https://rijournals.com/scientific-and-experimental-sciences/

RESEARCH INVENTION JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 4(3):31-36, 2024

©RIJSES Publications

ONLINE ISSN: 1115-618X

PRINT ISSN: 1597-2917

https://doi.org/10.59298/RIJSES/2024/433136

Nanoparticles in Medical Imaging: Enhancing Contrast Agents

Alberta Jeanne N.

School of Applied Health Sciences Kampala International University Uganda

ABSTRACT

Nanoparticles have emerged as revolutionary tools in medical imaging, offering novel solutions to enhance contrast agents for improved diagnostics. Contrast agents play a critical role in visualizing internal structures and functions, aiding the diagnosis and monitoring of various health conditions. However, traditional agents face limitations, including suboptimal imaging quality, biocompatibility challenges, and potential toxicity. Nanoparticles address these concerns through their unique properties, such as surface tunability, size optimization, and multifunctionality. This review examines the types, advantages, limitations, and functionalization of nanoparticles in medical imaging, highlighting their applications across modalities such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and optical imaging. Emphasis is placed on the synthesis, characterization techniques, and regulatory considerations necessary for clinical translation. By pushing the boundaries of imaging technology, nanoparticles hold promise for earlier detection, better treatment monitoring, and a new era of personalized diagnostics.

Keywords: Nanoparticles, Medical imaging, Contrast agents, Biocompatibility, MRI, CT imaging.

INTRODUCTION

Medical imaging has shown its significance in the real-time visualization of internal structures and functions, which is essential for diagnosing a variety of diseases and monitoring health conditions. The development of imaging modalities has driven discovery and introduced enabling biomarkers that have particularly improved diagnostic accuracy. However, the images acquired can be impaired by scattered radiation in the body, which can strongly degrade image quality, hindering magnetic resonance imaging, nuclear imaging, and especially extensive X-ray imaging modalities. Contrast agents are non-toxic chemicals typically used to enhance the image contrast of tissues and cells of interest in the body. Due to their efficiency in improving image quality, these agents enable visualization of vascular compartments, characterization of the liver and spleen, and also provide helpful tools to visualize tumors, and the brain, and track stem cells post-injection in clinics [1, 2]. Numerous types of contrast agents for MRI include extracellular, intravascular, dynamic, blood pool, and targeted agents, and new agents have been discovered and introduced in clinics and pre-clinics to enhance the signals of each tissue. Regarding X-ray imaging, the widely used classes of contrast agents are iodine-based agents, barium, and particulate agents. However, the use of contrast agents is not limited to diagnostic imaging. They also show improved image quality by introducing 3D images and can be used in other applications like quality control of drug-loaded nano-carriers. These applications are relevant in clinics since contrast agents, unlike drugs, are not absorbed, transformed, metabolized, or excreted by the body [3, 4]. To this aim, contrast agents must possess superior imaging capabilities such as high sensitivity and quantitatively accurate responses to the local microenvironment, as well as non-compromising design for biocompatibility to avoid undesired body responses, control of target or compartment selectivity to gather specific information about the disease, and the capacity to occupy, discriminate, and induce the compartment we examine. However, most available contrast agents do not meet all these requirements

due to their contrast mechanism, chemical biodegradability, and accumulation in the body. To meet these requirements, promising candidates are those prepared from advanced materials where the correlation between physicochemical properties and contrast signal response shows higher potential than small molecular agents. Among advanced materials, nanoparticles have garnered much attention as they can interact with electromagnetic irradiation due to their optical and electrical properties. Moreover, new applications of nanoparticles are ongoing and have been reported. In addition, applications of contrast agents must undergo regulatory review, and because of the potential side effects and their longer existence in the body compared to drugs, the regulations and therefore their translation to clinics are stringent. It is favorable for contrast agents to be prepared from biocompatible materials and to be continuously eliminated from the body with no accumulative features or side effects [5, 6].

