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ADVANCEMENT IN MICRO MRI PROBES OR NANO MRI PROBES

Aamir Rasheed[1*], Muahammad Ali Qureshi[2], Samavia Aftab[3]

*[*1]Department of Information & Communication Engineering, The Islamia University of Bahawalpur, Bahawalpur, 63100, Punjab, Pakistan.*

[2]Department of Biomedical engineering, The Islamia University of Bahawalpur, Bahawalpur, 63100, Punjab, Pakistan.

[3]Department of Ningbo Institute of Materials Technology and Engineering Chinese Academy of Sciences.

*[*1]m.aamirrasheed003@gmail.com, [2]ali.qureshi@iub.edu.pk*
[3]samaviaaftab2000@gmail.com

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Corresponding Author:

Abstract

MRI is a significant device in medicine as its standard probes and instru- ments possess low capability of detecting and differentiating various molecules. The improvement of micro and nano MRI probes has resulted in the present day where imaging is finer than the high-temperature superconductor coils and development of multifunctional nanoparticles. Such probes have targeted ligands and responsive materials that enable them to specifically interrogate particular of localization, and modu- late the imaging contrast upon detection of biological signals. It is used in used oncology, inflammatory studies, cardiovascular and neurology, because guided probes find faster application, continuous monitoring and concomitant therapy and diagnostics (theranostics). There are still signif- icant progresses, impediments that much to do with security, acceptance of new treatment and clinical use. In particular, these enhanced probes have demonstrated a resilience of up to 200-300 per cent of MRI sen- sitivity and signal-to-noise level in preclinical models as compared with standard representatives. This review evaluates technological, biomedi- cal and translational performances of micro and nano MRI probes, bothin terms of accomplishments and desired outcomes. With the imple- mentation of these new advanced systems, the precision of medicine may change to be more accurate in the identification of the disease whereby the therapies of the disease can be more accurately tracked and the image-guided therapies can be more accessible to individuals. MRI is a major tool in medicine, its standard probes and instruments have a low ability to detect and distinguishing different molecules. Advancements in micro/nano MRI probes have led to a time when imaging is more precise than to high-temperature superconductor coils and the creation of multifunctional nanoparticles. Targeted ligands and responsive materials in these probes allow them to selectively examine specific areas and to change the imaging contrast as biolog- ical signals are detected. Applications are seen in oncology, studies of inflammation, cardiovascular disorders and neurology, as guided probes enable faster detection, continuous monitoring and combining therapy and diagnostics (theranostic approaches). Important advances, barriers still exist when it comes to security, the acceptance of new treatments and clinical use. This review assesses technological, biomed- ical and translational aspects of micro/nano MRI probes, focusing on both achieved and desired results. The introduction of these new advanced systems could transform precision medicine by making dis- ease identification more precise, allowing better monitoring of thera- pies and making individualized image-guided therapies more available.

1. Introduction

Magnetic Resonance Imaging (MRI) is a leading technique in diagnostic medicine, prized for being safe, offering excellent contrast between soft tissues, and needing no ionizing radiation. Image-Guided Interventions are used to obtain clear images of the body in neurology, oncology, and cardiology, as well as to monitor different body functions [1]. Although MRI dramatically affects healthcare, standard technology still struggles with sensitivity, accuracy, and the ability to show small-scale activities and particles [2]. Gadolinium-based chelates are better than others and improve image clarity; they can spread to different parts of the body, can be toxic, and are less useful with early diseases or small biological changes [3]. Due to these limitations, researchers are now focusing on creating tiny micro-/nano-MRI tools. Such advanced probes, built from magnetic nanoparticles, engineered polymers, or hybrids, allow for flex- ible magnetism and accuracy on small scales [4]. Micro/nano MR probes can target specific cellular markers or disease microenvironments that are func- tionalized with peptides, antibodies, or aptamers, allowing high-resolution, real-time imaging that was not possible before [5]. Innovative or responsivefeatures in such probes help them respond to changes in the body, signifi- cantly improving how accurately a disease can be identified and treated using imaging guidance [6].

