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Integration of magnetic nanocomposites into biomedical imaging platforms

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A B S T R A C T

The integration of magnetic nanocomposites into biomedical imaging platforms is of importance due to a transformative approach to disease diagnosis and monitoring. This review discusses a thorough overview of magnetic nanocomposites, describing their types, structures, magnetic properties, synthesis methods, and surface functionalization strategies. Moreover, their applications across several imaging modalities, including MRI, MPI, CT, PET, and optical imaging, are assessed, showing their multifunctionality in terms of enhanced sensitivity and specificity in detecting cancer, neurological, and cardiovascular conditions. Recent developments in the design of bimodal and emerging trends, such as smart and targeted nanocomposites for theranostics, as well as the role of artificial intelligence in image analysis, are discussed, highlighting breakthroughs in real-time diagnostics and personalized medicine. Furthermore, this review emphasizes the potential to accelerate clinical translation and transform biomedical imaging through innovative nanotechnologies.

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1. Introduction

Nanotechnology is a multidisciplinary field involving the description of materials at the nanoscale, typically ranging from 1 to 100 nanometers [1]. In the field of biomedicine, nanotechnology enables the design of nanoparticles and nanocomposites that can interact with biological systems at the molecular and cellular levels, offering groundbreaking methods in diagnostics, imaging, drug delivery, and therapy [2]. Nanocomposites display outstanding potential for early cancer diagnosis and precise imaging. Utilizing various imaging techniques alongside fluorescence imaging in nanocomposites enables the development of contrast agents that suggest improved specificity and sensitivity [3, 4]. Magnetic nanoparticles (MNPs) are classified into magnetic nanocomposites, metal oxides, and pure metals. In order to make MNPs effective as nanocarriers for therapeutic applications, they need to show adequate bioactivity without inducing inflammation or cytotoxicity [5]. Among the different types of magnetic nanoparticles, only iron nanoparticles, mainly in their two oxidation states, magnetite and maghemite, fulfil these criteria. Iron is abundant in various organs such as the liver, spleen, and heart, and is essential for the structural integrity of vital biological molecules like hemoglobin, myoglobin, and ferritin, confirming their biocompatibility [6-8]. Incorporating magnetic nanocomposites into biomedical imaging platforms uses their distinct magnetic features and multifunctionality to increase diagnostic efficiency, especially in techniques such as magnetic resonance imaging, fluorescence imaging, and multimodal imaging systems [9, 10]. Combining magnetic nanoparticles with fluorescent entities creates multifunctional nanocomposites that enable bimodal imaging simultaneous MRI and fluorescence microscopy. These "two-in-one" nanocomposites facilitate real-time cell tracking, bioseparation, and multimodal diagnostics, enhancing sensitivity and specificity. Challenges such as fluorescence quenching by magnetic cores are addressed by innovative synthesis methods and surface engineering [11]. The up-to-date advancements in molecular diagnostic imaging devices such as traditional X-ray radiographs, ultrasonography, Computed Tomography (CT), Magnetic Particle Imaging (MPI), Positron emission tomography (PET), Single Photon Emission Computed Tomography (SPECT), and Magnetic Resonance Imaging (MRI) are helping clinicians accurately diagnose a range of injuries and illnesses [12, 13]. This integration requires crafting nanocomposites with a magnetic core and biocompatible surface coatings, which can be tailored with targeting ligands, fluorophores, or drug agents. This adaptable method allows for the targeted imaging of particular tissues or disease markers, boosting specificity while minimizing side effects [14]. Recent developments in the synthesis and surface functionalization of magnetic nanocomposites reveal their potential as versatile imaging agents. These materials can be engineered to exhibit strong superparamagnetic properties and can be functionalized to improve their biocompatibility and targeting capabilities [15, 16]. For instance, magnetic-fluorescent Fe_3O_4 quantum dot composites have been developed for bimodal imaging, which shows promise for both in vivo and in vitro applications [17, 18]. Furthermore, research has shown that multifunctional magnetic gold nanocomposites (MGNCs) enable simultaneous cancer imaging and therapy. These nanocomposites serve as effective MRI contrast agents and hyperthermal therapeutic platforms, demonstrating targeted uptake and dual functionality in epithelial cancer treatment [19]. In this review, we aim to explore the integration of magnetic nanocomposites into various biomedical imaging platforms, highlighting their unique properties and potential applications. By examining the fundamental aspects of magnetic nanocomposites, including their synthesis, surface functionalization, and biocompatibility, we will provide insights into how these materials enhance imaging modalities such as MRI, MPI, CT, PET, and optical imaging. Furthermore, we will discuss their applications in diagnostics and monitoring, particularly in cancer detection, neurological imaging, and real-time cellular analysis. Our investigation will also address future directions, including the development of smart nanocomposites and the role of artificial intelligence in imaging interpretation, ultimately paving the way for clinical advancements in this promising field.

