International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Emerging Trends in Targeted Magnetic Nanoparticle Imaging for Precision Medicine in Oncology

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Abstract:
In cancer care's dynamic landscape, targeted imaging is pivotal for advancing precision medicine. This review focuses on the role of magnetic nanoparticles (MNPs), particularly magnetic iron oxide nanoparticles (MIONPs) and superparamagnetic iron oxide nanoparticles (SPIONs), in personalized diagnostics and treatments for oncology. Current trends and future directions in MNP imaging, addressing challenges like biocompatibility, toxicity, and regulatory considerations, are discussed. The review explores MIONPs' theranostic potential, especially in brain drug delivery monitoring through magnetic resonance imaging (MRI) or magnetic particle imaging (MPI). Variousnanoparticle types, including SPIONs as MRI contrast agents, are highlighted. The article covers challenges in nanoparticle modification, including methoxy- polyethylene glycol (mPEG), and discusses gold nanoparticles (AuNPs) for photoacoustic imaging, as well as insights into fluorescent semiconductor quantum dots (QDs). The conclusion emphasizes rapid and accurate tumoridentification, introduces carbon nanotubes (CNTs) for cancer therapy and diagnosis, and underscores the transformative role of lipid-based nanocarriers incancer research. The multifaceted applications of nanotechnology in cancer diagnostics and treatment are discussed throughout, showcasing a paradigm shift.Crucial challenges in unlocking nanotechnology's full potential in cancer care, such as safety concerns, robust clinical trials, synthesis methods standardization, regulatory approval, biodegradability, tailoring nanotherapies, economic viability, ethical considerations, and interdisciplinary collaboration, are addressed. Addressing these challenges holds the promise of elevating nanotechnology into a potent force in the ongoing battle against cancer.

Keywords: Magnetic nanoparticles, Imaging, ligand, Gadolinium, Gold, Iron oxide, Manganese, Carbon nanotube, Lipid, Semiconductor, Contrast agent, Cancer, Nanocarrier.

1. Introduction:

In the ever-evolving field of cancer care, precise imaging plays a crucial role in advancing precision medicine. This review covers the transformative impact of precision medicine in cancer care, focusing on personalized diagnostics and treatments. It highlights the role of magnetic nanoparticles (MNPs) in targeted imaging, exploring current trends and future directions in MNP imaging for precision medicine in oncology. The article delves into MNP synthesis and functionalization, showcasing their versatility for

precise imaging and therapy. Recent advancements in targeting and imaging strategies are examined, addressing challenges such as biocompatibility, toxicity, and regulatory considerations in implementing targeted MNP imaging. The goal is to provide a thorough understanding of the evolving landscape of MNP imaging in oncology and its transformative impact on personalized cancer diagnostics and treatment in the era of precision medicine. In addition, the review explores the theranostic potential of 10 magnetic iron oxide nanoparticles (MIONPs) for brain disorders, particularly in monitoring drug delivery through magnetic resonance imaging (MRI) or magnetic particle imaging (MPI). The discussion includes various nanoparticle types, with a focus on superparamagnetic iron oxide nanoparticles (SPIONs) derived from iron oxide, showcasing their advantages in MRI contrast agents. Nanomaterial-based MRI contrast agents offer benefits like biostability, tunable biodistribution, adjustment of biocompatibility and imaging properties, and specific conjugation for targeted identification, enabling multimodal imaging with optical and magnetic properties. The article also covers photoacoustic (PA) imaging, a non-ionizing biomedical imaging modality, discussing gold nanoparticles (AuNPs) as effective PA contrast agents due to their strong and tunable optical absorptions. Various nano-contrast agents, including liposomes, microbubbles, superparamagnetic iron oxide (SPIO), and AuNPs, are explored. Most are modified with methoxy-polyethylene glycol (mPEG) for enhanced biocompatibility and half-life. However, challenges related to mPEG water- solubility reducing cell uptake are discussed, limiting sensitivity and signal intensity. Fluorescent semiconductor quantum dots (QDs) are highlighted for their superior optical properties in biomedical applications, with a focus on surface modification and functionalization to address challenges like potential toxicity and instability in biological environments. The review concludes by discussing the significance of rapid and accurate tumor identification, introducing carbon nanotubes (CNTs) as a potential tool in cancer therapy and diagnosis. Additionally, lipid-based nanocarriers are presented as a transformative platform in cancer research, emphasizing their diverse applications in therapy, diagnostics, and real-time monitoring.

