13), 0.93 (0.82-1.05), 0.88 (0.77-0.99),), for second, third, and fourth quartiles compared with the first quartile; with p for trend: 0.022). ApoB, LDL, and non-HDL were not associated with PCa risk. CONCLUSIONS: Our results show that low HDL and ApoA-I as well as increased lipid ratios are related to increased PCa risk. Experimental studies are required to tease out the underlying biological mechanisms linking these lipid components to PCa.

van Velzen, S. G. M., et al. (2022). "AI-Based Quantification of Planned Radiation Therapy Dose to Cardiac Structures and Coronary Arteries in Patients With Breast Cancer." Int J Radiat Oncol Biol Phys **112**(3): 611-620.

PURPOSE: The purpose of this work is to develop and evaluate an automatic deep learning method for segmentation of cardiac chambers and large arteries, and localization of the 3 main coronary arteries in radiation therapy planning on computed tomography (CT). In addition, a second purpose is to determine the planned radiation therapy dose to cardiac structures for breast cancer therapy. METHODS AND MATERIALS: Eighteen contrast-enhanced cardiac scans acquired with a dual-layer-detector CT scanner were included for method development. Manual reference annotations of cardiac chambers, large arteries, and coronary artery locations were made in the contrast scans and transferred to virtual noncontrast images, mimicking noncontrast-enhanced CT. In addition, 31 noncontrast-enhanced radiation therapy treatment planning CTs with corresponding dose-distribution maps of breast cancer cases were included for evaluation. For reference, cardiac chambers and large vessels were manually annotated in two 2-dimensional (2D) slices per scan (26 scans, totaling 52 slices) and in 3-dimensional (3D) scan volumes in 5 scans. Coronary artery locations were annotated on 3D imaging. The method uses an ensemble of convolutional neural networks with 2 output branches that perform 2 distinct tasks: (1) segmentation of the cardiac chambers and large arteries and (2) localization of coronary arteries. Training was performed using reference annotations and virtual noncontrast cardiac scans. Automatic segmentation of the cardiac chambers and large vessels and the coronary artery locations was evaluated in radiation therapy planning CT with Dice score (DSC) and average symmetrical surface distance (ASSD). The correlation between dosimetric parameters derived from the automatic and reference segmentations was evaluated with R(2). RESULTS: For cardiac chambers and large arteries, median DSC was 0.76 to 0.88, and the median ASSD was 0.17 to 0.27 cm in 2D slice evaluation. 3D evaluation found a DSC of 0.87 to 0.93 and an ASSD of 0.07 to 0.10 cm. Median DSC of the coronary artery locations ranged from 0.80 to 0.91. R(2) values of dosimetric parameters were 0.77 to 1.00 for the cardiac chambers and large vessels, and 0.76 to 0.95 for the coronary arteries. CONCLUSIONS: The developed and evaluated method can automatically obtain accurate estimates of planned radiation dose and dosimetric parameters for the cardiac chambers, large arteries, and coronary arteries.

van Velzen, S. G. M., et al. (2022). "AI-Based Radiation Dose Quantification for Estimation of Heart Disease Risk in Breast Cancer Survivors After Radiation Therapy." Int J Radiat Oncol Biol Phys **112**(3): 621-632.

PURPOSE: To investigate whether the dose planned for cardiac structures is associated with the risk of heart disease (HD) in patients with breast cancer treated with radiation therapy, and whether this association is modified by the presence of

coronary artery calcification (CAC). METHODS AND MATERIALS: Radiation therapy planning computed tomographic (CT) scans and corresponding dose distribution maps of 5561 patients were collected, 5300 patients remained after the exclusion of ineligible patients and duplicates; 1899 patients received their CT scan before 2011, allowing long follow-up. CAC was detected automatically. Using an artificial intelligence-based method, the cardiac structures (heart, cardiac chambers, large arteries, 3 main coronary arteries) were segmented. The planned radiation dose to each structure separately and to the whole heart were determined. Patients were assigned to a low-, medium-, or high-dose group based on the dose to the respective heart structure. Information on HD hospitalization and mortality was obtained for each patient. The association of planned radiation dose to cardiac structures with risk of HD was investigated in patients with and without CAC using Cox proportional hazard analysis in the long follow-up population. Tests for interaction were performed. RESULTS: After a median follow-up of 96.0 months (interquartile range, 84.2-110.4 months) in the long follow-up group, 135 patients were hospitalized for HD or died of HD. If the dose to a structure increased 1 Gy, the relative HD risk increased by 3% to 11%. The absolute increase in HD risk was substantially higher in patients with CAC (event-rate(low-dose) = 14-15 vs event-rate(high-dose) = 15-34 per 1000 person-years) than in patients without CAC (event-rate(low-dose) = 6-8 vs event-rate(high-dose) = 5-17 per 1000 person-years). No interaction between CAC and radiation dose was found. CONCLUSIONS: Radiation exposure of cardiac structures is associated with increased risk of HD. Automatic segmentation of cardiac structures enables spatially localized dose estimation, which can aid in the prevention of radiation therapy-induced cardiac damage. This could be especially valuable in patients with breast cancer and CAC.

Vanitha, K., et al. (2024). "Deep learning ensemble approach with explainable AI for lung and colon cancer classification using advanced hyperparameter tuning." BMC Med Inform Decis Mak **24**(1): 222.

Lung and colon cancers are leading contributors to cancer-related fatalities globally, distinguished by unique histopathological traits discernible through medical imaging. Effective classification of these cancers is critical for accurate diagnosis and treatment. This study addresses critical challenges in the diagnostic imaging of lung and colon cancers, which are among the leading causes of cancer-related deaths worldwide. Recognizing the limitations of existing diagnostic methods, which often suffer from overfitting and poor generalizability, our research introduces a novel deep learning framework that synergistically combines the Xception and MobileNet architectures. This innovative ensemble model aims to enhance feature extraction, improve model robustness, and reduce overfitting.Our methodology involves training the hybrid model on a comprehensive dataset of histopathological images, followed by validation against a balanced test set. The results demonstrate an impressive classification accuracy of 99.44%, with perfect precision and recall in identifying certain cancerous and non-cancerous tissues, marking a significant improvement over traditional approach.The practical implications of these findings are profound. By integrating Gradient-weighted Class Activation Mapping (Grad-CAM), the model offers enhanced interpretability, allowing clinicians to visualize the diagnostic reasoning process. This transparency is vital for clinical acceptance and enables more personalized, accurate treatment planning. Our study not only pushes the boundaries of medical imaging technology but also sets the stage for future research aimed at expanding these techniques to other types of cancer diagnostics.

Vareslija, D., et al. (2016). "Adaptation to AI Therapy in Breast Cancer Can Induce Dynamic Alterations in ER Activity Resulting in Estrogen-Independent Metastatic Tumors." Clin Cancer Res **22**(11): 2765-2777.

PURPOSE: Acquired resistance to aromatase inhibitor (AI) therapy is a major clinical problem in the treatment of breast cancer. The detailed mechanisms of how tumor cells develop this resistance remain unclear. Here, the adapted function of estrogen receptor (ER) to an estrogen-depleted environment following AI treatment is reported. EXPERIMENTAL DESIGN: Global ER chromatin immuno-precipitation (ChIP)-seq analysis of AI-resistant cells identified steroid-independent ER target genes. Matched patient tumor samples, collected before and after AI treatment, were used to assess ER activity. RESULTS: Maintained ER activity was observed in patient tumors following neoadjuvant AI therapy. Genome-wide ER-DNA-binding analysis in AI-resistant cell lines identified a subset of classic ligand-dependent ER target genes that develop steroid independence. The Kaplan-Meier analysis revealed a significant association between tumors, which fail to decrease this steroid-independent ER target gene set in response to neoadjuvant AI therapy, and poor disease-free survival and overall survival (n = 72 matched patient tumor samples, P = 0.00339 and 0.00155, respectively). The adaptive ER response to AI treatment was highlighted by the ER/AIB1 target

gene, early growth response 3 (EGR3). Elevated levels of EGR3 were detected in endocrine-resistant local disease recurrent patient tumors in comparison with matched primary tissue. However, evidence from distant metastatic tumors demonstrates that the ER signaling network may undergo further adaptations with disease progression as estrogen-independent ER target gene expression is routinely lost in established metastatic tumors. CONCLUSIONS: Overall, these data provide evidence of a dynamic ER response to endocrine treatment that may provide vital clues for overcoming the clinical issue of therapy resistance. Clin Cancer Res; 22(11); 2765-77. (c)2016 AACR.

Vazoura, G. P., et al. (2024). "AI potential in PET/CT cancer imaging." Hell J Nucl Med **27**(3): 212-221.

Positron emission tomography/computed tomography (PET/CT) is a hybrid medical imaging technique that combines PET and CT to provide detailed images of the body's anatomical structures and metabolic activity. It is frequently used for oncology and other medical diagnoses. This overview aims to examine how artificial intelligence (AI) has been used in PET/CT, based on recent state-of-art. There are a number of clinical questions in Nuclear Medicine, and AI could provide answers, having the capability to enhance various aspects of medical imaging. The overview focuses on how machine learning (ML) and deep learning (DL), enhance tumor segmentation, classification, diagnosis, disease-free survival prediction and treatment response prediction in oncology. The analysis showed that the application of AI provides reliable results, especially in the fields of classification and diagnosis. In addition, radiomics is a novel research field enabling quantitative analysis of medical images through feature extraction, utilized for AI model implementation. Despite these advances, addressing issues such as dataset size, standardization, and ethical concerns are essential for broad clinical integration of AI in PET/CT oncology imaging.

Venkatesh, K. P., et al. (2024). "Learnings from the first AI-enabled skin cancer device for primary care authorized by FDA." NPJ Digit Med **7**(1): 156.

The U.S. Food and Drug Administration's (FDA) recent authorization of DermaSensor, an AI-enabled device for skin cancer detection in primary care, marks a pivotal moment in digital health innovation. Clinically, the authorization of the first AI-enabled device for use by non-specialists for detecting skin cancer reinforces the feasibility of digital health technologies to bridge gaps in access and expertise in medical practice. The authorization also establishes a new regulatory precedent for FDA authorization of medical devices incorporating AI and machine learning (ML) technologies within dermatology. Together, this article uses the DermaSensor authorization to examine the clinical evidence and regulatory implications of emerging AI-enabled technologies in dermatology.

Venkatesh, K. P., et al. (2023). "AI-based skin cancer detection: the balance between access and overutilization." NPJ Digit Med **6**(1): 147.

Gregoor et al. evaluated the healthcare implications and costs of an AI-enabled mobile health app for skin cancer detection, involving 18,960 beneficiaries of a Netherlands insurer. They report a 32% increase in claims for premalignant and malignant skin lesions among app users, largely attributed to benign skin lesions and leading to higher annual costs for app users (euro64.97) compared to controls (euro43.09). Cost-effectiveness analysis showed a comparable cost to dermatologist-based diagnosis alone. This editorial emphasizes the balance in AI-based dermatology between increased access and increased false positives resulting in overutilization. We suggest refining the diagnostic schemas with new referral pathways to capitalize on potential savings. We also discuss the importance of econometric analysis to evaluate the adoption of new technologies, as well as adapting payment models to mitigate the risk of overutilization inherent in AI-based diagnostics such as skin cancer detection.

Verburg, F. and C. Reiners (2019). "Sonographic diagnosis of thyroid cancer with support of AI." Nat Rev Endocrinol **15**(6): 319-321.

Veseli, E. (2024). "Skin cancer and AI." Br Dent J **236**(8): 581-582.

Vidovic, T., et al. (2023). "AI-Predicted mTOR Inhibitor Reduces Cancer Cell Proliferation and Extends the Lifespan of C. elegans." Int J Mol Sci **24**(9).

The mechanistic target of rapamycin (mTOR) kinase is one of the top drug targets for promoting health and lifespan extension. Besides rapamycin, only a few other mTOR inhibitors have been developed and shown to be capable of slowing aging. We used machine learning to predict novel small molecules targeting mTOR. We selected one small molecule, TKA001, based on in silico predictions of a high on-target probability, low toxicity, favorable physicochemical properties, and preferable ADMET profile. We modeled TKA001 binding in silico by molecular docking and molecular dynamics. TKA001 potently inhibits both TOR complex 1 and 2 signaling in vitro. Furthermore,

TKA001 inhibits human cancer cell proliferation in vitro and extends the lifespan of Caenorhabditis elegans, suggesting that TKA001 is able to slow aging in vivo.

Vinhas, M., et al. (2024). "AI Applied to Volatile Organic Compound (VOC) Profiles from Exhaled Breath Air for Early Detection of Lung Cancer." Cancers (Basel) **16**(12).

Volatile organic compounds (VOCs) are an increasingly meaningful method for the early detection of various types of cancers, including lung cancer, through non-invasive methods. Traditional cancer detection techniques such as biopsies, imaging, and blood tests, though effective, often involve invasive procedures or are costly, time consuming, and painful. Recent advancements in technology have led to the exploration of VOC detection as a promising non-invasive and comfortable alternative. VOCs are organic chemicals that have a high vapor pressure at room temperature, making them readily detectable in breath, urine, and skin. The present study leverages artificial intelligence (AI) and machine learning algorithms to enhance classification accuracy and efficiency in detecting lung cancer through VOC analysis collected from exhaled breath air. Unlike other studies that primarily focus on identifying specific compounds, this study takes an agnostic approach, maximizing detection efficiency over the identification of specific compounds focusing on the overall compositional profiles and their differences across groups of patients. The results reported hereby uphold the potential of AI-driven techniques in revolutionizing early cancer detection methodologies towards their implementation in a clinical setting.

Volovat, S. R., et al. (2022). "Use of Personalized Biomarkers in Metastatic Colorectal Cancer and the Impact of AI." Cancers (Basel) **14**(19).

Colorectal cancer is a major cause of cancer-related death worldwide and is correlated with genetic and epigenetic alterations in the colonic epithelium. Genetic changes play a major role in the pathophysiology of colorectal cancer through the development of gene mutations, but recent research has shown an important role for epigenetic alterations. In this review, we try to describe the current knowledge about epigenetic alterations, including DNA methylation and histone modifications, as well as the role of non-coding RNAs as epigenetic regulators and the prognostic and predictive biomarkers in metastatic colorectal disease that can allow increases in the effectiveness of treatments. Additionally, the intestinal microbiota's composition can be an important biomarker for the response to strategies based on the immunotherapy of CRC. The identification of biomarkers in mCRC can be enhanced by developing artificial intelligence programs. We present the actual models that implement AI technology as a bridge connecting ncRNAs with tumors and conducted some experiments to improve the quality of the model used as well as the speed of the model that provides answers to users. In order to carry out this task, we implemented six algorithms: the naive Bayes classifier, the random forest classifier, the decision tree classifier, gradient boosted trees, logistic regression and SVM.

Vrdoljak, J., et al. (2023). "The Role of AI in Breast Cancer Lymph Node Classification: A Comprehensive Review." Cancers (Basel) **15**(8).

Breast cancer is a significant health issue affecting women worldwide, and accurately detecting lymph node metastasis is critical in determining treatment and prognosis. While traditional diagnostic methods have limitations and complications, artificial intelligence (AI) techniques such as machine learning (ML) and deep learning (DL) offer promising solutions for improving and supplementing diagnostic procedures. Current research has explored state-of-the-art DL models for breast cancer lymph node classification from radiological images, achieving high performances (AUC: 0.71-0.99). AI models trained on clinicopathological features also show promise in predicting metastasis status (AUC: 0.74-0.77), whereas multimodal (radiomics + clinicopathological features) models combine the best from both approaches and also achieve good results (AUC: 0.82-0.94). Once properly validated, such models could greatly improve cancer care, especially in areas with limited medical resources. This comprehensive review aims to compile knowledge about state-of-the-art AI models used for breast cancer lymph node metastasis detection, discusses proper validation techniques and potential pitfalls and limitations, and presents future directions and best practices to achieve high usability in real-world clinical settings.

Wahab, N., et al. (2023). "AI-enabled routine H&E image based prognostic marker for early-stage luminal breast cancer." NPJ Precis Oncol **7**(1): 122.

Breast cancer (BC) grade is a well-established subjective prognostic indicator of tumour aggressiveness. Tumour heterogeneity and subjective assessment result in high degree of variability among observers in BC grading. Here we propose an objective Haematoxylin & Eosin (H&E) image-based prognostic marker for early-stage luminal/Her2-negative BReAst CancEr that we term as the BRACE

marker. The proposed BRACE marker is derived from AI based assessment of heterogeneity in BC at a detailed level using the power of deep learning. The prognostic ability of the marker is validated in two well-annotated cohorts (Cohort-A/Nottingham: n = 2122 and Cohort-B/Coventry: n = 311) on early-stage luminal/HER2-negative BC patients treated with endocrine therapy and with long-term follow-up. The BRACE marker is able to stratify patients for both distant metastasis free survival (p = 0.001, C-index: 0.73) and BC specific survival (p < 0.0001, C-index: 0.84) showing comparable prediction accuracy to Nottingham Prognostic Index and Magee scores, which are both derived from manual histopathological assessment, to identify luminal BC patients that may be likely to benefit from adjuvant chemotherapy.

Waissengrin, B., et al. (2023). "Artificial intelligence (AI) molecular analysis tool assists in rapid treatment decision in lung cancer: a case report." J Clin Pathol **76**(11): 790-792.

Leptomeningeal involvement among non-small cell lung cancer (NSCLC) patients is an aggressive form of disease that requires quick and efficient treatment. In this case report, we describe a woman in her 40s with a presenting symptom of headache that ultimately was diagnosed as leptomeningeal spread from NSCLC adenocarcinoma. We identified EGFR mutation in less than 48 hours from the biopsy using imagene-artificial intelligence's real-time algorithmic solution on the pathological diagnostic slide.

Wan, H., et al. (2023). "CDKN2A was a cuproptosis-related gene in regulating chemotherapy resistance by the MAGE-A family in breast cancer: based on artificial intelligence (AI)-constructed pan-cancer risk model." Aging (Albany NY) **15**(20): 11244-11267.

