Role of Diffusion‑weighted MR Imaging in the evaluation of ovarian tumors

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Abstract: Introduction: Ovarian cancer is the fifth leading cause of death among women after (lung, breast, colorectal, and pancreatic cancers) and has a high likelihood of recurrence despite aggressive treatment strategies**.** It is considered the second most common gynecologic malignancy (after cervical Cancer). Diffusion-weighted imaging (DWI) is one of the evolving imaging technologies. It carries the potential to improve tissue characterization when findings are interpreted together with conventional MR imaging sequences. DWI has been widely used in neuroimaging for a number of years. Its application in abdominal and pelvic imaging has been limited by motion and susceptibility artifacts. However, the development of new imaging techniques, high gradient amplitudes and phased-array surface coils allowed much faster data acquisition with fewer artifacts, leading to significant improvement in the quality of image in body applications. **Experimental Methods:** This study included 20 patients with ovarian tumors. Examined by 1.5 T MRI using both conventional sequences as well as DWI and ADC map. Correlation with histo-pathological results was done. **Results:** Addition of DWI to the conventional MR images did not improve the sensitivity, but increased the specificity, PPV, NPV, accuracy from78.6%, 62.5, 91.7% and 80% to 85.7%, 71.4%, 92.3% and 85%. **Conclusion:** The combination of DWI to conventional MRI implies: (1) Using a completely noninvasive technique with no radiation exposure. (2) DWI might be an alternative for contrast administration especially for those were contrast intake is better avoided as during pregnancy. (3) It improves the specificity and accuracy of MRI and thus increasing the radiologist's confidence in image interpretation which will finally reflect on the patients' outcome and prognosis.

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1. Introduction:

Functional imaging is becoming increasingly important in the evaluation of cancer patients because of the limitations of morphologic imaging, particularly in the assessment of response to therapy. Recent technical advances allow the use of diffusion MR imaging in abdominal and pelvic applications after it has been established as a useful functional imaging tool in neurologic applications for a number of years. **(Whittaker et al, 2009)**

This unique noninvasive modality has demonstrated the capacity to help discriminate between benign and malignant lesions, increase the contrast between lesions and surrounding tissues, and improve the detection and delineation of peritoneal implants at both initial staging and follow-up. Moreover, diffusion-weighted imaging provides quantitative information about tissue cellularity that may be used to distinguish viable tumors from treatment-related changes **(Kyriazi et al, 2010).**

When diffusion-weighted MR imaging is used in gynecologic applications, cancers have shown lower apparent diffusion coefficient (ADC) values. Increasing ADC values is noted in carcinomas responding to radiation therapy, so it can be used as a biomarker for treatment response, and in the evaluation of recurrence, discriminating localized from multifocal disease which is a critical factor in opting for secondary cytoreduction **(Inada et al, 2008), (McVeigh et al, 2008).**

As for peritoneal implants from ovarian cancer, the diagnosis represents a privilege for diffusion weighted MR imaging, as the small seeds invaginated within peritoneal reflections, or coating the serosal surface of intestinal loops and solid viscera, are often masked by the similarity of their attenuation or signal intensity to that of adjacent structures using CT or conventional MRI. On diffusion-weighted imaging, malignant deposits on the visceral peritoneum are more conspicuous because of signal suppression from surrounding ascites, bowel contents, and fat **(Low et al, 2009).**

Avoiding the potential pitfalls, of the technique, can be accomplished when diffusion weighted images are interpreted in association with anatomic MR images. Increasing familiarity with diffusion coefficient calculation and software manipulation, will allow radiologists to provide new information for the diagnosis of patients with known or suspected gynecologic malignancies **(Fujii et al, 2008).**

Limitations of diffusion weighted MR imaging, in abdomen and pelvis, due to motion and susceptibility artifacts has been overcome by the development of new imaging techniques, particularly novel methods of data acquisition and parallel imaging, allowing much faster data acquisition with fewer artifacts, resulting in significant improvement in image quality in body applications **(Qayyum, 2009)**.