2. Methodical Approach:

This study adopts a systematic review approach to examine the role of Magnetic Nanoparticles (MNPs) in oncology imaging. The core objective is to intricately analyze and interpret the collected data in accordance with predefined research focus and criteria. The insights derived from this scrutiny play a pivotal role in charting the course for our future research endeavors.

2.1. Magnetic Iron Oxide Nanoparticles (MIONPs) for Brain Imaging

The inherently small size of MIONPs serves as a significant advantage, making them optimal for traversing the blood-brain barrier (BBB) for both imaging and drug delivery applications. Moreover, MIONPs offer a versatile surface chemistry that facilitates easy functionalization with various biological ligands, enhancing their specificity for diseased tissue and augmenting BBB penetration, positioning them as an ideal platform for brain imaging and drug delivery. In clinical scenarios, leveraging MIONPs as platforms involves surface functionalization with therapeutic agents for treatment, coupled with visualization and monitoring of treatment response through imaging techniques to assess theranostic efficacy. The subsequent sections delve into recent studies highlighting the use of MIONPs for imaging-guided drug delivery in various brain disorders, encompassing brain cancer, neurodegenerative diseases, and ischemic stroke. Finally, the article provides a perspective on the opportunities and challenges for the future clinical translation of MNP-based contrast agents in diagnosing brain diseases. Despite its widespread use, the coprecipitation method has limitations in controlling the size distribution of

MIONPs. The growth process of nanocrystals is solely governed by kinetic factors during coprecipitation, resulting in MIONPs with moderate crystallinity quality and suboptimal magnetic properties. Such defects may impede the application of MIONPs, particularly in imaging scenarios requiring high sensitivity. MIONPs, particularly as T1 or T2 contrast agents in MR imaging of glioblastoma multiforme (GBM), exhibit significant potential. In comparison to traditional Gd-based contrast agents, MIONPs show prolonged retention in circulation and enhanced tumor accumulation. Recent research with ultrafine iron oxide nanoparticles (uIONPs) demonstrates their promise in navigating the blood-brain tumor barrier, indicating improved imaging of GBM.

Also recognized as superparamagnetic iron oxide nanoparticles (SPIONs), MIONPs have been extensively studied as contrast agents to enhance the contrast in transverse (T2)-weighted MRI due to their intrinsic superparamagnetic properties. Recent developments show their promise as longitudinal (T1)-contrast agents in both research and clinical settings. MIONPs exhibit superior contrast, sensitivity, and spatial resolution across various clinical imaging modalities, including MRI, PET, photoacoustic imaging, and ultrasound. In the realm of MRI, MIONPs stand out for their ability to enhance proton relaxation, offering a heightened level of contrast that aids radiologists in identifying discrete lesions associated with metastasis or residual disease following surgical tumor removal.

2.2. Gadolinium based nanoparticles (Gd-NPs) for Molecular Imaging

Modifications and functionalizations of nanoparticles offer a platform for improving contrast media by enhancing specificity, prolonging circulation half- life, and ensuring in vitro and in vivo stability. The addition of targeting ligands further field of MRI, clinically available contrast agents are predominantly based on paramagnetic Gd complexes. While widely used, traditional agents like Magnevist enhances specificity, promoting increased interactions between nanoparticles and tumorous tissues. In the, Gadolinium (Gd) (III) chelate, face limitations such as potential biotoxicity, lower relaxivity, and shorter blood circulation time. Gadolinium (III)-based nanoparticles (Gd-NPs) have emerged as promising alternatives due to their thermodynamic and kinetic stability, high relaxivity, good water solubility, in vivo stability, low toxicity, and precise control over molecular size and functionalization. Despite advancements in enhancing relaxivity values and biocompatibility, concerns persist regarding the potential toxicity of nanomaterials and the release of Gd. Encapsulation and surface labeling have been explored to mitigate toxic effects, but further studies are warranted. Conjugating Gd-based contrast agents with ultra-small nanoparticles for rapid elimination may offer a solution to toxicity concerns. The concept of imparting multi-modality to Gd-based contrast agents has gained traction, representing the next generation of contrast agents. Combining Gd-Cas with other modalities, such as CT imaging and optical imaging, holds great promise for clinical applications. The integration of PET with Gd-CAs in MRI can provide high-resolution images with detailed anatomical information, offering a comprehensive and complementary approach to molecular imaging.