BACKGROUND: Before the discovery of cuproptosis, copper-loaded nanoparticle is a wildly applied strategy for enhancing the tumor-cell-killing effect of chemotherapy. Although copper(ii)-related researches are wide, details of cuproptosis-related bioprocess in pan-cancer are not clear yet now, especially for prognosis and drug sensitivity prediction yet now. METHODS: In this study, VOSviewer is used for the literature review, and R4.2.0 is used for data analysis. Public data are collected from TCGA and GEO, local breast cancer cohort is collected to verify the expression level of CDKN2A. RESULTS: 7036 published articles exhibited a time-dependent linear relationship (R=0.9781, p<0.0001), and breast cancer (33.4%) is the most researched topic. Cuproptosis-related-genes (CRGs)-based unsupervised clustering divides pan-cancer subgroups into four groups (CRG subgroup) with differences in prognosis and tumor immunity. 44 tumor-driver-genes (TDGs)-based prediction model of drug sensitivity and prognosis is constructed by artificial intelligence (AI). Based on TDGs and clinical features, a nomogram is (C- index: 0.7, p= 6.958e- 12) constructed to predict the prognosis of breast cancer. Importance analysis identifies CDKN2A has a pivotal role in AI modeling, whose higher expression indicates worse prognosis in breast cancer. Furthermore, inhibition of CDKN2A down-regulates decreases Snail1, Twist1, Zeb1, vimentin and MMP9, while E-cadherin is increased. Besides, inhibition of CDKN2A also decreases the expression of MEGEA4, phosphorylated STAT3, PD-L1, and caspase3, while cleaved-caspase3 is increased. Finally, we find down-regulation of CDKN2A or MAGEA inhibits cell migration and wound healing, respectively. CONCLUSIONS: AI identified CRG subgroups in pan-cancer based on CRGs-related TDGs, and 44-gene-based AI modeling is a novel tool to identify chemotherapy sensitivity in breast cancer, in which CDKN2A/MAGEA4 pathway played the most important role.

Wang, H., et al. (2020). "AI-Driver: an ensemble method for identifying driver mutations in personal cancer genomes." NAR Genom Bioinform **2**(4): lqaa084.

The current challenge in cancer research is to increase the resolution of driver prediction from gene-level to mutation-level, which is more closely aligned with the goal of precision cancer medicine. Improved methods to distinguish drivers from passengers are urgently needed to dig out driver mutations from increasing exome sequencing studies. Here, we developed an ensemble method, AI-Driver (AI-based driver classifier, https://github.com/hatchetProject/AI-Driver), to predict the driver status of somatic missense mutations based on 23 pathogenicity features. AI-Driver has the best overall performance compared with any individual tool and two cancer-specific driver predicting methods. We demonstrate the superior and stable performance of our model using four independent benchmarks. We provide pre-computed AI-Driver scores for all possible human missense variants (http://aidriver.maolab.org/) to identify driver mutations in the sea of somatic mutations discovered by personal cancer sequencing. We believe that AI-Driver together with pre-computed database will play vital important roles in the human cancer studies, such as identification of driver mutation in personal cancer genomes, discovery of targeting sites for cancer therapeutic

treatments and prediction of tumor biomarkers for early diagnosis by liquid biopsy.

Wang, H., et al. (2022). "Lncap-AI prostate cancer cell line establishment by Flutamide and androgen-free environment to promote cell adherent." BMC Mol Cell Biol **23**(1): 51.

BACKGROUND: To establish castration-resistant prostate cancer (CRPC) - Lncap androgen-independent (AI) cell line from Lncap androgen-dependent (AD) cell line, and explore the different molecular biological between these two cell lines. METHODS: The Lncap-AD cell line was cultured and passaged 60 times over 16 months. The morphology of the Lncap-AI cell line was observed. AR levels identification were detected in qRT-PCR and Western Blot assay. CCK-8, EdU assay, wound healing assay and cell adhesion assays were used to observe the ability of proliferation, migration, and adhesion. SEM and TEM were used to observe microculture structure. At last, the PSA secrete ability was evaluated by Elisa assay. RESULTS: The Lncap-AD cell line was cultured and passaged 60 times over 16 months. The Lncap-AI cell line showed a morphologic change at the end stage of culture, the cells turned slender and cell space turned separated compared to the Lncap-AD cell line. The relative levels of AR-related genes in the Lncap-AI cell line were up-regulation compared to the Lncap-AD cell line both in mRNA and protein levels. The expression of AR and HK2 proteins were influenced and down-regulation by Enzalutamide in the Lncap-AD cell line, but no obvious difference in Lncap-AI cell lines. Lncap-AI cell line showed strong viability of proliferation, migration, and adhesion by CCK-8, EdU assay, wound healing assay, and adhesion assay. The microstructure of Scanning Electron Microscopy (SEM) showed many synapses in the Lncap-AI cell line and PC3 cell line, but not in the Lncap-AD cell line. At last, the PSA secrete ability was evaluated by Elisa assay, and PCa cell lines showed no significant difference. CONCLUSION: Simulation of CRPC progression, Lncap-AD cell line turned to Lncap-AI cell line with androgen deprivation therapy.

Wang, J., et al. (2021). "Identifying the role of apolipoprotein A-I in prostate cancer." Asian J Androl **23**(4): 400-408.

Although localized prostate cancer (PCa) can be cured by prostatectomy and radiotherapy, the development of effective therapeutic approaches for advanced prostate cancer, including castration-resistant PCa (CRPC) and neuroendocrine PCa (NEPC), is lagging far behind. Identifying a novel prognostic and diagnostic biomarker for early diagnosis and intervention is an urgent clinical need. Here, we report that apolipoprotein A-I (ApoA-I), the major component of high-density lipoprotein (HDL), is upregulated in PCa based on both bioinformatics and experimental evidence. The fact that advanced PCa shows strong ApoA-I expression reflects its potential role in driving therapeutic resistance and disease progression by reprogramming the lipid metabolic network of tumor cells. Molecularly, ApoA-I is regulated by MYC, a frequently amplified oncogene in late-stage PCa. Altogether, our findings have revealed a novel indicator to predict prognosis and recurrence, which would benefit patients who are prone to progress to metastasis or even NEPC, which is the lethal subtype of PCa.

Wang, M., et al. (2024). "Comparative Analysis of AI-SONICTM Thyroid System and Six Thyroid Risk Stratification Guidelines in Papillary Thyroid Cancer: A Retrospective Cohort Study." Ther Clin Risk Manag **20**: 515-528.

AIM: The study aimed to compare the diagnostic performance of AI-SONICTM Thyroid System (AI-SONICTM) with six thyroid nodule ultrasound risk stratification systems, as well as the interobserver agreement among different-year ultrasound examiners using the same diagnostic approach. METHODS: This retrospective study included patients who underwent thyroid ultrasound examination and surgery between 2010 and 2022. Three ultrasound examiners with 2, 5, and 10 years of experience, respectively, used AI-SONICTM and six guidelines to risk-stratify the nodules. The diagnostic performance and interobserver agreement were assessed. RESULTS: A total of 370 thyroid nodules were included, including 195 papillary thyroid carcinomas (PTC) and 175 benign nodules. For physicians of varying seniority from low to high, AI-SONICTM had a moderate sensitivities of 82.56%, 83.08%, 84.62%, respectively, while AACE/ACE/AME had the highest diagnostic sensitivities (96.41%, 95.38%, 96.41%, respectively); And relatively higher specificities were 85.14%, 85.71%, 85.71% for KSThR, while moderate specificities with values of 84.0%, 85.14%, and 85.71%, respectively were found for AI-SONICTM; The accuracy was highest for ATA (excluding non-classifiable nodules), with values of 87.26%, 87.93%, and 88.82%, respectively, while the accuracy for AI-SONICTM were 83.24%, 84.05%, and 85.14%, respectively. The Kendall's tau coefficient indicated strong or moderate interobserver agreement among all examiners using different diagnostic methods (Kendall's tau coefficient >0.6, P<0.001). AI-SONICTM showed the highest interobserver agreement (Kendall's tau coefficient=0.995, P<0.001). A binary probit regression analysis showed that

nodules with cystic components had a significantly higher regression coefficient value of 0.983 (P=0.002), indicating that AI-SONICTM may have higher accuracy for nodules with cystic components. CONCLUSION: AI-SONICTM and the six thyroid nodule ultrasound risk stratification systems showed high diagnostic performance for papillary thyroid carcinoma. All examiners showed strong or moderate interobserver agreement when using different diagnostic methods. AI-SONICTM may have higher accuracy for nodules with cystic components.

Wang, N., et al. (2018). "Network Pharmacology-Based Validation of Caveolin-1 as a Key Mediator of Ai Du Qing Inhibition of Drug Resistance in Breast Cancer." Front Pharmacol **9**: 1106.

Chinese formulas have been paid increasing attention in cancer multidisciplinary therapy due to their multi-targets and multi-substances property. Here, we aim to investigate the anti-breast cancer and chemosensitizing function of Ai Du Qing (ADQ) formula made up of Hedyotis diffusa, Curcuma zedoaria (Christm.) Rosc., Astragalus membranaceus (Fisch.) Bunge, and Glycyrrhiza uralensis Fisch. Our findings revealed that ADQ significantly inhibited cell proliferation in both parental and chemo-resistant breast cancer cells, but with little cytotoxcity effects on the normal cells. Besides, ADQ was found to facilitate the G2/M arresting and apoptosis induction effects of paclitaxel. Network pharmacology and bioinformatics analysis further demonstrated that ADQ yielded 132 candidate compounds and 297 potential targets, and shared 22 putative targets associating with breast cancer chemoresponse. Enrichment analysis and experimental validation demonstrated that ADQ might improve breast cancer chemosensitivity via inhibiting caveolin-1, which further triggered expression changes of cell cycle-related proteins p21/cyclinB1 and apoptosis-associated proteins PARP1, BAX and Bcl-2. Besides, ADQ enhanced in vivo paclitaxel chemosensitivity on breast cancer. Our study not only uncovers the novel function and mechanisms of ADQ in chemosensitizing breast cancer at least partly via targeting caveolin-1, but also sheds novel light in utilizing network pharmacology in Chinese Medicine research.

Wang, S., et al. (2018). "Decoction of Chinese Herbal Medicine Fuzheng Kang-Ai Induces Lung Cancer Cell Apoptosis via STAT3/Bcl-2/Caspase-3 Pathway." Evid Based Complement Alternat Med **2018**: 8567905.

Decoction of Chinese herbal medicine (CHM) Fuzheng Kang-Ai (FZKA for short) has been applied as adjuvant treatment strategy in advanced lung cancer patients for decades. We previously showed that FZKA decoction inhibited proliferation of non-small cell lung cancer (NSCLC) cells through activation of AMP-activated protein kinase alpha (AMPKalpha) signaling pathway, followed by inducing insulin-like growth factor (IGF) binding protein 1 (IGFBP1) and forkhead homeobox type O3a (FOXO3a) proteins, and enhanced the inhibition effect of gefitinib in lung cancer cell growth via inactivating PI3-K/Akt-mediated suppressing of cell surface-associated mucin-1 (MUC1) expression. In this study, we investigated the molecular mechanism by which FZKA decoction affected cell apoptosis in lung cancer cells. Our results show that FZKA induced apoptosis in lung cancer cells. Mechanistically, FZKA activated the caspase-3, PARP, and caspase-9 activities. Both antiapoptotic and proapoptotic proteins from Bcl-2 family were deregulated by FZKA exposure in lung cancer cells. In addition, FZKA reduced protein expressions of signal transducer and activator of transcription 3 (STAT3) and Jun activation domain-binding protein 1 (Jab1), while it concomitantly increased p21 protein. Moreover, the inhibitor of caspase-3 resisted the effect of FZKA on induction of apoptosis. Finally, exogenous overexpression of STAT3 overcame FZKA-inhibited protein expressions of Bcl-2 and myeloid cell leukemia-1 (Mcl-1) as well as Bax and blocked FZKA-induced activities of caspase-3 and caspase-9. Our results show that FZKA decoction promotes lung cancer cell apoptosis through STAT3/Bcl-2/caspase-3 signaling pathways. This study unveils potential novel molecular mechanism by which FZKA controls growth of human lung cancer cells.

Wang, S., et al. (2020). "Fuzheng Kang-Ai decoction enhances the effect of Gefitinib-induced cell apoptosis in lung cancer through mitochondrial pathway." Cancer Cell Int **20**: 185.

BACKGROUND: Our previous clinical study has shown that Chinese herbal medicine (CHM) Fuzheng Kang-Ai (FZKA) decoction is effective in treating advanced lung cancer patients through prolonging the drug resistance to Gefitinib (GFTN). Our basic study found that FZKA decoction could enhance the inhibition effect of GFTN in lung cancer by inactivating PI3K/Akt pathway. Moreover, our recent work showed that FZKA induced lung cancer cell apoptosis via STAT3/Bcl-2/Caspase-3 pathway. Thus in this study, we aim to elucidate how FZKA enhances the effect of GFTN in lung cancer from the perspective of cell apoptosis. METHODS: Cell proliferation and colony formation assay were performed to detect the cell growth inhibition. Flow cytometry and TUNEL assay were carried out to test

the cell apoptosis. Mitochondrial membrane potential (MMP) assay was done to measure the alteration of MMP. Caspase-3/-9 activity assay was used to test the activity of caspase-3/-9. Western blot and qRT-PCR were done to detect the expression of STAT3 and Bcl-2 family as well as Caspase-3/-9 and Cyt-C at protein and mRNA levels, respectively. Transient transfection was performed to silence STAT3 using siSTAT3. Animal model was done to validate the molecular mechanisms in vivo and immunohistochemistry was done to detect the expression of Bax and Caspase-3. RESULTS: Firstly, our results showed that FZKA enhanced the inhibition effect of GFTN in lung cancer both in vitro and in vivo. Secondly, cell apoptosis was enhanced when treating lung cancer cells with both FZKA and GFTN, a process involving the mitochondria and the Bcl-2 family. And Bcl-2 family was involved in this process. Interestingly, STAT3 plays a critical role on mediating the above process. Last but not the least, the enhanced effect of cell apoptosis induction of GFTN by FZKA was validated in animal model. CONCLUSION: Our findings conclude that Fuzheng Kang-Ai decoction enhances the effect of GFTN-induced cell apoptosis in lung cancer through the mitochondrial pathway, providing a novel molecular mechanism by which FZKA sensitizes to GFTN by delaying drug resistance in treating lung cancer patients.

Wang, T. and X. Yang (2024). "Take CT, get PET free: AI-powered breakthrough in lung cancer diagnosis and prognosis." Cell Rep Med **5**(4): 101486.

PET scans provide additional clinical value but are costly and not universally accessible. Salehjahromi et al.(1) developed an AI-based pipeline to synthesize PET images from diagnostic CT scans, demonstrating its potential clinical utility across various clinical tasks for lung cancer.

Wang, W., et al. (2024). "AI-Enhanced Visual-Spectral Synergy for Fast and Ultrasensitive Biodetection of Breast Cancer-Related miRNAs." ACS Nano **18**(8): 6266-6275.

In biomedical testing, artificial intelligence (AI)-enhanced analysis has gradually been applied to the diagnosis of certain diseases. This research employs AI algorithms to refine the precision of integrative detection, encompassing both visual results and fluorescence spectra from lateral flow assays (LFAs), which signal the presence of cancer-linked miRNAs. Specifically, the color shift of gold nanoparticles (GNPs) is paired with the red fluorescence from nitrogen vacancy color centers (NV-centers) in fluorescent nanodiamonds (FNDs) and is integrated into LFA strips. While GNPs amplify the fluorescence of FNDs, in turn, FNDs enhance the color intensity of GNPs. This reciprocal intensification of fluorescence and color can be synergistically augmented with AI algorithms, thereby improving the detection sensitivity for early diagnosis. Supported by the detection platform based on this strategy, the fastest detection results with a limit of detection (LOD) at the fM level and the R(2) value of approximately 0.9916 for miRNA can be obtained within 5 min. Meanwhile, by labeling the capture probes for miRNA-21 and miRNA-96 (both of which are early indicators of breast cancer) on separate T-lines, simultaneous detection of them can be achieved. The miRNA detection methods employed in this study may potentially be applied in the future for the early detection of breast cancer.

Wang, X., et al. (2015). "A meta-analysis of Kang;ai injection combined with chemotherapy in the treatment of advanced non-small cell lung cancer." J Cancer Res Ther **11**(3): 558-564.

OBJECTIVE: The purpose of this study was to evaluate the Kang;ai injection combined with chemotherapy in the treatment of advanced non-small cell lung cancer (NSCLC) by meta-analysis. MATERIALS AND METHODS: Electronic search of the Cochrane library, PubMed, EMBASE, Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals (VIP), and Wanfang Database was conducted to collect appropriate studies about Kang;ai injection combined with chemotherapy versus chemotherapy alone in the treatment of NSCLC. All data were analyzed by using RevMan 5.2 software provided by Cochrane, which involved the odds ratio (OR) and 95% confidence intervals (95% CIs) calculated with fixed-effect models according to the heterogeneity test. RESULTS: Eighteen studies were included in this meta-analysis. The meta-analysis showed that Kang;ai injection combined with chemotherapy could enhance the efficacy of the tumor response (OR=1.51, 95% CI: 1.23-1.85, Z=3.94, P<0.0001), improve the quality of life (OR=3.37, 95% CI: 2.71-4.20, Z=10.86, P<0.00001), alleviate the adverse reaction of digestive tract (OR=0.42, 95% CI: 0.32-0.55, Z=6.34, P<0.00001) and reduce the risk of the bone marrow suppression (OR=0.38, 95% CI: 0.29-0.49, Z=7.37, P<0.00001) compared with chemotherapy alone. Asymmetries were observed in funnel plots, which indicated an evidence of publication bias. CONCLUSION: Kang;ai injection combined with chemotherapy can enhance the short-term efficacy, improve the quality of life, and alleviate the chemotherapy-induced adverse reaction in the treatment of advanced NSCLC, although these results

need to be further confirmed by more high-quality trials.

Wang, Y., et al. (2022). "The value of AI in the Diagnosis, Treatment, and Prognosis of Malignant Lung Cancer." Front Radiol **2**: 810731.

Malignant tumors is a serious public health threat. Among them, lung cancer, which has the highest fatality rate globally, has significantly endangered human health. With the development of artificial intelligence (AI) and its integration with medicine, AI research in malignant lung tumors has become critical. This article reviews the value of CAD, computer neural network deep learning, radiomics, molecular biomarkers, and digital pathology for the diagnosis, treatment, and prognosis of malignant lung tumors.

Wang, Z., et al. (2024). "Correction: A multi-task learning based applicable AI model simultaneously predicts stage, histology, grade and LNM for cervical cancer before surgery." BMC Womens Health **24**(1): 602.

Wang, Z., et al. (2024). "A multi-Task Learning based applicable AI model simultaneously predicts stage, histology, grade and LNM for cervical cancer before surgery." BMC Womens Health **24**(1): 425.