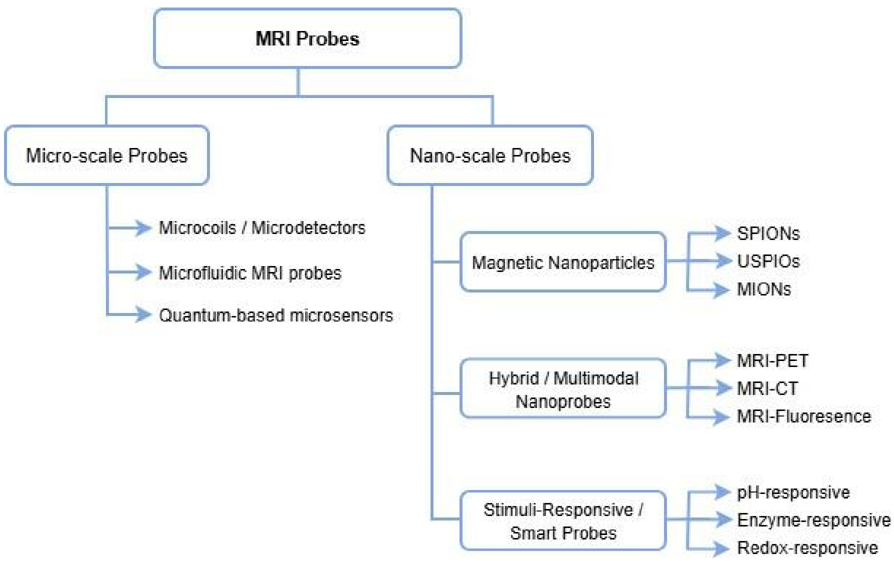

Fig. 1 Classification of MRI probes micro-scale and nanoscale probes for enhanced imaging and sensing

In these terms, this review provides a detailed background of the current developments in micro- and nanoscale MRI probes, emphasizing their poten- tial to transform biomedical imaging and precision medicine. In particular, the review is devoted to the recent advances in materials, hardware innovation, and surface functionalization that improve the performance of the probes. It also examines their various biomedical uses in cancer, inflammation, cardiovascular, and neurological diseases, as well as their application as theranostic platforms in combination with diagnosis and treatment [7]. In addition, the paper pro- vides a critical assessment of existing issues in clinical translation, such as safety, biocompatibility, clearance, and regulatory barriers, and talks about the prospects of quantum sensing, artificial intelligence, and biodegradable smart probes [8]. MRI probes represent a rapidly evolving class of diagnostic tools designed to enhance image contrast and specificity in biomedical imaging. These probes are generally classified into micro and nanoscale categories based on their dimensional characteristics and functional applications [9]. Micro-scale probes, including microcoils, microfluidic MRI probes, and quantum-based microsensors, are primarily utilized for high-resolution and localized imag- ing, enabling precise detection of microstructural and physiological variations within tissues.In contrast, nanoscale probes—comprising magnetic nanoparticles (such as SPIONs, USPIONs, and MIONs), hybrid or multimodal nanoprobes, and stimuli-responsive smart probes—offer molecular-level imaging and targeted

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contrast enhancement [10]. Magnetic nanoparticles serve as efficient contrast agents T1 or T2 due to their strong magnetic properties. At the same time, hybrid nanoprobes integrate MRI with complementary imaging modalities such as PET, CT, or fluorescence to achieve multimodal diagnostics. In addi- tion, stimuli-responsive probes that react to pH, enzyme activity, or redox conditions enable dynamic visualization of pathological microenvironments such as tumors or inflammatory sites [11]. Together, the development of micro- and nanoscale MRI probes has significantly advanced biomedical imag- ing by improving spatial resolution, sensitivity, and functional insight, thus facilitating early disease detection and personalized therapeutic monitoring.

The review follows the following structure: Section 2 deals with the techno- logical advances and design of probes; Section 3 addresses the topic of targeting and stimuli-responsive strategies; Section 4 focuses on biomedical uses; Section 5 lists insights on the clinical potential of the field; and Section 7 provides a conclusion about this field.

