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Magnetic Nanoparticle-Polymer Nanocomposites for Enhanced Magnetic Resonance Imaging (MRI) Contrast Agents: A Review

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Abstract—Magnetic nanoparticle-polymer nanocomposites have been well encouraged as magnetic resonance imaging (MRI) contrast agents with high performance. The advanced nanocomposites combine with magnetic contours such as superparamagnetism and high relaxivity, which are limited to nanoparticles with the structural and functional flexibility of polymers. Additionally, it improves the particular functionalisation, biocompatibility, and structure of imaging contrast agents, which raises the diagnostic yield. This paper discusses the various manufacturing processes for magnetic nanoparticle-polymer nanocomposites, their structure, and how they enhance MRI contrast. Their ability to improve diagnostics, reduce the required dosage, and allow real-time imaging makes these nanocomposites potent tools for the development of new medical imaging technologies. We also discuss future prospects and concerns with regard to the further advancement of these materials for clinic use.

Keywords: Magnetic nanoparticles, Polymer nanocomposites, magnetic resonance imaging (MRI), medical imaging technologies

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1. INTRODUCTION

Magnetic Resonance Imaging (MRI) is a crucial non-invasive imaging modality in medicine, offering enhanced diagnostic capabilities and producing crisp images of soft tissues [1]. Magnetic Resonance Imaging utilizes powerful magnetic fields to orient hydrogen nuclei in newly generated water molecules. When radiofrequency (RF) pulses are applied, the nuclei are disturbed off equilibrium and give signals back as they relax to being aligned. The signals are processed with advanced algorithms to create images, so that structures and pathologic conditions within the body can be displayed. Recent advances, such as high magnetic field MRI systems have increased the resolution of images and acquisition speed over time leading to better delineation among various anatomical structures with improved diagnostic utility. Certain diagnosis situations, like finding a small differentiation among very closely associated tissues or tumors may unresolve the issues in clinical study [2]. Consequently,

there is a growing interest in the research community to improve contrast by using new agents.

Contrast agents are particularly important in MRI to increase the visibility of selected tissues and discrimination between normal tissue, healthy organs, and pathological objects [3]. The area of interest for most contrast agents are gadolinium- based compounds, which effectively shorten the T1 relaxation times of neighboring hydrogen nuclei to yield brighter signal intensities from selected areas. Despite its safety, rare but serious risks associated with gadolinium use in patients with united renal function have mortified; as nephrogenic systemic fibrosis (NSF) [4]. Exposure and long-term tissue retention has raised concern for the appropriateness of this agent. In this context, to improve the safety profile, the nanoparticles based on manganese have been suggested as alternative effective T1-weighted contrast agents due to their relatively low toxicity and good relaxivity properties. Moreover, the incorporation superparamagnetic iron oxide nanoparticles (SPION) formulation has demonstrated an improved T2 contrast in addition to lowering administered dose requirements as compared with conventional gadolinium-based agents [5].

To date, there exists a familiar prosperity of magnetic nanoparticles (MNPs) enabling superparamagnetism, biocompatibility with sensible degrees of toxicity and acceptable behaviors within biological environments as contrast agents have been modified for directed imaging [6]. Metallic nanoparticles such as iron oxide, cobalt and nickel are known to significantly increase MRI contrast due to the generation of local magnetic fields leading to signal enhancement. Several studies have investigated the size-related effects of MNPs on imaging quality or contrast; usually, smaller particles (<20 nm) revealed improved T1 contrasts due to their higher surface area volume percentage which leads a better interaction with surrounding tissues [7].

The magnetic nanoparticle-polymer nanocomposites exhibits a potential enhanced in MNPs for MRI applications. These composites combine the magnetic properties of nanoparticles with functional versatility to yield added stability, biocompatibility and targeting ability for site-specific delivery of imaging agents [8]. Due to the increasing blood retention and low antigenicity of polyethylene glycol (PEG)-coated iron oxide nanoparticles, they could be even used for enhanced tumor targeting. The addition of stimuli-responsive polymers facilitates selective imaging agent, depending on varying exogenous conditions such as pH shifts in tumor microenvironment, which leads to enhanced in bioimaging efficiency. Hybrid imaging techniques in functionalizing MNPs with fluorescent dyes shows a dual-modality approach strengthening the diagnostic capabilities by yielding two types of information about tissue characteristics and function, has provide a powerful detection tool [9].

In this review, we have attempt to provide a systematic discussion on the recent developments in various types of magnetic nanoparticle-polymer nanocomposites that have recently emerged as new contrast agents with improved properties for MR imaging. Discussion over different synthesis methods (e.g., co-precipitation method, hydrothermal method and sol-gel technique), advanced characterization techniques like transmission electron microscope (TEM) and dynamic light scattering (DLS) to determine size distribution profiles as well morphology stability behavior in these composites provide the nature of the materials. Furthermore, specific techniques these nanocomposites exploit to generate improved contrast for imaging studies, and examine into how biocompatible and their safety profiles are needed for preclinical or clinical work. In this context, progress in the utilization of those nanocomposites for targeted imaging and therapy are discussed. Lastly, the review will discuss the challenges and opportunities in this area will guide future studies which address these issues to allow for novel, safe, more effective MRI contrast agents with substantial diagnostic improvements within clinical environments [10].

2. MAGNETIC NANOPARTICLES

The magnetic nanoparticles has occurred as a favourable approach for medical imaging, in particular engaged as contrast agents in MRI [11]. The exclusive magnetic property and capacity to functionalize the surface has facilitated to increase MRI resolution. The different types of magnetic nanoparticles used in MRI applications will be considered with respect to their structure and properties as contrast agents. Different types of magnetic nanoparticles, superparamagnetic iron oxide nanoparticles (SPIONs), maghemite-γ-Fe_2O_3 based SPIONs are extensively studied because their superparamagnetism. This distinct property helps SPIONs to enhance MRI contrast [12].

The synthesis of SPIONs through co-precipitation have developed 8 nm sized SPIONS, with saturation magnetisation value of 80 emu/g. While, thermal decomposition and hydrothermal synthesis which provided more control over size as well morphology. The polymer coatings and ligand functionalization are critical to improve biocompatibility and targeting efficiency of the nanomaterials with regard to human tissue [13]. Cobalt ferrite nanoparticles ($CoFe_2O_4$) possess good magnetic properties such as high saturation magnetisation and dimensional stability that make them suitable for MRI applications [14]. The cobalt ferrite nanoparticles have shown promise as agents for multimodal imaging with integrated MRI/fluorescence and computed tomography (CT) [15].