PURPOSE: To build an Mult-Task Learning (MTL) based Artificial Intelligence(AI) model that can simultaneously predict clinical stage, histology, grade and LNM for cervical cancer before surgery. METHODS: This retrospective and prospective cohort study was conducted from January 2001 to March 2014 for the training set and from January 2018 to November 2021 for the validation set at Beijing Chaoyang Hospital, Capital Medical University. Preoperative clinical information of cervical cancer patients was used. An Artificial Neural Network (ANN) algorithm was used to build the MTL-based AI model. Accuracy and weighted F1 scores were calculated as evaluation indicators. The performance of the MTL model was compared with Single-Task Learning (STL) models. Additionally, a Turing test was performed by 20 gynecologists and compared with this AI model. RESULTS: A total of 223 cervical cancer cases were retrospectively enrolled into the training set, and 58 cases were prospectively collected as independent validation set. The accuracy of this cervical cancer AI model constructed with ANN algorithm in predicting stage, histology, grade and LNM were 75%, 95%, 86% and 76%, respectively. And the corresponding weighted F1 score were 70%, 94%, 86%, and 76%, respectively. The average time consumption of AI simultaneously predicting stage, histology, grade and LNM for cervical cancer was 0.01s (95%CI: 0.01-0.01) per 20 patients. The mean time consumption doctor and doctor with AI were 581.1s (95%CI: 300.0-900.0) per 20 patients and 534.8s (95%CI: 255.0-720.0) per 20 patients, respectively. Except for LNM, both the accuracy and F-score of the AI model were significantly better than STL AI, doctors and AI-assisted doctors in predicting stage, grade and histology. ($P < 0.05$) The time consumption of AI was significantly less than that of doctors' prediction and AI-assisted doctors' results. ($P < 0.05$ CONCLUSION: A multi-task learning AI model can simultaneously predict stage, histology, grade, and LNM for cervical cancer preoperatively with minimal time consumption. To improve the conditions and use of the beneficiaries, the model should be integrated into routine clinical workflows, offering a decision-support tool for gynecologists. Future studies should focus on refining the model for broader clinical applications, increasing the diversity of the training datasets, and enhancing its adaptability to various clinical settings. Additionally, continuous feedback from clinical practice should be incorporated to ensure the model's accuracy and reliability, ultimately improving personalized patient care and treatment outcomes.

Warin, K., et al. (2022). "AI-based analysis of oral lesions using novel deep convolutional neural networks for early detection of oral cancer." PLoS One **17**(8): e0273508.

Artificial intelligence (AI) applications in oncology have been developed rapidly with reported successes in recent years. This work aims to evaluate the performance of deep convolutional neural network (CNN) algorithms for the classification and detection of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC) in oral photographic images. A dataset comprising 980 oral photographic images was divided into 365 images of OSCC, 315 images of OPMDs and 300 images of non-pathological images. Multiclass image classification models were created by using DenseNet-169, ResNet-101, SqueezeNet and Swin-S. Multiclass object detection models were fabricated by using faster R-CNN, YOLOv5, RetinaNet and CenterNet2. The AUC of multiclass image classification of the best CNN models, DenseNet-196, was 1.00 and 0.98 on OSCC and OPMDs, respectively. The AUC of the best multiclass CNN-base object detection models, Faster R-CNN, was 0.88 and 0.64 on OSCC and OPMDs, respectively. In comparison, DenseNet-196 yielded the best multiclass image classification performance with AUC of 1.00 and 0.98 on OSCC and OPMD, respectively. These values were inline with the

performance of experts and superior to those of general practictioners (GPs). In conclusion, CNN-based models have potential for the identification of OSCC and OPMDs in oral photographic images and are expected to be a diagnostic tool to assist GPs for the early detection of oral cancer.

Webster, P. (2024). "How AI-powered handheld devices are boosting disease diagnostics - from cancer to dermatology." Nat Med **30**(4): 914-915.

Wei, M. Y. K., et al. (2023). "Artificial intelligence (AI) in the management of colorectal cancer: on the horizon?" ANZ J Surg **93**(9): 2052-2053.

Wei, Y. Y., et al. (2019). "[Down-regulated PTTG1 expression promotes the senescence of human prostate cancer LNCaP-AI]." Zhonghua Nan Ke Xue **25**(3): 216-222.

OBJECTIVE: To investigate the effect of the down-regulated expression of pituitary tumor-transforming gene 1 (PTTG1) on the senescence of human castration-resistant prostate cancer LNCaP-AI cells. METHODS: Human castration-resistant prostate cancer LNCaP-AI cells were induced in vitro and transfected with siRNA targeting PTTG1 (the siRNA-PTTG1 group), the reagent lip3000 only (the mock group) or siRNA negative control vector (the NC group). All the cells were cultured in fetal bovine serum (FBS) or charcoal-stripped bovine serum (CSS) and counted with the cell counting chamber. The senescence characteristics of the transfected LNCaP-AI cells were examined by senescence-associated beta-galactosidase (SA-beta-Gal) staining, and the expressions of the senescence-related beta-galactosidase-1-like proteins (Glb1), the cyclin-dependent kinase inhibitors p-21CIP1 and p-27Kip1, and the chromatin-regulating heterochromatin protein 1gamma (HP1gamma) were detected by Western blot. RESULTS: The expression of PTTG1 in the human prostate cancer LNCaP-AI cells was significantly reduced in the siRNA-PTTG1 group compared with those in the mock and NC groups (0.21 +/- 0.01 vs 0.56 +/- 0.02 and 0.61 +/- 0.02, P < 0.05). Culture with FBS markedly increased while that with CSS decreased the number of LNCaP-AI cells transfected with siRNA, but both FBS and CSS enhanced the proliferation of the LNCaP-AI cells in the mock and NC groups. SA-beta-Gal staining revealed that reducing the expression of PTTG1 induced a remarkably higher positive rate of the LNCaP-AI cells in the siRNA-PTTG1 than in the mock and NC groups ([63.5 +/- 2.35] % vs [11.3 +/- 1.24] % and [12.4 +/- 1.15] %, P < 0.05). The siRNA-PTTG1 group, in comparison with the mock and NC groups, showed a significantly down-regulated expression of PTTG1 (0.21 +/- 0.01 vs 0.56 +/- 0.02 and 0.61 +/- 0.02, P < 0.05), but up-regulated expressions of p-21CIP1 (0.32 +/- 0.03 vs 0.20 +/- 0.02 and 0.21 +/- 0.03, P < 0.05), p-27Kip1 (0.38 +/- 0.02 vs 0.20 +/- 0.03 and 0.22 +/- 0.01, P < 0.05), Glb1 (0.24 +/- 0.01 vs 0.13 +/- 0.01 and 0.15 +/- 0.01, P < 0.05), and HP1gamma (0.41 +/- 0.01 vs 0.26 +/- 0.01 and 0.27 +/- 0.02, P < 0.05) in the LNCaP-AI cells. CONCLUSIONS: Down-regulated expression of PTTG1 induces senescence of human castration-resistant prostate cancer LNCaP-AI cells.

Weitz, M., et al. (2024). "Performance of an AI-powered visualization software platform for precision surgery in breast cancer patients." NPJ Breast Cancer **10**(1): 98.

Surgery remains the primary treatment modality in the management of early-stage invasive breast cancer. Artificial intelligence (AI)-powered visualization platforms offer the compelling potential to aid surgeons in evaluating the tumor's location and morphology within the breast and accordingly optimize their surgical approach. We sought to validate an AI platform that employs dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) to render three-dimensional (3D) representations of the tumor and 5 additional chest tissues, offering clear visualizations as well as functionalities for quantifying tumor morphology, tumor-to-landmark structure distances, excision volumes, and approximate surgical margins. This retrospective study assessed the visualization platform's performance on 100 cases with ground-truth labels vetted by 2 breast-specialized radiologists. We assessed features including automatic AI-generated clinical metrics (e.g., tumor dimensions) as well as visualization tools including convex hulls at desired margins around the tumor to help visualize lumpectomy volume. The statistical performance of the platform's automated features was robust and within the range of inter-radiologist variability. These detailed 3D tumor and surrounding multi-tissue depictions offer both qualitative and quantitative comprehension of cancer topology and may aid in formulating an optimal surgical approach for breast cancer treatment. We further establish the framework for broader data integration into the platform to enhance precision cancer care.

Westhaeusser, F., et al. (2024). "Robust, credible, and interpretable AI-based histopathological prostate cancer grading." medRxiv.

BACKGROUND: Prostate cancer (PCa) is among the most common cancers in men and its diagnosis requires the histopathological evaluation of biopsies by human experts. While several recent

artificial intelligence-based (AI) approaches have reached human expert-level PCa grading, they often display significantly reduced performance on external datasets. This reduced performance can be caused by variations in sample preparation, for instance the staining protocol, section thickness, or scanner used. Another limiting factor of contemporary AI-based PCa grading is the prediction of ISUP grades, which leads to the perpetuation of human annotation errors. METHODS: We developed the prostate cancer aggressiveness index (PCAI), an AI-based PCa detection and grading framework that is trained on objective patient outcome, rather than subjective ISUP grades. We designed PCAI as a clinical application, containing algorithmic modules that offer robustness to data variation, medical interpretability, and a measure of prediction confidence. To train and evaluate PCAI, we generated a multicentric, retrospective, observational trial consisting of six cohorts with 25,591 patients, 83,864 images, and 5 years of median follow-up from 5 different centers and 3 countries. This includes a high-variance dataset of 8,157 patients and 28,236 images with variations in sample thickness, staining protocol, and scanner, allowing for the systematic evaluation and optimization of model robustness to data variation. The performance of PCAI was assessed on three external test cohorts from two countries, comprising 2,255 patients and 9,437 images. FINDINGS: Using our high-variance datasets, we show how differences in sample processing, particularly slide thickness and staining time, significantly reduce the performance of AI-based PCa grading by up to 6.2 percentage points in the concordance index (C-index). We show how a select set of algorithmic improvements, including domain adversarial training, conferred robustness to data variation, interpretability, and a measure of credibility to PCAI. These changes lead to significant prediction improvement across two biopsy cohorts and one TMA cohort, systematically exceeding expert ISUP grading in C-index and AUROC by up to 22 percentage points. INTERPRETATION: Data variation poses serious risks for AI-based histopathological PCa grading, even when models are trained on large datasets. Algorithmic improvements for model robustness, interpretability, credibility, and training on high-variance data as well as outcome-based severity prediction gives rise to robust models with above ISUP-level PCa grading performance.

Weykamp, F., et al. (2024). "Daily AI-Based Treatment Adaptation under Weekly Offline MR Guidance in Chemoradiotherapy for Cervical Cancer 1: The AIM-C1 Trial." J Clin Med **13**(4).

(1) Background: External beam radiotherapy (EBRT) and concurrent chemotherapy, followed by brachytherapy (BT), offer a standard of care for patients with locally advanced cervical carcinoma. Conventionally, large safety margins are required to compensate for organ movement, potentially increasing toxicity. Lately, daily high-quality cone beam CT (CBCT)-guided adaptive radiotherapy, aided by artificial intelligence (AI), became clinically available. Thus, online treatment plans can be adapted to the current position of the tumor and the adjacent organs at risk (OAR), while the patient is lying on the treatment couch. We sought to evaluate the potential of this new technology, including a weekly shuttle-based 3T-MRI scan in various treatment positions for tumor evaluation and for decreasing treatment-related side effects. (2) Methods: This is a prospective one-armed phase-II trial consisting of 40 patients with cervical carcinoma (FIGO IB-IIIC1) with an age >/= 18 years and a Karnofsky performance score >/= 70%. EBRT (45-50.4 Gy in 25-28 fractions with 55.0-58.8 Gy simultaneous integrated boosts to lymph node metastases) will be accompanied by weekly shuttle-based MRIs. Concurrent platinum-based chemotherapy will be given, followed by 28 Gy of BT (four fractions). The primary endpoint will be the occurrence of overall early bowel and bladder toxicity CTCAE grade 2 or higher (CTCAE v5.0). Secondary outcomes include clinical feasibility, quality of life, and imaging-based response assessment.

Wieder, R. and N. Adam (2022). "Drug repositioning for cancer in the era of AI, big omics, and real-world data." Crit Rev Oncol Hematol **175**: 103730.

Drug repositioning in cancer has been pursued for years because of slowing drug development, increasing costs, and the availability of drugs licensed for other indications with anticancer effects in the laboratory. Repositioning has encountered obstacles due to generally insufficient single-agent clinical anticancer effects of licensed drugs and a subsequent reluctance by pharmaceutical companies to invest in phase III combination studies with them. Here we review potential machine learning/artificial intelligence (ML/AI) approaches for using real-world data (RWD) that could overcome the limitations of clinical trials and retrospective analyses. We outline a two-tiered filtering approach of identifying top-ranked drugs based on their drug-target binding affinity scores while considering their challenges and matching the top-ranked drugs with their top-ranked specific scenarios from among the multitude of real-world scenarios for efficacy and safety. This approach will generate RWD scenario-specific hypotheses that can be tested in randomized

clinical trials with high probabilities of success.

Wiklund, P., et al. (2023). "Incidental pulmonary embolism in patients with cancer: prevalence, underdiagnosis and evaluation of an AI algorithm for automatic detection of pulmonary embolism." Eur Radiol **33**(2): 1185-1193.

OBJECTIVES: To assess the prevalence of reported and unreported incidental pulmonary embolism (iPE) in patients with cancer, and to evaluate an artificial intelligence (AI) algorithm for automatic detection of iPE. METHODS: Retrospective cohort study on patients with cancer with an elective CT study including the chest between 2018-07-01 and 2019-06-30. All study reports and images were reviewed to identify reported and unreported iPE and were processed by the AI algorithm. RESULTS: One thousand sixty-nine patients (1892 studies) were included. Per study, iPE was present in 75 studies (4.0%), of which 16 (21.3%) were reported. Unreported iPE had a significantly lower number of involved vessels compared to reported iPE, with a median of 2 (interquartile range, IQR, 1-4) versus 5 (IQR 3-9.75), p < 0.001. There were no significant differences in age, cancer type, or attenuation of the main pulmonary artery. The AI algorithm correctly identified 68 of 75 iPE, with 3 false positives (sensitivity 90.7%, specificity 99.8%, PPV 95.6%, NPV 99.6%). False negatives occurred in cases with 1-3 involved vessels. Of the unreported iPE, 32/59 (54.2%) were proximal to the subsegmental arteries. CONCLUSION: In patients with cancer, the prevalence of iPE was 4.0%, of which only 21% were reported. Greater than 50% of unreported iPE were proximal to the subsegmental arteries. The AI algorithm had a very high sensitivity and specificity with only three false positives, with the potential to increase the detection rate of iPE. KEY POINTS: * In a retrospective single-center study on patients with cancer, unreported iPE were common, with the majority lying proximal to the subsegmental arteries. * The evaluated AI algorithm had a very high sensitivity and specificity, so has the potential to increase the detection rate of iPE.

Williams, C. J. M., et al. (2023). "Associations between AI-Assisted Tumor Amphiregulin and Epiregulin IHC and Outcomes from Anti-EGFR Therapy in the Routine Management of Metastatic Colorectal Cancer." Clin Cancer Res **29**(20): 4153-4165.

PURPOSE: High tumor production of the EGFR ligands, amphiregulin (AREG) and epiregulin (EREG), predicted benefit from anti-EGFR therapy for metastatic colorectal cancer (mCRC) in a retrospective analysis of clinical trial data. Here, AREG/EREG IHC was analyzed in a cohort of patients who received anti-EGFR therapy as part of routine care, including key clinical contexts not investigated in the previous analysis. EXPERIMENTAL DESIGN: Patients who received panitumumab or cetuximab +/- chemotherapy for treatment of RAS wild-type mCRC at eight UK cancer centers were eligible. Archival formalin-fixed paraffin-embedded tumor tissue was analyzed for AREG and EREG IHC in six regional laboratories using previously developed artificial intelligence technologies. Primary endpoints were progression-free survival (PFS) and overall survival (OS). RESULTS: A total of 494 of 541 patients (91.3%) had adequate tissue for analysis. A total of 45 were excluded after central extended RAS testing, leaving 449 patients in the primary analysis population. After adjustment for additional prognostic factors, high AREG/EREG expression (n = 360; 80.2%) was associated with significantly prolonged PFS [median: 8.5 vs. 4.4 months; HR, 0.73; 95% confidence interval (CI), 0.56-0.95; P = 0.02] and OS [median: 16.4 vs. 8.9 months; HR, 0.66 95% CI, 0.50-0.86; P = 0.002]. The significant OS benefit was maintained among patients with right primary tumor location (PTL), those receiving cetuximab or panitumumab, those with an oxaliplatin- or irinotecan-based chemotherapy backbone, and those with tumor tissue obtained by biopsy or surgical resection. CONCLUSIONS: High tumor AREG/EREG expression was associated with superior survival outcomes from anti-EGFR therapy in mCRC, including in right PTL disease. AREG/EREG IHC assessment could aid therapeutic decisions in routine practice. See related commentary by Randon and Pietrantonio, p. 4021.

Wise, J. (2023). "NICE says there is insufficient evidence to support use of AI for lung cancer diagnosis." BMJ **383**: 2284.

Wong, A. J. N., et al. (2024). "Navigating the Future of Prostate Cancer Care: AI-Driven Imaging and Theranostics Through the Lens of RELAINCE." J Nucl Med **65**(10): 1503-1504.

Workman, P., et al. (2019). "Transforming cancer drug discovery with Big Data and AI." Expert Opin Drug Discov **14**(11): 1089-1095.

Wu, D. Y., et al. (2024). "Long overdue national big data policies hinder accurate and equitable cancer detection AI systems." J Med Imaging Radiat Sci **55**(4): 101387.

Wu, K., et al. (2019). "Efficacy and Safety of Xiao Ai Ping Injection Combined with Chemotherapy in Advanced Gastric Cancer: A Systematic Review and Meta-Analysis." Evid Based Complement Alternat Med **2019**: 3821053.