2. Technological Innovations in Micro Nano MRI Probes

2.1. Advances in Hardware and Materials

MRI hardware has played a key role in improving the performance of view- ing tiny or microscopic structures. Significant innovation is the appearance of High-Temperature Superconductor (HTS) coils. With reduced electrical resis- tance, HTS coils noticeably increase the signal-to-noise ratio compared to conventional copper coils. It helps spot weak signals from micro/nano devices and in microscopy of small biological structures [12]. New developments in simple, cryogen-free HTS coil systems increase their usefulness in hospitals and science fields. Workers are still trying to solve superconductor problems and make HTS work with existing MRI equipment. HTS has advanced, and the miniaturization of detection hardware has led to the development of micro coils and sensors at the nanoscale. Local high-resolution pictures and molec- ular data can be captured using micro coils ranging from hundreds to several micrometers in diameter. Diamond nitrogen-vacancy centers and other quan- tum sensors are being examined for their superior ability to sense magnetic fields at the nanoscale level [13]. Miniature components for MRI systems are in the early stages of use. They promise to make MRI useful for cellular and molecular research, filling a gap between traditional and modern research needs.

2.2. Magnetic Nanoparticles as MRI Probes

Superparamagnetic iron oxide nanoparticles (SPIONs) and ultra-small SPI- ONs (USPIOs) are two of the most significant medical innovations [14]. Their strong magnetic properties, compatibility with the body, and varied surface.

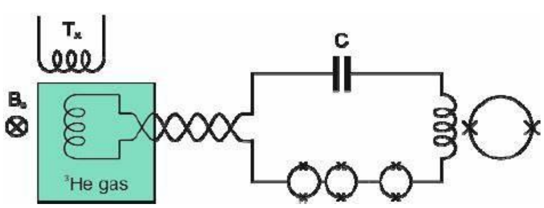

Fig. 2 HTS coil circuit for enhanced MRI sensitivity

Chemistry have made these nanoparticles, generally no more than 150 nanome- ters in size, the new standard in MRI probes. The primary function of SPIONs is to reduce the signal in the areas they accumulate, making those areas easier to spot. USPIOs, on the contrary, serve as both T1 and T2 agents if their size is appropriate and the magnetic core meets specific needs, making imaging more flexible. Nanoparticle performance is strongly affected by their size, shape, and coating. Generally, small nanoparticles circulate longer and enter tissues more easily, but larger particles often end up in the RES, a group of immune cells. Structural changes to nanoparticles, such as making them into rods and cubes or adding porosity, may change their magnetic performance and usefulness [15]. The biocompatibility, blood half-life, and targeting of nanoparticles are also influenced by surface coatings, whether using polyethylene glycol (PEG), dextran, or bioactive ligands. For example, using PEG reduces the chance that immune cells will notice the particle. It allows the nanoparticles to remain in the body longer, targeting molecules (peptides, antibodies, or aptamers) that guide them to the required biomarkers or specific areas. These new and flexible MRI probes now exist to respond to triggers, including pH, enzymes, or redox conditions, which means that they can only show contrast when something is wrong and hide from non-pathological tissue [16]. Despite these developments, some obstacles remain, such as lowering iron levels to prevent overload, ensuring that nanoparticles do not clump, and keeping production reliable. However, in clinical and preclinical studies, magnetic nanoparticles are being proven safe and effective, since SPION-based devices are permitted for a few diagnostic purposes.

2.3. Multimodal and Hybrid Probes (e.g., PET MRI)

Scientists have now invented multifunctional probes that combine several imag- ing techniques into one device. Nanoprobes designed for combined PET MRI or MRI fluorescence imaging accommodate a simultaneous collection of anatomical, functional, and molecular data. A combination of magnetic particles, radioisotopes, and special dyes in these probes allow them to combine the accuracy of MRI with the powerful sensitivity of PET and the fast fluores- cence image [17]. Effective probes for two or more modalities, the stability of each imaging agent, how it is absorbed in the body, and the chances of mutual interference are all important factors to consider. By way of illustra- tion, nanoparticle surface modification has to prevent any interference with their magnetic functions or ability to be guided to the target.