2. Experimental Methods:

This study was performed on 20 cases of ovarian tumors. Two cases were excluded from the final comparative statistical analysis. They were outpatients and we could not follow their operative details or get their pathology.

The study was conducted in AL Hussein university hospital. Most of the patients were referred from the gynecology & Obstetric department during the period from 15 Jan. 2017 to 30 April 2017.

The patients' age ranged from 21 to 75 year old.

Ten patients presented by abdominal enlargement, six were complaining of long standing abdominal pain, Two came with other different complaints; one came complaining with frequency of micturition, dysuria, loss of weight and one was accidentally discovered during US examination.

All cases had been subjected to the following:

1- Full history taking with a special emphasis on:

- Age.
- Parity.
- Age of menarche.
- Time of menopause.
- Past history of gynecological troubles or operations.
- Positive family history of gynecological malignancy.

2- Routine laboratory investigation for all patients including: kidney functions tests.

3- Ultrasound examination:

All patients had undergone preliminary pelvic ultrasound to exclude benign functional pure cystic lesions. The examination was done on ultrasound machine Toshiba xario 200, trans-abdominal and trans-vaginal ultrasound approaches using 3-4 MHz and 7-8 MHz probes respectively. Color Doppler was superimposed on masses to detect vascularity.

3. Results:

Addition of DWI to the conventional MR images did not improve the sensitivity, but increased the specificity, PPV, NPV, accuracy from78.6%, 62.5, 91.7% and 80% to 85.7%,71.4%, 92.3% and 85%.

	MRI Results	**DWI Results**
Sensitivity	100%	83.3%
Specificity	78.6%	85.7%
PPV	62.5 %	71.4%
NPV	91.7%	92.3%
Accuracy	80%	85%

4. Discussion:

Ovarian cancer is a leading cause of death among women. It is the second most common gynecological cancer and the fifth most common cancer in women. Unfortunately most women are diagnosed with late stage disease, which has a poor survival rate. Proper diagnosis of cancer can help finding more available treatment options and in turn better prognosis. **(Jemal et al, 2009). (Hippisley-Cox et al, 2012).**

Proper management depends on proper preoperative assessment, with the help of clinical examination, laboratory tests and different imaging modalities. Thus, helping to inform the patient about the surgical route and the feasibility of conservative treatment. **(Thomassin-Naggara et al, 2011).**

Accurate characterization of an adnexal mass as being benign can avoid unnecessary surgery especially in postmenopausal women and can help young women wishing to preserve childbearing potential to go for conservative surgery. **(Thomassin-Naggara et al, 2009).**

Ultrasonography is used as the first-line imaging technique for detecting adnexal masses but with less accuracy for complex or indeterminate masses, even when combined with color Doppler imaging. **(Kinkel et al, 2000).**

MR imaging has shown to be more specific and accurate than US and Doppler assessment in characterizing adnexal masses. In addition, it is the best method in delineation of local spread to the pelvic organs. **(Hulse et al, 2004).**

DWI is one of the promising new functional imaging techniques. As long as interpretation of DWI is combined with the conventional MR images and with realizing of the possible pitfalls, it has recently shown to be effective in the differentiation of benign from malignant adnexal masses. **(Fujii et al, 2008), (Thomassin-Naggara et al, 2011).**

In this study, the sensitivity of MRI (which was100%) while that of DWI was (83.3%). The specificity was higher for DWI (85.7%) compared to conventional MRI sequences (78.6%) and so addition of DWI to the MRI is expected to increase the specificity of examination.

Regarding the mean **ADC values** forsolid malignant lesions was ($0.6x\ 10^{-3} \pm 0.11$ SD mm^2/s), while that for solid benign lesions was ($1.2 \times 10^{-3} \pm 0.6$ SD mm^2/s), with p value = 0.058, however p value was considered < 0.05 of statistical significance. The lack of statistical difference between the solid components of the malignant tumors may be attributed to the relatively small number of cases (twenty cases) included in our study and also to the inclusion of mature cystic teratoma in the benign category.