Xiao Ai Ping injection (XAPI), extracted from the Chinese herbal medicine Marsdenia tenacissima, is widely used in the adjuvant treatment of tumors in China. The present study aimed to evaluate the efficacy and safety of XAPI combined with chemotherapy for treating patients with advanced gastric cancer. Seven databases were searched for relevant studies published up to October 1, 2018, and Review Manager 5.3 software and Stata 12.0 software were used for meta-analysis. Fourteen studies, representing 1097 enrolled patients, were included in our analysis. Compared with chemotherapy alone, combination treatment with XAPI and the XELOX regimen (capecitabine plus oxaliplatin) was found to improve the objective response rate (ORR) [RR=1.36; 95%CI (1.10, 1.70); P=0.006], disease control rate (DCR) [RR=1.15; 95% CI (1.04, 1.28); P=0.010], and Karnofsky Performance Status (KPS) improvement rate [RR=1.51; 95%CI (1.14, 2.00); P=0.004] and to reduce the incidence of leukopenia [RR=0.68; 95%CI (0.55,0.84); P=0.0005], liver damage [RR=0.59; 95% CI (0.37, 0.92); P=0.02], renal impairment [RR=0.39; 95% CI (0.18, 0.85); P=0.02], and hand-foot syndrome [RR=0.56; 95%CI (0.35,0.90); P=0.02]. However, median progression-free survival (PFS), 1-year survival rate, and median overall survival (OS) were not extended by XAPI plus XELOX. Combination treatment with XAPI and the SOX regimen (tegafur plus oxaliplatin) did not improve ORR or DCR, but it did enhance the KPS improvement rate [RR=1.73; 95%CI (1.23,2.43); P=0.002] and reduce the incidence of nausea and vomiting [RR=0.66; 95% CI (0.50, 0.88); P=0.004]. XAPI in combination with the FOLFOX regimen (fluorouracil/calcium folinate/oxaliplatin) enhanced only the KPS improvement rate [RR=1.68; 95%CI (1.18,2.39); P=0.004] and had no significant effect on ORR or DCR or the incidence of adverse events. A single study reported that XAPI combined with the CPT-11 regimen (irinotecan) was superior to chemotherapy alone with respect to DCR and also reduced the incidence of leukopenia, liver damage, and hand-foot syndrome during chemotherapy, while prolonging PFS. Finally, one study reported that XAPI combined with the TP regimen (palitaxel plus cisplatin) improved ORR and KPS improvement rate to a greater extent than TP alone. Although the present review has some limitations, the findings suggest that XAPI combined with chemotherapy may represent a beneficial treatment strategy, particularly the combination of XAPI and XELOX.

Wu, X. Q., et al. (2012). "[Effects of ru'ai shuhou recipe on the matrix metalloproteinases and the inhibitive factors in the recurrence and metastasis of HER2 positive breast cancer]." Zhongguo Zhong Xi Yi Jie He Za Zhi **32**(11): 1526-1530.

OBJECTIVE: To observe the anti-tumor recurrent and metastatic efficacy of Ru'ai Shuhou Recipe (RSR) on HER2 positive breast cancer, to evaluate the effects of RSR on the expressions of matrix metalloproteinases (MMPs) and the tissue inhibitor of metalloproteinases (TIMPs) in the recurrence and metastasis of HER2 positive breast cancer, thus revealing its anti-tumor recurrent and metastatic mechanisms. METHODS: Selected were 30-week-old HER2/neu transgenic spontaneous breast cancer mice FVB/neu. The primary tumor resection was carried out. After surgery they were randomly divided into the blank control group, the RSR group, the Herceptin group, and the combination group (RSR + Herceptin group). The treatment lasted for 4 months. The inhibition rate of the recurrent tumor volume and the inhibition rate of the lung metastasis were evaluated. The expressions of matrix metalloproteinase-2 (MMP-2), matrix metalloproteinase-9 (MMP-9), tissue inhibitor of metalloproteinase (TIMP-1), and TIMP-2 in the recurrent tumor tissue were detected using Western blot. RESULTS: By the end of the treatment the average recurrent tumor volume was 11.11 +/- 8.71 cm3 in the blank control group and 5.56 +/- 5.55 cm3 of the RSR group, showing statistical difference between the two groups (P = 0.037). The average lung metastatic nodule was 16 in the blank control group and 10 in the RSR group. The inhibition rate of lung metastasis was 37. 85% in the RSR group, but with no statistical significance. The expression level of activated MMP-2 in the RSR group was down-regulated when compared with the blank control group, the Herceptin group, and the combination group (P < 0.05). The expression of MMP-9 of the RSR group, the Herceptin group, and the combination group was significantly down-regulated when compared with the blank control group (P < 0.05). The expression of MMP-9 of the RSR group and the combination group was further down-regulated when compared with the Herceptin group (P < 0.05). The expressions of both TIMP-1 and TIMP-2 of the RSR group, the Herceptin group, and the combination group were all up-regulated when compared with the blank control group (P < 0.05). The increased expression of TIMP-1 was more significantly in the RSR group and the combination group when compared with the Herceptin group (P < 0.05). It was higher in the combination group than in

the RSR group (P < 0.05). CONCLUSIONS: RSR could inhibit the tumor recurrence of FVB/neu mice. It could reduce the degradation of extracellular matrix and increase the protective effects of extracellular matrix. It might achieve its anti-tumor effect through effecting the invasive and metastatic capabilities of breast tumor cells.

Wu, X. Q., et al. (2010). "[Effect of ru'ai shuhou recipe on immune response in HER2/neu tranagenic mice undergoing breast cancer carcinogenesis process]." Zhongguo Zhong Xi Yi Jie He Za Zhi **30**(7): 717-719, 756.

OBJECTIVE: To explore the immune response induced by HER2/neu oncogene in the breast cancer (BC) carcinogenesis process and the immunological mechanism of Ru'ai Shuhou Recipe (RSR) in the prevention and treatment of BC. METHODS: HER2/neu transgenic spontaneous breast tumor model mice were fed with RSR from 5 weeks old, the occurrence of breast tumor in them was observed, and the changes of T cell-mediated immune response and associated cytokines were detected during the carcinogenesis process, i. e., when mice aged between 15 and 25 weeks. RESULTS: RSR showed significant effects in postponing and reducing the carcinogenesis of primary breast tumor, up-regulating the amount of T cell in splenic lymphocyte in tumor-bearing mice, promoting the proliferation of T lymphocyte, and inducing the secretion of cytokines such as interleukin-2, interleukin-12 and interferon-y. CONCLUSIONS: A serial immune response reveals in the carcinogenesis process. The immunologic function of HER-2/neu transgenic mice is significantly different to that of the same strain non-transgenic mice. Effect of RSR in preventing and postponing breast cancer carcinogenesis is possibly realized through enhancing the anti-tumor immune response of transgenic mice themselves.

Wu, Y. J. and F. Z. Wu (2024). "AI-Enhanced CAD in Low-Dose CT: Balancing Accuracy, Efficiency, and Overdiagnosis in Lung Cancer Screening." Thorac Cancer.

Xiao, Q., et al. (2021). "High-throughput proteomics and AI for cancer biomarker discovery." Adv Drug Deliv Rev **176**: 113844.

Biomarkers are assayed to assess biological and pathological status. Recent advances in high-throughput proteomic technology provide opportunities for developing next generation biomarkers for clinical practice aided by artificial intelligence (AI) based techniques. We summarize the advances and limitations of cancer biomarkers based on genomic and transcriptomic analysis, as well as classical antibody-based methodologies. Then we review recent progresses in mass spectrometry (MS)-based proteomics in terms of sample preparation, peptide fractionation by liquid chromatography (LC) and mass spectrometric data acquisition. We highlight applications of AI techniques in high-throughput clinical studies as compared with clinical decisions based on singular features. This review sets out our approach for discovering clinical biomarkers in studies using proteomic big data technology conjoined with computational and statistical methods.

Xie, H., et al. (2024). "Apolipoprotein A-I levels in the survival of patients with colorectal cancer: a retrospective study." Front Endocrinol (Lausanne) **15**: 1318416.

BACKGROUND: Abnormal lipid levels have been associated with cancer incidence and progression. However, limited studies have investigated the relationship between apolipoprotein A-I (ApoA-I) and colorectal cancer (CRC). This study assessed the significance of ApoA-I levels in progression-free survival (PFS) and overall survival (OS) of patients with CRC. METHODS: Survival curves were compared using Kaplan-Meier analysis, while the predictive values of various lipid indicators in CRC prognosis were evaluated based on receiver operating characteristic curves. The factors influencing PFS and OS in patients with CRC were analyzed using Cox proportional hazards regression models. Finally, the relationship between ApoA-I level and disease recurrence was investigated through logistic regression analysis. The optimal Apo-I level was determined through maximally selected rank statistics. RESULTS: Using the optimal ApoA-I cutoff value (0.9 g/L), the 1,270 patients with CRC were categorized into low (< 0.9 g/L, 275 cases) and high (>/=0.9 g/L, 995 cases) ApoA-I groups. Compared with other lipid indicators, ApoA-I demonstrated superior predictive accuracy. The high ApoA-I group exhibited significantly higher survival rates than the low ApoA-I group (PFS, 64.8% vs. 45.2%, P < 0.001; OS, 66.1% vs. 48.6%, P < 0.001). Each one-standard-deviation increase in ApoA-I level was related to a 12.0% decrease in PFS risk (hazard ratio [HR] 0.880; 95% confidence interval [CI], 0.801-0.968; P = 0.009) and an 11.2% decrease in OS risk (HR 0.888; 95%CI, 0.806-0.978; P = 0.015). Logistic regression analysis revealed that patients with low ApoA-I had a 32.5% increased risk of disease recurrence (odds ratio [OR] 0.675; 95%CI, 0.481-0.946; P = 0.0225) compared with those with high ApoA-I. PFS/OS nomograms based on ApoA-I demonstrated excellent prognostic prediction

accuracy. CONCLUSIONS: Serum ApoA-I level may be a valuable and non-invasive tool for predicting PFS and OS in patients with CRC.

Xie, J., et al. (2024). "PathMethy: an interpretable AI framework for cancer origin tracing based on DNA methylation." Brief Bioinform **25**(6).

Despite advanced diagnostics, 3%-5% of cases remain classified as cancer of unknown primary (CUP). DNA methylation, an important epigenetic feature, is essential for determining the origin of metastatic tumors. We presented PathMethy, a novel Transformer model integrated with functional categories and crosstalk of pathways, to accurately trace the origin of tumors in CUP samples based on DNA methylation. PathMethy outperformed seven competing methods in F1-score across nine cancer datasets and predicted accurately the molecular subtypes within nine primary tumor types. It not only excelled at tracing the origins of both primary and metastatic tumors but also demonstrated a high degree of agreement with previously diagnosed sites in cases of CUP. PathMethy provided biological insights by highlighting key pathways, functional categories, and their interactions. Using functional categories of pathways, we gained a global understanding of biological processes. For broader access, a user-friendly web server for researchers and clinicians is available at https://cup.pathmethy.com.

Xie, J. Y., et al. (1995). "[Experimental study on effect of kang ai-bao II to cancer cells with cell CT analysis in mice]." Zhongguo Zhong Xi Yi Jie He Za Zhi **15**(5): 293-295.

The result of the experiment indicated that Kang Ai-bao II ([symbol: see text] II) had a destructive effect on DNA and RNA of cancer cells. Our study provided the basis for the clinical practice. The effect of Kang Ai-bao II on U14 cancer cell in C57 BL mice was investigated with confocal laser scanning microscopy.

Xie, X., et al. (2024). "SERS-based AI diagnosis of lung and gastric cancer via exhaled breath." Spectrochim Acta A Mol Biomol Spectrosc **314**: 124181.

Distinct diagnosis between Lung cancer (LC) and gastric cancer (GC) according to the same biomarkers (e.g. aldehydes) in exhaled breath based on surface-enhanced Raman spectroscopy (SERS) remains a challenge in current studies. Here, an accurate diagnosis of LC and GC is demonstrated, using artificial intelligence technologies (AI) based on SERS spectrum of exhaled breath in plasmonic metal organic frameworks nanoparticle (PMN) film. In the PMN film with optimal structure parameters, 1780 SERS spectra are collected, in which 940 spectra come from healthy people (n = 49), another 440 come from LC patients (n = 22) and the rest 400 come from GC patients (n = 8). The SERS spectra are trained through artificial neural network (ANN) model with the deep learning (DL) algorithm, and the result exhibits a good identification accuracy of LC and GC with an accuracy over 89 %. Furthermore, combined with information of SERS peaks, the data mining in ANN model is successfully employed to explore the subtle compositional difference in exhaled breath from healthy people (H) and L/GC patients. This work achieves excellent noninvasive diagnosis of multiple cancer diseases in breath analysis and provides a new avenue to explore the feature of disease based on SERS spectrum.

Xiong, Z., et al. (2024). "Precision HER2: a comprehensive AI system for accurate and consistent evaluation of HER2 expression in invasive breast Cancer." BMC Cancer **24**(1): 1204.

BACKGROUND: With the development of novel anti-HER2 targeted drugs, such as ADCs, it has become increasingly important to accurately interpret HER2 expression in breast cancer. Previous studies have demonstrated high intra-observer and inter-observer variabilities in evaluating HER2 staining by human eyes. There exists a strong requirement to develop artificial intelligence (AI) systems to achieve high-precision HER2 expression scoring for better clinical therapy. METHODS: In the present study, we collected breast cancer tissue samples and stained consecutive sections with anti-Calponin and anti-HER2 antibodies. High-quality digital images were selected from immunohistochemical slides and interpreted as HER2 3+, 2+, 1+, and 0. AI models were trained and assessed using annotated training and testing sets. The AI model was trained to automatically identify ductal carcinoma in situ (DCIS) by Calponin staining and myoepithelial annotation and filter out DCIS components in HER2-stained slides using image-overlapping techniques. Furthermore, we organized two-phase validation studies. In phase one, pathologists interpreted 112 HER2 whole-slide images (WSIs) without AI assistance, whereas in phase two, pathologists read the same slides using the AI system after a washing period of 2 weeks. RESULTS: Our AI model greatly improved the accuracy of reading (0.902 vs. 0.710). The number of HER2 1 + patients misdiagnosed as HER2 0 was significantly reduced (32/279 vs. 65/279), and they benefitted from ADC drugs. In addition, the AI algorithm improved the intra-group consistency of HER2 readings by pathologists with different years of experience (intra-class correlation coefficient [ICC]: 0.872-0.926 vs. 0.818-0.908), with

the improvement most pronounced among junior pathologists (0.885 vs. 0.818). CONCLUSIONS: We proposed a high-precision AI system to identify and filter out DCIS components and automatically evaluate HER2 expression in invasive breast cancer.

Xu, K., et al. (2023). "AI Body Composition in Lung Cancer Screening: Added Value Beyond Lung Cancer Detection." Radiology **308**(1): e222937.

Background An artificial intelligence (AI) algorithm has been developed for fully automated body composition assessment of lung cancer screening noncontrast low-dose CT of the chest (LDCT) scans, but the utility of these measurements in disease risk prediction models has not been assessed. Purpose To evaluate the added value of CT-based AI-derived body composition measurements in risk prediction of lung cancer incidence, lung cancer death, cardiovascular disease (CVD) death, and all-cause mortality in the National Lung Screening Trial (NLST). Materials and Methods In this secondary analysis of the NLST, body composition measurements, including area and attenuation attributes of skeletal muscle and subcutaneous adipose tissue, were derived from baseline LDCT examinations by using a previously developed AI algorithm. The added value of these measurements was assessed with sex- and cause-specific Cox proportional hazards models with and without the AI-derived body composition measurements for predicting lung cancer incidence, lung cancer death, CVD death, and all-cause mortality. Models were adjusted for confounding variables including age; body mass index; quantitative emphysema; coronary artery calcification; history of diabetes, heart disease, hypertension, and stroke; and other PLCO(M2012) lung cancer risk factors. Goodness-of-fit improvements were assessed with the likelihood ratio test. Results Among 20 768 included participants (median age, 61 years [IQR, 57-65 years]; 12 317 men), 865 were diagnosed with lung cancer and 4180 died during follow-up. Including the AI-derived body composition measurements improved risk prediction for lung cancer death (male participants: chi(2) = 23.09, P < .001; female participants: chi(2) = 15.04, P = .002), CVD death (males: chi(2) = 69.94, P < .001; females: chi(2) = 16.60, P < .001), and all-cause mortality (males: chi(2) = 248.13, P < .001; females: chi(2) = 94.54, P < .001), but not for lung cancer incidence (male participants: chi(2) = 2.53, P = .11; female participants: chi(2) = 1.73, P = .19). Conclusion The body composition measurements automatically derived from baseline low-dose CT examinations added predictive value for lung cancer death, CVD death, and all-cause death, but not for lung cancer incidence in the NLST. Clinical trial registration no. NCT00047385 (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Fintelmann in this issue.

Xu, S., et al. (2019). "Ai-lncRNA EGOT enhancing autophagy sensitizes paclitaxel cytotoxicity via upregulation of ITPR1 expression by RNA-RNA and RNA-protein interactions in human cancer." Mol Cancer **18**(1): 89.

BACKGROUND: The biology function of antisense intronic long noncoding RNA (Ai-lncRNA) is still unknown. Meanwhile, cancer patients with paclitaxel resistance have limited therapeutic options in the clinic. However, the potential involvement of Ai-lncRNA in paclitaxel sensitivity remains unclear in human cancer. METHODS: Whole transcriptome sequencing of 33 breast specimens was performed to identify Ai-lncRNA EGOT. Next, the role of EGOT in regulation of paclitaxel sensitivity was investigated. Moreover, the mechanism of EGOT enhancing autophagy sensitizes paclitaxel cytotoxicity via upregulation of ITPR1 expression by RNA-RNA and RNA-protein interactions was investigated in detail. Furthermore, upstream transcriptional regulation of EGOT expression was also investigated by co-immunoprecipitation and chromatin immunoprecipitation. Finally, clinical breast specimens in our cohort, TCGA and ICGC were applied to validate the role of EGOT in enhancing of paclitaxel sensitivity. RESULTS: EGOT enhances autophagosome accumulation via the up-regulation of ITPR1 expression, thereby sensitizing cells to paclitaxel toxicity. Mechanistically, on one hand, EGOT upregulates ITPR1 levels via formation of a pre-ITPR1/EGOT dsRNA that induces pre-ITPR1 accumulation to increase ITPR1 protein expression in cis. On the other hand, EGOT recruits hnRNPH1 to enhance the alternative splicing of pre-ITPR1 in trans via two binding motifs in EGOT segment 2 (324-645 nucleotides) in exon 1. Moreover, EGOT is transcriptionally regulated by stress conditions. Finally, EGOT expression enhances paclitaxel sensitivity via assessment of cancer specimens. CONCLUSIONS: These findings broaden comprehensive understanding of the biology function of Ai-lncRNAs. Proper regulation of EGOT may be a novel synergistic strategy for enhancing paclitaxel sensitivity in cancer therapy.