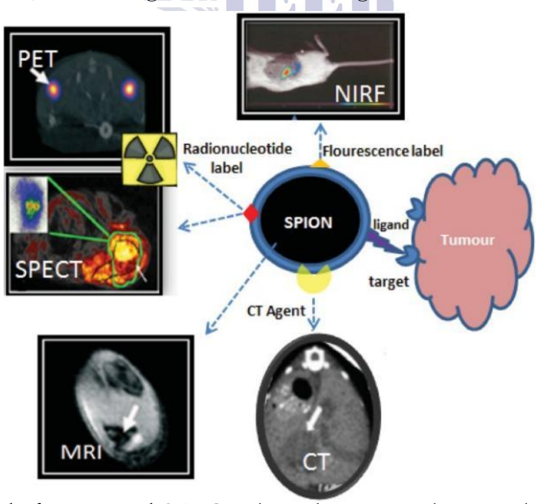

Fig. 3 Schematic showing multifunctional SPION-based nanoprobes used for targeted tumor imaging with multiple modalities MRI, CT, PET, SPECT, and NIR fluorescence through surface labeling and targeting ligands

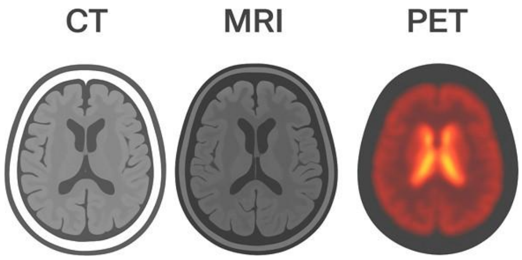

Fig. 4 CT, MRI, and PET brain images

PET/MRI "super probes" allow clinicians to spot a lesion through MRI and measure its metabolic activity using PET. Multimodal probes ready for medi- cal use are slowed by regulatory challenges, which involve product development and safety checks. Future work is expected to focus on making the probes more suitable for clinical needs and integrating various imaging techniques, including photoacoustic and quantum imaging [18].

3. Design Strategies for Targeted Micro Nano MRI Probes

3.1. Surface Functionalization and Targeting Ligands

The main advantage of the most modern MRI probes in micro and nanosystems is that they concentrate on the site of disease, helping to increase diagnos- tic accuracy and sensitivity. The basic method for achieving this selectivity is to change the nanoparticle surfaces by adding ligands that can detect and attach to signs of disease in the blood. The unique benefits for the design of MRI probes, peptides, aptamers, and antibodies are now considered the main classes of targeting ligands [19]. RGD peptides provide high accuracy, pose lit- tle risk of causing an immune response, and allow easy modification to attach to many tumor or inflammation-specific surface proteins. Aptamers, which are short single-stranded nucleic acids, can be quickly made, modified chem- ically, and specifically chosen for their strong binding to targets at low cost. Although antibodies and fragments are the most specific type, they can some- times be unstable and are usually more expensive to make and change. Two types of mechanisms are available for targeted delivery: passive and active. In passive targeting, leaky vessels inside tumors (EPR effect) cause nanopar- ticles to collect mostly in and around them. Although it seems simple, the effect of EPR changes significantly depending on the patient or their cancer and cannot target the cell or receptor level [20]. Active targeting feature lig- ands that link to specific markers found only in cancer cells, cells involved in inflammation, or other diseased sites. Probes modified with AFP or GPC-3 lig- ands have effectively located hepatocellular carcinoma. Multi-liganded probes are also improving the process of concentrating nanoparticles. Being careful is crucial here because being over-targeted may result in early removal by cells in the body, and being under-targeted could weaken the benefits of imaging. The density of ligands, along with the size and surface charge of the particles, also decides their half-life in blood, where they are found in the body, and the chance of finding their intended target [21].

3.2. Stimuli-Responsive and Smart Probes

The newest MRI probes use regular targeting, respond to nearby harmful con- ditions in the body, and turn on contrast when useful, making them "smart." They are designed to overcome the main problem by reducing unwanted back- ground noise and increasing the range between healthy and compromised tissue. Many researchers have built pH-responsive probes to detect acid sur- roundings at most tumor or inflammation sites [22]. In the circulatory phase, these liposomes do not show MRI contrast but transform or bind together in response to acids within the tumor, making them highly visible on MRI images. Nanoprobes engineered with enzymes respond to disease-related enzymes, cut- ting special bonds or layers around the particle so that only at the targeted site does the imaging signal appear. When exposed to the excessive glutathione or reactive oxygen species present in some diseased tissues, redox-responsive systems can change either the relaxivity of the probe or trigger drug release. Such probes improve the accuracy of tests and allow new ways for theranos- tics to combat diseases [23]. Medicines only released from nanoparticles in diseased tissue keep side effects to a minimum and can be monitored by MRI throughout treatment. Although preclinical results are encouraging, the use of these therapies in the clinic is slowed by challenges in synthesis, the potential impacts on the immune system, and strict requirements for correct activation. This merging of surface treatment methods with stimuli-responsive engineer- ing allows the field to develop precise imaging techniques that use advanced microprobes to help monitor and direct therapy with minor undesired damage [24].