2. Magnetic nanocomposites: Fundamentals

2.1. Types and structures

Magnetic nanocomposites are multi-component materials that combine nanosized magnetic particles with organic or inorganic matrices to achieve enhanced magnetic and functional properties [20, 21]. The novel nanocomposites combine various materials, including liquid crystals, silica, gels, renewable polymers, carbon, and magnetic particles. They hold significant applications in medical diagnosis, therapy, catalysis, and separation. These nano-carriers include nanofibers, spherical nanoparticles nanosheets, nanotubes, and highly porous nanocomposites [22]. The domain of magnetic nanocomposites encompasses a wide array of diverse materials and material combinations, along with an extensive range of applications, spanning from technical fields to biomedical uses applications. Common structural types include core–shell structures, where magnetic nanoparticles such as Fe_3O_4 are coated with shells like silica, polymers, or noble metals such as gold to provide chemical stability, biocompatibility, and surface functionality. More complex structure include yolk–shell and Janus particles; in yolk–shell structures, the magnetic core is separated from the shell by a void, while Janus particles exhibit asymmetric surface properties, enabling multifunctionality [20], shown in Fig. 1. Polymer-based nanocomposites consist of magnetic nanoparticles dispersed within polymer matrices, where uniform dispersion critically affects mechanical and magnetic properties [23]. Additionally, template-based nanocomposites involve magnetic nanostructures deposited within porous templates, such as porous silicon, allowing precise control over the shape, size, and spatial arrangement of the magnetic phase [24]. The morphology and structure of these composites strongly influence their magnetic behavior and application potential.

2.2. Properties and behavior

The magnetic properties of nanocomposites depend on the size, shape, distribution, and interaction of the magnetic nanoparticles within the matrix [27]. Nanocomposites may exhibit ferromagnetic hysteresis or superparamagnetic behavior without remanence, depending on particle size and composition. Magnetic anisotropy, influenced by shape anisotropy such as elongated nanowires and spatial arrangement within templates, affects coercivity and remanence [28].It is shown that the magnetic iron oxide nanoparticles include superparamagnetic iron oxide nanoparticles (SPIONs), which have gained attention due to their ability to load biologically active agents for various applications [29]. Magnetite@silica nanoparticles exhibit excellent biocompatibility, making them suitable for biomedical applications. They serve as outstanding contrast agents in imaging studies, particularly in cellular MRI. Their magnetic properties enhance image contrast, allowing better visualization of cellular structures and processes (Fig. 2).