Manganese-based nanoparticles such as manganese oxide (MnO) and manganese ferrite ($MnFe_2O_4$) are also investigated for their superparamagnetic prop-

erties to use them as MRI contrast agents [16]. The manganese ferrite nanoparticles showed enhanced MRI contrast and photothermal properties which enabled simultaneous cancer imaging and treatment. The ability to obtain improved relaxivity values of 12 mM^{-1} s^{-1}, positions Mn-based nanoparticles as interesting candidates that could probably advance detection sensitivity in early-stage tumour imaging. The ongoing research on the synthesis, functionalisation and varied applications of MNPs has made medical imaging namely MRI one of the most fascinating fields for such a revolutionary discovery. The ability of these agents to enhance imaging contrast, as well as provide therapeutic benefits supports a growing importance in the age of precision medicine [17].

The difference between SPIONs and cobalt ferrite nanoparticles is in magnetic saturation, coercivity and relaxivity which determine the applicability of these nanoparticles as MRI contrast enhancement agents. This is an important characteristic of SPIONs recommended for use in medical applications of NPs is based on magnetite (Fe_3O_4) or maghemite (γ-Fe_2O_3) because their small particle size demonstrates superparamagnetic activity, which in turn has high magnetic permeability but no remnant magnetism when the magnetic field is turned off. Using this property, the SPIONs can generate high T2-weighted contrast by creating varying local magnetic field that influences T2 shortening in target tissues and hence improves the contrast in the respective tissues.

Comparing SPIONs with cobalt ferrite ($CoFe_2O_4$) nanoparticles, the later exhibit higher MS and coercivity values due to presence of Co^{3+} ions. This higher magnetic saturation may in turn manifest into increased T2 relaxivity and therefore additionally improving the contrast in particular utility. But, the main problem of cobalt ferrite is its higher coercivity hence there may exist residual magnetism, an aspect that can provoke aggregation tendencies and bio compatibility concerns [18, 19].

The synthesis of magnetic nanoparticle-polymer composites can be carried out using different techniques and these techniques have their individual merits and demerits. The co-precipitation of magnetic nanoparticles from metal salts in the presence of a base followed by polymer coating is the most common and has the benefits of ease and reproducibility but lacks the ability to control the particle size distribution. The major advantage of thermal decomposition is that particle size and crystallinity can be controlled effectively and hence uniform nanoparticles are formed, but they need high temperature and toxic organic solvent with the disadvantage of safety and environmental impacts. The microemulsion process has a tight control of particle size and provides good stability but is cumbersome and difficult to optimize for large-scale production. The sol–gel synthesis of nanocomposites is characterized by high purity and homogeneity of the synthesized material, but requires longer synthesis time due to a necessity to apply the post-synthesis heat treatments for stabilization. Electrospinning electrospins webs of fibrous polymer matrices with densely packed magnetic nanoparticles, which are useful for applications demanding high surface interaction; however, it uses expensive equipment and technical difficulties in particle well-dispersedness. Both methods are useful in producing magnetic nanoparticle-polymer composites for MRI applications and have their unique strength based on the area of use, particle properties and production needs hence a variety of techniques are available to researchers [20].

3. POLYMER MATRICES FOR MRI CONTRAST AGENTS

The hybridization of magnetic nanoparticles with polymer matrices has improves the imaging efficacy as MRI contrast agents. The stabilisation of nanoparticles for prolonged use and added biocompatibility, functionality, and imaging ability are mediated by interaction with surrounding functional matrices.

3.1. Types of Polymers

3.1.1. Biodegradable polymers. Biodegradable polymers are indispensable in the preparation of MRI contrast agents, particularly for biomedical applications. Due to which these polymers can biodegrade in the body and this would allow elimination of nanocomposite after their usage, hence safe for long-time toxicity [20]. The most commonly used biodegradable polymers include polylactic acid (PLA), polycaprolactone (PCL) and poly(lactic-co-glycolic acid) (PLGA). The incorporation of degradable polymers in magnetic nanoparticle formulations enhances biocompatibility and reduces the adverse effects arising from non-degradabie materials. Their degradation products are commonly non-toxic and biocompatible for easy metabolism from the body, making them ideal candidates to design molecular-targeted MRI contrast agents that can offer precise imaging of tumours or specific tissues before subsequent clearance [21].

3.1.2. Non-biodegradable polymers. Magnetic nanoparticle-polymer nanocomposites based on non-biodegradable polymers are most commonly used in MRI applications. These polymers have excellent mechanical and stability properties, rendering them well-suited for the formulation of long-lived contrast agents. The polyethylene glycol (PEG), and polystyrene, as well as polyvinyl alcohol (PVA) are used as non-biodegradable polymers, although they contain many risks, possess a great advantage in homogeneity and dispersion stability for proper imaging performance [22]. As these polymers are modified by increasing the hydrophilicity so that nanoparticles would remain stable in biological environments, preventing NP aggregation, which could affect adversely

on imaging quality [23]. This ensures that the contrast chemicals do not lose their potency during imaging procedures.

3.1.3. Smart polymers. New types of materials called smart polymers, or stimuli-responsive polymers are used for MRI contrast agents. These polymers can change their physicochemical properties in response to a particular stimulus, such as temperature, pH, light or magnetic field. These polymers are designed to play a role as contrast agents and it respond to a certain biological conditions, thereby enhancing the contrast at specific sites [24]. This sensitivity allows the development of dynamic imaging systems that can respond to the changes in physiological parameters. This advancements could provide better diagnostic accuracy and therapeutic outcome regarding MRI techniques.

Polymer-coated or polymer functionalized magnetic nanoparticles are fabricated by placing it as core-shell or modifying the external surface area with substances. This technique improves dispersion in biological fluids, prevents aggregation and ensures the required magnetic properties for imaging [25]. Functionalisation of the polymeric shell with targeting ligands (antibodies or peptides), which allow selective binding to specific cells or organs. These polymer magnetic nanoparticles enhace relaxivity, allowing for a more sensitive imaging using MRI contrast. Secondly, they can serve as carriers to deliver therapeutics and allows the combination of both imaging and drug delivery aspects in a single dual-functional (diagnosis-treatment) system. These can be based on biodegradable, or degradability- and cytotoxicity-tuned polymer-coated magnetic nanoparticles that may have high potential as responsive targeted contrast agents for MRI [26].