Xu, W., et al. (2024). "Consistency of CSCO AI with Multidisciplinary Clinical Decision-Making Teams in Breast Cancer: A Retrospective Study." Breast Cancer (Dove Med Press) **16**: 413-422.

BACKGROUND: The Chinese Society of Clinical Oncology Artificial Intelligence System (CSCO AI) serves as a clinical decision support

system developed utilizing Chinese breast cancer data. Our study delved into the congruence between breast cancer treatment recommendations provided by CSCO AI and their practical application in clinical settings. METHODS: A retrospective analysis encompassed 537 breast cancer patients treated at the Second Affiliated Hospital of Anhui Medical University between January 2017 and December 2022. Proficient senior oncology researchers manually input patient data into the CSCO AI system. "Consistent" and "Inconsistent" treatment categories were defined by aligning our treatment protocols with the classification system in the CSCO AI recommendations. Cases that initially showed inconsistency underwent a second evaluation by the Multi-Disciplinary Treatment (MDT) team at the hospital. Concordance was achieved when MDTs' treatment suggestions were in the 'Consistent' categories. RESULTS: An impressive 80.4% concurrence was observed between actual treatment protocols and CSCO AI recommendations across all breast cancer patients. Notably, the alignment was markedly higher for stage I (85.02%) and stage III (88.46%) patients in contrast to stage II patients (76.06%, P=0.023). Moreover, there was a significant concordance between invasive ductal carcinoma and lobular carcinoma (88.46%). Interestingly, triple-negative breast cancer (TNBC) exhibited a high concordance rate (87.50%) compared to other molecular subtypes. When contrasting MDT-recommended treatments with CSCO AI decisions, an overall 92.4% agreement was established. Furthermore, a logistic multivariate analysis highlighted the statistical significance of age, menstrual status, tumor type, molecular subtype, tumor size, and TNM stage in influencing consistency. CONCLUSION: In the realm of breast cancer treatment, the alignment between recommendations offered by CSCO AI and those from MDT is predominant. CSCO AI can be a useful tool for breast cancer treatment decisions.

Xue, Z., et al. (2024). "Cleaning and Harmonizing Medical Image Data for Reliable AI: Lessons Learned from Longitudinal Oral Cancer Natural History Study Data." Proc SPIE Int Soc Opt Eng **12931**.

For deep learning-based machine learning, not only are large and sufficiently diverse data crucial but their good qualities are equally important. However, in real-world applications, it is very common that raw source data may contain incorrect, noisy, inconsistent, improperly formatted and sometimes missing elements, particularly, when the datasets are large and sourced from many sites. In this paper, we present our work towards preparing and making image data ready for the development of AI-driven approaches for studying various aspects of the natural history of oral cancer. Specifically, we focus on two aspects: 1) cleaning the image data; and 2) extracting the annotation information. Data cleaning includes removing duplicates, identifying missing data, correcting errors, standardizing data sets, and removing personal sensitive information, toward combining data sourced from different study sites. These steps are often collectively referred to as data harmonization. Annotation information extraction includes identifying crucial or valuable texts that are manually entered by clinical providers related to the image paths/names and standardizing of the texts of labels. Both are important for the successful deep learning algorithm development and data analyses. Specifically, we provide details on the data under consideration, describe the challenges and issues we observed that motivated our work, present specific approaches and methods that we used to clean and standardize the image data and extract labelling information. Further, we discuss the ways to increase efficiency of the process and the lessons learned. Research ideas on automating the process with ML-driven techniques are also presented and discussed. Our intent in reporting and discussing such work in detail is to help provide insights in automating or, minimally, increasing the efficiency of these critical yet often under-reported processes.

Yadav, K. K. (2018). "How AI Is Optimizing the Detection and Management of Prostate Cancer." IEEE Pulse **9**(5): 19.

Annually, approximately 20 million men are prostate-specific-antigen screened, and 1.3 million undergo an invasive biopsy to diagnose roughly 200,000 new cases, 50% of which end up being indolent. Approximately 30,000 men die of prostate cancer (PCa) yearly. Importantly, an estimated US$8 billion is spent on unnecessary biopsies. Thus, an integrative analysis and predictive model of prognosis is needed to help identify only lethal and aggressive forms of the disease.

Yamaguchi, R. and H. Yasui (2021). "[A Future Perspective on Cancer Precision Medicine Accelerated by AI and Data Science]." Gan To Kagaku Ryoho **48**(12): 1415-1419.

In this article, we give a perspective for the future of cancer precision medicine that has been accelerated by AI and data science with massive production of personal omics data by new measurement technologies.

Yan, H., et al. (2024). "AI-Powered cellular morphometric biomarkers discovered in needle

biopsy of prostatic cancer predict neoadjuvant androgen deprivation therapy response and prognosis: an international multicenter retrospective study." medRxiv.

It is imperative to identify patients with prostate cancer (PCa) who will benefit from androgen receptor signaling inhibitors that can impact quality of life upon prolonged use. Using our extensively-validated artificial-intelligence technique: cellular morphometric biomarker via machine learning (CMB-ML), we identified 13 CMBs from whole slide images of needle biopsies from the trial specimens (NCT02430480 , n=37) that accurately predicted response to neoadjuvant androgen deprivation therapy (NADT) (AUC: 0.980). Notably, 13-CMB model stratified PCa patients into responder and non-responder groups after NADT treatment in an independent hospital cohort (n=122) that significantly associated with pathologic complete response (p=0.0005), biochemical-recurrence-free survival (p=0.024) and mTOR signaling pathway (p=0.03), suggesting potentially more clinical benefit from mTOR inhibitors in non-responder group. Additionally, genetic and genomic analysis revealed interplay between genetic variants and CMBs on NADT resistance, and provided molecular annotations for CMBs. Overall, prospective clinical implementation of 13-CMB model could assist precision care of PCa patients. SIGNIFICANCE: We describe a highly accurate CMB model to predict the therapeutic benefit in prostate cancer patients and uncover the complex interplay between genetic variants and CMBs on NADT resistance. Our model relies only on widely available needle biopsy specimens and provides a robust and cost-effective solution for clinical implementation.

Yan, H. and K. Suzuki (2024). "Prognostic AI Model for Precise Surgical Decision-making in Non-Small Cell Lung Cancer." Radiology **313**(2): e241370.

Yan, K., et al. (2023). "SynAI: an AI-driven cancer drugs synergism prediction platform." Bioinform Adv **3**(1): vbad160.

SUMMARY: The SynAI solution is a flexible AI-driven drug synergism prediction solution aiming to discover potential therapeutic value of compounds in early stage. Rather than providing a finite choice of drug combination or cell lines, SynAI is capable of predicting potential drug synergism/antagonism using in silico compound SMILE (Simplified Molecular Input Line Entry System) sequences. The AI core of SynAI platform has been trained against cell lines and compound pairs listed by NCI (National Cancer Institute)-Almanac and DurgCombDB datasets. In total, the training data consists of over 1 200 000 in vitro synergism tests on 150 cancer cell lines of different organ origins. Each cell line is tested against over 6000 pairs of FDA (Food and Drug Administration) approved compound combinations. Given one or both candidate compound in SMILE sequence, SynAI is able to predict the potential Bliss score of the combined compound test with the designated cell line without the needs of compound synthetization or structural analysis; thus can significantly reduce the candidate screening costs during the compound development. SynAI platform demonstrates a comparable performance to existing methods but offers more flexibilities for data input. AVAILABILITY AND IMPLEMENTATION: The evaluation version of SynAI is freely accessible online at https://synai.crownbio.com.

Yan, W., et al. (2023). "MiR-200/183 family-mediated module biomarker for gastric cancer progression: an AI-assisted bioinformatics method with experimental functional survey." J Transl Med **21**(1): 163.

BACKGROUND: Gastric cancer (GC) is a major cancer burden throughout the world with a high mortality rate. The performance of current predictive and prognostic factors is still limited. Integrated analysis is required for accurate cancer progression predictive biomarker and prognostic biomarkers that help to guide therapy. METHODS: An AI-assisted bioinformatics method that combines transcriptomic data and microRNA regulations were used to identify a key miRNA-mediated network module in GC progression. To reveal the module's function, we performed the gene expression analysis in 20 clinical samples by qRT-PCR, prognosis analysis by multi-variable Cox regression model, progression prediction by support vector machine, and in vitro studies to elaborate the roles in GC cells migration and invasion. RESULTS: A robust microRNA regulated network module was identified to characterize GC progression, which consisted of seven miR-200/183 family members, five mRNAs and two long non-coding RNAs H19 and CLLU1. Their expression patterns and expression correlation patterns were consistent in public dataset and our cohort. Our findings suggest a two-fold biological potential of the module: GC patients with high-risk score exhibited a poor prognosis (p-value < 0.05) and the model achieved AUCs of 0.90 to predict GC progression in our cohort. In vitro cellular analyses shown that the module could influence the invasion and migration of GC cells. CONCLUSIONS: Our strategy which combines AI-assisted bioinformatics method with experimental and clinical validation suggested that the miR-200/183 family-mediated

network module as a "pluripotent module", which could be potential marker for GC progression.

Yanagawa, M. and A. Hata (2024). "Transforming Lung Cancer Screening with AI: Comprehensive Evaluation and Personalized Medicine Prospects." Radiology **312**(3): e242118.

Yang, B., et al. (2024). "AI-powered genomic mutation signature for predicting immune checkpoint inhibitor therapy outcomes in gastroesophageal cancer: a multi-cohort analysis." Discov Oncol **15**(1): 507.

BACKGROUND: Immune checkpoint inhibitors (ICIs) have significantly transformed the treatment of gastroesophageal cancer (GEC). However, the lack of reliable prognostic biomarkers hinders the ability to predict patient response to ICI therapy. METHODS: In this study, we engineered and validated a genomic mutation signature (GMS) utilizing an innovative artificial intelligence (AI) algorithm to forecast ICI therapy outcomes in GEC patients. We further explored immune profiles across subtypes through comprehensive multiomics analysis. Our investigation of drug sensitivity data from the Genomics of Drug Sensitivity in Cancer (GDSC) database led to the identification of trametinib as a potential therapeutic agent. We subsequently evaluated trametinib's efficacy in AGS and MKN45 cell lines using Cell Counting Kit-8 (CCK8) assays and clonogenic experiments. RESULTS: We developed a GMS by integrating 297 algorithms, enabling autonomous prognosis prediction for GEC patients. The GMS demonstrated consistent performance across three public cohorts, exhibiting high sensitivity and specificity for overall survival (OS) at 6, 12, and 18 months, as shown by Receiver Operator Characteristic Curve (ROC) analysis. Notably, the GMS surpassed traditional clinical and molecular features, including tumor mutational burden (TMB), programmed death-ligand 1 (PD-L1) expression, and microsatellite instability (MSI), in predictive accuracy. Low-risk samples exhibited elevated levels of cytolytic immune cells and heightened immunogenic potential compared to high-risk samples. Our investigation identified trametinib as a potential therapeutic agent. An inverse correlation was observed between GMS and trametinib IC50. Moreover, the high-risk-derived AGS cell line showed increased sensitivity to trametinib compared to the low-risk-derived MKN45 cell line. CONCLUSION: The GMS utilized in this study successfully demonstrated the ability to reliably predict the survival advantage for patients with GECs undergoing ICI therapy.

Yang, D. D., et al. (2020). "Prognostic value of the serum apolipoprotein B to apolipoprotein A-I ratio in metastatic colorectal cancer patients." J Cancer **11**(5): 1063-1074.

Background: The aim of our research was to assess the prognostic value of the apolipoprotein B (ApoB) to apolipoprotein A-I (ApoA-I) ratio (ApoB/ApoA-I) in metastatic colorectal cancer (mCRC) patients. Methods: We randomly assigned 838 patients into the training cohort (n=578) and the validation cohort (n=260). The cut-off value of the ApoB/ApoA-I in the training cohort identified by a receiver operating characteristic (ROC) curve was 0.69 and was further validated in the validation cohort. A propensity score matching (PSM) analysis was carried out to eliminate the imbalance in the baseline characteristics of the high and low ApoB/ApoA-I group. The PSM cohort of 542 mCRC patients was generated. We also validated our main findings and conclusions with an independent cohort (n=150). Univariate and multivariate analyses were conducted to explore the independent prognostic value of the ApoB/ApoA-I in the training cohort (n=578), the validation cohort (n=260), the PSM cohort (n=542) and the independent cohort (n=150). Results: Patients in the high ApoB/ApoA-I group had significantly shorter overall survival compared to those in the low ApoB/ApoA-I group in the training cohort, the validation cohort, the PSM cohort and the independent cohort (P <0.01). Multivariate analysis indicated that the ApoB/ApoA-I was an independent prognostic index for OS in the training cohort [hazard ratio (HR):1.371; 95% confidence interval (CI):1.205-1.870, P=0.045], the validation cohort (HR: 1.924; 95% CI: 1.360-2.723, P<0.001), the PSM cohort (HR: 1.599; 95% CI: 1.287-1.988, P<0.001) and the independent cohort (HR: 1.949; 95% CI: 1.014-3.747, P=0.046). Conclusions: An increased baseline serum ApoB/ApoA-I is an independent prognostic factor for a poor prognosis in mCRC patients.

Yang, D. D., et al. (2024). "AI-derived Tumor Volume from Multiparametric MRI and Outcomes in Localized Prostate Cancer." Radiology **313**(1): e240041.

Background An artificial intelligence (AI)-based method for measuring intraprostatic tumor volume based on data from MRI may provide prognostic information. Purpose To evaluate whether the total volume of intraprostatic tumor from AI-generated segmentations (V(AI)) provides independent prognostic information in patients with localized prostate cancer treated with radiation therapy (RT) or radical prostatectomy (RP). Materials and Methods For this retrospective, single-center

study (January 2021 to August 2023), patients with cT1-3N0M0 prostate cancer who underwent MRI and were treated with RT or RP were identified. Patients who underwent RT were randomly divided into cross-validation and test RT groups. An AI segmentation algorithm was trained to delineate Prostate Imaging Reporting and Data System (PI-RADS) 3-5 lesions in the cross-validation RT group before providing segmentations for the test RT and RP groups. Cox regression models were used to evaluate the association between V(AI) and time to metastasis and adjusted for clinical and radiologic factors for combined RT (ie, cross-validation RT and test RT) and RP groups. Areas under the receiver operating characteristic curve (AUCs) were calculated for V(AI) and National Comprehensive Cancer Network (NCCN) risk categorization for prediction of 5-year metastasis (RP group) and 7-year metastasis (combined RT group). Results Overall, 732 patients were included (combined RT group, 438 patients; RP group, 294 patients). Median ages were 68 years (IQR, 62-73 years) and 61 years (IQR, 56-66 years) for the combined RT group and the RP group, respectively. V(AI) was associated with metastasis in the combined RT group (median follow-up, 6.9 years; adjusted hazard ratio [AHR], 1.09 per milliliter increase; 95% CI: 1.04, 1.15; P = .001) and the RP group (median follow-up, 5.5 years; AHR, 1.22; 95% CI: 1.08, 1.39; P = .001). AUCs for 7-year metastasis for the combined RT group for V(AI) and NCCN risk category were 0.84 (95% CI: 0.74, 0.94) and 0.74 (95% CI: 0.80, 0.98), respectively (P = .02). Five-year AUCs for the RP group for V(AI) and NCCN risk category were 0.89 (95% CI: 0.80, 0.98) and 0.79 (95% CI: 0.64, 0.94), respectively (P = .25). Conclusion The volume of AI-segmented lesions was an independent, prognostic factor for localized prostate cancer. (c) RSNA, 2024 Supplemental material is available for this article.

Yang, S. J., et al. (2020). "[Establishment and clinical testing of pancreatic cancer Faster R-CNN AI system based on fast regional convolutional neural network]." Zhonghua Wai Ke Za Zhi **58**(7): 520-524.

Objective: To investigate the effectiveness of an enhanced CT automatic recognition system based on Faster R-CNN for pancreatic cancer and its clinical value. Methods: In this study, 4 024 enhanced CT imaging sequences of 315 patients with pancreatic cancer from January 2013 to May 2016 at the Affiliated Hospital of Qingdao University were collected retrospectively, and 2 614 imaging sequences were input into the faster R-CNN system as training dataset to create an automatic image recognition model, which was then validated by reading 1 410 enhanced CT images of 135 cases of pancreatic cancer.In order to identify its effectiveness, 3 750 CT images of 150 patients with pancreatic lesions were read and a followed-up was carried out.The accuracy and recall rate in detecting nodules were recorded and regression curves were generated.In addition, the accuracy, sensitivity and specificity of Faster R-CNN diagnosis were analyzed, the ROC curves were generated and the area under the curves were calculated. Results: Based on the enhanced CT images of 135 cases, the area under the ROC curve was 0.927 calculated by Faster R-CNN. The accuracy, specificity and sensitivity were 0.902, 0.913 and 0.801 respectively.After the data of 150 patients with pancreatic cancer were verified, 893 CT images showed positive and 2 857 negative.Ninety-eight patients with pancreatic cancer were diagnosed by Faster R-CNN.After the follow-up, it was found that 53 cases were post-operatively proved to be pancreatic ductal carcinoma, 21 cases of pancreatic cystadenocarcinoma, 12 cases of pancreatic cystadenoma, 5 cases of pancreatic cyst, and 7 cases were untreated.During 5 to 17 months after operation, 6 patients died of abdominal tumor infiltration, liver and lung metastasis.Of the 52 patients who were diagnosed negative by Faster R-CNN, 9 were post-operatively proved to be pancreatic ductal carcinoma. Conclusion: Faster R-CNN system has clinical value in helping imaging physicians to diagnose pancreatic cancer.

Yang, X. B., et al. (2018). "Gefitinib plus Fuzheng Kang'ai Formula () in Patients with Advanced Non-Small Cell Lung Cancer with Epidermal Growth Factor Receptor Mutation: A Randomized Controlled Trial." Chin J Integr Med **24**(10): 734-740.