Nanoparticles as Contrast Agents

At their most basic level, modern-day medical imaging techniques aim to improve the visibility of tissues and organs to detect abnormalities and diseases. Contrast agents are by far the most widely used 'medicines' in radiology today, augmenting the contrast between abnormal and normal tissues or different organs. Currently, most contrast agents are based on low-molecular-weight chelates of both natural and artificial metals. While the use of these agents has vastly improved the performance of various imaging systems, there are significant limitations in spatial and functional areas. To overcome these limitations, several nanoscale particles have been proposed as next-generation contrast agents. In this paper, we shall focus our attention on the applications of nanoparticles as contrast agents for medical imaging. Accordingly, numerous questions regarding clinical utility, biocompatibility, and possible cytotoxicity issues must be addressed as functional nanoparticles are to be translated successfully from the chemistry laboratory to the clinical department and into the community [7, 8]. Several important advantages of nanoparticles make them attractive for targeting imaging as well, such as their surface tunability, small size, and ability to be present for long periods of time in the blood, among others. Furthermore, nanoparticulate contrast agents generate variable contrast and are surface-modifiable for targeted imaging applications. Adding additional ligands creates the possibility for signaling, cellular-penetrating, or targeting moieties to be added to the nanoparticle surface, thus enhancing the capabilities of the nanoparticle as a multimodal platform. They can serve as both targeted therapeutic carriers as well as contrast imaging agents. Nanoparticles have been shown to exploit physical properties and biological behaviors to offer imaging advantages such as increased resolution and free contrast inversion due to their physical properties and surface chemistry. They retain imaging agents locally when they are injected into the body. These unique properties allow for unique imaging functionalities; for instance, some particles provide feedback or monitoring of their own presence or biological activity within the diseased tissue in case of therapy. Finally, some nanoparticulate imaging agents that are designed to produce one type of image can also produce another type of image. This feature is known as multifunctionality. In all cases, we are most concerned with severe problems of potential safety and biocompatibility issues, which must be tackled so that the unique features of nanoparticles can be exploited in molecular imaging [9, 10].

Types of Nanoparticles Used

Nanoparticles, which are frequently made of hydrophilic polymers, come in several different forms, including metals, polymers, lipids, silica, quantum dots, and various bismuth oxide structures. Silica nanoparticles are recognized for their versatility, but their lack of surface charge (and therefore poor stability) is compensated for by the fact that they can be easily modified chemically. The molecules were attached to the surface of the freshly synthesized silica nanoparticles to create positively chargeable contrast agents. It was shown that remodeled nanoparticles, provide an easy and effective way of adjusting their size and surface charge. A similar approach was used to engineer nanoparticles with interesting magnetic and fluorescent properties. Metal-based nanoparticles are usually more expensive to fabricate; however, some nanoparticles based on metal for use as contrast agents to improve MRI images have been developed. These include a moldable MRI contrast agent and another developed for hepatic MRI imaging. The Advantageous Surface Design can improve MR brain imaging [11, 12]. In conclusion, our understanding of the benefits of utilizing nanoparticle contrast agents is that these unique benefits aid in enhancing imaging performance and pushing the boundaries of technological advancements. By tailoring the particles' properties, it is easy to identify exactly where a certain type of particle has gone in the human body [13, 14].

Advantages and Limitations

The use of nanoparticles as contrast agents presents a set of advantages. The bioavailability of the contrast is improved by modifying their surface with biocompatible polymers. In addition, several functionalities can be added to the nanoparticles to enhance the imaging resolution, the capacity to target specific bodies and cells, and other enhanced imaging modalities. This versatility increases the range of nanoparticle imaging applications. Despite the obvious advantages, the use of nanoparticles as contrast agents also presents some limitations. One possible drawback could be the potential triggers of a toxic effect from the escalated number of nanoparticles—either in their elemental core or modified as they transit through the body. This raises valid doubts and caution toward the use and accumulation of nanoparticles in organs. An in-depth insight into these factors is crucial, as it is expected to require a period of time and extensive research before nanoparticles' clinical circulation becomes permissible. Regulatory norms and testing need to be designed, and the nanoparticle contrast agents scrutinized carefully based on their efficacy and toxicity. One means to gauge accurately if nanoparticles offer potential overall effects in a disease is to contemplate their prospective toxicities. This helps identify any interference between the therapy and the contrast agent. If possible, investigations must portray the overall functionality and efficacy incorporating, for instance, the safety and tolerability of the nanoparticles when applied in humans [15, 16]. There are several successful applications of nanoparticles in medical imaging techniques. However, there are also some challenges in the clinical applications of nanoparticles because of their possible toxicity. The standard requirements and protocols should be consistent with a toxicity assessment for the nanoparticles in a reasonable dose. The toxicity assessment, including an imaging agent application, should be performed to determine the overall benefit/risk ratio. The primary performance consideration is inevitably a balance among effectiveness, appropriateness, expansion, distortion, and contribution to the overall technical performance and safety. Most of the currently used applications do not require a sensitometric analysis to determine diagnostic efficacy, also targeting prospective clinical use. Regulatory constraints must also be cleared, and therefore the majority of the clinical devices and techniques necessitate operational approvals. The other main consideration for the clinical applications is the investment reliability, even if the nanoparticle is not yet regulated. This is the case for most imaging techniques, particularly oncological, where incomplete phase III investigations leave the nanoparticle halfway between experimental and approved therapeutic tools [17, 18].