The selection of polymers suitable for magnetic nanoparticle-polymer composites entails the two important parameters, biocompatibility and biodegradability, when used in MRI applications. Biocompatibility is very important since it ensures that the composites have minimal detrimental immunological and cytotoxicity response that ensures that the composite performs optimally within biological systems. Materials including polyethylene glycol (PEG), chitosan and poly (lactic–co–glycolic) acid (PLGA) are often selected due to their non-cytotoxic, non-immunogenic characteristics that allow biocompatibility with tissues and cells. Other biocompatible layers are also used to extend and possess the nanocomposite in this regions for good image resolution and distinctiveness [27].

Another critical factor affecting the choice of the polymer is biodegradability since it affects the stability and removal of this composite material from the body. Some polymers are synthesized to be biodegradable with non-hazardous byproducts; this minimizes the problems related with nanoparticle deposition and permits friendly elimination after diagnosis. This property is most desirable in clinical applications where multiple MRIs may be conducted perhaps because of some chronic condition, as it minimizes the chances of having some residual effect on tissues. Nevertheless, controlled degradation is critically important to ensure stability and avoid premature degradation that could seriously undermine the potential of a nanocomposite as a contrast agent.

The polymers property have direct impact on the nanocomposite stability and performance during MRI. Stable dispersion of the nanocomposite is enabled by biocompatibility of polymers which avoids aggregation that may affect MRI signal strength; biodegradability of polymers makes the composite safe, degrading in a controlled time manner thus improving the composite's clinical relevance. Such selection of polymers leads to more stable and high-quality images in comparison with earlier systems, allowing to follow the safety and regulation requirements for medical applications [28].

3.2. Properties Enhancing MRI Efficacy

3.2.1. Biocompatibility. Biocompatibility is an essential property of MRI contrast agents that determine the safety as well as efficacy during imaging. The presence of biocompatible polymers helps in the cellular uptake, enhances interactions with target tissues and eventually improves imaging quality [29]. Nanoparticle compositions research revealed that polymers such as polyethylene gycol (PEG) and chitosan significantly increase biocompatibility by reducing cytotoxicity. Covalent linking PEG chains through a process called "PEGylation" has reduced protein adsorption and immunogenicity, and increasing circulation half-life in blood stream. Improved biocompatibility, would improve the safety of contrast agents being used at clinical sites [30].

3.2.2. Tailored relaxation periods. Tuning the relaxation times of magnetic NPs is key towards improving their performance as a contrast agent for MRI. The selection of appropriate polymers and disposition of composite structures could also change the relaxation properties of nanoparticles [32]. By tuning nanoparticle size, coating thickness or polymer interactions this can potentially allow researchers to develop contrast agents with an optimal T1/T2 relaxivity profile for their in-vivo studies. The T1 and T2 relaxation times more accurately determining contrast for different tissue types by adjusting hydrophilic-hydrophobic segment ratio in block copolymers coated nanoparticles. The incorporation of gadolinium (Gd)-based contrast agents within polymeric scaffolds has proved to boost T1 relaxivity leading to a significant increase in tumour detectability. Relaxation times have been shown to be explicit of different tissues, and the tailored relaxation will improve diagnostic accuracy in MRI scans which has the potentiality for earlier detection or surveillance for disease [33].

3.3. Characterization Techniques

The characterization of manganese ferrite nanoparticles for MRI contrast involves DLS, TEM and MRI phantom studies which possesses profound information pertaining to the imaging ability of the valued nanoparticles. DLS is used to determine particle size distribution and zeta potential in order to determine the stability of colloids, which is critical to in vivo benefits. Research has demonstrated that manganese ferrite NPs with high zeta potential values has suffered less aggregation in biological media, which enhances distribution and stability and, therefore, the reliability of MRI signal. TEM is used to show morphology, size distribution, and distribution of the Mn ferrite particles within the polymeric phases, which is necessary for the stability of magnetic relaxivity. The reduced size variation and the uniform polymer coating thickness identified through TEM analysis are also proportional to the improvement of MRI contrast, since uniform dispersion does not hinder the imaging quality. Supporting these analyses MRI phantom studies mimic the tissue conditions to determine the T1 and T2 relaxivities that influence the contrast effectiveness of the nanocomposites. Higher T2 relaxivity in MRI phantom test of Mn-ferrite composites also confirms its potentiality of MRI contrast agents to help the researchers to tune up these new nanocomposites for in-vivo imaging purposes [34].

4. MAGNETIC NANOPARTICLES-POLYMER COMPOSITES

Nanocomposites combined the unique magnetic properties of nanoparticles with the advantages offered by polymers: they could improve imaging performance, assist in targeting delivery and provide multifunctionality. The nanocomposite particles of iron oxide or cobalt ferrite core that are stabilized by polymer matrices [35]. The surface functionalisation strategies such as site-specific moieties (antibodies, peptides) and imaging enhancers have markedly improved the performance of these formulations. The magnetic nanoparticle-polymer composites functionalised with targeting ligands have shown selective adhesion to cancer cells in some reports and improved MRI sensitivity for tumour identification. Further, the introduction of therapeutic agents within these nano-composites has opened up new prospects in offering both imaging and treatment simultaneously i.e., theranostics. This technique allows clinicians to see the tumour during targeted therapy, improving patient care [36]. Optimal integration of magnetic nanoparticles into polymer matrices is crucial in designing effective nanocomposites for MRI contrast agents. It was recently found that superparamagnetic iron oxide (SPIO) nanoparticles can be encapsulated successfully in matrices of polylactic acid, through which they are more well-dispersed and exhibit the magnetic properties required for enhanced MRI contrast [37].

The chemical bond linking the nanoparticles and polymer boosts interaction providing greater stability as well as functionality. This significantly increases the in vivo circulation time and imaging potential of magnetic nanoparticle-polymer composites tolerated on a silane-based, covalent linkage [38]. Magnetic iron nanoparticles of under 10 nm, shows increased in surface-to-volume ratio, results in higher relaxivity both for T1 and T2. Such magnetic properties are tailored using surface modifications, e.g. functionalising with carboxyl or amine groups to promote the interfacial interaction of nanoparticles-polymers. The characteristics of the polymer, such as viscosity and molecular weight also have an influence over the dispersed/stability of nanostructures within the matrix.