OBJECTIVE: To evaluate the effect of Fuzheng Kang'ai Formula (, FZKA) plus gefitinib in patients with advanced non-small cell lung cancer with epidermal growth factor receptor (EGFR) mutations. METHODS: A randomized controlled trial was conducted from 2009 to 2012 in South China. Seventy chemotherapynaive patients diagnosed with stage IIIB/IV non-small cell lung cancer with EGFR mutations were randomly assigned to GF group [gefitinib (250 mg/day orally) plus FZKA (250 mL, twice per day, orally); 35 cases] or G group (gefitinib 250 mg/day orally; 35 cases) according to the random number table and received treatment until progression of the disease, or development of unacceptable toxicities. The primary endpoint [progression-free survival (PFS)] and secondary endpoints [median survival time (MST), objective response rate (ORR), disease control rate (DCR) and safety] were observed. RESULTS: No patient was excluded after randomization. GF group had significantly longer PFS and MST compared

with the G group, with median PFS of 12.5 months (95% CI 3.30-21.69) vs. 8.4 months (95% CI 6.30-10.50; log-rank P<0.01), MST of 21.5 months (95% CI 17.28-25.73) vs. 18.3 months (95% CI 17.97-18.63; log-rank P<0.01). ORR and DCR in GF group and G group were 65.7% vs. 57.1%, 94.3% vs. 80.0%, respectively (P>0.05). The most common toxic effects in the GF group and G group were rash or acne (42.8% vs. 57.1%, P>0.05), diarrhea (11.5% vs. 31.4%, P<0.05), and stomatitis (2.9% vs. 8.7%, P>0.05). CONCLUSION: Patients with advanced non-small cell lung cancer selected by EGFR mutations have longer PFS, MST with less toxicity treated with gefitinib plus FZKA than gefitinib alone.

Yang, X. B., et al. (2016). "[Effect of Fuzheng Kang'ai Recipe Combined Gefitinib on Lung Cancer A549 Cells and Its Mecha- nism Research]." Zhongguo Zhong Xi Yi Jie He Za Zhi **36**(11): 1340-1344.

Objective To observe the effect of Fuzheng Kang'ai Recipe (FKR) combined ge- fitinib on the proliferation and apoptosis of lung cancer A549 cells , and to study its potential synergistic mechanish with gefitinib. Methods The effects of FKR (0. 211, 0. 316, 0. 474, 0. 711, 1. 067, 1. 600, 2. 400, 3. 600 mg/mL) combined gefitinib (3. 95, 5. 92, 8. 18, 13. 33, 20. 00, 30. 00, 45. 00, 67. 50 mumol/ L) on the proliferation of A549 cells were detected by MTT assay. The apoptosis of A549 cells in the control group (complete culture medium) , FKR (1. 6 mg/mL) , gefitinib (45 mumol/L) , and FKR plus gefitinib (1. 6 mg/mL +45 mumol/L) were detected by flow cytometry (FCM). Their expressions of epidermal growth factor receptor (EGFR) , phosphorylating epidermal growth factor receptor (p-EGFR) , enhancer of zeste homolog 2 (EZH2), peroxisome proliferator-activated receptor-gamma (PPAR-gamma) , and P53 protein in A549 cells were detected by Western blot. Results Both FKR and gefitinib could inhibit the proliferation of A549 cells. The apoptotic rate was 12. 6% +/-4. 5% in the FKR combined gefitinib group, obviously higher than that of the FKR group (4. 6% +/- 0. 7%) and the gefitinib group (7. 8% +/- 2. 7%) , showing statistical difference (P <0. 05). Compared with the control group, the expressions of p-EGFR and EZH2 were sig- nificantly down-regulated (P <0. 05) , the expressions of PPAR-gamma and P53 protein were up-regulated in the FKR combined gefitinib group (P <0. 05); the expression of EZH2 was down-regulated in the gefitinib group and the FKR group (P <0. 05) ; the expression of PPAR-y was up-regulated in the FKR group (P < 0. 05). Compared with the gefitinib group, the expression of p-EGFR was down-regulated, and the expression of PPAR-gamma was up-regulated in the FKR combined gefitinib group (both P <0. 05). Compared with the FKR group, the expression of p-EGFR was down-regulated in the FKR combined gefitinib group (P < 0. 05). Conclusions Combination of FKR and gefitinib could significantly inhibit the proliferation and growth of A549 cells,and induce cell apoptosis. Its potential synergistic mechanism of anti-tumor activities might be associated with down-regulating mRNA expressions of p-EGFR and EZH2, and up-regulating protein expressions of PPAR-y and P53.

Yang, X. B., et al. (2015). "Fuzheng Kang'ai decoction combined with gefitinib in advanced non-small cell lung cancer patients with epidermal growth factor receptor mutations: study protocol for a randomized controlled trial." Trials **16**: 146.

BACKGROUND: Patients with advanced non-small cell lung cancer (NSCLC) harboring mutations of the epidermal growth factor receptor (EGFR) gene respond well to the EGFR tyrosine kinase inhibitor (TKI) gefitinib. Chinese herbal medicine (CHM) has been used as a complementary therapy for cancer for decades in China. CHM was proved to be effective in improving the quality of life (QOL) and reducing the toxicity associated with chemotherapy in patients with NSCLC. The purpose of the present trial is to determine whether CHM (Fuzheng Kang'ai decoction (FZKA), a CHM formula) combined with gefitinib results in longer progression-free survival with less toxicity than gefitinib alone. METHODS/DESIGN: This is a randomized, placebo-controlled, double-blind trial. This trial is designed to determine if CHM (FZKA) combined with gefitinib results in longer progression-free survival with less toxicity than gefitinib alone. A total of 70 NSCLC patients with EGFR mutations will be randomly assigned to treatment group (gefitinib plus FZKA granules) or control group (gefitinib plus placebo). The primary endpoint is progression-free survival. Secondary endpoints are: (1) overall survival; (2) disease control rate; (3) QOL, measured with the questionnaire of Functional Assessment of Cancer Therapy-lung (FACT-L 4.0) and Lung Cancer Symptom Scale and (4) safety. DISCUSSION: In previous clinical practice, we found that CHM (FZKA) could improve the therapeutic efficacy of gefitinib. This study will provide objective evidence to evaluate the efficiency of CHM combined with gefitinib in NSCLC patients with EGFR mutations, and may provide a novel regimen for patients with NSCLC. TRIAL REGISTRATION: Chinese Clinical Trial Registry (www.chictr.org): ChiCTR-IOR-14005679 , registered 17 December 2014.

Ye, J., et al. (2019). "Serum Apolipoprotein A-I Combined With C-Reactive Protein Serves As A Novel Prognostic Stratification System For Colorectal Cancer." Cancer Manag Res **11**: 9265-9276.

BACKGROUND AND OBJECTIVE: Noninvasive prognostic tools for colorectal cancer (CRC) are urgently needed. This study was designed to investigate the prognostic value of preoperative serum lipid and lipoprotein concentrations (including ApoA-I, Apo-B, HDL-C, LDL-C, TC and TG) and CRP levels retrospectively in CRC patients. METHODS: Preoperative serum lipid and lipoprotein concentrations (including ApoA-I, Apo-B, HDL-C, LDL-C, TC and TG) and CRP levels were analyzed retrospectively in 250 patients with CRC. The prognostic significance of these indexes was determined by univariate and multivariate Cox hazard models. RESULTS: CRC patients with higher levels of ApoA-I and HDL-C and lower levels of CRP had significantly longer overall survival (OS, log rank test, $p<0.05$). Based on univariate analysis, ApoA-I levels ($p=0.002$), CRP levels ($p=0.007$), HDL-C levels ($p=0.005$), pT classification ($p=0.005$), pN classification ($p<0.001$), pM classification ($p<0.001$) and pTNM stage ($p<0.001$) were significantly associated with OS. Multivariate Cox proportional hazards regression analysis indicated that ApoA-I levels (HR: 1.52, $p=0.023$), CRP levels (HR: 1.85, $p=0.035$) and pTNM stage (HR: 2.53, $p< 0.001$) were independent predictors of CRC survival. The included patients were then stratified into three tiers based on the ApoA-I and CRP levels. In the whole cohort, the OS and disease-free survival differed significantly between the low-risk (ApoA-I>/=1.08 mg/dL and CRP<3.04 mg/dL), medium-risk (ApoA-I>/=1.08 mg/dL or CRP<3.04 mg/dL), and high-risk (ApoA-I<1.08 mg/dL and CRP >/=3.04 mg/dL) groups ($p=0.001$ and $p=0.004$). CONCLUSION: Decreased levels of ApoA-I and HDL-C and increased levels of CRP were predictive of poor prognosis among patients with CRC. In addition, the combination of ApoA-I and CRP can serve as a novel prognostic stratification system for more accurate clinical staging of CRC.

Yin, P., et al. (2023). "A generalized AI method for pathology cancer diagnosis and prognosis prediction based on transfer learning and hierarchical split." Phys Med Biol **68**(17).

Objective.This study aims to propose a generalized AI method for pathology cancer diagnosis and prognosis prediction based on transfer learning and hierarchical split.Approach.We present a neural network framework for cancer diagnosis and prognosis prediction in pathological images. To enhance the network's depth and width, we employ a hierarchical split block (HS-Block) to create an AI-aided diagnosis system suitable for semi-supervised clinical settings with limited labeled samples and cross-domain tasks. By incorporating a lightweight convolution unit based on the HS-Block, we improve the feature information extraction capabilities of a regular network (RegNet). Additionally, we integrate a Convolutional Block Attention Module into the first and last convolutions to optimize the extraction of global features and local details. To address limited sample labels, we employ a dual-transfer learning (DTL) mechanism named DTL-HS-Regnet, enabling semi-supervised learning in clinical settings.Main results.Our proposed DTL-HS-Regnet model outperforms other advanced deep-learning models in three different types of cancer diagnosis tasks. It demonstrates superior feature extraction ability, achieving an average sensitivity, specificity, accuracy, and F1 score of 0.9987, 1.0000, 1.0000 and 0.9992, respectively. Furthermore, we evaluate the model's capability to directly extract prognosis prediction information from pathological images by constructing patient cohorts. The results show that the correlation between DTL-HS-Regnet predictions and the presence of cancer-associated fibroblasts is comparable to that of pathologists.Significance.Our proposed AI method offers a generalized approach for cancer diagnosis and prognosis prediction in pathology. The outstanding performance of the DTL-HS-Regnet model demonstrates its potential for improving current practices in image digital pathology, expanding the boundaries of cancer treatment in two critical areas.

Yokoyama, K., et al. (1985). "[Effects of bronchial artery infusion (B-AI) with single use of MMC after intravenous peplomycin (PEP) administration in lung cancer]." Gan To Kagaku Ryoho **12**(2): 265-269.

Effects of BAI therapy on 86 cases of lung cancer were evaluated in three groups: single-use of MMC group after intravenous PEP administration (PEP (iv).MMC group), PEP and MMC combination use group (PEP + MMC group) and single use of MMC group. Tumor regression rate determined by chest X-ray film 2 or 3 weeks after BAI was highest in the PEP (iv).MMC group followed by the PEP + MMC and MMC group. Cavity formation was more typical in the group treated with PEP + MMC. Histopathological effects were best for the PEP + MMC group followed by those of the PEP (iv).MMC and MMC group. As for side effects, pulmonary fibrosis and necrotizing bronchitis were noted in 8% of the PEP + MMC group, but side effects in the other two groups were mild. In conclusion single use of MMC after intravenous PEP administration was

found to be the best way to give BAI in these three groups.

Yoo, H., et al. (2021). "AI-based improvement in lung cancer detection on chest radiographs: results of a multi-reader study in NLST dataset." Eur Radiol **31**(12): 9664-9674.

OBJECTIVE: Assess if deep learning-based artificial intelligence (AI) algorithm improves reader performance for lung cancer detection on chest X-rays (CXRs). METHODS: This reader study included 173 images from cancer-positive patients (n = 98) and 346 images from cancer-negative patients (n = 196) selected from National Lung Screening Trial (NLST). Eight readers, including three radiology residents, and five board-certified radiologists, participated in the observer performance test. AI algorithm provided image-level probability of pulmonary nodule or mass on CXRs and a heatmap of detected lesions. Reader performance was compared with AUC, sensitivity, specificity, false-positives per image (FPPI), and rates of chest CT recommendations. RESULTS: With AI, the average sensitivity of readers for the detection of visible lung cancer increased for residents, but was similar for radiologists compared to that without AI (0.61 [95% CI, 0.55-0.67] vs. 0.72 [95% CI, 0.66-0.77], p = 0.016 for residents, and 0.76 [95% CI, 0.72-0.81] vs. 0.76 [95% CI, 0.72-0.81, p = 1.00 for radiologists), while false-positive findings per image (FPPI) was similar for residents, but decreased for radiologists (0.15 [95% CI, 0.11-0.18] vs. 0.12 [95% CI, 0.09-0.16], p = 0.13 for residents, and 0.24 [95% CI, 0.20-0.29] vs. 0.17 [95% CI, 0.13-0.20], p < 0.001 for radiologists). With AI, the average rate of chest CT recommendation in patients positive for visible cancer increased for residents, but was similar for radiologists (54.7% [95% CI, 48.2-61.2%] vs. 70.2% [95% CI, 64.2-76.2%], p < 0.001 for residents and 72.5% [95% CI, 68.0-77.1%] vs. 73.9% [95% CI, 69.4-78.3%], p = 0.68 for radiologists), while that in cancer-negative patients was similar for residents, but decreased for radiologists (11.2% [95% CI, 9.6-13.1%] vs. 9.8% [95% CI, 8.0-11.6%], p = 0.32 for residents and 16.4% [95% CI, 14.7-18.2%] vs. 11.7% [95% CI, 10.2-13.3%], p < 0.001 for radiologists). CONCLUSIONS: AI algorithm can enhance the performance of readers for the detection of lung cancers on chest radiographs when used as second reader. KEY POINTS: * Reader study in the NLST dataset shows that AI algorithm had sensitivity benefit for residents and specificity benefit for radiologists for the detection of visible lung cancer. * With AI, radiology residents were able to recommend more chest CT examinations (54.7% vs 70.2%, p < 0.001) for patients with visible lung cancer. * With AI, radiologists recommended significantly less proportion of unnecessary chest CT examinations (16.4% vs. 11.7%, p < 0.001) in cancer-negative patients.

Yoon, J. H., et al. (2023). "Standalone AI for Breast Cancer Detection at Screening Digital Mammography and Digital Breast Tomosynthesis: A Systematic Review and Meta-Analysis." Radiology **307**(5): e222639.

Background There is considerable interest in the potential use of artificial intelligence (AI) systems in mammographic screening. However, it is essential to critically evaluate the performance of AI before it can become a modality used for independent mammographic interpretation. Purpose To evaluate the reported standalone performances of AI for interpretation of digital mammography and digital breast tomosynthesis (DBT). Materials and Methods A systematic search was conducted in PubMed, Google Scholar, Embase (Ovid), and Web of Science databases for studies published from January 2017 to June 2022. Sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) values were reviewed. Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 and Comparative (QUADAS-2 and QUADAS-C, respectively). A random effects meta-analysis and meta-regression analysis were performed for overall studies and for different study types (reader studies vs historic cohort studies) and imaging techniques (digital mammography vs DBT). Results In total, 16 studies that include 1 108 328 examinations in 497 091 women were analyzed (six reader studies, seven historic cohort studies on digital mammography, and four studies on DBT). Pooled AUCs were significantly higher for standalone AI than radiologists in the six reader studies on digital mammography (0.87 vs 0.81, P = .002), but not for historic cohort studies (0.89 vs 0.96, P = .152). Four studies on DBT showed significantly higher AUCs in AI compared with radiologists (0.90 vs 0.79, P < .001). Higher sensitivity and lower specificity were seen for standalone AI compared with radiologists. Conclusion Standalone AI for screening digital mammography performed as well as or better than radiologists. Compared with digital mammography, there is an insufficient number of studies to assess the performance of AI systems in the interpretation of DBT screening examinations. (c) RSNA, 2023 Supplemental material is available for this article. See also the editorial by Scaranelo in this issue.

Yu, C. and E. J. Helwig (2022). "The role of AI technology in prediction, diagnosis and treatment of colorectal cancer." Artif Intell Rev **55**(1): 323-343.

Artificial intelligence (AI) is a fascinating new technology that incorporates machine learning and neural networks to improve existing technology or create new ones. Potential applications of AI are introduced to aid in the fight against colorectal cancer (CRC). This includes how AI will affect the epidemiology of colorectal cancer and the new methods of mass information gathering like GeoAI, digital epidemiology and real-time information collection. Meanwhile, this review also examines existing tools for diagnosing disease like CT/MRI, endoscopes, genetics, and pathological assessments also benefitted greatly from implementation of deep learning. Finally, how treatment and treatment approaches to CRC can be enhanced when applying AI is under discussion. The power of AI regarding the therapeutic recommendation in colorectal cancer demonstrates much promise in clinical and translational field of oncology, which means better and personalized treatments for those in need.

Yu, R., et al. (2023). "PI-RADS(AI): introducing a new human-in-the-loop AI model for prostate cancer diagnosis based on MRI." Br J Cancer **128**(6): 1019-1029.

BACKGROUND: This study aims to develop and validate an artificial intelligence (AI)-aided Prostate Imaging Reporting and Data System (PI-RADS(AI)) for prostate cancer (PCa) diagnosis based on MRI. METHODS: The deidentified MRI data of 1540 biopsy-naive patients were collected from four centres. PI-RADS(AI) is a two-stage, human-in-the-loop AI capable of emulating the diagnostic acumen of subspecialists for PCa on MRI. The first stage uses a UNet-Seg model to detect and segment biopsy-candidate prostate lesions, whereas the second stage leverages UNet-Seg segmentation is trained specifically with subspecialist' knowledge-guided 3D-Resnet to achieve an automatic AI-aided diagnosis for PCa. RESULTS: In the independent test set, UNet-Seg identified 87.2% (628/720) of target lesions, with a Dice score of 44.9% (range, 22.8-60.2%) in segmenting lesion contours. In the ablation experiment, the model trained with the data from three centres was superior (kappa coefficient, 0.716 vs. 0.531) to that trained with single-centre data. In the internal and external tests, the triple-centre PI-RADS(AI) model achieved an overall agreement of 58.4% (188/322) and 60.1% (92/153) with a referential subspecialist in scoring target lesions; when one-point margin of error was permissible, the agreement rose to 91.3% (294/322) and 97.3% (149/153), respectively. In the paired test, PI-RADS(AI) outperformed 5/11 (45.5%) and matched the performance of 3/11 (27.3%) general radiologists in achieving a clinically significant PCa diagnosis (area under the curve, internal test, 0.801 vs. 0.770, $p < 0.01$; external test, 0.833 vs. 0.867, $p = 0.309$). CONCLUSIONS: Our closed-loop PI-RADS(AI) outperforms or matches the performance of more than 70% of general readers in the MRI assessment of PCa. This system might provide an alternative to radiologists and offer diagnostic benefits to clinical practice, especially where subspecialist expertise is unavailable.