Synthesis and Functionalization of Nanoparticles

Synthesis and functionalization of nanoparticles represent the first essential steps for the development of medical imaging contrast agents. Nanoparticle synthesis can be fulfilled by different methods: some of the major strategies can be classified into three groups, i.e., chemical, physical, and biological routes. Despite the numerous advantages of chemical methodologies, in terms of reproducibility and scalability of product synthesis, they often present several drawbacks, such as the use of toxic precursors, high pressures and temperatures, the impossibility of controlling particle capping and functionalization, and the production of relevant amounts of waste. Even though physical approaches could overcome most of these issues, they would be affected by a lower possibility of controlling the finally determined size, size distribution, and morphology, whose optimization is critical for final imaging performance, since those features affect relaxation times for a given concentration. Lastly, biological synthesis is connected with a growing but still limited number of viable strategies, mainly silver, iron, and other metal nanoparticles' biosynthesis. The low levels of waste, excellent reproducibility, and capability to tailor metal nanoparticle dimensions and functionalization with enzymes may be some attractive features for imaging, even though their relation to clinical translation is still lacking [19, 20]. Nanoparticle functionalization, usually applied as a bi-layered coating, aims at improving biocompatibility and introducing tailored cell-type targeting. In this field, particles should preferably be endowed with a long blood residence time due to a controlled blood circulatory half-life. The final design and performance of nanoparticles are also closely related to the synthesis of their structural and functional features, such as size, shape, crystalline form, composition, solubility, and storage stability. Once in vitro and in vivo, nanoparticles are expected to recognize the specific biological tissue of interest, depending on the conditions, and release therapeutic and/or informational molecules in a specific target site when triggered. The use of nanotechnology for the preparation of contrast agents is an ongoing, strongly dynamic, and expanding field, and several promising approaches have been recently proposed [21, 22].

Characterization Techniques for Nanoparticles

Associated with nanoparticles and their application in medical imaging diagnostics, the production batch quality must be assessed. Generally, the following techniques are proposed and well used: transmission electron microscopy, X-ray diffraction, dynamic light scattering, zeta potential assay, and UV-VIS-NIR optical characterization. However, different techniques are developed to obtain different types of information, such as electronic, magnetic, thermal, catalytic properties, and shape anisotropy, to develop them with in-depth, detailed characterization so that one can improve their suitability for the best possible medical imaging application [23, 24]. The characterization of nanoparticles is of utmost importance, especially for potential medical imaging applications. Such information includes considerable parameters other than just nanoparticle size, e.g., shape. The above-mentioned characteristics determine the potential usefulness of nanoparticles as contrast-creating substances in medical imaging, ensuring that manufactured batches are consistent and reliable. What is more intriguing is the distribution and clearance of contrast-generating nanoparticles into biological media, particularly blood and lymph, which affects, for instance, the nanoparticles required for strongly vascularizing organs. Accurate information on the size, shape, surface charge, and nanoparticle stability in the applied environment ensures the best contrast results in the applied imaging scenarios [25, 26].

Applications of Nanoparticles in Medical Imaging

The potential of nanoparticles in medical imaging has various applications, and their uses are likely to be part of routine clinical tools that enable earlier diagnosis and better monitoring of treatment. In general, we can classify the applications of nanoparticles in medical imaging according to the imaging modality as follows—these applications will on some occasions make possible a performance in medical diagnosis that was completely inconceivable until recent times. For instance, these nanoparticles can enhance the sensitivity and resolution of imaging techniques. This is feasible just by using contrasting agents that can specifically increase the contrast between different biological tissues, organs, or vessels. In recent years, practical applications for nanoparticle contrast agents have already been proven for the in vivo imaging of a wide range of organs, such as tumors by MRI and myocardium by CT [27, 28]. Similarly, this nanoparticle-based image contrast has already achieved routine diagnostics for in vivo sentinel lymph node identification and/or imaging-guided surgery. In many cases, nanoparticles are the only materials able to provide such excellent information. In theoretical discussions of so-called 'impossible diagnosis,' it has been claimed that under some conditions, cancer diagnoses at an early stage would be impossible, even using a combination of the most advanced imaging techniques. 'Impossible' diagnosis mainly refers to the early-stage diagnosis of tiny tumors, i.e., a typical diagnostic imaging tool at the pre-micrometer scale is standard histopathology of biopsies. Recent discussions have introduced gold nanoparticles as a new class of photothermal enhancing agents that can obtain enhanced dark-field imaging of individual non-diffracting nanoparticles and even clinical dark-field hyperspectral microscopy images of cancer biopsy specimens small enough not to affect the positive evaluations by pathologists [19, 29].