4.1. Targeted and Sustained Drug Release Mechanisms

One of the primary aspects for magnetic nanoparticle-polymer nanocomposites is to deliver stimuli-responsive imaging or therapeutic agents in different applications. Thermoresponsive polymers such as poly(*N*-isopropylacrylamide) (PNIPAMs) may be tailored to release these contrast agents in response to higher temperatures. The drug release through the heat treatments was involved in hyperthermia, but using PNIPAM-based nanocomposites has exhibited a dual imaging and also therapeutic advantages [39]. The PNIPAM-functionalized magnetic nanoparticles has showed a temperature-triggered drug release and demonstrated its application as MRI-guided therapeutic strategy. In a similar manner, pH-responsie polymers may improve the release of drugs in cancerous tumour environments with low regional pH levels compared to normal tissues. The targeting approach improves the imaging and therapeutic efficacy by focusing the effect of treatment with minimal collateral damage to normal tissues [40].

The magnetic nanoparticle-polymer composites, functionalised with antibodies against cancer-specific markers (e.g., HER2/EGFR) have significantly improved tumour targeting and imaging contrast. The chemical utility of polymer nanocomposites is foreseen to be related with the magnofeatic targeting. Nanocomposites guided with the aid of an external magnetic field to the specific sites in biological systems has increased the localisation and minimise inward systemic toxicity. The presence of magnetic field, during MRI scanning (external or internal) has enhances localization of the particles at tumour sites has enhanced imaging contrast [41].

4.2. Functionalization Approaches

4.2.1. Conjugation of targeting ligands. Functionalizing the surface is a main strategy for enhancing magnetic properties of nanocomposites for its potential applications in MRI. A targeting ligand is attached to the surface of magnetic nanoparticles; it can then bind

selectively to specific cells or tissue. Common targeting ligands include antibodies, peptides or small molecules that can recognize the upregulated receptors on target cells. The sol–gel process is a bottom up approach that provides an excellent route to achieve this functionalisation. In this process, the colloidal suspension (sol) is created by resuspend solid nanoparticles in a monomer solution. As the aging process proceeds, a three-dimensional interconnecting network (gel) is formed. This method has been recently engaged in the synthesis of magnetite (Fe_3O_4) nanoparticles embedded within a polymer matrix and further functionalized with specific targeting ligands such as folic acid or RGD peptides [42]. These modifications increased the cellular uptake and imaging contrast in cancerous tissues, thereby showing that sol–gel method has a great potential for developing advanced MRI contrasting agents.

Focused manner, spatially selective delivery of magnetic nanoparticle can effectively reduce the dosage necessary to label tumor cells and minimize off-target toxicity lest side effects, thus such could increase security and effectiveness for MRI treatment (43). The anti-HER2 antibody-conjugated magnetic nanoparticles had significantly higher uptake in HER2-positive breast cancer cells compared to non-targeted nanoparticles for MRI enhancement. The surface coatings can improve the biocompatibility of nanocomposites which results better circulation times and reduced immune responses. The most efficient surface-coating approach has been demonstrated using polyethylene glycol (PEG) podocytes. The hydrophobicity of GEN and SPIOs, PEGylation reduces protein adsorption decreasing their circulation time in blood stream which is indispensable for better functionality when used as MRI contrast agents for therapeutics. Longer circulation times may also lead to longer imaging times such, resulting in improved anatomical illustration as well [44].

4.2.2. MRI Contrast enhancing modifications. MRI contrast agents have progressed since the introduction of Gd- based agents has improved MRI visibility of soft tissues by T1 contrast. Yet, these agents raised safety concerns and when used for long-term retention into kidneys-compromised patients, the search for other materials ensued. The superparamagnetic iron oxide nanoparticles (SPION) advanced T2 – weighted imaging and similarity in liver and lymph node contrast imaging. However, main challenges of stability, aggregation or biocompatibility significantly hampered their broader implementation.

Over the past few years, the magnetic nanoparticle-polymer nanocomposites have come up as an innovative invention that is highly versatile for the improvement of MRI technology due to high relaxivity and targeting characteristics of the magnetic nanoparticles as well as good stability and processes of the polymer matrices. Including not only enhancing image contrast and resolution, but also modifying the functional characteristics such as site-selective adhesion and stimulated drug discharge. Polymer conjugation resolves past challenges through improving stability and biocompatibility, reducing the aggregation potential, and increasing circulation time. This evolution demonstrates a considerable development, placing magnetic nanoparticle–polymer composites on the cutting edge of MRI CA technology with applications in diagnostic imaging and potentially in the field of theranostics for cancer treatment.

Hybrid magnetic nanoparticles composed of nickel and iron oxide have demonstrated the largest improvements in MRI contrast due to their high magnetism, with discussed longitudinal relaxivity profiles. The incorporation of specific functional moieties can increase interactions with protons in surrounding tissues to alter relaxation times and enhance contrast. The introduction of carboxyl or hydroxil groups into the surface of magnetic nanoparticles, so improving their properties for T1 and/or a dual effect (T1/T2) as a function consequence by accessibilizing H NMR water molecules closer to these particles. The amino group-modified dextran-coated iron oxide nanoparticles for increases in T2 relaxivity and signal enhancement on MRI [45]. Table 1, summarize the magnetic nanoparticles and polymer magnetic nanomaterials properties, applications and relevant references for both MRI contrast agents; the significant index was given as to their therapeutic outcome.

5. POTENTIAL MECHANISMS OF CONTRAST ENHANCEMENT IN MRI

The magnetic resonance imaging (MRI) contrast enhancement is inherently linked to the alteration of proton relaxation times in tissues. Magnetic nanoparticles can enhance contrast mechanisms when incorporated into polymer matrices [55]. MRI scan takes the advantage of radiofrequency pulse alters the alignment of protons emit energy that is detected by the MRI machine and retain to their original state. This procedure is characterized by two main relaxation times.

T1 is the time it takes for protons to realign with and parallel the magnetic field after they have been disturbed. The T1-weighted imaging was utilized for obtaining anatomical images with a good contrast between fat and water by measuring the longitudinal relaxation time of spins in tissues (Tl), and the use of contrast agents will decrease T1 times,by allowing more signal coming from specific area to generate brighter pictures. Gadolinium-based agents for T1-shortening are widely known, and efficacious Gd-chelates with improved relaxivity properties [56].