2.3. Iron Oxide Nanoparticles (IONPs) based biomarkers for cancer detection

SPIONs, with their ability to attain the highest drug targeting efficiency among nano-carriers, benefit from localized application of an external magnetic field to the target organ. This facilitates the accumulation of magnetic nanoparticles at the site of drug action, presenting a synergistic combination of MRI and nanotechnology. This synergy plays a vital role in real-time monitoring of therapeutic outcomes, potentially mitigating multi-drug resistance in communicable diseases, addressing antimicrobial drug resistance in infectious diseases, and reducing drug toxicity. The success of this treatment strategy hinges on the identification of robust biomarkers that can correlate with the diseased

stage or treatment response in a patient-tailored manner, thus minimizing adverse drug toxicity. In a clinical setting, a quantifiable biomarker should be extractable from various biospecimens, such as blood, sweat, urine, tissues, or cerebral spinal fluid (CSF). Diagnostic imaging biomarkers, expressed as bio-signals detectable through electromagnetic, photonic, or acoustic signals emitted by the patient, offer a non-invasive alternative to invasive assessments involving tissue biopsies or CSF. For MRI-based imaging technology, these biomarkers must exhibit sensitivity, specificity, biological relevance, quantifiability, reproducibility, and cost-effectiveness. The favorable characteristics of iron-oxide- based SPIONs, coupled with their cost-effectiveness, position them as valuable tools in disease diagnosis. Iron-oxide-based nanoparticles (IONPs) serve as T2 contrast agents, but their properties can be engineered for use as T1 contrast agents. Due to the oxidative characteristics and high toxicity levels of pure metals, despite their higher magnetization (Ms), they are deemed unsuitable for in vivo use. Therefore, the most widely used magnetic iron oxide nanoparticles are magnetite (Fe_3O_4) and maghemite (c-Fe_2O_3), both possessing cubic inverse spinel structures and finding applications in various healthcare sectors. These nanoparticles exhibit high chemical/colloidal stability and biocompatibility. Through surface modification of magnetite and maghemite, the resulting superoxide nanoparticles (SPIONs) can shorten the T1 and T2 proton relaxation times.

Table 1: Biomarkers utilizing MRI-IONPs for cancer diagnosis in clinical settings.

Biomarker	Application	Characteristics	Contrast Agent type
Detection and Characterization	BI-RADS PI-RADS LI-RADS	Lesion morphology	T2, T1
Staging	TNM staging	Tumor morphology, presence and number of nodes, metastases	T2, T1
Response	Treatment response in solid tumor	Change in tumor size	T2, T1

Positron Emission Tomography (PET), while extremely sensitive, suffers from low resolution. Grafting a radionuclide onto a polymer-coated SPION offers a high-resolution, quantitative approach with no penetration limit. Common agents like iodine and noble metals (gold and silver) are employed for Computed Tomography (CT) imaging. These substances can be directly applied to the surface of IONPs, applied as coatings, or regarded as hetero structured nanoparticles. IONPs with a hydrodynamic diameter of 20 to 30 nm exhibit prolonged circulation periods, proving beneficial for imaging lymphography, inflammation, and blood pools. Upon intravenous administration, IONPs circulate in the bloodstream, partially extravasate into tissues over time, and are eventually removed by the lymph system, accumulating in macrophages in lymph nodes. This leads to alterations in signal intensities in various MRI imaging sequences. The signal intensity in T2 and T2*-weighted MR imaging diminishes or increases in T1-weighted imaging due to the circulation and accumulation of IONPs. Metastatic manifestation in lymph nodes results in reduced nodal macrophage concentration and compromised lymph node function. Metastasis may further reduce macrophage functioning and decrease phagocytic activity, resulting in lower IONP uptake and brighter malignant lymph nodes in T2/T2*-weighted imaging.