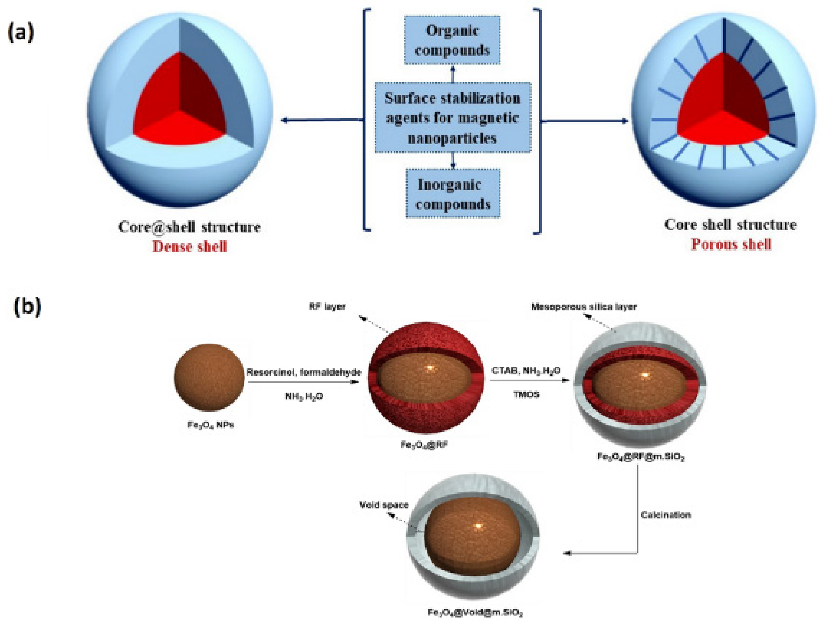

Fig. 1. (a) Core–shell structures [25], (b) Yolk–shell structure of magnetic nanocomposites [26].

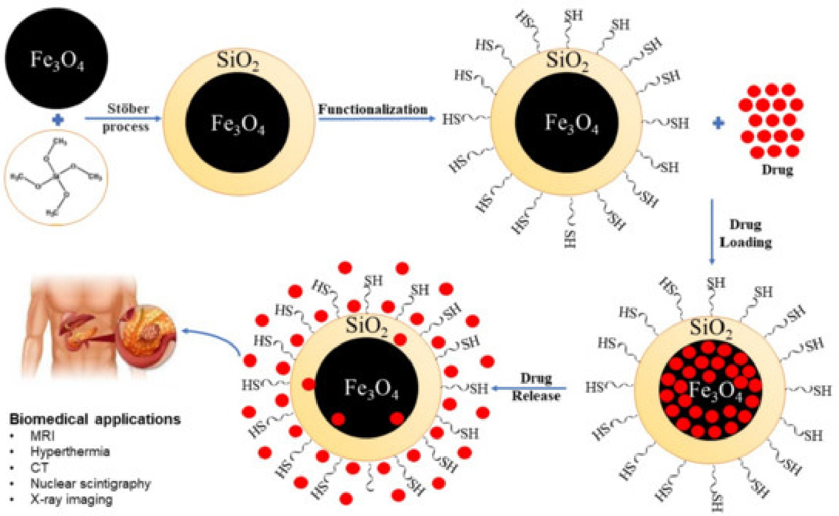

Fig. 2. Synthesis of Magnetite@silica nanoparticles [25].

Magnetic coupling between adjacent nanoparticles or nanostructures also plays a critical role; controlling morphology to reduce coupling can increase coercivity. Furthermore, the magnetic properties such as coercivity and remanence vary with temperature, influenced by particle size and magnetic domain structure. These properties can be finely tuned by controlling synthesis parameters and composite fabrication [30].

2.3. Synthesis techniques

Currently, bottom-up chemical synthesis methods are used to create inorganic nanoparticles for biomedical purposes. This technique involves the chemical assembly of small atoms and molecules through nucleation and growth processes, culminating in the formation of larger aggregates and eventually nanoparticles. Furthermore, bottom-up techniques can be categorized into hydrolytic and non-hydrolytic synthetic routes, depending on the type of solvent used [31]. Magnetic nanocomposites are synthesized using various chemical and physical methods tailored to achieve desired structures and properties. Co-precipitation is a widely used chemical method to produce magnetic nanoparticles, which are often subsequently coated or embedded within matrices. Sol-gel and chemical deposition techniques enable the formation of coatings or shells on magnetic cores to create core–shell structures. Electrodeposition into templates allows magnetic metals like nickel or cobalt to be deposited into porous silicon or alumina templates, forming nanowires or particles with controlled shape and arrangement. Physical methods such as laser ablation or thermal decomposition are also employed to produce nanoparticles with controlled size and crystallinity. The choice of synthesis method influences particle size, crystallinity, surface chemistry, and ultimately magnetic behavior. Guo et al.[32] showcased an easy and affordable method for producing a unique form of magnetite: monodisperse superparamagnetic single-crystal magnetite nanoparticles that feature a mesoporous structure (MSSMN). This is achieved via a straightforward solvothermal process, opening up exciting possibilities in drug delivery applications. Similarly, Tseng et al. [33] developed a theranostic platform integrating MRI and computed tomography (CT) capabilities, utilizing pH-sensitive nano-carriers to enhance drug delivery alongside imaging potential, which illustrates the effective synergy between drug delivery and imaging technology. Moreover, Hui et al. [34] prepared core-shell nanoparticles (NPs) of silica-coated magnetite (Fe_3O_4@SiO2) with controlled silica shell thicknesses via a modified Stöber method, utilizing 20 nm hydrophilic Fe_3O_4 NPs as seeds.

