

Nanomaterials based exogenous contrast agents for MRI

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INTRODUCTION

Imaging is not only an important tool in academia to understand the fundamentals of biology at molecular or cellular level but also is a primary tool for early detection of disease in medical sciences. Because these two fields, molecular biology and in vivo imaging have so much in common in terms of research and development, a new discipline, called molecular imaging (MI) came into existence recently [1]. MI is a non-invasive method to obtain tissue information in real time that is similar to what is generated from histopathological results of several surgical diagnoses of human tissue(s). MI techniques are widely used to obtain tissue orientation, disease detection, monitoring biological changes at the cellular level before and after a therapeutic treatment. Traditional MI techniques that are currently used in medical practices include X-ray computed tomography (CT), fluorescence imaging (FI), Positron emission tomography (PET), near infrared imaging (NIR), Photo acoustic imaging (PAI), ultrasound, Magnetic resonance imaging (MRI), etc. [2].

Magnetic resonance imaging (MRI)

MRI is one of the several promising imaging techniques that are currently used in clinical practices for early detection of any disease or to follow the tissue biological functions. It is a non-invasive clinical diagnosis owing to its high degree of soft tissue contrast, special resolution, and tissue penetration. MRI relies on strong magnetic fields and radio frequencies (RFs), and uses different relaxation properties of the hydrogen atoms of water, lipids and protein molecules (endogenous contrast agents) present in the living tissues, to produce anatomical images with good spatial and temporal resolution [3]. The proton relaxation times that relate to the MRI signal intensity, are of two types: (a) spin-lattice relaxation also called longitudinal relaxation, T₁, and (b) spin-spin relaxation also called transverse relaxation, T₂. Even though the presence of a huge amount of water (proton density) in the body helps to generate relatively high-quality MR images from soft tissues, but still there are some cases where the image contrast is so poor that it barely helps to make the right diagnosis. In such cases, the physicians either need to depend on the histopathological examinations of tissue biopsies or another alternative is to use some exogenous contrast agent that predominantly interacts with the endogenous contrast agent, i.e. protons in water and helps to increase the magnetic field or selectively shortens the water proton relaxation times and thus helps to get the better contrast/resolution MR images for accurate diagnosis. The imaging modality that involves the use of an exogenous contrasting agent depends on the accumulation of the contrasting agent at the disease site. So, the site selectivity of the contrasting agent is an important criterion for their proper choice and should be administered to the diseased area.

Several inorganic, organic as well as composite exogenous contrast agents have been investigated and clinically used for MRI. Gd(III)

(Gadolinium (III)) metal ion with seven unpaired electrons when forms chelate complexes, are the most stable, reduced cytotoxic effect and are clinically used contrast agents for MRI [4-6]. The other metal ion complexes that involve Mn²⁺ with five unpaired electrons, has also been explored as contrast agent for MRI [7]. Even though, several contrast agents that are chelated complexes of Gd have been approved by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) for their clinical use, but the World Health Organization (WHO) showed some concern in relation to the risk of nephrogenic systemic fibrosis and so restricted their use.

Rapid growth in Nano science and their effect on almost every aspect of human society from academia to business to health opens up new avenues for their further research and developments. Numerous research is going on globally to develop nanomaterials-based contrast agents to improve the MRI contrasting effect for better resolution, high stability under physiological conditions, low toxicity, and sufficiently high magnetic field. For example, iron oxide nanoparticles [8-10] as well as their surface modifications by PEGs, polyethyleneimines, and other biocompatible motifs such as peptides, and liposomes are reported to increase the image contrast for magnetic resonance imaging (MRI) by enhancing their retention and optical properties [11-13]. Hayashi et al. reported that Nano clusters of modified superparamagnetic iron oxide nanoparticles (SPION) with folic acid (FA) and polyethylene glycol (PEG), (FA-PEG-SPION NCs) shows enhanced MRI contrast activity with neither liver nor kidney toxicity. Xie et al. reported the formation of ultra-small superparamagnetic iron oxide nanoparticles (USPIONs) with diameter less than 10 nm when conjugated with 4-methylcatechol and a cyclic arginine-glycine-aspartic acid (cRGD) peptide for tumor-specific MRI targeting [14]. Alloys of iron oxide nanomaterials, in which one iron atom is replaced by another magnetic metal ion called ferrites such as Mn-Ferrites [15] and Mn-Ferrites when deposited on graphene oxide surface [16] are reported to be potential candidates for MRI contrasting agents. Heterocyclic organic compounds such as metalloporphyrins, their related tetrapyrrolic macrocycles such as phthalocyanines, naphthalocyanines etc. as well as the conjugates of these macrocycles have also been thoroughly investigated as contrasting agents for MRI [17-21]. For example, Jahanbin et al. reported a gadolinium meso-tetrakis(4-pyridyl) porphyrin, [Gd(TpyP)] chelate when conjugated with chitosan nanoparticles (CNs), [Gd(TpyP)-CNs] have potential to be used as contrast agents for MRI. Other metalloporphyrins containing Mn(III) ions have also been reported for their usage as molecular MRI probes for in vivo imaging [18,19].