4. Biomedical Applications of Micro Nano MRI Probes

4.1. Cancer Imaging and Theranostics

Cancer imaging is where micro/nano MRI probes have their most signifi- cant impact since they significantly improve sensitivity and specificity while introducing ”theranostics” [25]. MRI’s use in seeing the structure of tumors is valuable, but it is not as precise at the molecular level needed to spot tumors early or understand them well. Nanoscale probes that carry targeting molecules have greatly improved how we image cancers by displaying unique molecules found in cancer cells [26]. Hepatocellular carcinoma (HCC), which is often not discovered until it is advanced and carries a poor outlook, targeted MRI probes linked to AFP and GPC-3 ligands have proven effective at gath- ering in malignant tissues, making it easier to detect and prevent mistakes. SPIONs and nanocarriers with Gd enhance imaging sharply and improve the ability to divide and classify tumors at the molecular level [27]. An important development is the growth of theranostic nanoprobes, which unite tests and treatments in a single structure. Such probes help deliver medicines directly to the tumor, followed by an MRI that guides them and helps view their progress. Gold nanotechnology has played a pivotal role in advancing cancer therapy, particularly by enabling highly specific and efficient targeted drug delivery systems [28] (Al-Thani 2024). As an illustration, SPIONs and gold nanoparti- cles filled with anticancer drugs and covered to target tumors support precise diagnosis, guided treatment with images and examination once the treatment is finished, helping to approach personalized oncology. Even with supportive evidence from these models, bringing these discoveries into standard patient care is not easy because they need approval, must be produced and must be shown to be safe.

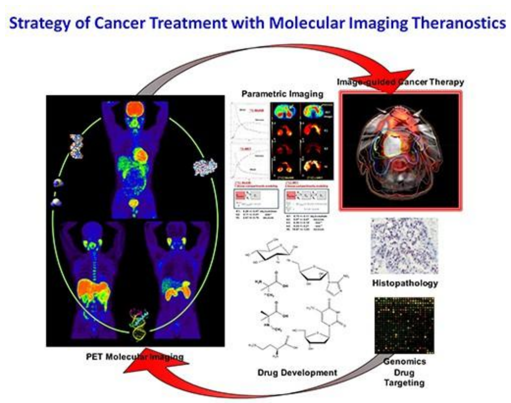

Fig. 5 Molecular imaging theranostics integrates PET imaging, drug development, genomics, and image-guided therapy for personalized cancer treatment