Yu, Y., et al. (2024). "Multimodal data fusion AI model uncovers tumor microenvironment immunotyping heterogeneity and enhanced risk stratification of breast cancer." MedComm (2020) **5**(12): e70023.

Breast cancer is the leading cancer among women, with a significant number experiencing recurrence and metastasis, thereby reducing survival rates. This study focuses on the role of long noncoding RNAs (lncRNAs) in breast cancer immunotherapy response. We conducted an analysis involving 1027 patients from Sun Yat-sen Memorial Hospital, Sun Yat-sen University, and The Cancer Genome Atlas, utilizing RNA sequencing and pathology whole-slide images. We employed unsupervised clustering to identify distinct lncRNA expression patterns and developed an AI-based pathology model using convolutional neural networks to predict immune-metabolic subtypes. Additionally, we created a multimodal model integrating lncRNA data, immune-cell scores, clinical information, and pathology images for prognostic prediction. Our findings revealed four unique immune-metabolic subtypes, and the AI model demonstrated high predictive accuracy, highlighting the significant impact of lncRNAs on antitumor immunity and metabolic states within the tumor microenvironment. The AI-based pathology model, DeepClinMed-IM, exhibited high accuracy in predicting these subtypes. Additionally, the multimodal model, DeepClinMed-PGM, integrating pathology images, lncRNA data, immune-cell scores, and clinical information, showed superior prognostic performance. In conclusion, these AI models provide a robust foundation for precise prognostication and the identification of potential candidates for immunotherapy, advancing breast cancer research and treatment strategies.

Yu, Y., et al. (2024). "AI predictive modeling of survival outcomes for renal cancer patients undergoing targeted therapy." Sci Rep **14**(1): 26156.

Renal clear cell cancer (RCC) is a complex disease that is challenging to predict patient outcomes. Despite improvements with targeted therapy, personalized treatment planning is still needed. Artificial intelligence (AI) can help address this

challenge by developing predictive models that accurately forecast patient survival periods. With AI-powered decision support, clinicians can provide patients with tailored treatment plans, enhancing treatment efficacy and quality of life. The study analyzed 267 patients with renal clear cell carcinoma, focusing on 26 who received targeted drug therapy. The data was refined by excluding 8 patients without enhanced CT scans. The research team categorized patients into two groups based on their expected lifespan: Group 1 (over 3 years) and Group 2 (under 3 years). The UPerNet algorithm was used to extract features from CT tumor markers, validating their effectiveness. These features were then used to develop an AI-based predictive model trained on the dataset. The developed AI model demonstrated remarkable accuracy, achieving a rate of 93.66% in Group 1 and 94.14% in Group 2. In conclusion, our study demonstrates the potential of AI technology in predicting the survival time of RCC patients undergoing targeted drug therapy. The established prediction model exhibits high predictive accuracy and stability, serving as a valuable tool for clinicians to facilitate the development of more personalized treatment plans for patients. This study highlights the importance of integrating AI technology in clinical decision-making, enabling patients to receive more effective and targeted treatment plans that enhance their overall quality of life.

Yu, Z. H., et al. (2024). "Enhancing Breast Cancer Diagnosis: A Nomogram Model Integrating AI Ultrasound and Clinical Factors." Ultrasound Med Biol **50**(9): 1372-1380.

PURPOSE: A novel nomogram incorporating artificial intelligence (AI) and clinical features for enhanced ultrasound prediction of benign and malignant breast masses. MATERIALS AND METHODS: This study analyzed 340 breast masses identified through ultrasound in 308 patients. The masses were divided into training (n = 260) and validation (n = 80) groups. The AI-based analysis employed the Samsung Ultrasound AI system (S-detect). Univariate and multivariate analyses were conducted to construct nomograms using logistic regression. The AI-Nomogram was based solely on AI results, while the ClinAI- Nomogram incorporated additional clinical factors. Both nomograms underwent internal validation with 1000 bootstrap resamples and external validation using the independent validation group. Performance was evaluated by analyzing the area under the receiver operating characteristic (ROC) curve (AUC) and calibration curves. RESULTS: The ClinAI-Nomogram, which incorporates patient age, AI-based mass size, and AI-based diagnosis, outperformed an existing AI-Nomogram in differentiating benign from malignant breast masses. The ClinAI-Nomogram surpassed the AI-Nomogram in predicting malignancy with significantly higher AUC scores in both training (0.873, 95% CI: 0.830-0.917 vs. 0.792, 95% CI: 0.748-0.836; p = 0.016) and validation phases (0.847, 95% CI: 0.763-0.932 vs. 0.770, 95% CI: 0.709-0.833; p < 0.001). Calibration curves further revealed excellent agreement between the ClinAI-Nomogram's predicted probabilities and actual observed risks of malignancy. CONCLUSION: The ClinAI- Nomogram, combining AI alongside clinical data, significantly enhanced the differentiation of benign and malignant breast masses in clinical AI-facilitated ultrasound examinations.

Zamanian-Daryoush, M. and J. A. DiDonato (2015). "Apolipoprotein A-I and Cancer." Front Pharmacol **6**: 265.

High-density lipoprotein (HDL) and apolipoprotein A-I (apoA-I), the predominant protein in plasma HDL, have long been the focus of intense studies in the field of atherosclerosis and cardiovascular disease. ApoA-I, in large part, is responsible for HDL assembly and its main atheroprotective function, that of shuttling excess cholesterol from peripheral tissues to the liver for excretion (reverse cholesterol transport). Recently, a protective role for HDL in cancer was suggested from several large clinical studies where an inverse relationship between plasma HDL-cholesterol (HDL-C) levels and risk of developing cancer was noted. This notion has now been tested and found to be supported in mouse tumor studies, where increasing levels of apoA-I/HDL were discovered to protect against tumor development and provision of human apoA-I was therapeutic against established tumors. This mini-review discusses the emerging role of apoA-I in tumor biology and its potential as cancer therapeutic.

Zamanian-Daryoush, M., et al. (2020). "Apolipoprotein A-I anti-tumor activity targets cancer cell metabolism." Oncotarget **11**(19): 1777-1796.

Previously, we reported apolipoprotein A-I (apoA-I), the major protein component of high-density lipoprotein (HDL), has potent anti-melanoma activity. We used DNA microarray and bioinformatics to interrogate gene expression profiles of tumors from apoA-I expressing (A-I Tg(+/-)) versus apoA-I-null (A-I KO) animals to gain insights into mechanisms of apoA-I tumor protection. Differential expression analyses of 11 distinct tumors per group with > 1.2-fold cut-off and a false discovery rate adjusted p < 0.05, identified 176

significant transcripts (71 upregulated and 105 downregulated in A-I Tg(+/-) versus A-I KO group). Bioinformatic analyses identified the mevalonate and de novo serine/glycine synthesis pathways as potential targets for apoA-I anti-tumor activity. Relative to A-I KO, day 7 B16F10L melanoma tumor homografts from A-I Tg(+/-) exhibited reduced expression of mevalonate-5-pyrophosphate decarboxylase (Mvd), a key enzyme targeted in cancer therapy, along with a number of key genes in the sterol synthesis arm of the mevalonate pathway. Phosphoglycerate dehydrogenase (Phgdh), the first enzyme branching off glycolysis into the de novo serine synthesis pathway, was the most repressed transcript in tumors from A-I Tg(+/-). We validated our mouse tumor studies by comparing the significant transcripts with adverse tumor markers previously identified in human melanoma and found 45% concordance. Our findings suggest apoA-I targets the mevalonate and serine synthesis pathways in melanoma cells in vivo, thus providing anti-tumor metabolic effects by inhibiting the flux of biomolecular building blocks for macromolecule synthesis that drive rapid tumor growth.

Zehra, T., et al. (2023). "Ki-67 Quantification in Breast Cancer by Digital Imaging AI Software and its Concordance with Manual Method." J Coll Physicians Surg Pak **33**(5): 544-547.

OBJECTIVE: To validate the concordance of automated detection of Ki67 in digital images of breast cancer with the manual eyeball / hotspot method. STUDY DESIGN: Descriptive study. Place and Duration of the Study: Jinnah Sindh Medical University, Karachi, from 1st January to 15th February 2022. METHODOLOGY: Glass slides of cases diagnosed as invasive ductal carcinoma (IDC) were obtained from the Agha Khan Medical University Hospital, selected retrospectively and randomly from 60 patients. They were stained with the Ki67 antibody. An expert pathologist evaluated the Ki67 index in the hotspot fields using eyeball method. Digital images were taken from the hotspots using a camera attached to the microscope. The images were uploaded in the Mindpeak software to detect the exact percentage of Ki67-positive cells. The results obtained through automated detection were compared with the results reported by expert pathologists to see the differential outcome. RESULTS: The manual and automated scoring methods showed strong positive concordance (p <0.001). CONCLUSION: Automated scoring of Ki-67 staining has tremendous potential as the issues of lack of consistency, reproducibility, and accuracy can be eliminated. In the era of personalised medicine, pathologists can efficiently give a precise clinical diagnosis with the support of AI. KEY WORDS: Artificial intelligence, Algorithms, Breast cancer, Deep learning, Image detection, Ki-67.

Zeng, T., et al. (2024). "AI diagnostics in bone oncology for predicting bone metastasis in lung cancer patients using DenseNet-264 deep learning model and radiomics." J Bone Oncol **48**: 100640.

This study aims to predict bone metastasis in lung cancer patients using radiomics and deep learning. Early prediction of bone metastasis is crucial for timely intervention and personalized treatment plans. This can improve patient outcomes and quality of life. By integrating advanced imaging techniques with artificial intelligence, this study seeks to enhance predictive accuracy and clinical decision-making. METHODS: We included 189 lung cancer patients, comprising 89 with non-bone metastasis and 100 with confirmed bone metastasis. Radiomic features were extracted from CT images, and feature selection was performed using Minimum Redundancy Maximum Relevance (mRMR) and Least Absolute Shrinkage and Selection Operator (LASSO). We developed and validated a radiomics model and a deep learning model using DenseNet-264. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, and specificity. Statistical comparisons were made using the DeLong test. RESULTS: The radiomics model achieved an AUC of 0.815 on the training set and 0.778 on the validation set. The DenseNet-264 model demonstrated superior performance with an AUC of 0.990 on the training set and 0.971 on the validation set. The DeLong test confirmed that the AUC of the DenseNet-264 model was significantly higher than that of the radiomics model ($p < 0.05$). CONCLUSIONS: The DenseNet-264 model significantly outperforms the radiomics model in predicting bone metastasis in lung cancer patients. The early and accurate prediction provided by the deep learning model can facilitate timely interventions and personalized treatment planning, potentially improving patient outcomes. Future studies should focus on validating these findings in larger, multi-center cohorts and integrating clinical data to further enhance predictive accuracy.

Zhang, B., et al. (2023). "Machine Learning and AI in Cancer Prognosis, Prediction, and Treatment Selection: A Critical Approach." J Multidiscip Healthc **16**: 1779-1791.

Cancer is a leading cause of morbidity and mortality worldwide. While progress has been made in the diagnosis, prognosis, and treatment of cancer patients, individualized and data-driven care remains

a challenge. Artificial intelligence (AI), which is used to predict and automate many cancers, has emerged as a promising option for improving healthcare accuracy and patient outcomes. AI applications in oncology include risk assessment, early diagnosis, patient prognosis estimation, and treatment selection based on deep knowledge. Machine learning (ML), a subset of AI that enables computers to learn from training data, has been highly effective at predicting various types of cancer, including breast, brain, lung, liver, and prostate cancer. In fact, AI and ML have demonstrated greater accuracy in predicting cancer than clinicians. These technologies also have the potential to improve the diagnosis, prognosis, and quality of life of patients with various illnesses, not just cancer. Therefore, it is important to improve current AI and ML technologies and to develop new programs to benefit patients. This article examines the use of AI and ML algorithms in cancer prediction, including their current applications, limitations, and future prospects.

Zhang, J., et al. (2024). "External validation of AI for detecting clinically significant prostate cancer using biparametric MRI." Abdom Radiol (NY).

Zhang, P., et al. (2024). "Advancing Cancer Prevention through an AI-Based Integration of Traditional and Western Medicine." Cancer Discov **14**(11): 2033-2036.

Traditional Chinese medicine has accumulated a wealth of experiences in individualized cancer prevention and serves as a complement to Western medicine. We propose an artificial intelligence-based integration of traditional and Western medicine as a new paradigm for cancer prevention, encompassing cancer risk screening and preventive intervention, which will provide new solutions for cancer prevention and offer fresh perspectives for traditional medicine research worldwide.

Zhang, W. H., et al. (2024). "Development and validation of AI models using LR and LightGBM for predicting distant metastasis in breast cancer: a dual-center study." Front Oncol **14**: 1409273.

OBJECTIVE: This study aims to develop an artificial intelligence model utilizing clinical blood markers, ultrasound data, and breast biopsy pathological information to predict the distant metastasis in breast cancer patients. METHODS: Data from two medical centers were utilized, Clinical blood markers, ultrasound data, and breast biopsy pathological information were separately extracted and selected. Feature dimensionality reduction was performed using Spearman correlation and LASSO regression. Predictive models were constructed using LR and LightGBM machine learning algorithms and validated on internal and external validation sets. Feature correlation analysis was conducted for both models. RESULTS: The LR model achieved AUC values of 0.892, 0.816, and 0.817 for the training, internal validation, and external validation cohorts, respectively. The LightGBM model achieved AUC values of 0.971, 0.861, and 0.890 for the same cohorts, respectively. Clinical decision curve analysis showed a superior net benefit of the LightGBM model over the LR model in predicting distant metastasis in breast cancer. Key features identified included creatine kinase isoenzyme (CK-MB) and alpha-hydroxybutyrate dehydrogenase. CONCLUSION: This study developed an artificial intelligence model using clinical blood markers, ultrasound data, and pathological information to identify distant metastasis in breast cancer patients. The LightGBM model demonstrated superior predictive accuracy and clinical applicability, suggesting it as a promising tool for early diagnosis of distant metastasis in breast cancer.

Zhang, W. Y., et al. (2024). "Revolutionizing adjuvant development: harnessing AI for next-generation cancer vaccines." Front Immunol **15**: 1438030.

With the COVID-19 pandemic, the importance of vaccines has been widely recognized and has led to increased research and development efforts. Vaccines also play a crucial role in cancer treatment by activating the immune system to target and destroy cancer cells. However, enhancing the efficacy of cancer vaccines remains a challenge. Adjuvants, which enhance the immune response to antigens and improve vaccine effectiveness, have faced limitations in recent years, resulting in few novel adjuvants being identified. The advancement of artificial intelligence (AI) technology in drug development has provided a foundation for adjuvant screening and application, leading to a diversification of adjuvants. This article reviews the significant role of tumor vaccines in basic research and clinical treatment and explores the use of AI technology to screen novel adjuvants from databases. The findings of this review offer valuable insights for the development of new adjuvants for next-generation vaccines.

Zhang, X., et al. (2019). "Potential Applications of DNA, RNA and Protein Biomarkers in Diagnosis, Therapy and Prognosis for Colorectal Cancer: A Study from Databases to AI-Assisted Verification." Cancers (Basel) **11**(2).

In order to find out the most valuable

biomarkers and pathways for diagnosis, therapy and prognosis in colorectal cancer (CRC) we have collected the published CRC biomarkers and established a CRC biomarker database (CBD: http://sysbio.suda.edu.cn/CBD/index.html). In this study, we analysed the single and multiple DNA, RNA and protein biomarkers as well as their positions in cancer related pathways and protein-protein interaction (PPI) networks to describe their potential applications in diagnosis, therapy and prognosis. CRC biomarkers were collected from the CBD. The RNA and protein biomarkers were matched to their corresponding DNAs by the miRDB database and the PubMed Gene database, respectively. The PPI networks were used to investigate the relationships between protein biomarkers and further detect the multiple biomarkers. The Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway enrichment analysis and Gene Ontology (GO) annotation were used to analyse biological functions of the biomarkers. AI classification techniques were utilized to further verify the significances of the multiple biomarkers in diagnosis and prognosis for CRC. We showed that a large number of the DNA, RNA and protein biomarkers were associated with the diagnosis, therapy and prognosis in various degrees in the CRC biomarker networks. The CRC biomarkers were closely related to the CRC initiation and progression. Moreover, the biomarkers played critical roles in cellular proliferation, apoptosis and angiogenesis and they were involved in Ras, p53 and PI3K pathways. There were overlaps among the DNA, RNA and protein biomarkers. AI classification verifications showed that the combined multiple protein biomarkers played important roles to accurate early diagnosis and predict outcome for CRC. There were several single and multiple CRC protein biomarkers which were associated with diagnosis, therapy and prognosis in CRC. Further, AI-assisted analysis revealed that multiple biomarkers had potential applications for diagnosis and prognosis in CRC.

Zhang, X., et al. (2020). "Novel MicroRNA Biomarkers for Colorectal Cancer Early Diagnosis and 5-Fluorouracil Chemotherapy Resistance but Not Prognosis: A Study from Databases to AI-Assisted Verifications." Cancers (Basel) **12**(2).

Colorectal cancer (CRC) is one of the major causes of cancer death worldwide. In general, early diagnosis for CRC and individual therapy have led to better survival for the cancer patients. Accumulating studies concerning biomarkers have provided positive evidence to improve cancer early diagnosis and better therapy. It is, however, still necessary to further investigate the precise biomarkers for cancer early diagnosis and precision therapy and predicting prognosis. In this study, AI-assisted systems with bioinformatics algorithm integrated with microarray and RNA sequencing (RNA-seq) gene expression (GE) data has been approached to predict microRNA (miRNA) biomarkers for early diagnosis of CRC based on the miRNA-messenger RNA (mRNA) interaction network. The relationships between the predicted miRNA biomarkers and other biological components were further analyzed on biological networks. Bayesian meta-analysis of diagnostic test was utilized to verify the diagnostic value of the miRNA candidate biomarkers and the combined multiple biomarkers. Biological function analysis was performed to detect the relationship of candidate miRNA biomarkers and identified biomarkers in pathways. Text mining was used to analyze the relationships of predicted miRNAs and their target genes with 5-fluorouracil (5-FU). Survival analyses were conducted to evaluate the prognostic values of these miRNAs in CRC. According to the number of miRNAs single regulated mRNAs (NSR) and the number of their regulated transcription factor gene percentage (TFP) on the miRNA-mRNA network, there were 12 promising miRNA biomarkers were selected. There were five potential candidate miRNAs (miRNA-186-5p, miRNA-10b-5, miRNA-30e-5p, miRNA-21 and miRNA-30e) were confirmed as CRC diagnostic biomarkers, and two of them (miRNA-21 and miRNA-30e) were previously reported. Furthermore, the combinations of the five candidate miRNAs biomarkers showed better prediction accuracy for CRC early diagnosis than the single miRNA biomarkers. miRNA-10b-5p and miRNA-30e-5p were associated with the 5-FU therapy resistance by targeting the related genes. These miRNAs biomarkers were not statistically associated with CRC prognosis.

