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A systematic review: Advanced magnetic nanotheranostics

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Abstract

Scientific progress in chemistry, physics, technology, and medicine has led to the development of high-sensitivity biomedical imaging systems, crucial for identifying illnesses and interpreting physiological phenomena. Modalities like MRI, PET, CT, SPECT, optical fluorescence imaging, ultrasound, and photoacoustic imaging are widely used. The pursuit of precise imaging has driven the exploration of multi-modality approaches, combining the strengths of different modalities. Magnetic nanoparticles, due to their customizable features, have become a key platform for contrast agents in MRI. Their adaptability also makes them valuable in multi-modal imaging, combining features like MRI-optical and MRI-PET/SPECT for precise imaging. Current discussion delves into the unique magnetic properties of nanoparticles, their synthesis methods, and applications across diverse fields. External magnetic fields play a role in the agglomeration of superparamagnetic iron oxide nanoparticles (SPIONs), impacting their biological effects. In nanomedicine, engineered magnetic nanoparticles guide drug delivery, hyperthermia cancer therapy, and tissue engineering. However, concerns arise about increased cytotoxicity and resistance to biodegradation compared to bulk counterparts. Moreover, role of magnetic stimuli in neurogenesis, emphasizing both potential benefits and risks. Additionally, a magneto-nanomechanical approach is discussed, involving the mechanical activation of functionalized magnetic nanoparticles for targeted drug delivery and cancer cell destruction. The application of magnetic nanoparticles as carriers for therapeutic DNA, particularly in gene delivery using surface-modified nanoparticles, represents a promising avenue for cancer management. The text underscores the need for further research to optimize parameters for in vitro and in vivo treatments. Overall, the integration of magnetic nanoparticles in various biomedical applications showcases their versatility and potential impact on advancing medical technologies.

Keywords: Molecular Imaging; Magnetic Nanoparticles; Nanomedicine; MRI; Nanotheranostics; Multimodal Imaging Agents; Contrast Agents

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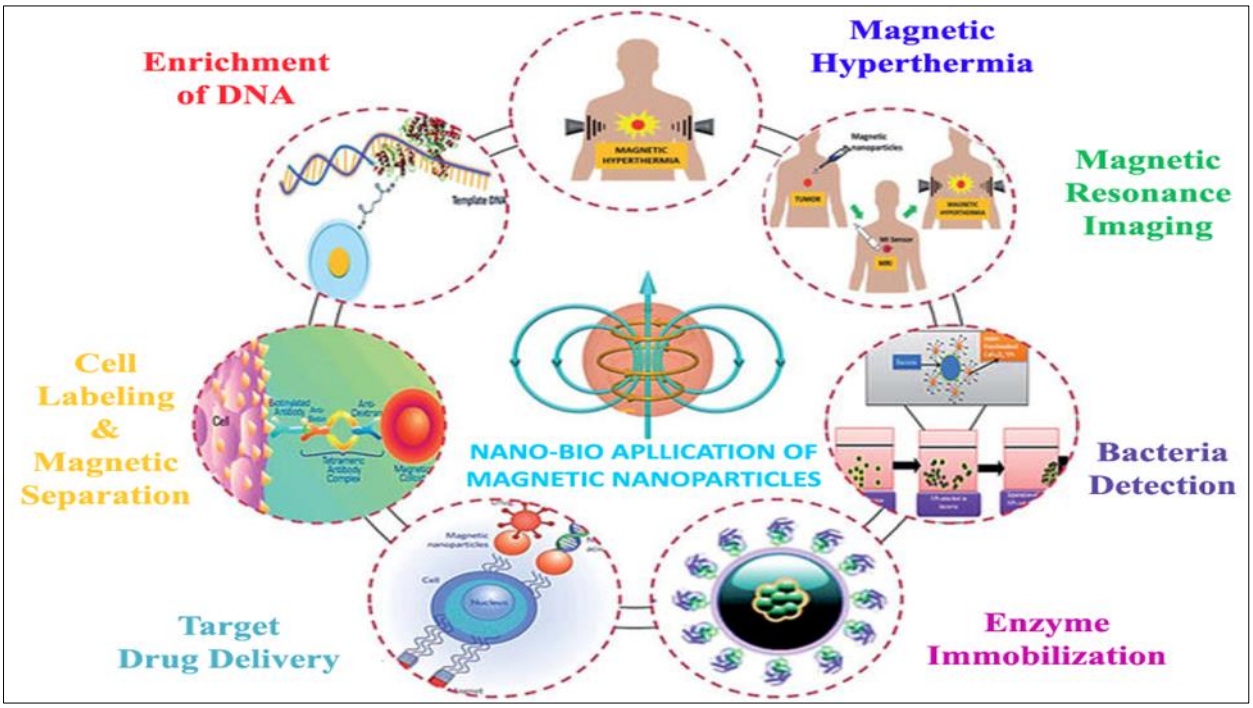
Graphical Abstract