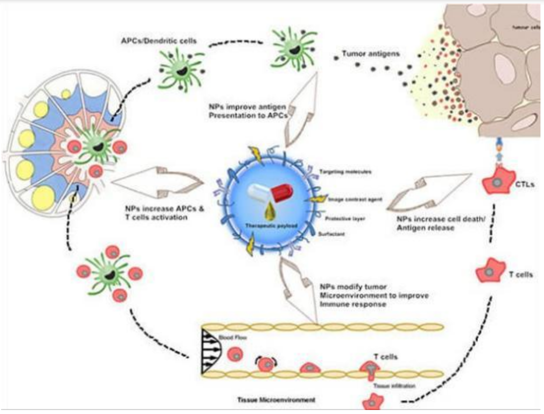

Fig. 6 : Theranostic nanoprobe for targeted tumor imaging and therapy

4.2. Inflammation, Infection, and Cardiovascular Imaging

Oncology micro nano MRI agents, especially SPIONs and their miniature ver- sions have proven very useful for imaging and following the progress of varied pathologies, such as inflammation, infection, and heart disease. The feature that makes SPIONs easy for macrophages to remove has allowed researchers to track inflammation in plaques, weak cardiac lesions and places where infection occurs. Because MRI can spot the presence of SPIONs in inflammation-affected tissues, it can tell if inflammation is going on before any apparent physical differences open, helping interventions can be provided sooner [29]. Smarter SPIONs, built to react in inflammatory areas or coated with chemicals that stick to P-selectin and VCAM-1, make it possible to track the progress of stroke, myocardial infarction and autoimmune diseases and identify those at a higher risk. Nanoparticles made to be taken up by macrophages can make infected tissue visible, which can be recognized from sterile inflammation in imaging. Thanks to SPIONs, scientists can trace how immune cells spread throughout the body and study the body's reaction to disease and specific drug treatments [30]. Although there is good evidence for SPION-enhanced MRI in animals and some studies in patients, important reasons for not using them, as usual, are more concerned about safety than accuracy, challenging iron saturation in certain diseases and the need for regulatory support.

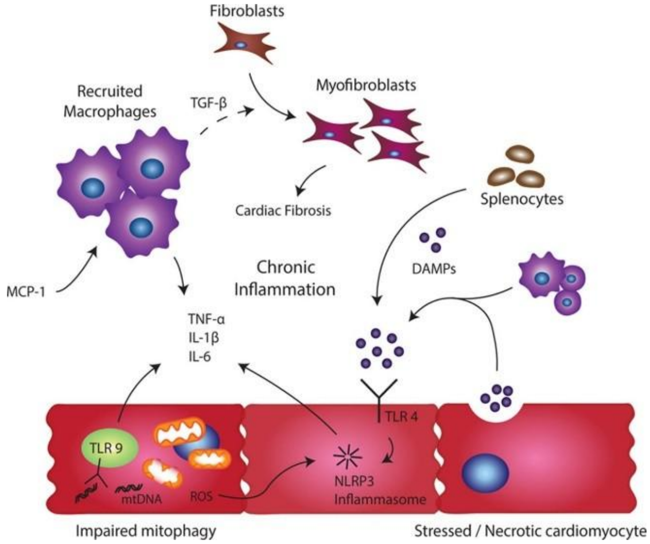

Fig. 7 Mechanism of chronic inflammation and cardiac fibrosis showing the roles of impaired mitophagy, inflammatory cytokines, recruited immune cells, and fibroblast activa- tion in heart disease progression.

4.3. Other Applications: Neurology, Renal, Gastrointestinal, etc.

Further proof of how versatile micro/nano MRI probes are is found in their use for neurology, renal and gastrointestinal imaging. With USPIOs, it is now possible to use MRI to detect neuroinflammation, detect MS lesions early and measure how tightly the blood-brain barrier is sealed, which traditional MRI. In regenerative medicine and immunotherapy, researchers can track how stem cells or immune cells are inside the body thanks to functionalized SPIONs [31]. Through renal imaging with targeted nanoprobes, physicians can assess kidney inflammation, transplant rejection, and the early stages of fibrosis, a problem currently difficult to evaluate non-invasively. Similarly, nanoparticles taken orally or injected into a vein support detecting and evaluating inflamma- tory bowel disorders and the non-surgical mapping of gastrointestinal tumors. These treatments into the clinical setting remains challenging even with these latest discoveries. Challenges concerning delivering probes, their lasting safety and making sense of observed signal changes must be solved to get the best from micro/nano MRI probes across multiple body systems.

Table 1: ***Application Summary of Micro/Nanoscale MRI Probes***

Application Area	Probe Type	Targeting/ Mechanism	Imaging Mode(s)	Stage
Oncology	SPIONs, Gd-NPs	AFP, GPC-3, pH-responsive	MRI / PET-MRI	Preclinical–Clinical
Cardiovascular	SPIONs	VCAM-1, macrophage uptake	MRI	Preclinical
Neurology	USPIOs	BBB permeability	MRI	Preclinical
Inflammation	Dextran-coated SPIONs	Macrophage accu-mulation	MRI	Clinical (Feru-moxytol)
Theranostics	Au@SPION hybrids	Drug release + imaging	MRI / NIR / CT	Preclinical

5. Clinical Translation and Current Challenges

5.1. Preclinical and Clinical Trials Overview

Micro/nano MRI probes have made significant progress in clinical use thanks to a solid foundation from research and the first phases of studies in people. Researchers have primarily focused on SPIONs, as several different formula- tions, like ferumoxytol and ferumoxtran, have been allowed into clinical use for vascular imaging, the identification of lymph nodes and locating areas of inflammation. According to clinical studies, these drugs help increase the accuracy of diagnoses in oncology, neurology and cardiovascular fields [32]. Good results in the first batch of studies, few nano MRI probes have becomeapproved for use. Although ferumoxytol is approved for treating iron deficiency, its use for MRI is increasing, but its broader acceptance in imaging is limited by safety and standardization problems. Complex probe production, different pharmacokinetic patterns in patients and the absence of standard clinical out- come measures have caused the translation process to move slowly. Probes for imaging with PET MRI or several other modalities are not yet fully used, as studies mostly use them only in animals or very carefully controlled groups of humans [33].

