

New player in the market: Magnetic Nanoparticles as contrast agent for Magnetic Resonance Imaging

Taekwon Kong

The Hill School, 860 Beech St, Pottstown, PA 19464 The United States of America

tkong@thehill.org

Abstract: Climate has changed considerably in the last decade, which has drastically affected the quality of life. Several biological entities like viruses, bacteria, protozoa and multicellular parasites pose continues threat to humans and other mammals due to change in the climate. Many prevalent human infections including malaria, dengue fever and cholera are climate sensitive. Significant efforts have been made to counter these effects and improve the quality of life in past few years. According to the United Nations sustainable development goals, there has been a significant reduction in the number of people infected with HIV, malaria and tuberculosis in past few years. New HIV infections have reduced by 38% in the year 2013. Also the global malaria incidence rate has fallen by 37%. The improved quality of life is a direct result of development of new technology in the form of mobile applications, sensitive diagnostic tools and better treatments.

[Taekwon Kong. **New player in the market: Magnetic Nanoparticles as contrast agent for Magnetic Resonance Imaging.** *N Y Sci J* 2016;9(11):62-64]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 9. doi: [10.7537/marsnys091116.09](https://doi.org/10.7537/marsnys091116.09).

Keywords: New player, market, Magnetic Nanoparticles, agent, Magnetic Resonance Imaging

1. Introduction

Diagnosis is an important aspect of medical treatment and sensitive tools are needed to reach to a correct conclusion. In past decade several new techniques have emerged and evolved that has improved the quality of life. One such technique that is used very commonly for diagnosis of abnormalities within the body is magnetic resonance imaging or MRI (Sahoo et al., 2005). MRI utilizes magnetic resonance spectroscopy to analyze hydrogen atoms that are naturally present in tissues in form of water or proteins. Hydrogen nuclei behave like compass needles that are partially aligned by a strong magnetic field. These nuclei undergo rotation when radio waves are used externally and they subsequently oscillate in the magnetic field and return to equilibrium simultaneously releasing radio waves. This is detected using antennas and can be used for making detailed images of the body. Each tissue returns to its equilibrium state after excitation by independent processes of T1 (spin-lattice) and T2 (spin-spin) relaxation.

2. Methods

The T1 time of a tissue is the time taken by excited nuclei to recover and be available for next excitation. Different tissues have different T1 times depending upon the frequency of hydrogen ions in the tissue. The contrast in the image comes from different T1 times of different tissues. For example fat has higher frequency of hydrogen ions as compared to cerebrospinal fluid (CSF) because of which the hydrogen atoms in fat recover faster more rapidly along the longitudinal axis. When a second pulse is

applied, the longitudinal magnetization flips to transverse plane. The net magnetization vector of fat can be flipped easily into the X-Y plane as compared to CSF. Therefore fat has higher signal and appears bright on a T1 contrast image and low signal CSF will be dark.

The T2 time determines how quickly an MRI signal fades after excitation and it occurs because of energy transfer between spins. For example the energy exchange in the hydrogen atom in fat is more efficient than in water. Because of which, hydrogen in the fat loses transverse magnetization more rapidly than in CSF. Therefore transverse magnetization of fat reduces faster than that of CSF. In this case since the magnitude of transverse magnetization in CSF is large it appears very bright compared to fat in T2 contrast image.

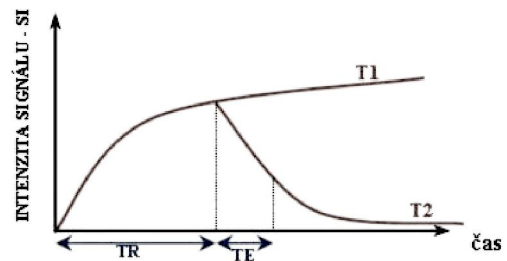


Figure 1. Effects of repetition time (TR) and echo time (TE) on the signal

Magnetization is recovered after changing the repetition time (TR) in T1-weighted image however, magnetization is allowed to decay after changing echo time (TE) in T2-weighted image. As shown in the

figure 1, the effects of TR and TE determine the actual image contrast, which would in-turn be responsible for demonstrating and visualizing various anatomical structures and pathologies associated with them.