Roca et al. [34] employed the sol-gel method for the coating of silica on maghemite nanospheres. The literature presents numerous studies on micro-emulsion and reverse micro-emulsion techniques that illustrate silica coating methods for iron oxide. These synthesis approaches provide considerable benefits in producing specific nanoparticles and hold important implications for biomedical applications.

2.4. Surface functionalization

Surface modification of magnetic nanocomposites is critical for enhancing stability, dispersibility, and compatibility with biological systems. Polymer coatings such as polyethylene glycol (PEG) or polystyrene improve colloidal stability and provide functional groups for further conjugation [35].

Silica and noble metal shells, like gold, protect magnetic cores from oxidation and enhance biocompatibility, enabling biofunctionalization. Attachment of biomolecules such as antibodies or peptides allows targeted biomedical applications including drug delivery and imaging [36]. Controlling surface chemistry is essential for optimizing environmental or biological media interactions. These surface treatments significantly expand the applicability of magnetic nanocomposites in fields such as biomedicine and environmental remediation. One promising strategy for synthesizing functionalized magnetic nanocomposites involves the use of metal-organic frameworks (MOFs) that can integrate magnetic functionality with therapeutic and diagnostic capabilities. Gao et al. [37] reported on the synthesis of a nanoscale MOF that exhibits exceptional biocompatibility and strong magnetic resonance imaging (MRI) capability, along with targeted drug delivery properties.

3. Biomedical imaging modalities

With continuous research aimed at improving their design for increased multifunctionality, specificity, and sensitivity in clinical diagnostics and theranostics applications, magnetic nanoparticles particularly those based on iron oxide are frequently employed to improve contrast and enable targeted imaging. The main benefits, drawbacks, underlying mechanisms, and illustrations of magnetic nanocomposites utilized in MRI, CT, PET, MPI, fluorescence, and multimodal imaging are presented in Table 1.

Table 1
Biomedical imaging modalities.

Imaging modality	Advantages	Disadvantages	Mechanisms	Examples of magnetic nanocomposites	Refs.
Magnetic resonance imaging (mri)	• High spatial resolution and non-invasive imaging • Magnetic nanoparticles (mnps) enhance contrast at cellular/molecular levels • Tunable magnetic properties and surface chemistry allow targeted imaging • Can be combined with therapeutic delivery (theranostics)	• Contrast depends on nanoparticle composition, size, surface properties, and aggregation • Requires careful nanoparticle design for stability and biocompatibiliy	• Based on interaction of magnetic field with tissue protons • Mnps alter relaxation times (T2, T2*) of nearby nuclei, enhancing contrast	• Iron oxide nanoparticles coated with organic ligands or polymers for improved stability and targeting • Dual-modal MRI probes combining magnetic nanoparticles with other imaging agents	[31, 38-41]
Magnetic particle imaging (mpi)	• High sensitivity and specificity for magnetic nanoparticles • High temporal and spatial resolution • Quantitative imaging without tissue attenuation • Suitable for functional and quantitative imaging	• Newer modality with limited clinical availability • Requires specialized nanoparticle tracers and reconstruction algorithms	• Detection of nonlinear magnetization response of magnetic nanoparticles under oscillating magnetic fields	• Iron oxide nanoparticles as tracers for MPI to detect and quantify nanoparticle distribution in vivo	[38, 42]
Computed tomography (ct)	• High spatial resolution anatomical imaging • Magnetic nanocomposites can enhance contrast	• Lower sensitivity for molecular imaging compared to MRI or PET • Radiation exposure	• X-ray attenuation differences enhanced by nanoparticles containing high atomic number elements	• Magnetic nanoparticles combined with CT contrast agents for multimodal imaging (e.g., MRI/CT)	[39]
Positron emission tomography (pet)	• High sensitivity for molecular and functional imaging • Quantitative imaging of tracer distribution	• Low spatial resolution • Requires radioactive tracers	• Detection of gamma rays from positron-emitting radionuclide-labeled nanoparticles	• Magnetic nanoparticles labeled with PET isotopes for MRI/PET multimodal imaging	[43]
Optical Imaging and Fluorescence	• High sensitivity for molecular imaging • Real-time imaging capability • Useful for cellular and molecular level studies	• Limited tissue penetration depth • Autofluorescence background can reduce contrast	• Emission of light from fluorescently labeled nanoparticles upon excitation	• Magnetic nanoparticles conjugated with fluorescent dyes for MRI/optical multimodal imaging	[44]
Multimodal imaging	• Combines strengths of multiple modalities (e.g., MRI/PET, MRI/CT, MRI/optical) • Provides complementary anatomical, functional, and molecular information • Enables theranostics (therapy + diagnostics)	• Complexity in nanoparticle design and synthesis • Potential for increased toxicity or altered pharmacokinetics	• Integration of multiple imaging mechanisms via multifunctional magnetic nanocomposites	• Core-shell or core-satellite magnetic nanocomposites enabling MRI/SERS, MRI/PET, MRI/CT/optical imaging • Nanoparticles designed for simultaneous imaging and drug delivery	[31, 42]