Table 2: Key stages in the development pipeline of micro- and nanoscale MRI probes, from materials discovery to clinical translation

Stage	Meaning
Materials Science	Scientists choose or synthesize the basic materials (e.g., iron oxide, polymers, quantum materials) that will form the probe.
Probe Design	Engineers design the probe's size, surface coating, tar- geting ligands, and responsiveness (e.g., pH, enzymes).
Preclinical Validation	The probe is tested in lab experiments and animal models to check imaging quality, targeting accuracy, and performance.
Safety & Biocompatibility	Toxicology, biodistribution, clearance, and immune response are studied to ensure the probe is safe in bio-logical systems.
Regulatory Trials	Human clinical trials (Phase I–III) evaluate safety, dosing, efficacy, and performance in real patients.
Clinical Translation	Once approved by regulatory agencies (e.g., FDA, EMA), the probe can be used in hospitals and medi- cal imaging settings.

Table 3: ***Timeline of key nano MRI probes and clinical milestones***

Year	Nano MRI Probe	Application Area	Stage	Notes
1996	Ferumoxides (Feridex)	Liver lesion imaging	FDA Approved	First SPION-based liver contrast agent; later withdrawn.
2000	Ferumoxtran-10	Lymph node, tumor detection	Clinical Trials	Used in EU for lymph node imaging; not FDA approved.
2009	Ferumoxytol (Feraheme)	Iron defi- ciency therapy, MRI	FDA Approved (therapy), label (MRI)	Approved for anemia; widely used off-label for Off-vascular and tumor MRI.
2010–2015	USPIOs (ultra-small SPIONs)	Inflammation, cell track-ing	Preclinical	Enhanced sensitivity for tracking inflamma- tion and immune cells.
2016–2022	Hybrid PET/MRI NPs	Multimodal imaging	Preclinical/T	riaClos mbined PET/MRI probes in animal and select human studies.
2023	Biodegradable SPIONs	Cancer, theranos- tics	Preclinical	Focus on improved safety, targeted deliv- ery,and controlled clearance.

5.2 Safety, Biocompatibility, and Clearance

Clinical use of nano MRI probes is unlikely until their safety can be ensured. There are worries about excess iron accumulation and about the risk of adverse effects on the immune system if iron is given often or to people system is less efficient. Whether nanoparticles end up in the kidneys for removal or build up over time in the liver, spleen and bone marrow is being closely watched. Ways to solve these issues involve altering particle size (smaller SPIONs clear more easily from the body), making the particle surface neutral or hydrophilic (such as by using PEG) and creating formulations for safe metabolism [34] (Yang et al., 2023). Various reasons, a few agents have been taken off the market, making it clear that firms must continue to carefully study the long-term safety of their medicines in those who might be more at risk.

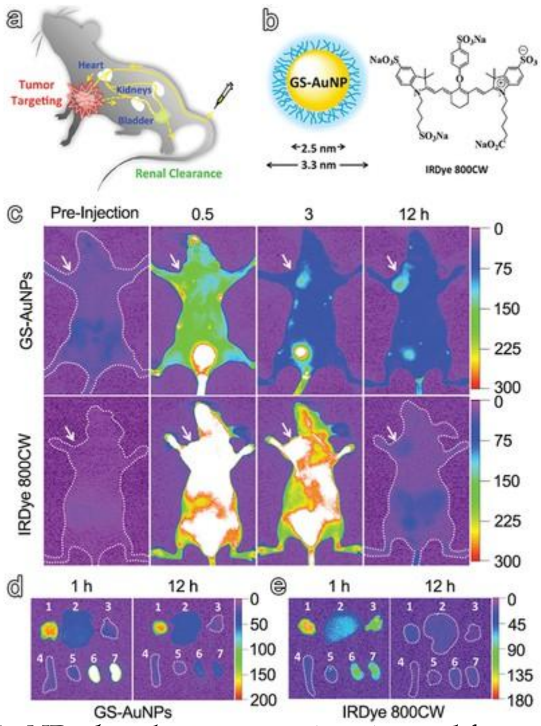

Fig. 8: Tumor-targeted GS-AuNPs show better tumor imaging and faster clearance than IRDye 800CW