3. Results

Even though different types of tissue can be differentiated by difference in T1 and T2 relaxation times, natural differences in relaxation time between region of interest (normal verses affected) are relatively small and the therefore the contrast of image is poor. Therefore contrast agents like Gadolinium ions or manganese ions are used that are known to produce hyper intense signals in T1 weighted images (Moon et al., 2015). T2 contrast agents on the other hand produce low intense signal in T2 weighted areas, thereby making the affected area look darker.

Besides Gadolinium based contrast agents, super paramagnetic nanoparticles have emerged as effective contrast agents for T2 weighing. Magnetic iron oxide nanoparticles have been extensively used as MRI contrast agents due to their ability to shorten T2 relaxation times in liver, spleen and bone marrow. These nanoparticles have dimensions in nanometer range and are considered as zero dimensional materials. They exhibit quantum mechanical properties because of their small size, which also bring about changes in the physico-chemical properties of the particles. These changes include differential dependence on optical absorption and emission of semiconductor particles on their sizes, enhanced catalytic properties of metallic particles, and single domain magnetic behavior in magnetic particles.

Due to their ultrafine size, biocompatibility and super paramagnetic properties magnetic nanoparticles have found application in several biomedical processes like contrast agents in medical imaging and carriers for targeted drug delivery. Besides diagnosis, nanoparticles are also used in the field of cancer therapy (Blasaik et al., 2013).

Among the several magnetic nanoparticles used for the purpose of medical imaging including magnetite ($\gamma\text{-Fe}_2\text{O}_3$) and hematite ($\alpha\text{-Fe}_2\text{O}_3$), iron oxide nanoparticles, Fe_3O_4 or magnetite are most famously used because of its proven biocompatibility. These magnetic particles in the bulk form show a unique property known as ferrimagnetism. Ferrimagnetism is a property of a material that is generated by spins of electrons. Electrons produce a small magnetic field when they spin and orbit around the nucleus. For many atoms, the combination of the electrons in their orbit cancel out each other thereby generates a net magnetic moment of zero. Unlike these materials, electron fields in ferromagnetic

materials do not cancel out each other thereby producing a net magnetic moment. Such materials when are exposed to magnetic field align the spin magnetic moments of electrons in the direction of field and therefore show the property of ferrimagnetism.

Ferromagnetic materials are further characterized by existence of spin domain structures. Domains are the physical regions within the material, which possess a net magnetic moment generated by spins of individual unpaired electrons. Within a domain the magnetic field is intense, but in a bulk sample the material will be usually demagnetized due to cancellation of the magnetic moment from different domains. When external magnetic field is applied these domains reorient and the magnetic moment of the ferromagnet aligns with the magnetic field applied. Once the field is removed the ferromagnet retains the new orientation of the domains and acts like a magnet even after field is removed. This happens because domain wall tend to get fixed in its new orientation and does not change back to original form. Effect of domain is visible only in large magnets where several domains are present together. When the size of magnet is reduced to nanometer range it does not show domain effect because they have only single domain. These single domain particles are called as super paramagnetic particles. Unlike ferromagnetic particles that retain new orientation of spins of electrons even after magnetic field is removed, these super paramagnetic particles revert back to original confirmation (Orsucci et al., 2013; Granitzer et al., 2015).

4. Discussions

The way SPIONS are produced has an influence on properties of these particles that includes toxicity, magnetic moments and biocompatibility. An essential characteristic of an effective MRI contrast agent is high saturation magnetization value. Magnetization values for SPIONS fall in the range from 30-50emu/g. The size and distribution of SPIONS is also an important consideration as it can influence biocompatibility and bio-distribution in vivo. Other properties such as high colloidal stability and low toxicity are equally important because they increase the chance of a SPION to be used as a contrast agent commercially. SPIONS are produced by a method of co-precipitation. The precipitation method is the simplest pathway to obtain super paramagnetic iron oxide particles or SPIONS. Co-precipitating a stoichiometric mixture of ferrous and ferric salts in an aqueous medium produces SPIONS. In the co-precipitation process there are two main processes involved. The first is a short single burst of nucleation followed by growth of the nuclei. This method is

better since large quantities of SPIONS can be obtained in one go but there is considerable difference in the size of particles obtained which can cause problem with bio-distribution of nanoparticles. Another method involves co-precipitation of ferrous and ferric salts in alkaline solution. In this method size of particle decreases as the pH and or Fe^{3+}/Fe^{2+} ratio, increase and as the ionic strength in the medium increases. These particles tend to aggregate and this aggregation can be prevented by addition of surfactant during or after precipitation. It also helps in making a suitable colloidal solution (Lodhia et al., 2009).