1. Introduction

Scientific advances in the fields of chemistry, physics, technology, and medicine over the last few decades have produced high-sensitivity and high-resolution biomedical imaging systems that help with identifying illnesses and physiological phenomenon interpretation (Webb, 2022). MRI, positron emission tomography (PET), computed tomography (CT)(Norris & Caprioli, 2013), single-photon emission computed tomography (SPECT), optical fluorescence imaging, ultrasound (US) imaging, and photoacoustic (PA) imaging are currently the representative imaging modalities used in preclinical research or clinical settings (Q. Li et al., 2013). The demand for precise imaging of small biological targets in intricate surroundings has led to the ongoing development of new imaging techniques and performance enhancement experiments (Noble et al., 2016). A technique being researched is the idea of multi-modality, which combines the advantages of multiple imaging modalities with the shortcomings of a single modality. Utilizing imaging agents is another tactic to get around intrinsic instrumental constraints, including the sensitivity or resolution of a specific imaging method, and ultimately improve the precision of biomedical imaging (Hsu, Markey, & Wang, 2013). Specifically, because of their easily conjugated physiologically functional units, variable size, and magnetism, magnetic nanoparticles have been used as a platform for MRI contrast agents. Utilizing imaging agents is another tactic to get around intrinsic instrumental constraints, including the sensitivity or resolution of a specific imaging method, and ultimately improve the precision of biomedical imaging (C. Li, Chen, Zhang, Wu, & Wang, 2020). In particular, because of their easily conjugated physiologically functional units, customizable features including size and magnetism, magnetic nanoparticles have been used as a platform for MRI contrast agents. For instance, precise control over the size or composition of the nanomaterials can optimize the magnetic characteristics, such as saturation magnetization (ms), which influences the MRI contrast proportionately (Grillo et al., 2016). Furthermore, nanoparticles may carry a variety of imaging moieties, including fluorescent compounds and radioisotopes, thanks to their surface functionalization, which makes them valuable in multi-modal imaging systems (Farzin, Sheibani, Moassesi, & Shamsipur, 2019). In fact, because of their adaptability, magnetic nanoparticles have emerged as a key platform for multi-modal imaging applications like MRI-optical and MRI-PET/SPECT, which combine the best features of each imaging modality to produce incredibly precise images (Shahdoosti, Tabatabaei, & Control, 2019). Magnetic nanoparticles conjugated with secondary imaging components are one method used. These nanoparticles are made to produce sufficient signals in a variety of imaging modalities, such as MRI, which can have the required high sensitivity and spatial resolution, or optical, PET, or SPECT, for example. The biological targets can be scanned with high accuracy when these signals are integrated in a complimentary way (Jovicic, Li, & Richardson, 2013). The alternative method does not require additional imaging moieties and instead leverages the intrinsic magnetic characteristics of magnetic nanoparticles as a source of multi-modal imaging signals (Shin, Choi, Kim, & Cheon, 2015). With the development of various novel imaging methods (such as MPI, MMUS, and MPA) that directly view nanoparticles, it is now possible to pinpoint the location of the magnetic

nanoparticles. It is possible to combine these magnetic nanoparticle-based imaging methods with more traditional imaging methods (such as MRI and US) (Shin et al., 2015). The exact distribution of magnetic nanoparticles can be accurately determined by overlaying images from different modalities, eliminating the influence of background signals. This could ultimately result in more accurate illness diagnosis (Foster et al., 2014). These multi-modal imaging techniques based on magnetic nanoparticles are being actively investigated to increase the precision of cell tracking in regenerative medicine, cardiovascular disease imaging, and cancer diagnostics (Liu, Li, Tong, Yeom, & Kuzminski, 2015).