4. Applications in diagnostics and monitoring

Common metal-based nanoparticles utilized in cancer diagnostics are silver, gold, and iron oxide nanoparticles [45]. To bind to cancer cells specifically, these nanoparticles can be coupled to antibodies or other targeted ligands. They may be found using a variety of imaging methods, including CT, MRI, and PET, and work as contrast agents [46, 47].

By using cellular and molecular pathways, metal-based nanoparticles have the ability to trigger antitumor immune responses, which enhances their potential for cancer diagnostics [48, 49].

4.1. Cancer detection and tumor imaging

Magnetic nanoparticles are frequently used for tumor imaging in cancer diagnosis. MRI creates high-contrast, detailed pictures of malignancies by using the magnetic characteristics of nanoparticles [50]. Additionally, hybrid magnetic nanostructures are used in cancer medication administration, diagnostics, and magnetic separation. These multipurpose nanocomposites make it possible to effectively separate cancer cells from complicated biological samples via magnetic separation, which speeds up detection and subsequent analysis [51].

Furthermore, circulating tumor cells (CTCs) may be extracted from the bloodstream using magnetic nanoparticles. For instance, CTCs can be captured and separated by magnetic nanocomposites of ferroplatinum iron oxide (Fe_3O_4-FePt) [52].The ability to isolate and analyze CTCs from blood samples makes this technique important for cancer diagnosis and prognosis [53].

Since the nanoparticles may be loaded with imaging agents, magnetic separation presents the possibility of multimodal imaging, allowing for simultaneous imaging and diagnosis and a more thorough comprehension of the tumor. For the purpose of early cancer identification and prognosis, it also aids in the isolation and detection of tumor-associated biomarkers, such as proteins, DNA, or RNA [50, 54].

Fortunati et al. [55]. have employed magnetic nanoparticles conjugated with the radiotracer 67Ga-DOTATATE for PET imaging of neuroendocrine tumors which give precise tumor localization and increased accumulation in tumor tissues.

Additionally, Han et al. [56] demonstrated that a nanocomposite with a gold nanoshell and a magnetic PPy/Fe3O4 core successfully improves contrast for both MRI and X-ray CT imaging in detecting cancer cells. Additionally, it offers a powerful platform for cancer treatment guided by multimodal imaging.

4.2. Neurological imaging

Magnetic nanoparticles incorporated into composite materials are used in neurological imaging using magnetic nanocomposites to improve brain imaging methods and allow more focused neurological therapies [57].

Because of their superparamagnetic characteristics, which enhance image resolution and specificity for brain tissues, magnetic iron oxide nanoparticles, or MIONPs, are frequently utilized as contrast agents in MRI. In order to overcome obstacles like the blood-brain barrier, these nanoparticles can also act as drug delivery vehicles, enabling theranostic applications that combine therapeutic administration straight to the brain with diagnostic imaging [57, 58].