T2 is the time required for protons to lose phase coherence between neighboring spins of adjacent protons after an RF pulse has tipped aligned nuclei away

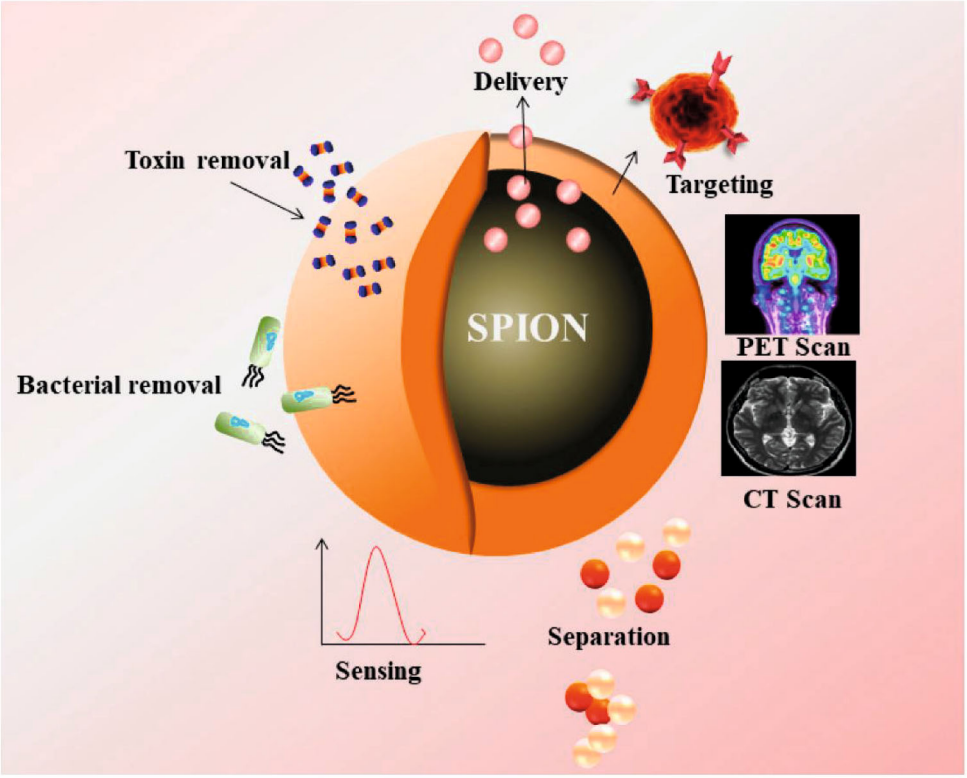

Fig. 1. Schematic diagram illustrates SPIONs' role in enhancing imaging precision and therapeutic outcomes through magnetic targeting and controlled release mechanisms [10].

from Boltzmann Equilibrium. T2 contrast agents darken images in T2-weighted scans by reducing the normally increased signal profile of tissue with lengthened transverse relaxiation times. Superparamagnetic nanoparticles induce strong dephasing of protons, thereby greatly shortened T2 relaxation times and increased contrast in particular tissues. This was realised by a recent study demonstrating that iron oxide nanoparticles (IONPs) are excellent T2-weighted MRI contrast agents, with smaller IONP s being considerably more relaxive than their larger counterparts resulting in strongly enhanced image contrasts [57].

Magnetic nanoparticles influence the relaxation times of proximal protons via multiple mechanisms. Magnetic nanoparticles generate localised magnetic fields that perturb neighbouring proton performance. Various types of magnetic particles and their structural has largely affect the relaxation dynamics of T1 or T2 relaxation times. The enhanced in local magnetic field effects produced by the combination of magnetic nanoparticles with a polymer matrix gave rise to considerable T2 contrast for Liver imaging. The physical state and composition are important parameters that define their magnetic characteristics [58, 59].

6. MAGNETIC RESONANCE IMAGING APPLICATIONS

The use of magnetic nanoparticle-polymer nanocomposites as MRI contrast agents has established a new era in imaging technology. Many pre-clinical studies and the clinical applications demonstrate the potential of these systems to enhance image quality and provide specialised imaging capabilities. Preclinical studies help to fill the gap between bench research and human application, providing valuable evidence of effectiveness as well safety for newly developed MRI contrast agents. Various methods has been used by the scientist to measure retrieval effectiveness of magnetic nanoparticle-polymer nanocomposites versus conventional contrast agents [60].

6.1. In Vivo Imaging Studies

The vivo imaging studies are an indispensable tool to understand the fate of magnetic nanoparticle-polymer nanocomposites inside biological systems. Several key factors such as fluorescence imaging, gamma scintigraphy or magnetic resonance imaging techniques are commonly used as options for tracking the distribution of nanocomposites in the organism [61]. Understanding the pharmacokinetics, biodistribution

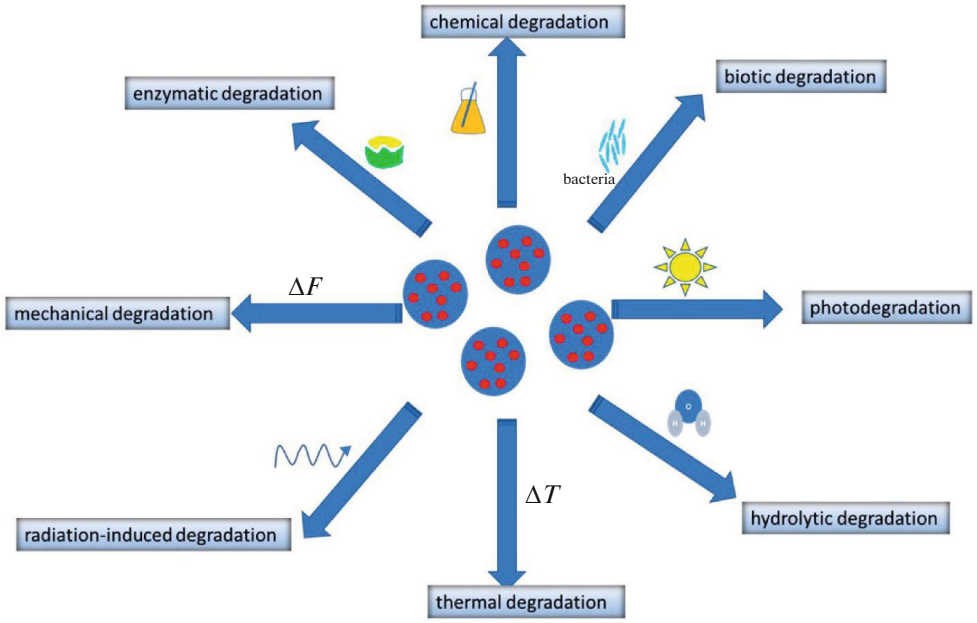

Fig. 2. Possible mechanisms of polymeric nanoparticle degradation, illustrating various pathways including hydrolysis, enzymatic degradation, oxidation, and pH-triggered cleavage [21].