2. Discussion

Due to finite size effects, characterized by a high surface-to-volume ratio and unique crystal structures, magnetic nanoparticles exhibit fascinating and notably different magnetic properties in comparison to their bulk counterparts. These nanoparticles can be synthesized using diverse methods, including chemical and physical approaches, allowing for precise control over sizes, enabling comparisons with biological entities spanning from cells (10–100 μm) and viruses to genes and proteins (3–50 nm). The optimization of factors such as nanoparticle size, size distribution, agglomeration, coating, and shapes, coupled with their distinct magnetic characteristics, has driven the widespread application of these nanoparticles across various fields[1]. Applied magnetic fields can induce the development of elongated linear chains of magnetic nanoparticles (MNPs), contrasting with the tendency of MNPs to form smaller clusters or shorter linear segments in the absence of a magnetic field. Additionally, the application of magnetic fields can align disordered MNP chains parallel to the field direction. When ferromagnetic or superparamagnetic nanoparticle solutions are allowed to dry under such applied magnetic fields, the resulting outcome is regularly spaced linear chains. This formation arises from attractive interactions within the chains and repulsive interactions between them. Whether derived from Magnetic Field Driven Self-Assembly (MFDSA) or alternative methods, these chains of MNPs exhibit magnetic anisotropy along the chain axis due to dipolar coupling among the nanoparticles [2].

Magnetic nanoparticles find diverse applications in medicine, electronics, environmental remediation, and materials sciences. Understanding the impact of a magnetic field on the interaction between cells and magnetic nanoparticles (MNPs) is crucial for potential gene and drug delivery. A pulsed magnetic field enhances the uptake and transportation of MNPs across cell monolayers, unlike a constant field. In both conditions, low temperatures significantly impede MNP transport, suggesting an active mechanism like endocytosis. Under a constant magnetic field, hindered MNP transport is observed due to the formation of large magnetically induced MNP aggregates, surpassing endocytic vesicle size (>2 μm). Consequently, a pulsed magnetic field improves cellular uptake and MNP transport across cell barriers compared to a constant field, promoting accumulation while minimizing magnetically induced MNP aggregation at the cell surface[3].

Engineered magnetic nanoparticles (MNPs) advance medicine with simultaneous functionalization and guidance by a magnetic field. They are applied in MRI, guided drug/gene delivery, magnetic hyperthermia cancer therapy, tissue engineering, cell tracking, and bio-separation. Theragnostic applications combine therapeutic and diagnostic functions, demonstrated in MRI-guided cell replacement and cancer-specific gene delivery imaging. However, certain MNP properties, like increased reactivity and resistance to biodegradation, heighten cytotoxicity compared to bulk counterparts. Oxidative stress, a three-tier nanotoxicity paradigm (ROS activation, pro-inflammatory response, DNA damage), becomes apparent. In vivo, MNPs encounter challenges from RES macrophages, neutralizing toxicity but reducing circulation time. This discussion delves into MNP roles in intracellular uptake, biodistribution, macrophage recognition, and cytotoxicity, reviewing current studies, addressing nanotoxicity assessment caveats, and suggesting engineering strategies for optimal biomedical use [4].Superparamagnetic iron oxide nanoparticles (SPIONs) are promising in diverse nanomedicine applications, such as targeted imaging/drug delivery, tissue engineering, hyperthermia, and gene therapy, owing to their favorable biocompatibility and unique magnetic properties. Recent advances reveal that external magnetic fields can induce significant agglomeration of SPIONs in their colloidal suspension. This agglomeration, influenced by changes in the physicochemical properties of colloidal nanoparticles, has the potential to modify their established biological impacts. It is explored the cellular uptake and toxicity of SPIONs before and after exposure to external magnetic fields, demonstrating notable changes in the size and zeta potential of different SPION types. For example, exposure to external magnetic fields led to particle size variations in plain, positive, and negative SPIONs from 74, 94, and 59 nm to 327, 294, and 393 nm, respectively[5]. Considering that nanoparticle size and surface charge govern the protein corona profile and therapeutic/toxic effects, it is reasonable to anticipate that external magnetic fields may significantly influence the biological effects of nanoparticles and cellular responses[6].