T2-weighted images exhibit a 40% shift in signal intensity after injecting tumor-bearing mice with human transferrin proteins attached to SPIONs. Herceptin, a cancer-specific antibody binding to the HER2 receptor present in breast cancer cells, yields darker images in T2-weighted MRI when using 9-nm nanocrystals as a model probe functionalized with the conjugated ligand for Herceptin. Over the years, numerous MRI biomarkers have been reported, and the detection of these imaging biomarkers using nanoparticles, especially SPIONs, necessitates careful consideration of nanoparticle formulation and the attachment of specific biomarkers.

2.4. Manganese Oxide Nanoparticles (MONs) for tumor imaging

To enhance imaging contrast sensitivity, various T1- or T2-MRI contrast agents based on manganese (Mn) have been developed. Gadolinium (Gd) and iron oxide nanoparticles (Fe3O4 NPs) face limitations in clinical applications due to intrinsic dark signals and susceptibility artifacts, making it challenging to distinguish small early-stage tumors from hypointense areas. Mn-based contrast agents are considered ideal substitutes due to their bright signals and good biocompatibility. These can be categorized into Mn2+ composites and manganese oxide nanoparticles (MONs). However, Mn2+ complexes have short blood circulation times, and high doses can accumulate in the brain, causing manganese poisoning. MnO nanoparticles, on the other hand, show potential as T1-weighted MR contrast agents. Surface coating methods, such as polymer functionalization, silica coating, and phospholipid modification, are employed to enhance the relaxation rate of MnO nanoparticles. For instance, attaching PEGylated bis-phosphonate dendrons (PDns) to the surface of MnO improves colloidal stability, relaxation performance, and rapid excretion ability, reducing in vivo toxicity. The structure of MnO also influences its relaxation properties, with octagonal MnO nanoparticles exhibiting larger surface areas and enhanced low-temperature ferromagnetic behavior. Manganese oxide nanoparticles (MONs) have been developed as T1 contrast agents due to their good biocompatibility, relatively high magnetization spin, and rapid water proton exchange rate. MONs, as opposed to Gd-based agents, hold significant clinical relevance for cancer detection and diagnosis.

2.5. Gold nanoparticles (Au-NPs/GNPs) for cancer imaging

AuNPs of various shapes and sizes, such as nanospheres, nanorods, nanoshells, nanoprisms, nanocages, nanostars, and nanovesicles, exhibit distinct and tunable absorption spectra in the near-infrared region, making them valuable for PA imaging. Beyond plasmonic AuNPs, there are numerous other PA contrast agents. AuNP-based PA imaging is well-suited for detecting different tumor types, benefiting from their accumulation in tumors via the enhanced permeability and retention effect or functionalization for receptor-mediated binding. This imaging approach aids in locating tumors, monitoring vasculature heterogeneities, and tracking therapeutic agent accumulation in real-time. Due to their fine-tunable surface plasmon resonance peaks, photothermal conversion efficiency, and biocompatibility, AuNPs serve as promising exogenous contrast agents for PA imaging and image-guided therapy. Composites like AuNP–magnetic nanoparticle composites and triple-modality MRI–PA imaging–Raman imaging nanoparticles enhance PA imaging contrast when combined with other imaging modalities, showing potential for more accurate tumor imaging. To impart tumor specificity to PEG-NPs, targeted contrast agents were created by conjugating anti-tumor antibodies, ligands, and peptides with nanoprobes. Active tumor- targeting and cell uptake of PEG-NPs are crucial for improved sensitivity in targeted diagnostics. Methoxy-PEG hapten, FDA-approved for human use, can modify nanoprobes like SPIO, AuNP, and microbubbles, enhancing their biocompatibility and half-life in vivo. Results indicate that one-step formulation of mPEG × HER2 BsAbs with multiple PEG-NPs enhances HER2 targeting to HER2-

positive tumor cells, providing a universal and direct formulation for developing targeted PEG- NPs for multimodality imaging in clinical applications.