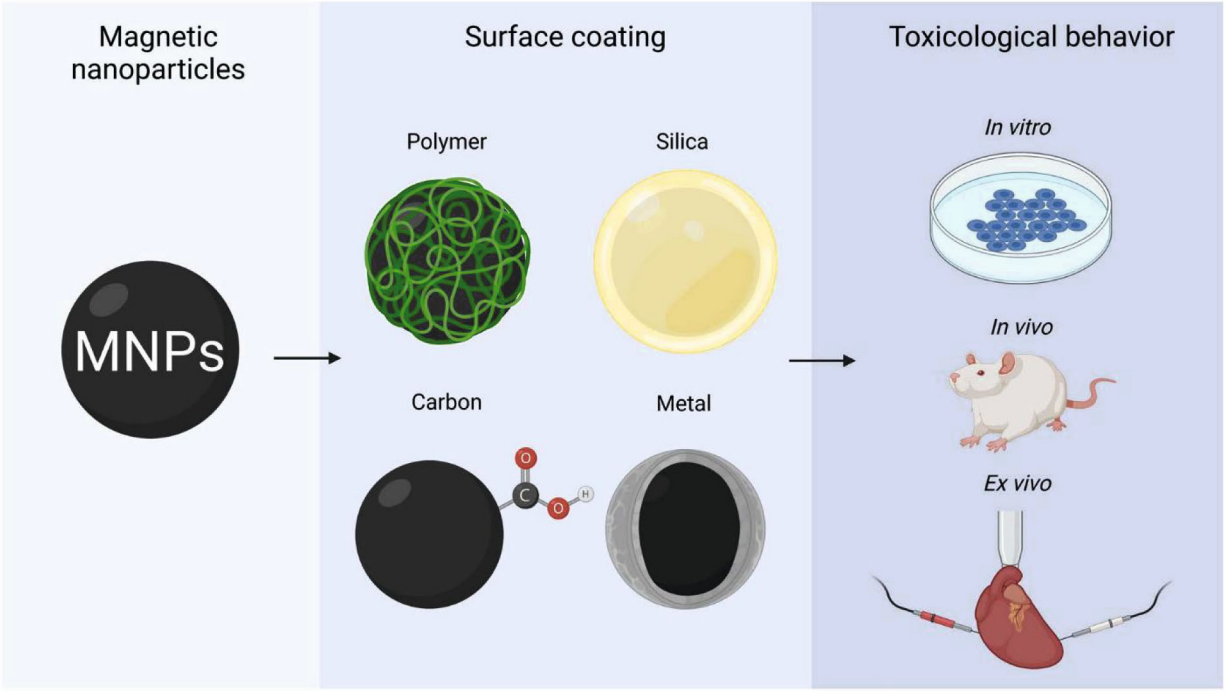

Fig. 3. Schematic illustration of magnetic nanoparticles (MNPs) and their surface coatings, including polymer, silica, carbon, and metal, influencing their behavior in toxicological evaluations [44].

and elimination of different contrast agents is essential for evaluating their effectiveness as well as safety profiles. The magnetic nanoparticles mostly accumulate in the liver and spleen, but a significant part of them colocalised to tumour sites which could be targeted for imaging [62]. MRI imaging with localised drug delivery helps the clinicians to image tumor. Animal model experimental studies also highlight the need for toxic-

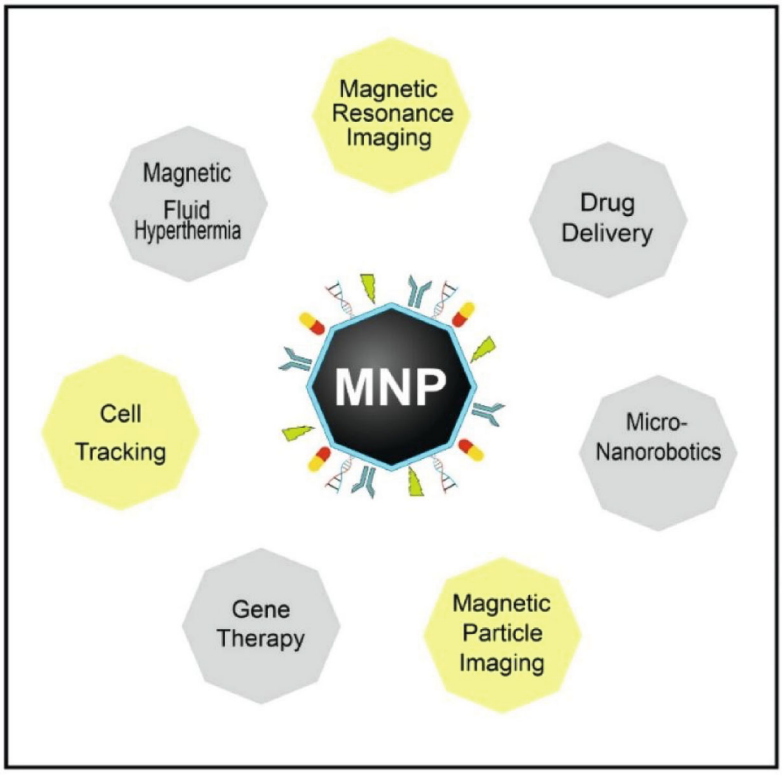

Fig. 4. Biomedical applications of magnetic nanoparticles (MNPs) leveraging their unique magnetic properties, small particle size, and surface functionalization for both diagnostic imaging (yellow) and therapeutic purposes (grey) [60].