Neurodevelopmental processes in pluripotent cells, involving proliferation and differentiation, respond to external natural forces. Despite the presence of biogenic magnetite nanoparticles in the central nervous system and continuous exposure to Earth's magnetic fields, the role of electromagnetic stimuli in neurogenesis remains poorly understood. The inclusion of 0.5% MNPs in collagen-based coatings aids in the in vitro migration and neuronal maturation of mESCs and

hiPSCs. Additionally, applying a 0.4 Tesla electromagnetic field (EMF) perpendicular to the cell culture plane notably stimulates proliferation and directs fate decisions in pluripotent stem cells, dependent on their origin and developmental stage. Mechanistic analysis highlights the modulation of ionic homeostasis and the expression of proteins related to cytostructural, liposomal, and cell cycle checkpoint functions as fundamental for the impact of electromagnetic stimuli on neural lineage specification and proliferation. These findings not only reveal the potential of magnetic stimuli as modulators of neural differentiation and function but also emphasize the risks associated with excessive magnetic stimulation, especially affecting more vulnerable neurons, such as dopaminergic neurons[7].Extensive research has been conducted on the magneto-nanomechanical approach to stimulate biochemical systems, involving the mechanical activation of functionalized magnetic nanoparticles using a low-frequency alternating magnetic field. This method offers specificity at the cellular or molecular level and precise spatial control at the nanometer scale. It explores various types of magnetic nanoparticles and shows promise in therapy for targeted drug delivery, controlled drug release, and cancer cell destruction. The approach can influence the properties and functions of macromolecules or cellular membranes attached to them, causing periodic deformations on the nanometer scale. Effective in vitro and in vivo treatment requires specific AMF parameters and MNP design considerations [8].

One of the most promising advanced approaches, serving as an alternative to traditional chemotherapies for cancer management, involves the utilization of therapeutic DNA to rectify genetic defects or RNA interference for gene silencing. For instance, siRNA molecules are employed to selectively suppress abnormal gene expressions or genetic mutations in cancer cells. However, the efficacy of DNA and RNA molecules on their own is limited due to their susceptibility in complex physiological environments. Consequently, magnetic nanoparticles (NPs) are being increasingly explored as carriers for gene delivery [9]. The bonding of DNA with magnetic nanoparticles is primarily accomplished through surface modification of the nanoparticles with polyethyleneimine (PEI), particularly those with low molecular weight. This modification demonstrates robust binding affinity and effective protection of nucleic acids, making it well-suited for transfection purposes [10].

3. Conclusion

In conclusion, applied magnetic field can affect the size and morphology of magnetic nanoparticles. The use of magnetic nanoparticles in biomedical imaging has led to the development of multi-modal imaging systems, which combine different modalities to create precise images. These nanoparticles have customizable features and are easily conjugated with physiologically functional units, making them ideal for use in MRI contrast agents. The use of pulsed magnetic fields can enhance cellular uptake and transport, making them useful for drug and gene delivery. However, challenges such as cytotoxicity and oxidative stress need to be considered. Magnetic nanoparticles also show promise in neurodevelopmental processes and cancer management, with surface modifications being effective in ensuring robust binding affinity and protection of nucleic acids during transfection. Overall, the ongoing advancements in magnetic nanoparticle research have the potential to revolutionize biomedical imaging and therapeutic interventions.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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