CONCLUSION

Nanoparticles are redefining the capabilities of contrast agents in medical imaging. Their small size, surface tunability, and multifunctionality enable enhanced visualization of biological tissues and organs, leading to improved diagnostic accuracy and therapy monitoring. Despite their potential, challenges such as toxicity, regulatory hurdles, and scalability need to be addressed to facilitate clinical translation. Advances in synthesis, functionalization, and characterization techniques continue to mitigate these issues, showcasing nanoparticles as a promising frontier in medical imaging. Future research and collaboration between materials science, medicine, and regulatory bodies are vital to unlocking their full potential, paving the way for transformative diagnostics and personalized healthcare solutions.

REFERENCES

1. Jiang Z, Zhang M, Li P, Wang Y, Fu Q. Nanomaterial-based CT contrast agents and their applications in image-guided therapy. Theranostics. 2023;13(2):483.
2. 2. Nowak A, Pacek G, Mrozik A. Transformation and ecotoxicological effects of iodinated X-ray contrast media. Reviews in Environmental Science and Bio/Technology. 2020 Jun;19(2):337-54. springer.com
3. Pareri AU, Koijam AS, Kumar C. Breaking the silence of tumor response: Future prospects of targeted radionuclide therapy. Anti-Cancer Agents in Medicinal Chemistry-Anti-Cancer Agents). 2022 Jun 1;22(10):1845-58. [HTML]

4. Vignati A, Giordanengo S, Fausti F, Martì Villarreal OA, Mas Milian F, Mazza G, Shakarami Z, Cirio R, Monaco V, Sacchi R. Beam monitors for tomorrow: the challenges of electron and photon FLASH RT. Frontiers in Physics. 2020 Sep 14;8:375. frontiersin.org
5. Bouafia A, Laouini SE, Ahmed AS, Soldatov AV, Algarni H, Feng Chong K, Ali GA. The recent progress on silver nanoparticles: synthesis and electronic applications. Nanomaterials. 2021 Sep 6;11(9):2318. mdpi.com
6. AlZaidy GA. Boosting of the optical properties, and electrical conductivity of polymethyl methacrylate (PMMA)/Polystyrene (PS) Blend with zinc oxide nanoparticles for high-performance energy storage devices. Journal of Inorganic and Organometallic Polymers and Materials. 2024 Jun 25:1-2. [HTML]
7. Chen X, Argandona SM, Melle F, Rampal N, Fairen-Jimenez D. Advances in surface functionalization of next-generation metal-organic frameworks for biomedical applications: design, strategies, and prospects. Chem. 2024 Feb 8;10(2):504-43. cell.com
8. Chakraborty K, Tripathi A, Mishra S, Mallick AM, Roy RS. Emerging concepts in designing next-generation multifunctional nanomedicine for cancer treatment. Bioscience Reports. 2022 Jul;42(7):BSR20212051. portlandpress.com
9. Chakraborty G, Meher M, Dash S, Rout RN, Pradhan S, Sahoo D. Strategies for Targeted Delivery via Structurally Variant Polymeric Nanocarriers. ChemistrySelect. 2023 Aug 4;8(29):e202301626. [HTML]
10. Shang K, Xu C, Cao Z, Cui M, Sun J, Xiao H, Zhang L, Wang Y, Han H. Polymer-based delivery systems with metal complexes as contrast agents for medical imaging. Coordination Chemistry Reviews. 2024 Nov 1;518:216071. [HTML]
11. Truong TT, Mondal S, Doan VH, Tak S, Choi J, Oh H, Nguyen TD, Misra M, Lee B, Oh J. Precision-engineered metal and metal-oxide nanoparticles for biomedical imaging and healthcare applications. Advances in Colloid and Interface Science. 2024 Jul 31:103263. [HTML]
12. Jeon M, Halbert MV, Stephen ZR, Zhang M. Iron oxide nanoparticles as T1 contrast agents for magnetic resonance imaging: fundamentals, challenges, applications, and prospectives. Advanced Materials. 2021 Jun;33(23):1906539. nih.gov
13. Honmane SM, Charde MS, Salunkhe SS, Choudhari PB, Nangare SN. Polydopamine surface-modified nanocarriers for improved anticancer activity: Current progress and future prospects. OpenNano. 2022 Jul 1;7:100059. sciencedirect.com
14. Javed R, Sajjad A, Naz S, Sajjad H, Ao Q. Significance of capping agents of colloidal nanoparticles from the perspective of drug and gene delivery, bioimaging, and biosensing: An insight. International Journal of Molecular Sciences. 2022 Sep 10;23(18):10521. mdpi.com
15. Schöckel L, Jost G, Seidensticker P, Lengsfeld P, Palkowitsch P, Pietsch H. Developments in X-ray contrast media and the potential impact on computed tomography. Investigative radiology. 2020 Sep 1;55(9):592-7. [HTML]
16. Lucchetti D, Colella F, Artemi G, Haque S, Sgambato A, Pellicano R, Fagoonee S. Smart nano-sized extracellular vesicles for cancer therapy: potential theranostic applications in gastrointestinal tumors. Critical Reviews in Oncology/Hematology. 2023 Sep 9:104121. [HTML]
17. Younis NK, Ghoubaira JA, Bassil EP, Tantawi HN, Eid AH. Metal-based nanoparticles: Promising tools for the management of cardiovascular diseases. Nanomedicine: Nanotechnology, Biology and Medicine. 2021 Aug 1;36:102433. sciencedirect.com
18. Siddique S, Chow JC. Application of nanomaterials in biomedical imaging and cancer therapy. Nanomaterials. 2020 Aug 29;10(9):1700.
19. Ansari AA, Parchur AK, Thorat ND, Chen G. New advances in pre-clinical diagnostic imaging perspectives of functionalized upconversion nanoparticle-based nanomedicine. Coordination Chemistry Reviews. 2021 Aug 1;440:213971. [HTML]
20. Soufi GJ, Iravani S. Eco-friendly and sustainable synthesis of biocompatible nanomaterials for diagnostic imaging: current challenges and future perspectives. Green Chemistry. 2020;22(9):2662-87.
21. Akhlaghi N, Najafpour-Darzi G. Manganese ferrite (MnFe2O4) Nanoparticles: From synthesis to application-A review. Journal of Industrial and Engineering Chemistry. 2021 Nov 25;103:292-304. [HTML]