2.6. Semiconductor Quantum Dots (QDs) for cancer imaging

While QDs offer advantages in imaging and spectroscopy, barriers exist that impede their widespread use in bioimaging. Concerns include potential toxicity from heavy metal ion release, pH-sensitive photoluminescence, and prolonged retention in animals. To address these issues, researchers have explored surface decoration with biocompatible molecules and conjugation with targeting ligands. Design considerations for in vivo imaging probes encompass factors like potential toxicity, interference with normal biology, circulation lifetime, optimal excitation/emission wavelengths, ligand-conjugation chemistry, and cost- effectiveness. Recent developments include a core/shell nanoprobe for dual-modality imaging in breast cancer, comprising an iron oxide (IO) NP core and silica shell layers with embedded CdSe/ZnS and NIR fluorescent CdSeTe/CdS QDs. Targeted delivery using an anti-HER2 antibody demonstrated enhanced tumor-specific accumulation. Another instance involves a targeted dual-modality fluorescence/positron emission tomography (PET) probe based on QDs labeled with 64Cu, showing specific binding in tumor-bearing mice. Vascular-specific targeting of QDs was observed with minimal extravasation. Quantum dots, among various nanoparticle types, stand out for their inherent advantages. However, achieving effective tumor targeting remains a key challenge. The focus on targeting tumor vasculature rather than tumor cells emerges as a promising strategy, given that many QD-based probes face limitations in extravasation compared to smaller molecules or proteins.

2.7. Carbon Nanotubes (CNTs) for cancer diagnosis

Characterized by their cylindrical shape, CNTs belong to the fullerene family of carbon allotropes. Currently, two main types of CNTs are employed for biomedical applications: single-walled carbon nanotubes (SWCNTs) with a single layer of graphene and a diameter of 1.2–2 nm, possessing a thermal conductivity of 6000 W/m*K but lower purity; and multi-walled carbon nanotubes (MWNTs) with multiple layers. Researchers have developed a nanoprobe using CNTs enriched with silver nanoparticles and functionalized with streptavidin. This innovative immunoassay, deployed for detecting tumor markers like α-fetoprotein or carcinoembryonic antigen, demonstrated high precision in detection. By utilizing screen-printer carbon electrodes and overcoming common electrochemical immunoassay barriers, such as cross talk and deoxygenation, this immunoassay provides a sensitive and improved method for tumor marker detection. In the realm of electrical immunosensors, a novel approach was taken for prostate antigen (PSA) detection using MWNTs, gold nanoparticles, and secondary antibody (Ab2) and 6-ferrocenyl hexanethiol (Fc) labels. This electrical immunosensor exhibited a low detection limit of 5.4 pg·mL−1 in serum samples, showcasing the potential for early cancer detection. Similarly, a biosensing nanoprobe for detecting the breast cancer biomarker CA 15-3 was developed using polymerase chain reaction (PCR). The biosensor, with a lower detection limit of 0.001–0.01 U/mL, demonstrated sensitivity in identifying CA 15-3. Vertical aligned carbon nanotubes (VACNTs) were employed in the development of an electrical spectroscopy device for diagnosing cancer metastasis at the single-cell level. By electrically coupling CNT beams with the cell membrane, the device provided information on electronic resonance and ionic permeability, enabling the diagnosis of metastatic colon and breast cancer cells. This method offers the potential for early cancer detection and improved diagnosis with minimal cells compared to traditional tissue-based methods. Carbon nanotubes present an advantage in circumventing cellular autofluorescence, enhancing the detection of cells with low receptor expression. Additionally, the attachment of nanomaterials to targeting agents, such as epithelial cell adhesion

molecules (EpCAMs), holds promise for improved cancer diagnosis and treatment. The development of multifunctional nanoprobes demonstrates the evolving role of nanotechnology in advancing less toxic and more effective cancer treatments.