Zhang, Y., et al. (2024). "Eurochevalierines A-I, Sesquiterpene Alkaloid Hybrids with Anti-Triple Negative Breast Cancer Activity from Penicillium sp. HZ-5." J Agric Food Chem **72**(30): 16801-16811.

Nine new sesquiterpene alkaloids, eurochevalierines A-I (1-9), were separated from the rice cultures of the endophytic fungus Penicillium sp. HZ-5 originated from the fresh leaf of Hypericum wilsonii N. Robson. The structures' illumination was conducted by single-crystal X-ray diffraction, extensive spectroscopic analysis, alkaline hydrolysis reaction, and Snatzke's method. Importantly, the antitumor activities screen of these isolates indicated that 1 could suppress triple negative breast cancer (TNBC) cell proliferation and induce apoptosis, with an IC(50) value of 5.4 muM, which is comparable to the positive control docetaxel (DXT). Flow

cytometry experiments mentioned that compound 1 significantly reduced mitochondrial membrane potential (MMP) of TNBC cells. In addition, 1 could activate caspase-3 and elevated the levels of reactive oxygen species (ROS) and expressions of suppressive cytokines and chemokines. Further Western blot analysis showed that 1 could selectively induce mitochondria-dependent apoptosis in TNBC cells via the BAX/BCL-2 pathway. Remarkably, these finding provide a new natural product skeleton for the treatment of TNBC.

Zhang, Y. and X. Yang (2018). "Prognostic Significance of Pretreatment Apolipoprotein A-I as a Noninvasive Biomarker in Cancer Survivors: A Meta-Analysis." Dis Markers **2018**: 1034037.

BACKGROUND: Numerous studies have reported the prognostic significance of serum apolipoprotein A-I (ApoA-I) in various cancers, but the results have been inconsistent. The current meta-analysis was performed to investigate the association between ApoA-I level and prognosis in human malignancies. METHODS: A literature search was performed using the electronic platforms of the PubMed, Cochrane Library, Web of Science, Embase, Wanfang, and China National Knowledge Infrastructure (CNKI) databases to obtain eligible articles published up to May 20, 2018. Pooled hazard ratios (HRs) with 95% confidence intervals (95% CIs) were calculated to assess the prognostic values of the ApoA-I level in cancers using STATA 12.0 software. RESULTS: A total of 14 studies involving 9295 patients were included. The results indicated that low ApoA-I level was significantly associated with poor overall survival (OS) (HR = 0.52, 95% CI: 0.44-0.61). Significant relationships between the ApoA-I level and OS were specifically detected in nasopharyngeal carcinoma (NPC, HR = 0.63, 95% CI: 0.54-0.73), colorectal cancer (CRC, HR = 0.48, 95% CI: 0.19-0.76), and hepatocellular carcinoma (HCC, HR = 0.46, 95% CI: 0.27-0.65). The subgroup analyses for OS also further confirmed the prognostic significance of the ApoA-I level in cancers. Moreover, lower Apo A-I was associated with unfavorable cancer-specific survival (CSS, HR: 0.47, 95% CI: 0.19-0.76) in cancers, and low ApoA-I level was clearly associated with inferior total time to recurrence (TTR, HR: 0.43, 95% CI: 0.29-0.58) in HCC, poorer locoregional recurrence-free survival (LRFS) and distant metastasis-free survival (DMFS) (HR: 0.58, 95% CI: 0.42-0.74 for LRFS; HR: 0.65, 95% CI: 0.41-0.89 for DMFS) in NPC, and shorter disease-free survival (DFS, HR: 0.64, 95% CI: 0.43-0.84) in cancers. Conclusions. Low ApoA-I level might be an unfavorable prognostic factor in multiple malignancies, and serum ApoA-I could serve as a noninvasive marker to predict cancer prognosis.

Zhao, Y., et al. (2020). "CUP-AI-Dx: A tool for inferring cancer tissue of origin and molecular subtype using RNA gene-expression data and artificial intelligence." EBioMedicine **61**: 103030.

BACKGROUND: Cancer of unknown primary (CUP), representing approximately 3-5% of all malignancies, is defined as metastatic cancer where a primary site of origin cannot be found despite a standard diagnostic workup. Because knowledge of a patient's primary cancer remains fundamental to their treatment, CUP patients are significantly disadvantaged and most have a poor survival outcome. Developing robust and accessible diagnostic methods for resolving cancer tissue of origin, therefore, has significant value for CUP patients. METHODS: We developed an RNA-based classifier called CUP-AI-Dx that utilizes a 1D Inception convolutional neural network (1D-Inception) model to infer a tumor's primary tissue of origin. CUP-AI-Dx was trained using the transcriptional profiles of 18,217 primary tumours representing 32 cancer types from The Cancer Genome Atlas project (TCGA) and International Cancer Genome Consortium (ICGC). Gene expression data was ordered by gene chromosomal coordinates as input to the 1D-CNN model, and the model utilizes multiple convolutional kernels with different configurations simultaneously to improve generality. The model was optimized through extensive hyperparameter tuning, including different max-pooling layers and dropout settings. For 11 tumour types, we also developed a random forest model that can classify the tumour's molecular subtype according to prior TCGA studies. The optimised CUP-AI-Dx tissue of origin classifier was tested on 394 metastatic samples from 11 tumour types from TCGA and 92 formalin-fixed paraffin-embedded (FFPE) samples representing 18 cancer types from two clinical laboratories. The CUP-AI-Dx molecular subtype was also independently tested on independent ovarian and breast cancer microarray datasets FINDINGS: CUP-AI-Dx identifies the primary site with an overall top-1-accuracy of 98.54% in cross-validation and 96.70% on a test dataset. When applied to two independent clinical-grade RNA-seq datasets generated from two different institutes from the US and Australia, our model predicted the primary site with a top-1-accuracy of 86.96% and 72.46% respectively. INTERPRETATION: The CUP-AI-Dx predicts tumour primary site and molecular subtype with high accuracy and therefore can be used to assist the diagnostic work-up of cancers of unknown primary or uncertain origin using a common and accessible

genomics platform. FUNDING: NIH R35 GM133562, NCI P30 CA034196, Victorian Cancer Agency Australia.

Zhao, Y. Y., et al. (2022). "GPX4 Plays a Crucial Role in Fuzheng Kang'ai Decoction-Induced Non-Small Cell Lung Cancer Cell Ferroptosis." Front Pharmacol **13**: 851680.

Background: Fuzheng Kang'ai decoction (FZKA) has been widely used to treat Non-Small Cell Lung Cancer (NSCLC) patients in China for decades, showing definitively curative effects in clinic. Recently, we found that FZKA could induce NSCLC cell ferroptosis, another type of programmed cell death (PCD), which is totally different from cell apoptosis. Therefore, in the present study, we aim to discover the exact mechanism by which FZKA induces NSCLC cell ferroptosis, which is rarely studied in Traditional Chinese Medicine (TCM). Methods: Cell proliferation assay were performed to detect the cell viability. Cell ferroptosis triggered by FZKA was observed by performing lipid peroxidation assay, Fe(2+) Ions assay, and mitochondrial ultrastructure by transmission electron microscopy. Ferroptosis inhibitors including liproxstatin-1 and UAMC 3203 were used to block ferroptosis. The ratio of GSH/GSSG was done to measure the alteration of oxidative stress. Western blot and qRT-PCR were carried out to detect the expression of solute carrier family 7 member 11 (SLC7A11), solute carrier family 3 member 2 (SLC3A2) and glutathione peroxidase 4 (GPX4) at protein and mRNA levels, respectively. Lentivirus transfection was performed to overexpress GPX4 stably. Animal model was done to verify the effect of FZKA-induced ferroptosis in NSCLC in vivo and immunohistochemistry was done to detect the expression of SLC7A11, SLC3A2 and GPX4 at protein level. Results: First of all, in vitro experiments confirmed the inhibition effect of FZKA on NSCLC cell growth. We then, for the first time, found that FZKA induced NSCLC cell ferroptosis by increasing lipid peroxidation and cellular Fe(2+) Ions. Moreover, characteristic morphological changes of NSCLC cell ferroptosis was observed under transmission electron microscopy. Mechanistically, GPX4, as a key inhibitor of lipid peroxidation, was greatly suppressed by FZKA treatment both at protein and mRNA levels. Furthermore, system xc(-) (SLC7A11 and SLC3A2) were found to be suppressed and a decreased GSH/GSSG ratio was observed at the same time when treated with FZKA. Notably, overexpressing GPX4 reversed the effect of FZKA-induced NSCLC cell ferroptosis significantly. Finally, the above effect was validated using animal model in vivo. Conclusion: Our findings conclude that GPX4 plays a crucial role in FZKA-induced NSCLC cell ferroptosis, providing a novel molecular mechanism by which FZKA treats NSCLC.

Zheng, C. L., et al. (2022). "Kang-Ai Injection Inhibits Gastric Cancer Cells Proliferation through IL-6/STAT3 Pathway." Chin J Integr Med **28**(6): 524-530.

OBJECTIVE: To explore the mechanisms underlying the proliferative inhibition of Chinese herbal medicine Kang-Ai injection (KAI) in gastric cancer cells. METHODS: Gastric cancer cell lines MGC803 and BGC823 were treated by 0, 0.3%, 1%, 3% and 10% KAI for 24, 48 and 72 h, respectively. The cell proliferation was evaluated by 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2-H-tetrazolium bromide (MTT) assay. The apoptosis and cell cycle were evaluated by flow cytometry. Interleukin (IL)-6 mRNA and protein expression levels were detected by quantitative real-time polymerase chain reaction (qRT-PCR) and enzyme-linked immune sorbent assay (ELISA), respectively. The protein expression levels of cyclin A, cyclin E, cyclin B1, cyclin D1, p21, retinoblastoma (RB), protein kinase B (AKT), extracellular regulated protein kinases (ERK), signal transducer and activator of transcription (STAT) 1 and STAT3 were detected by Western blot. RESULTS: KAI inhibited the proliferation of MGC803 and BGC823 gastric cancer cells in dose- and time-dependent manner. After treated with KAI for 48 h, the proportion of G1 phase was increased, expression level of cyclin D1 and phosphorylation-RB were down-regulated, whereas the expression of p21 was up-regulated (all $P<0.01$). Furthermore, 48-h treatment with KAI decreased the phosphorylation level of STAT3, inhibited the mRNA and protein expressions of IL-6 (all $P<0.01$). IL-6 at dose of 10 ng/mL significantly attenuated the proliferative effect of both 3% and 10% KAI, and recovered KAI-inhibited STAT3 phosphorylation and cyclin D1 expression level (all $P<0.01$). CONCLUSION: KAI exerted an anti-proliferative function by inhibiting IL-6/STAT3 signaling pathway followed by the induction of G(1) phase arrest in gastric cancer cells.

Zheng, F., et al. (2016). "Chinese Herbal Medicine Fuzheng Kang-Ai Decoction Inhibited Lung Cancer Cell Growth through AMPKalpha-Mediated Induction and Interplay of IGFBP1 and FOXO3a." Evid Based Complement Alternat Med **2016**: 5060757.

The aim of this study is to investigate the actions of Chinese herbal medicine, called "Fuzheng Kang-Ai" (FZKA for short) decoction, against non-small cell lung cancer (NSCLC) and its mechanisms in vitro and in vivo. We showed that the effect of

FZKA decoction significantly inhibited growth of A549 and PC9 cells. Furthermore, FZKA increased phosphorylation of AMP-activated protein kinase alpha (AMPKalpha) and induced protein expression of insulin-like growth factor (IGF) binding protein 1 (IGFBP1) and forkhead homeobox type O3a (FOXO3a). The specific inhibitor of AMPKalpha (Compound C) blocked FZKA-induced protein expression of IGFBP1 and FOXO3a. Interestingly, silencing of IGFBP1 and FOXO3a overcame the inhibitory effect of FZKA on cell growth. Moreover, silencing of IGFBP1 attenuated the effect of FZKA decoction on FOXO3a expression, and exogenous expression of FOXO3a enhanced the FZKA-stimulated phosphorylation of AMPKalpha. Accordingly, FZKA inhibited the tumor growth in xenograft nude mice model. Collectively, our results show that FZKA decoction inhibits proliferation of NSCLC cells through activation of AMPKalpha, followed by induction of IGFBP1 and FOXO3a proteins. Exogenous expression of FOXO3a feedback enhances FZKA decoction-stimulated IGFBP1 expression and phosphorylation of AMPKalpha. The reciprocal interplay of IGFBP1 and FOXO3a contribute to the overall responses of FAKA decoction.

Zhou, H., et al. (2024). "AI-guided histopathology predicts brain metastasis in lung cancer patients." J Pathol **263**(1): 89-98.

Brain metastases can occur in nearly half of patients with early and locally advanced (stage I-III) non-small cell lung cancer (NSCLC). There are no reliable histopathologic or molecular means to identify those who are likely to develop brain metastases. We sought to determine if deep learning (DL) could be applied to routine H&E-stained primary tumor tissue sections from stage I-III NSCLC patients to predict the development of brain metastasis. Diagnostic slides from 158 patients with stage I-III NSCLC followed for at least 5 years for the development of brain metastases (Met(+), 65 patients) versus no progression (Met(-), 93 patients) were subjected to whole-slide imaging. Three separate iterations were performed by first selecting 118 cases (45 Met(+), 73 Met(-)) to train and validate the DL algorithm, while 40 separate cases (20 Met(+), 20 Met(-)) were used as the test set. The DL algorithm results were compared to a blinded review by four expert pathologists. The DL-based algorithm was able to distinguish the eventual development of brain metastases with an accuracy of 87% ($p < 0.0001$) compared with an average of 57.3% by the four pathologists and appears to be particularly useful in predicting brain metastases in stage I patients. The DL algorithm appears to focus on a complex set of histologic features. DL-based algorithms using routine H&E-stained slides may identify patients who are likely to develop brain metastases from those who will remain disease free over extended (>5 year) follow-up and may thus be spared systemic therapy. (c) 2024 The Authors. The Journal of Pathology published by John Wiley & Sons Ltd on behalf of The Pathological Society of Great Britain and Ireland.

Zhou, Y., et al. (2023). "Multi-clinical index classifier combined with AI algorithm model to predict the prognosis of gallbladder cancer." Front Oncol **13**: 1171837.

OBJECTIVES: It is significant to develop effective prognostic strategies and techniques for improving the survival rate of gallbladder carcinoma (GBC). We aim to develop the prediction model from multi-clinical indicators combined artificial intelligence (AI) algorithm for the prognosis of GBC. METHODS: A total of 122 patients with GBC from January 2015 to December 2019 were collected in this study. Based on the analysis of correlation, relative risk, receiver operator characteristic curve, and importance by AI algorithm analysis between clinical factors and recurrence and survival, the two multi-index classifiers (MIC1 and MIC2) were obtained. The two classifiers combined eight AI algorithms to model the recurrence and survival. The two models with the highest area under the curve (AUC) were selected to test the performance of prognosis prediction in the testing dataset. RESULTS: The MIC1 has ten indicators, and the MIC2 has nine indicators. The combination of the MIC1 classifier and the "avNNet" model can predict recurrence with an AUC of 0.944. The MIC2 classifier and "glmet" model combination can predict survival with an AUC of 0.882. The Kaplan-Meier analysis shows that MIC1 and MIC2 indicators can effectively predict the median survival of DFS and OS, and there is no statistically significant difference in the prediction results of the indicators (MIC1: chi(2) = 6.849, P = 0.653; MIC2: chi(2) = 9.14, P = 0.519). CONCLUSIONS: The MIC1 and MIC2 combined with avNNet and mda models have high sensitivity and specificity in predicting the prognosis of GBC.

Zhu, J. and L. Tian (2024). "Cost-effectiveness of Kang Ai injection plus chemotherapy vs. Shenqi Fuzheng injection plus chemotherapy in the first-line treatment of advanced non-small cell lung cancer." Front Med (Lausanne) **11**: 1363484.

OBJECTIVE: This study aimed to evaluate the cost-effectiveness of two Chinese patent medicines, including Kang Ai injection and Shenqi Fuzheng injection with each combined with platinum-based chemotherapy as the first-line

treatment for patients with advanced non-small cell lung cancer (NSCLC) in China. METHODS: From Chinese healthcare system perspective, a three state Markov model with a cycle of 3 weeks and a 10-year horizon was constructed to derive the incremental cost-effectiveness ratio (ICER). Since only individual patient data of progression-free survival (PFS) of Kang Ai injection group can be obtained, we extrapolated median overall survival (mOS) of Kang Ai injection group and median progression-free survival (mPFS) and mOS of Shenqi Fuzheng injection group based on published literature and methods. Then survival curves were estimated by the method of declining exponential approximation of life expectancy (DEALE), which is based on the assumption that survival follows a declining exponential function. We performed one-way sensitivity analysis and probabilistic sensitivity analysis to test the robustness. Additionally, a scenario analysis was adopted to investigate the impact of using best-fitting distribution for PFS curve of Kang Ai injection group on the economic conclusion. RESULTS: The base-case result indicated that Kang Ai injection group provided 0.217 incremental quality-adjusted life years (QALYs) at an incremental cost of $103.38 compared with Shenqi Fuzheng injection group. The ICER was $476.41/QALY, which was much lower than the willingness to pay threshold of one time the GDP per capita of China in 2022 ($12,070/QALY). Deterministic sensitivity analysis result showed that ICER was most sensitive to the changes in odds ratio (OR) value. The probabilistic sensitivity analysis confirmed the robustness of base-case analysis results. The scenario analysis result showed that by using Log-Normal distribution to fit the PFS curve of Kang Ai injection group and shortening the time horizon to 5 years, the ICER was $4,081.83/QALY, which was still much lower than the willingness to pay threshold. CONCLUSION: Kang Ai injection combined with platinum-based chemotherapy appeared to be more cost-effective for the treatment of advanced NSCLC than Shenqi Fuzheng injection combined with platinum-based chemotherapy.

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