22. Sim S, Wong NK. Nanotechnology and its use in imaging and drug delivery. Biomedical reports. 2021 May;14(5):42.
23. Caputo F, Mehn D, Clogston JD, Rösslein M, Prina-Mello A, Borgos SE, Gioria S, Calzolai L. Asymmetric-flow field-flow fractionation for measuring particle size, drug loading and (in) stability of nanopharmaceuticals. The joint view of European Union Nanomedicine Characterization Laboratory and National Cancer Institute-Nanotechnology Characterization Laboratory. Journal of Chromatography A. 2021 Jan 4;1635:461767. sciencedirect.com

24. Li X, Li W, Wang M, Liao Z. Magnetic nanoparticles for cancer theranostics: Advances and prospects. Journal of Controlled Release. 2021 Jul 10;335:437-48.
25. Nam J, Kim M. Advances in materials and technologies for digital light processing 3D printing. Nano Convergence. 2024 Nov 4;11(1):45.
26. Pourmadadi M, Tajiki A, Hosseini SM, Samadi A, Abdouss M, Daneshnia S, Yazdian F. A comprehensive review of synthesis, structure, properties, and functionalization of MoS2; emphasis on drug delivery, photothermal therapy, and tissue engineering applications. Journal of Drug Delivery Science and Technology. 2022 Oct 1;76:103767. escholarship.org
27. Yi Z, Luo Z, Qin X, Chen Q, Liu X. Lanthanide-activated nanoparticles: a toolbox for bioimaging, therapeutics, and neuromodulation. Accounts of Chemical Research. 2020 Oct 26;53(11):2692-704.
28. Yi Z, Luo Z, Qin X, Chen Q, Liu X. Lanthanide-activated nanoparticles: a toolbox for bioimaging, therapeutics, and neuromodulation. Accounts of Chemical Research. 2020 Oct 26;53(11):2692-704.
29. Zhou J, Chen L, Chen L, Zhang Y, Yuan Y. Emerging role of nanoparticles in the diagnostic imaging of gastrointestinal cancer. InSeminars in Cancer Biology 2022 Nov 1 (Vol. 86, pp. 580-594). Academic Press.

CITE AS: Alberta Jeanne N. (2024). Nanoparticles in Medical Imaging: Enhancing Contrast Agents. RESEARCH INVENTION JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 4(3):31-36.
https://doi.org/10.59298/RIJSES/2024/433136