Table 2: CNTs for cancer diagnosis

Type of Nanoparticle	Size	Type of cancer detected	Method
single-walled carbon nanotubes conjugated with cyclic ArgGly-Asp (RGD) peptides	Diameter: 1–2 nm Length: 50-300 nm	Human Glioblastoma	Photoacoustic imaging
Carboxylated SWNTs with anti-HER2 chicken IgY antibody	Diameter: 1.17±0.28 nm Length: 88.00 ± 43.68 nm	Breast Cancer	Raman spectrometry
Short single-walled carbon nanotubes (SWNTs) functionalized by PEGylated phospholipids	Length~140 nm	Breast Cancer	Near infrared photoluminescence
Multilayers enzyme-coated MWNTs	Diameter: 20 nm Length: 3µm	Liver Cancer marker	Chemiluminescence
Single-walled carbon nanotubes (SWNTs)	Diameter: 1.6 nm Length: 83nm	Breast Cancer, Lymphoma	Near infrared photoluminescence
M13-stabilized single- walled carbon nanotubes (SWNTs)	Diameter: 6 nm Length: 880 nm	Ovarian Cancer	Fluorescence imaging
EGF functionalized SWNTs	Diameter: 0.7–2.1 nm Length: 0.2–3 µm	Pancreatic Cancer	Raman Spectroscopy
Dendrimer functionalized MWNTs	Diameter: 30–70 nm Length:100–2µm	Cervix Cancer	Fluorescence Imaging
ICG dyed single-walled carbon nanotubes (SWNTs-ICG)	N/A	Breast cancer (sentinel lymph nodes) Bladder cancer	Photoacoustic imaging
PEGylated SWCNT CD44 nanocarriers conjugated with superparamagnetic iron oxide nanoparticles (SPIONs) or radioactive Gallium-67	Diameter: 1–2 nm Length:200 nm	Breast cancer	MRI, Single Photon Emission Computed Tomography, Near-Infrared fluorescence imaging
Anti-EpCAM antibodies functionalized SWNTs	Diameter: 0.7 to 1.7 nm,	Breast cancer	Raman spectroscopy

	Length: 0.3 to 3µm		
PEGylated SWNTs	N/A	Metastatic breast cancer	NIR-II fluorescent imaging
RGD-conjugated silica-coated gold nanorods on the surface of MWNTs	Diameter:20~ 30 nm	Gastric cancer	Photoacoustic imaging
SWCNTs exchanged into a biocompatible surfactant, C18-PMHmPEG	Diameter 0.7–1.1 nm	Breast Cancer	Near infrared photoluminescence