A comparative study was carried out by **Hottat and colleagues** in **2008 on** 35 women to determine the accuracy of DWI imaging in the characterization of ovarian masses in patients undergoing pelvic MRI. The study included 26 benign tumors, 8 malignant tumors and 1 borderline tumor. Malignant lesions only showed definite high signal intensity in DW images. Addition of DWI to conventional MRI has increased the specificity from 81% to 85% respectively which is comparable to our study where the specificity increased from 78.6% to 85.7%. In their study the sensitivity of both was 100%. In our study, there was one false negative case which lower sensitivity of DWI (83.3%) compared to MRI sensitivity (100%).

Another study was conducted by **Fujii and colleagues** in **2008** on 123 ovarian lesions including 42 malignant and 81 benign lesions, most malignant ovarian tumors as well as some of the mature cystic teratomas showed high signal intensity on **DWI**. In contrast, most benign tumors did not show abnormal signal intensity on DWI. This agree with our results where we have five tumors out of six malignant tumors and two cases of mature cystic teratomas showed high signal on DWI, this may be attributed to keratinoid substance and Rokitansky protuberance.

Also those authors concluded that the **mean ADC value** of the solid portion in malignant tumors did not significantly differ from that in the benign lesions **(Fujii et al, 2008)**. In this study, we did not observe significant difference between the benign and the malignant solid or cystic component.

In 2009, Thomassin-Naggara et al evaluated the contribution of DWI in conjunction with morphological criteria to characterize77 complex adnexal masses (30 benign and 47 malignant). In their results, low **signal intensity** both on DWI and T2-weighted images in the solid component of mixed adnexal masses may predict benignity. This result matched with our result.

Regarding the, **ADC** measurements in the solid component, it did not contribute to differentiating benign from malignant adnexal masses. They concluded that the decreased **mean ADC values** in benign lesions may be attributed to dense network of collagen fibers within the extracellular matrixin benign fibrous tumors which were included in their study, as fibromas, Brenner tumors, and cystadenofibromas. In our study all the benign tumors did not show high signal on DWI except for two cases of mature teratomas.

Another study was carried out by **Li and colleagues** in **2011** on 127 patients with pelvic masses, (46 benign and 85 malignant). The purpose of this study was to evaluate differences in ADC values for the solid component of benign and malignant ovarian surface epithelial tumors with the goal of differentiating benign versus malignant ovarian tumors preoperatively.

The **mean ADC value** measured for the **cystic** component did not differ significantly between benign and malignant masses. Unlike that measured for the **solid** component which significantly differed between the benign and malignant lesions. **Mean ADC value** for **benign lesions** was1.69 x 10^{-3} ± 0.25 SD mm^2/s, and for the **malignant** was 1.03 x 10^{-3} ± 0.22 SD mm^2/s. The lower ADC value sassociated with the malignant group were found to be statistically significant. Their results suggest that an ADC value ≥ 1.25 x 10^{-3} mm^2/s may be an optimal cutoff value for differentiating benign and malignant ovarian tumors.

Also in their study, the sensitivity, specificity, PPV, NPV and accuracy of **conventional MR imaging** all have increased from 91.8%, 78.3%, 88.6%, 83.7%, and 87.0% respectively to 96.5%, 89.1%, 94.3%, 93.2%, and 93.1% after adding **DWI** to the conventional MR. This was comparable to our study. Addition of DWI to conventional raises the specificity, PPV, NPV and accuracy from 78.6%, 62.5, 91.7% and 80% to 85.7%, 71.4%, 92.3% and 85% with no improvement for the sensitivity.

A similar study was carried out by **Takeuchi and colleagues** at **2010** on 47 women (33malignant, 6 borderline, and 10 benign tumors). Regarding the **signal intensity**, the solid portion of all malignant tumors showed homogeneous or heterogeneous high intensity on DWI, whereas only 3 of the benign tumors (3 the comas) showed high intensity. However the presence of low intensity on T2-weighted images was suggestive for benign fibrous tumor. In our study all benign tumors including the ovarian fibroma did not show high signal on the DWI (except for the mature cystic teratoma tumors).

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