Multifunctional magnetic nanocomposites can be designed to increase contrast in magnetic resonance imaging and induce magnetic hyperthermia for medicinal purposes. Precise control over the behavior of these nanocomposites in imaging and therapy contexts is made possible by their magnetic confinement [59]. A study by Kreisl et al. [60] demonstrated that PET can distinguish between different elements of the neuroimmune response and is a good tool for measuring neuroinflammation. Similar findings have been made by a few but increasing research that show PET imaging of neuroinflammation may be useful in medication discovery.

4.3. Cardiovascular and inflammatory disease monitoring

Numerous cardiovascular conditions, such as atherosclerosis, thrombosis, and myocardial abnormalities, can be identified early. SPIO targeted with anti-VCAM-1 and the particular peptide VCAM-1 is used to identify atherosclerosis early. E-selectin, a proinflammatory marker for endothelial cells involved in angiogenesis, tumor endothelial proliferation, and atherosclerosis, is another element utilized in these investigations. The level of the aforementioned component in the in vitro culture media may be shown by MRI using SPIO coupled with human anti-Eselectin. The precise identification of αIIb-β3-released from active platelets provides the basis for the diagnosis of thrombosis. RGD conjugated SPIO RGD, a ring acid peptide made up of the three amino acids arginine, glycine, and separate, is used to detect activated platelets [61].

RGD with SPIO for improved detection In contrast to SPIO, it does not give a marker and permits the viewing of clots measuring 0.2 mm by 0.2 mm in diameter. Myocardial infarction is diagnosed using single-crystalline iron oxide (MION) nanoparticles linked to antimyosine, which are based on the electrostatic or covalent interaction between antibody lysine groups and potassium periodide-activated surface hydroxyl groups. Compared to a normal cell, the membrane of a myocardial infarction cell is more porous. In contrast to the sample without marker, SPIO coupled with antimyosine Fab efficiently enters the injured cell, recognizes myosin, and appears in black on pictures of the afflicted region [62].

4.4. Real-time cellular and molecular imaging

The development of molecular imaging technologies is essential to applied and research sciences. By making it easier for the technology to interact with the biological structure, molecular imaging, which lies at the intersection of physics and life sciences, produces an image at the molecular level [63]. There are several definitions for molecular imaging, which is a quantifiable, reproducible, non-invasive technique that allows imaging of the target macromolecules or biological processes in living things. This approach is useful because alterations in molecular profiles or cellular activity precede the impact of anatomy in many disease disorders [64].

Rapid disease diagnosis, more precise assessment of the severity of the illness and the patient's potential for treatment to minimize treatment procedures, it enhances our comprehension of how cells interact with their surroundings and allows us to demonstrate the therapeutic agent's effect. As a result, it is expected that molecular imaging will have a significant impact in both therapeutic and laboratory settings [63]. In vivo NIR-IIb molecular imaging of PD-L1 and CD8 in a study by Zhong et al. [65] showed that immunotherapy-induced cytotoxic T cells were present in the tumor microenvironment, and that immune activation had changed CD8 signals in the tumor and spleen. Fig. 3 illustrates different applications of magnetic nanocomposites in diagnostics and monitoring.

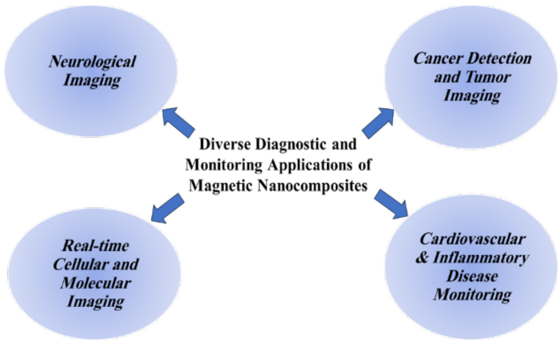

Fig. 3. Various diagnostic and monitoring applications of magnetic nanocomposites.

5. Future directions and innovations

Medical imaging, vital for visualizing tissues and organs, includes techniques like X-ray, CT, MRI, PET, SPECT, ultrasound, and mammography. These methods are key in diagnosing conditions such as cancer, heart disease, neurological disorders, and fractures. Advances like PET/CT, 3D ultrasound, and combined PET/MRI offer higher resolution and safer, more accurate diagnostics. Looking ahead, ongoing technological innovations are expected to transform medical imaging into routine, precise tools for detecting and managing complex diseases, enhancing healthcare outcomes with improved resolution, sensitivity, and safety [13].