2.8. Lipid-based nanoparticles (lipid-NPs) for cancer diagnosis

Lipid-based nanocarriers, composed of biocompatible lipids like phospholipids, cholesterol, and triglycerides, represent an idealistic drug delivery system. These carriers boast superior biocompatibility and biodegradability, minimizing toxicity compared to alternative drug delivery systems such as polymeric nanoparticles. Lipid-based nanocarriers exhibit a remarkable capacity for targeted drug delivery, enhancing bioavailability while avoiding side effects. Conjugation with specific ligands, such as folate and PSMA, ensures precise targeting of cancer cells. Additionally, these nanocarriers can be modified with various targeting moieties to improve their specificity, providing a versatile tool for personalized medicine. Recent research has explored diverse lipid-based nanocarriers, including liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and lipid polymer hybrid nanoparticles (LPHNPs). These carriers have shown promising results in cancer therapy, combining drug delivery with diagnostic imaging. In a groundbreaking study, liposomes conjugated with vasoactive intestinal peptide (VIP) receptors demonstrated enhanced imaging and pharmacokinetics in breast cancer cells. The incorporation of targeting moieties, such as immunoglobulin M (IgM) and specific antibodies, significantly improved cellular uptake and tumor accumulation. Lipid-based nanoparticles contribute to early cancer diagnosis through innovative techniques like single photon emission computed tomography (SPECT/CT) imaging. Advanced formulations, carrying anti-CD44 and anti-IL6R antibodies, exhibit specific targeting of the tumor microenvironment (TME), inhibiting metastasis in breast cancer models. Extracellular vesicles (EVs) derived from lipid-based nanocarriers, including tumor-derived EVs (TDEVs), have shown promise as fluid biopsy biomarkers. TDEVs, extracted from blood and urine, contain molecular components specific to tumors, offering a potential breakthrough in cancer diagnosis and management. The integration of theranostic nanocarriers into personalized medicine has demonstrated promising results. These nanocarriers, equipped with monitoring biosensors, enable non-invasive monitoring of treatment efficacy, allowing clinicians to adjust drug dosage in real-time. Lipid-based nanocarriers stand at the forefront of cancer research, offering a multifaceted approach to targeted drug delivery, imaging, and real-time monitoring. As a versatile and biocompatible platform, these nanocarriers hold the key to advancing personalized cancer therapy, with the potential to revolutionize the landscape of cancer diagnosis and treatment. Continued research in this domain promises exciting breakthroughs and enhanced therapeutic efficacy in the fight against cancer.

3. Findings & Discussions:

MIONPs, known for their small size, excel in brain imaging and drug delivery by efficiently crossing the blood-brain barrier. Their adaptable surface chemistry enhances precision for diseased tissue, making them effective drug delivery platforms in clinical settings. Despite limitations in the coprecipitation method affecting their properties, recent studies highlight MIONPs' role in imaging- guided drug delivery, especially in MR imaging for glioblastoma. Nanoparticle modifications, like adding targeting ligands, enhance contrast media in MRI, addressing limitations of traditional Gd-based agents. SPIONs, benefiting from an external magnetic field, excel in targeted drug delivery, offering real-time therapeutic monitoring. Identifying biomarkers from bodily fluids provides a non-invasive alternative to tissue biopsies, contributing to personalized medicine. Manganese-based agents in MRI, avoiding dark signals, show promise in early tumor detection. Gold nanoparticles in various shapes prove effective for photoacoustic imaging, especially in tumor detection. Quantum dots face challenges but hold potential for dual-modality imaging in breast cancer. Carbon nanotubes improve cell detection, aiding in cancer diagnosis and treatment. Lipid-based nanocarriers, with superior biocompatibility, enable targeted drug delivery and contribute to breakthroughs in cancer therapy and diagnosis through innovative imaging techniques.

Table 2: Summary of MNPs in oncology imaging

Magnetic Nanoparticle	Composition	Surface Modification	Targeted Biomarker	Imaging Enhancement
Superparamagnetic Iron Oxide (SPIO)	Fe3O4	Dextran, PEG	Various cancer biomarkers	T2-weighted contrast
Gadolinium-based Nanoparticles	Gadolinium (Gd)	Silica, Lipid	Tumor-specific ligands	T1-weighted contrast
Iron Oxide Nanoparticles	Fe2O3, Fe3O4	Silica, Polymer	HER2, EGFR, etc.	T2-weighted contrast
Manganese Oxide Nanoparticles	MnO	Silica, PEG	CD44, Integrins, etc.	T1/T2-weighted contrast
Gold Nanoparticles	Gold (Au)	PEG, Antibodies	EpCAM, CEA, etc.	Photoacoustic imaging
Quantum Dots	Semiconductor	Polymer, Ligands	VEGF, EGFR, etc.	Fluorescence imaging
Carbon Nanotubes	Carbon	PEG, Antibodies	Various cancer biomarkers	Photoacoustic imaging
Lipid-based Nanoparticles	Lipids	PEG, Ligands	Folate, PSMA, etc.	MRI and Drug delivery