Bare nanoparticles are inherently unstable under physiological conditions and are therefore coated with biocompatible polymer that improves colloidal stability and prevents agglomeration and precipitation of the particle in the media. Since these particles are injected in a human body they should exhibit low toxicity and high shelf life (Blasaik et al., 2013). Coating of the particle with organic layer prevents action of immune system on the particle and therefore helps in increasing the circulation half-life of the particles. Core particle is generally covered with several monolayers of inert material and the composition of the layer depends on the application of nanoparticle. The most common coating is polyethylene glycol, polyvinyl alcohol, starch, albumin and so on. While this layer improves the shelf life of nanoparticles, it also can be used for targeting the nanoparticle to a particular organ. Studies have shown that polysaccharide modified super paramagnetic iron oxide nanoparticles can be used as a contrast agent for diagnosing liver diseases. Diseased liver cells express specific protein receptors, which have an affinity for carbohydrate polymer. These nanoparticles accumulate in the liver and improves the resolution of magnetic resonance imaging.

The recent development in the synthesis and characterization of magnetic nanoparticles as MRI contrast agent has allowed the emergence of a variety of new biomedical applications including imaging assisted drug and gene delivery, molecular targeting of chronic diseases such as cancer and so on. Because of their very strong influence on transverse relaxivity, super paramagnetic nanoparticles are used in variety of clinical application like lymph node and spleen imaging. The Fe_3O_4 particles that have carboxy terminal on their surface can also bind to fluorescent molecules or drugs, which can be targeted at a particular tissue. These particles offer a great advantage in the medical imaging and have improved the resolution of MRI imaging by manifold.

11/15/2016

Acknowledgements

Author is grateful to Dr. Shukhrat Muradov for research and academic support to carry out this work.

Corresponding Author

Taekwon Kong
The Hill School, 860 Beech St, Pottstown, PA 19464
The United States of America
tkong@thehill.org

References

1. Cully, Megan, 2016. Drug delivery Nanoparticles improve profile of molecularly targeted cancer drug. *Nature Reviews Drug Discovery*, 15(4), 231.
2. Granitzer, P.; Rumpf, K.; Coffer, J.; Poelt, P.; Reissner, M., 2015. Assessment of Magnetic Properties of Nanostructured Silicon Loaded with Superparamagnetic Iron Oxide Nanoparticles. *ECS Journal of Solid State Science and Technology*, 4(5), N44-N46.
3. Rajesh, E. M.; Shamili, K.; Rajendran, R.; Elango, M.; Shankar, S. R. Madhan, 2014. Superparamagnetic nanoparticles of iron oxide: synthesis and characterization. *Advanced Science, Engineering and Medicine*, 6(3), 268-272.
4. Moon, MyeongJu; Thomas, Reju George; Heo, Seon-u; Park, Myong-Suk; Bae, Woo Kyun; Heo, Suk Hee; Yim, Nam Yeol; Jeong, Yong Yeon, 2015. A Hyaluronic Acid-Conjugated Gadolinium Hepatocyte-Specific T1 Contrast Agent for Liver Magnetic Resonance Imaging. *Molecular Imaging and Biology*, 17(4), 497-503.
5. Orsucci, Franco F.; Sala, Nicoletta, 2013. Ferrofluids, 13-28.
6. Sahoo, Yudhisthira; Goodarzi, Alireza; Swihart, Mark T.; Ohulchanskyy, Tymish Y.; Kaur, Navjot; Furlani, Edward P.; Prasad, Paras N., 2005. Aqueous Ferrofluid of Magnetite Nanoparticles: Fluorescence Labeling and Magnetophoretic Control. *Journal of Physical Chemistry B*, 109(9), 3879-3885.
7. Barbara Blasiak, Frank C. J. M. van Veggel, and Boguslaw Tomanek, 2013 Applications of Nanoparticles for MRI Cancer Diagnosis and Therapy *Journal of Nanomaterials*, 2013.
8. Lodhia J, Mandarano G, Ferris Nj, Eu P, Cowell S., 2009 Development and use of iron oxide nanoparticles (Part 1): Synthesis of iron oxide nanoparticles for MRI, 2.