5.1. Smart nanocomposites for theranostics

Smart nanocomposites, especially magnetic nanomaterials, are revolutionizing cancer theranostics by enabling precise, multifunctional diagnosis and treatment. These innovative materials respond to specific stimuli such as pH, temperature, or enzymes allowing targeted drug delivery and enhanced imaging of tumor microenvironments while minimizing toxicity [66-68]. Their ability to combine magnetic properties with fluorescence creates versatile platforms for simultaneous imaging, therapy, and cell tracking [69-71]. Despite manufacturing complexities, these smart nanocomposites hold significant promise for personalized cancer management, advancing high-resolution, non-invasive biomedical imaging and integrated treatment strategies [71-73].

5.2. Artificial intelligence in imaging interpretation

Artificial intelligence (AI), encompassing machine learning and deep learning, enhances medical imaging by improving diagnosis, lesion segmentation, image analysis, and biomarker detection. AI evaluates image quality, interprets data, and aids in reports, significantly impacting oncologic imaging. For example, in lung cancer, AI helps distinguish benign from malignant nodules. Traditional AI relied on predefined features based on expert knowledge, while modern deep learning, especially convolutional neural networks (CNNs), learns from data to improve diagnostic accuracy. As technology advances, AI systems are expected to become more sensitive and reliable, transforming medical imaging and diagnosis [13, 71].

5.3. Regulatory and clinical translation pathways

Nanomedicine, especially nanoparticle drug delivery systems (NNMs), faces hurdles in safety, biocompatibility, manufacturing standards, and regulatory approval. Reliable, standardized formulations are essential for clinical acceptance. Although most NNMs target cancer, their use in inflammatory and other diseases is expanding. Slow clinical progress results from inconsistent characterization, quality control issues, and variability in outcomes, emphasizing the need for thorough evaluation of biocompatibility, pharmacokinetics, and manufacturing processes. Successful translation requires early collaboration with regulators and meticulous safety studies [74, 75]. In tissue regeneration, magnetic actuation shows promise for regulating stem cells, notably adult mesenchymal stromal cells (MSCs) from tissues like bone marrow or adipose tissue. These cells have shown therapeutic potential in various conditions, avoiding ethical concerns linked to embryonic cells [76]. In nanomedicine, iron oxide nanoparticles (IONPs) conjugated with optical probes enable multimodal imaging and therapy. However, toxicity concerns, especially with quantum dots, highlight the need for safer alternatives like carbon quantum dots. The combination of IONPs with approved dyes like Indocyanine Green offers a promising path toward safe, effective nanomedicines. Overcoming regulatory and safety challenges is vital for moving these innovations from preclinical research to clinical practice [77].

6. Conclusion

Magnetic nanocomposites have emerged as versatile and powerful agents in the landscape of biomedical imaging, offering unprecedented opportunities for early diagnosis, precise disease monitoring, and targeted therapy. Their ability to combine magnetic and fluorescent functionalities, along with customizable surface modifications, enhances the sensitivity and specificity of various imaging modalities. As research progresses, innovative synthesis strategies and surface functionalization techniques are addressing existing challenges, such as biocompatibility and fluorescence quenching, paving the way for broader clinical translation. The future of this field is poised to benefit from smart nanostructures and artificial intelligence-driven image analysis, which will further refine diagnostic capabilities and therapeutic interventions. Overall, magnetic nanocomposites are set to play a crucial role in advancing personalized medicine and improving health outcomes through more accurate and minimally invasive diagnostic solutions.

Author contributions

Mehrasa Nikandish: Investigation, Writing—Original Draft Preparation, Writing—Review and Editing; **Hawraa Alsayegh:** Conceptualization, Writing—Original Draft Preparation, Writing—Review and Editing; **Mehrnaz Baneshi:** Writing—Original Draft Preparation, Writing—Review and Editing; **Zahra Mozaffarian:** Writing—Original Draft Preparation, Writing—Review and Editing.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

No data is available.

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