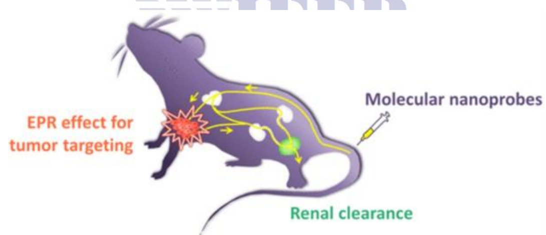

Fig. 9 Tumor targeting and renal clearance of molecular nanoprobes

5.3: Limitations and Unmet Needs

Probe design and early clinical outcomes have advanced, significant unresolved problems exist. Some weaknesses in using biomarkers include that targets do not work reliably for every disease; often, they are not sensitive enough to spot rare substances and the outcomes from treatment change from one group of patients to another. Guidelines for employing novel nano MRI probes are complicated, preventing their quick use in medical practice [35]. There is an urgent requirement for shared standards, better insights into in vivo actions and extensive studies to assess their clinical value.

5.3 Limitations and Unmet Needs Probe design and early clinical out- comes have advanced, significant unresolved problems exist. Some weaknesses in using biomarkers include that targets do not work reliably for every disease; often, they are not sensitive enough to spot rare substances and the outcomes from treatment change from one group of patients to another. Guidelines for employing novel nano MRI probes are complicated, preventing their quick use in medical practice [35]. There is an urgent requirement for shared standards, better insights into in vivo actions and extensive studies to assess their clinical value.

6. Future Perspectives and Research Directions

The area of micro/nano MRI probes is expanding quickly thanks to advances in new technologies and a move towards personalized and precise medicine. Researchers are also exploring quantum ways to sense and use diamond NV centres, which could lead to imaging with MRI at the single-molecule or cel- lular level. These quantum sensors will likely enable more explicit images and help identify otherwise unknown biological functions without harming the subject. Even though translating them into clinical MRI is not easy, studies point to quantum technologies as having the potential to transform the field of biomedical imaging. At the same time, AI and machine learning help plan and improve new MRI probes. Studying large datasets on nanoparticles, their activities with biology, and their imaging results helps AI quickly pick out ideal probe features, anticipate what they do inside the patient's body, and tailor the choice to patient-related data. These technologies are expected to make developing probes easier and improve the safety and usefulness of clini- cal procedures. Diagnosis strategies of the future expect personalized imaging and theranostics to play a key role. A single nano platform combining imag- ing technology and on-demand treatment can create new ways to give precise therapy and constantly check its effectiveness. Future investigations should focus on inventing biodegradable multifunctional probes that can target dif- ferent sites and be turned on and off as necessary. Because of this, chemical, physical, engineering, biological and clinical medicine experts will have to col- laborate, handling the most significant issues in safety, official permission and the large-scale making of such products [19]. Continued advancement backed by in-depth studies needs to happen to turn the great potential of micro nano MRI probes into routine use in healthcare.

7. Conclusion

Micro/nano MRI probes have enabled us to diagnose illnesses with enhanced accuracy and description at the molecular level. Improved probe designs, functionalised surfaces and smarter, responsive elements have made these tech- nologies much more sensitive, specific and suitable for personalized therapy using imaging. Progress and promising research results suggest that tissue engineering still faces serious challenges in keeping therapy safe for long, ensur- ing it works well with the body, getting regulatory approval and carrying out large patient trials. These challenges can only be overcome by combining approaches and the latest technology. Micro/nano MRI probes will majorly impact medicine by allowing for earlier diagnosis, better monitoring of treat- ments and attaining true precision in diagnostics and theranostics. These special tools may become important to modern non-invasive imaging if research and clinical studies continue.

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