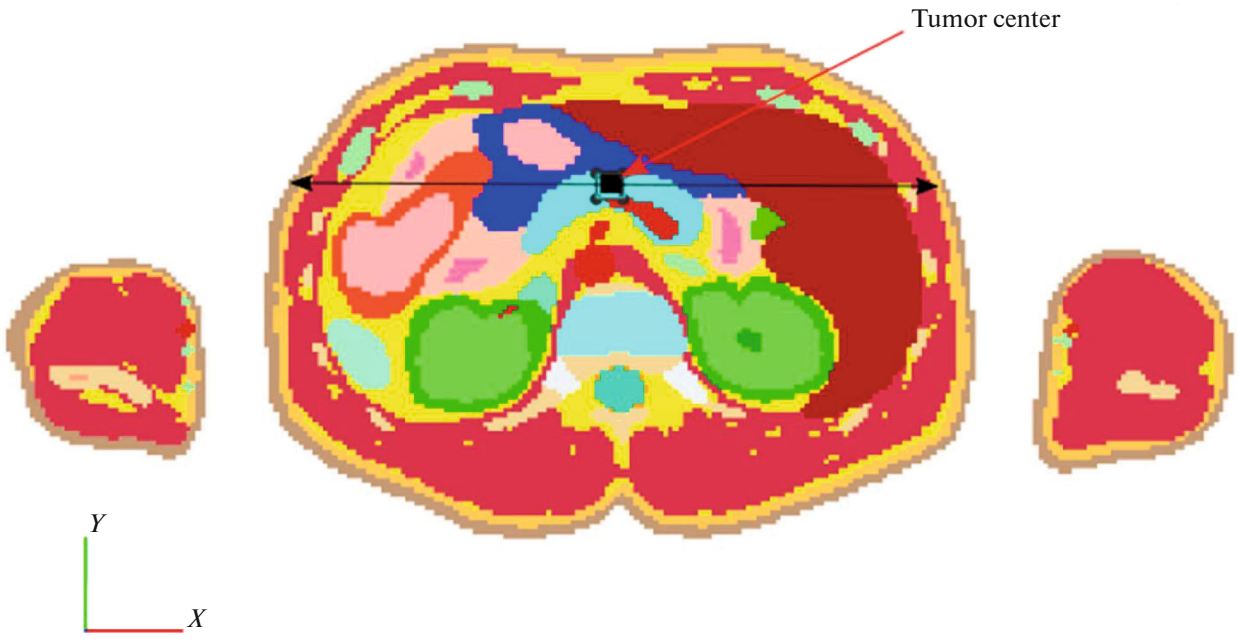

Fig. 5. Representation of magnetic nanoparticles (MNPs) with various surface coatings (polymer, silica, carbon, and metal) and their corresponding toxicological behavior studied across different platforms (in vitro, in vivo, and ex vivo). Surface modifications enhance the functionality of MNPs in biomedical applications while toxicological assessment provides insights into their safety and biocompatibility [64].

Table 1. This table integrates the key properties and applications of magnetic nanoparticles (MNPs)

Nanomaterial	Property	Details	Applications	Reference
Magnetic Nanoparticles (MNPs)	Multifunctional potential agent	MNPs can be utilized in both diagnostic and therapeutic roles in cancer, facilitating MRI imaging, drug delivery, and hyperthermia	Employed in cancer therapy and diagnostics, including MRI imaging and hyperthermia	[46]
Lipid-Based Nanoparticles	Contrast-enhanced MRI capabilities	These nanoparticles enhance the MRI contrast, which improves the sensitivity of molecular imaging for cancer detection	Primarily used for contrast-enhanced MRI and molecular imaging in cancer diagnosis	[47]
Magnetic Nanoparticles (MNPs)	Diagnostic and therapeutic applications	Functionalized MNPs are effective in cancer therapy, improving imaging and drug delivery methods	Applications include MRI imaging, drug delivery systems, and hyperthermia in cancer therapy	[48]
Engineered Magnetic Nanoparticles	Improved MRI contrast and detection methods	Engineered MNPs enhance MRI contrast and improve detection sensitivity, leading to better diagnostic accuracy	Used to enhance contrast in MRI, increasing diagnostic capabilities for cancer detection	[49]
Functional Nanoparticles	MRI contrast enhancement	These nanoparticles are specifically designed to improve MRI contrast, making imaging clearer and more informative	Applied in MRI to provide clearer and more accurate imaging results	[50]
Nano MRI Contrast Agents	High-resolution imaging capabilities	Small-sized nanoparticles are effective MRI contrast agents that provide safer and higher-resolution imaging than larger particles	Utilized in MRI for high-resolution imaging, enhancing diagnostic accuracy	[51]
Magnetic Nanoparticles (MNPs)	Cancer diagnosis, drug delivery, and treatment	MNPs serve multiple roles in cancer management, from diagnostic imaging to therapeutic applications like hyperthermia	Used for cancer diagnosis, drug delivery, and treatment methods, including magnetic hyperthermia	[52]
Iron Oxide Nanoparticles	Targeted imaging and diagnostics	Iron oxide nanoparticles enable targeted imaging capabilities, enhancing the specificity of cancer diagnostics	Employed for targeted cancer imaging and diagnostics, particularly using MRI	[52]
Magnetic Nanoparticles	Ultrahigh-resolution imaging	These nanoparticles facilitate ultrahigh-resolution susceptibility-weighted imaging, providing detailed visualization of tumor vascular structures	Advanced imaging of brain tumors through enhanced susceptibility-weighted MRI	[54]

ity analysis to avoid any potential toxicological effects, immunogenic responses as well as adverse events associated with nanocomposites in vivo.

6.2. Clinical Applications

The potential results from preclinical studies have enabled different clinical usages of magnetic nanoparticle-polymer nanocomposites by means of MR imaging [63]. At present, Clinical case studies have shown the efficacy of magnetic nanoparticle-polymer or MNP Clinically, breast cancer patient and glioblastoma studies show increased image quality as well tumor diagnosis with respect to gadolinium-based contrast agents. Better visualisation leads to better

tumour characterisation, staging and treatment planning. Indeed, some ongoing clinical trials are assessing multifunctional nanocomposites for MRI combined with other imaging modalities on the same particle including fluorescence and computed tomography (CT). Multimodal approaches for seeking to deliver more complete diagnostic information, hence improving concomitant patient care and treatment planning [64]. Preliminary studies have indicated that combining MRI with fluorescence imaging could enable the identification of very small tumors not visible on an MR image alone. Magnetic nanoparticle-polymer nanocomposites are being explored for local therapy delivery (chemo and radiotherapy) under real-time imaging translation. The fusion of AI into such an approach makes therapy more efficient and helps care providers track therapeutic outcomes, ultimately managing patients in a better way.