CONCLUSIONS

Recent development in nanotechnology, synthesis and functionalization of nanomaterials with desired properties, and advancement in imaging modalities seemed to work together to significantly improve the diagnostic limits from tissue to the cellular to even deep down to molecular level for early diagnosis and prognosis of disease such as cancers. The use of nanoparticles/nanomaterials as imaging probes has several advantages over small molecular conventional imaging agents. Various nanomaterials-

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based contrast agents have been developed that may have potential to be used in MRI clinical diagnosis to enhance image contrast and/or to provide better resolution. Although, the stability of inorganic nanoparticles is a potential advantage over conventional ones but, the clearance of inorganic nanoparticles and their long-term toxicity need to be examined very carefully before they go the next phase, clinical trials. Considering human health and early diagnosis of a disease, there is an urgent need of an ideal contrast agent for multimodal imaging technique. Despite all these pros and cons related to the advancement and clinical applications of nanomaterials, the future of nanomaterials to be used as a multimodal theranostics agents seems to be very promising.

REFERENCES

1. Kherlopian AR, Song T, Duan Q, et al. A review of imaging techniques for systems biology. *BMC Sys Biol.* 2008;2:74.
2. Weissleder R, Pittet MJ. Imaging in the era of molecular oncology. *Nature.* 2008;452:580-89.
3. Lam T, Pouliot P, Avti PK, et al. Superparamagnetic iron oxide based nanoprobes for imaging and theranostics. *Adv. Colloid Interface Sci.* 2013;2:95-113.
4. Shao Y, Tian X, Hu W, et al. The properties of Gd₂O₃-assembled silica nanocomposite targeted nanoprobes and their application in MRI. *Biomaterials.* 2012;33:6438-46.
5. Park JY, Baek MJ, Choi ES, et al. Paramagnetic ultrasmall gadolinium oxide nanoparticles as advanced t1 mri contrast agent: Account for large longitudinal relaxivity, optimal particle diameter, and in vivo T1 MR images. *ACS Nano.* 2009;3:3663-69.
6. Hifumi H, Yamaoka S, Tanimoto A, et al. Dextran coated gadolinium phosphate nanoparticles for magnetic resonance tumor imaging. *J Mater Chem.* 2009;19:6393-99.
7. Silva AC, Bock NA. Manganese-enhanced MRI: An exceptional tool in translational neuroimaging. *Schizophr. Bull.* 2008;34:595-604.
8. Hayashi K, Nakamura M, Sakamoto W, et al. Superparamagnetic nanoparticle clusters for cancer theranostics combining magnetic resonance imaging and hyperthermia treatment. *Theranostics.* 2013;3:366-76.
9. Tian Q, Hu J, Zhu Y, et al. Sub-10 nm Fe₃O₄@Cu₂-xS Core-Shell Nanoparticles for Dual-Modal Imaging and Photothermal Therapy. *J Am Chem Soc.* 2013;135:8571-577.
10. Yu J, Yang C, Li J, et al. Multifunctional Fe₃C₂ Nanoparticles: A targeted theranostic platform for magnetic resonance imaging and photoacoustic tomography-guided photothermal therapy. *Adv Mater.* 2014;26:4114-120.
11. Ferguson RM, Khandhar AP, Arami H, et al. Tailoring the magnetic and pharmacokinetic properties of iron oxide magnetic particle imaging tracers. *Biomed Tech (Berl).* 2013;58:493-507.
12. Ling D, Hyeon T. Chemical design of biocompatible iron oxide nanoparticles for medical applications. *Small.* 2013;9:1450-66.
13. Rosen JE, Chan L, Shieh DB, et al. Iron oxide nanoparticles for targeted cancer imaging and diagnostics. *Nanomed. Nanotech. Biol Med.* 2012;8:275-90.
14. Xie J, Chen K, Lee HY, et al. Ultrasmall c(RGDyK)-coated Fe₃O₄ nanoparticles and their specific targeting to integrin alpha(v)beta3-rich tumor cells. *J Am Chem Soc.* 2008; 130:7542-543.
15. Yang H, Zhang C, Shi X, et al. Water-soluble superparamagnetic manganese ferrite nanoparticles for magnetic resonance imaging. *Biomaterials.* 2010;31:3667-73.
16. Yang Y, Shi H, Wang Y, et al. Graphene oxide/manganese ferrite nanohybrids for magnetic resonance imaging, photothermal therapy and drug delivery. *J Biomater Appl.* 2016;30:810-22.
17. Jahanbin T, Sauriat DH, Spearman P, et al. Development of Gd(III) porphyrin-conjugated chitosan nanoparticles as contrast agents for magnetic resonance imaging. *Mater Sci Eng.* 2015;52:325-32.
18. Cheng W, Haedicke IE, Nofiele J, et al. Complementary strategies for developing GD-free high-field T1 MRI contrast agents based on MnIII Porphyrins. *J Med Chem.* 2014;57:516-20.
19. Mouraviev V, Venkatraman TN, Tovmasyan A, et al. Mn porphyrins as novel molecular magnetic resonance imaging contrast agents. *J Endourol.* 2012;26:1420-24.
20. Calvete MJF, Pinto S MA, Pereira MM, et al. Metal coordinated pyrrole-based macrocycles as contrast agents for magnetic resonance imaging technologies: Synthesis and applications. *Coord Chem Rev.* 2017;333:82-107.
21. Aydın TD, Garifullin R, Şentürk B, et al. Design of a Gd-DOTA-phthalocyanine conjugate combining mri contrast imaging and photosensitization properties as a potential molecular theranostic. *Photochem Photobiol.* 2014; 90:1376-86.