4. Conclusion:

The multifaceted applications of nanotechnology in the field of medical imaging and drug delivery

represent a paradigm shift in cancer diagnostics and treatment. Magnetic nanoparticles, such as MIONPs and SPIONs, exhibit remarkable potential for brain imaging and targeted drug delivery, surpassing traditional agents. Innovations in contrast media, like Gd-based nanoparticles and Mn-based agents, address limitations and contribute to enhanced imaging sensitivity. Gold nanoparticles and quantum dots offer versatility in imaging modalities, while carbon nanotubes revolutionize cancer diagnostics by overcoming autofluorescence and enabling precise tumor marker detection. The advent of lipid-based nanocarriers further propels personalized cancer therapy, offering targeted drug delivery with minimal toxicity. Collectively, these advancements underscore the transformative impact of nanotechnology on the landscape of cancer diagnosis and treatment, providing novel avenues for early detection, real-time monitoring, and improved therapeutic efficacy. Continued research and optimization of synthesis methods will undoubtedly contribute to overcoming challenges and unlocking the full potential of nanotechnology in the fight against cancer.

5. Future challenges:

Unlocking the full potential of nanotechnology in cancer diagnostics and treatment presents several crucial challenges. Ensuring the safe application of nanotechnology in medical contexts, addressing potential toxicity concerns, and conducting robust clinical trials are imperative steps. Understanding the long- term biocompatibility of nanomaterials, standardizing synthesis methods, and navigating regulatory frameworks for approval are essential for scalable manufacturing and widespread adoption. The creation of biodegradable nanomaterials that efficiently clear from the body is crucial, alongside tailoring nanotherapies to individual patient responses. Developing economically viable manufacturing processes and demonstrating overall economic benefits are pivotal for adoption. Ethical considerations, including privacy and consent, require thoughtful examination and the establishment of responsible guidelines. Lastly, effective interdisciplinary collaboration among researchers, clinicians, engineers, and regulatory bodies is imperative for accelerating progress and finding comprehensive solutions to multifaceted challenges in the future of nanomedicine.

6. Abbreviations:

MNP - Magnetic Nanoparticle
MIONP - Magnetic Iron Oxide Nanoparticle MRI - Magnetic Resonance Imaging
MPI - Magnetic Particle Imaging
SPION - Superparamagnetic Iron Oxide Nanoparticle PA - Photoacoustic Imaging
AuNP - Gold Nanoparticles
SPIO - Superparamagnetic Iron Oxide CNT - carbon nanotube
BBB - Blood-Brain Barrier GBM - Glioblastoma Multiforme
uIONP - Ultrafine Iron Oxide Nanoparticle Gd-NP - Gadolinium Based Nanoparticle PET – Positron Emission Tomography IONP - Iron Oxide Nanoparticles
CSF - Cerebral Spinal Fluid CT - Computed Tomography
MON - Manganese Oxide Nanoparticles
BI-RADS - Breast Imaging Reporting and Data System PI-RADS - Prostate Imaging and Data System
LI-RADS - Liver Imaging Reporting and Data System PEG - Polyethylene Glycol
mPEG - Methoxypolyethylene Glycol
HER2 - Human Epidermal Growth Factor Receptor 2 PDns - PEGylated Bis-Phosphonate Dendrons

SWCNT - Single-Walled Carbon Nanotube
MWNT - Multi-Walled Carbon Nanotube PSA - Prostate Antigen
Ab2 - Secondary Antibody
PCR - Polymerase Chain Reaction
VACNT - Vertical Aligned Carbon Nanotube SLN - Solid Lipid Nanoparticle
NLC - Nanostructured Lipid Carrier SPIO - Superparamagnetic Iron Oxide QD - Quantum Dot
EPR - Enhanced Permeability and Retention
EGFR - Human Epidermal Growth Factor Receptor
BsAb - Bispecific Antibody
Dig – Digoxigenin
FDA - Food and Drug Administration
PSMA - Prostate-Specific Membrane Antigen EpCAM - Epithelial Cell Adhesion Molecule LPHNP - Lipid Polymer Hybrid Nanoparticle VIP - Vasoactive Intestinal Peptide
IgM - immunoglobulin M
SPECT - Single Photon Emission Computed Tomography TME - Tumor Microenvironment
EV - Extracellular Vesicle TDEV - tumor-derived EVs

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