7. CHALLENGES AND LIMITATIONS

The magnetic stability and biocompatibility in the preparation of magnetic nanoparticle-polymer composites have paved way to new approaches in the utilization of such material as contrast agent in MRI in a clinical manner. Stability is one of the biggest challenges in nanoparticles applications, and this is mostly addressed by using surface functionalization where chemical moieties such as carboxyl, amino or PEG can be incorporated to address issues of aggregation. Concerning these features, PEGylation has gained interest mainly because of the increased colloidal stability, minimized non-specific protein binding, and increased circulation time in physiological environment needed for better imaging properties. Accomplished work has revealed that SPIONs can be effectively PEGylated to enable enhanced circulation in the systemic circulation with decreased immunogenicity, primarily enhancing their application in imaging and therapy [65].

Another promising approach for the enhancement of stability of nanocomposites can be represented by core-shell structures where the biocompatible shell is formed around the magnetic core. This design safeguards the magnetic core from oxidative decay while at the same time improving the life and efficiency of the nanoparticles. The preparation and synthesis of different nanocarriers point out that polydopamine can be used as a shell material, providing enhanced biocompatibility of the nanoparticles as well as functionalization of the nanoparticles for targeted delivery that enhances the stability and reduces susceptibility to degradation of the nanoparticles. In addition, the encapsulation of the polymer in hydrogels or other biodegradable systems has been proposed to protect nanoparticles from external environments, these include pH changes, ion concentrations and temperature variations which are essential to sustain the DP nanoparticles efficiency in the biological environment [66].

From biocompatibility perspective, the PEG, PVA and poly(lactic-co-glycolic acid) (PLGA) coatings has proved highly effective in reducing toxicity and increasing cell camaraderie. These coatings can be designed to address the needs of an application, for example, cancer imaging that incorporative bio-responsive materials such as pH sensitive polymers. New advances in the conjugation of specific targeting moieties like antibodies and peptides have enhanced the exquisite targeting capabilities of these multifaceted nanocomposites while decreasing systemic toxicity to healthy tissues. This targeted functionalization not only increases biocompatibility but also amplifies the uses of these nanocomposites; particularly in controlled drug delivery and molecular imaging [67].

As a result of green synthesis methods, there has been a research into the synthesis of less toxic reagents which are harmless or biocompatible when synthesizing nanoparticles from chemical solutions. The application of plants extracts, microbial system and other GREEN processes has attracted interest because they offer methods of producing nanoparticles that have few side effects and high safety measures. The newer articles have given better reports in synthesizing the magnetic nanoparticles from plantation extract in green synthesis which improves the biocompatibility and reduces the cytotoxicity of the composite thus providing good future for the medical nanomaterials.

Still, there are still barriers in regulation and production of AM parts. Current works of standardization organizations such as the FDA and EMA are oriented at creating standard procedures for the synthesis, characterization, and testing of magnetic nanoparticle-polymer composites. This is significant for making the experiment reproducible, accrete, seared for clinical uses. In addition, the methods for large scale production, including micro fabrication for creating nanocomposites are on the way of being established with a view of standardization for clinical applications. They afford a better control of size and size distribution of particulates and it is an ideal characteristic for stability and compatibility required in clinical applications [68].

In the course of furthering the study of these challenges, the composite has shown capability to become further established as a highly stable, biocompatible, and efficient tool for MRI applications. Advancements made in the areas of surface modification, drug conjugation and green syntheses, together with continuous attempts in crossing the barriers of FDA approval and up-scaling of these nanocomposites ensure a bright future for clinical diagnosis and therapy especially for cancer diagnosis and therapy.

8. FUTURE DIRECTION

The concept of magnetic nanoparticle-polymer nanocomposites can provide a novel development to MRI CA by improving image resolution and introducing developments in multiply modal imaging. New green 'green' chemistries of synthesizing magnetic nanoparticles employing bio resources such as plant extracts or microbial systems provide useful strategies for the preparation of such particles with a sustainability angle with regard to their intended biomedical uses while at the same time retaining optimal characteristics. Similarly, a promising avenue of investigation for future work is the synthesis of stimuli-responsive magnetic nanoparticles capable of targeted drug release together with imaging in response to certain biological cues (for instance, pH, temperature, enzymes), which could improve the performance of theranostic cancer treatments [69].

The advance in polymer technology also has a significant contribution towards power systems development. Long-term stable nanocomposites can be achieved by incorporating conductive and biodegradable polymers in the hybrid polymer matrices, moreover, the stimuli responsive hydrogels might enhance MRI contrast and stimuli triggered release of drugs. Further increase of nanoparticle relaxivity in the polymer matrices could lead to better suited MRI contrast agents for particular imaging purposes.

The MRI can be combined with another imaging modality like CT or fluorescence to improve the diagnostic accuracy in an organ multimodal imaging is one of the futuristic directions in diagnosis. Magnetic nanoparticles may be used as ideal tumour-targeting agents which, when used in tandem with imaging techniques such as SPECT or PET that may be performed in real-time, would increase the diagnostic accuracy. Such techniques in magnetic nanoparticle – polymer composites may enhance disease diagnosis and intervention results by providing desirable anatomic and physiologic information required for therapeutic procedures [70].

9. CONCLUSIONS

The magnetic nanoparticle-polymer nanocomposites (MSNPNs) are considered as potential MRI CA for using them in gaining image efficiency and accuracy. This section provides essential results and recommendations for future growth of these composites in medical imaging for use. Promising results show that MSNPNs, in particular those containing SPION and cobalt ferrites, achieve superior relaxivities to MRI conventional contrast media, which result in better image contrasts and resolution. In addition, polymer functionalization ensures specific targeting on tissues or cells resulting in aconcentration of the nanocomposites in the targeted tissues or cells which reduces on the toxicity hence enhance safety on the thoroughly therapeutic. This approach is particularly useful for tumor imaging and multi-modal imaging paradigms, as is evidenced by emerging proof of concept, preclinical, and initial clinical observations.

Although the above-mentioned nanocomposites are having immense potential, key issues related with stability and biocompatibility that are necessary for clinical applicability are still defying key developments. Thus, next studies should be aimed at improving the formulation to resolve stability problems, allowing the safe transition of MSNPNs from basic research to clinical applications in the future. It is crucial to solve these challenges in order to understand the whole potential of MSNPNs as stable MRI contrast agents which can enhance diagnostic performances and therefore patients' lives.

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CONFLICT OF INTEREST

The authors of this work declare that they have no conflicts of interest.

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