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Positron emission tomography imaging using radiolabeled iron oxide nanomaterials

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Abstract

This review aims to demonstrate the usability of radiolabeled iron oxide nanoparticles (IONPs) as PET imaging contrast agents and their perspectives in biomedical research and clinical practice. Magnetite and maghemite IONPs are superparamagnetic and released for multiple biomedical uses. Combining these nanoparticles with PET imaging significantly improves diagnostic capacities and treatment outcomes. Chelating agents and direct incorporation during synthesis are two techniques used in radiolabeling of nanoparticles to monitor particles in vivo. The review covers the background information on PET imaging, the opportunities provided by IONPs, and possible difficulties when using them. With new advancements in bimodal IONP templates, it is possible to use MRI and PET simultaneously for single-cell resolution imaging. The prospects centre on improving IONP safety and efficiency, utilizing nanomaterials with the 52Mn label, and applying IONPs in multimodal imaging. Copper-64 has also emerged as applicable in nuclear medicine, particularly in cancer diagnosis, using the copper-64 as a radiolabeling agent. These new generation automobiles of radiolabeled IONPs for PET imaging are a significant advancement to molecular and cellular imaging with possible enhancements in diagnostic precision and elements of precision medicine.

Keywords: PET; Multimodal imaging; Biomedical application; Cancer diagnosis; Personalized medicine

1. Introduction

Clinical / Imaging In the identification of diseases, Imaging is used in the determination of the extent and degree of ailments in order to administer standard pathological processes. Hence, it can be considered that for diagnosis of the disease, it is of crucial significance to get the true, three-dimensional picture, or 'scans' of the body areas that depict cells, tissues and organs and their functions [1]. These images also come useful during and after treatment to establish the efficacy of the treatment to be provided. As of now, the main forms of clinical imaging techniques and platforms are radiography or X-ray, CT or computer axial tomography, MRI or magnetic resonance imaging, PET or positron emission tomography, SPECT or single photon emission computed tomography, and optical and ultrasound Imaging. A summary of X-ray, CT, MRI and PET is that these are rated clinically as noninvasive 'gold standard' imaging devices presently in use around the world are noninvasive and versatile to visualize the different forms and functions of human anatomy in three dimensions, in addition to being non-angiographic.

In the introduction section, several types of clinical imaging modalities and peculiarities of PET imaging, like stealth, biodistribution, signal-to-noise, sensitivity, and specificity, are described. The technique of PET radioisotopes and labelling is presented with regard to the need to establish cost-efficient radiolabeling procedures [2]. It alerts the

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peculiarities of iron oxide nanomaterials that make it to be used in both PET and MRI. Last but not least, the arrangement of the sequel chapters is explained.

2. The Application of Iron Oxide Nanomaterials in Biomedical Field

Iron oxide can be used in many types of applications, and the fast advancement of magnetic nanomaterials in the past ten years has boosted the research interest in a number of aspects. Among all these kinds of nano-sized iron, Fe3O4 (magnetite) and γ-Fe2O3 (maghemite) nanoparticles are the most popular for biomedical uses [3]. They exhibit superparamagnetism which can be applied in Magnetic Particle Imaging (MPI), Magnetic Fluid Hyperthermia (MFH), MRI contrast agents and also Magnetic Cell/Molecular S separation.

In the case of the synthesis of the magnetic NPs, one can now find many methods for the preparation with moderate composition, size, and shape. The kind of facilities that can be employed in the biological and toxicological investigations of ultra-small magnetic NPs with a narrow size distribution. The uses of iron oxide NPs in biomedical sciences are mainly based on the superparamagnetic nature, the dependence of the magnetism on size, rapid magnetic response and particularly on the surface effects [4]. Small size effects imply that there is an increase in the surface-to-volume ratio, enabling many compounds like starch, dextran, polyethyleneimine, and organic molecules to have a large tendency to adhere at the nanoparticle surface, increasing the solubility of the nanomaterials in biologically friendly solutions, and therefore providing bio-compatibility.

3. Methods in Molecular Biology, vol. 454, Radio Labeling Techniques in Iron Oxide Nanoparticles

Classifying inorganic or organic nanomaterials according to the abundance of petrol to generalize the easy commercial deployment is the efficient approach to accomplish the inorganic-isotopic hybrid model. Thus, the problem of identification and differentiation of iron oxides has become an object of rather intensive investigation in the past decades [5]. When synthesizing the Fe_3O_4 NPs, the OH- ions in the chemical process could act as functional groups which could be used for exchanging the metallic ion with the radioisotope. Often it can be done and applied with regard to the gross yield. Therefore, the strategy based on superparamagnetism and facile surface ligand chemistry has come true, and the labelled Fe_3O_4 NPs were successfully developed and applied to various practices and showed great potential. It is seen that they exhibit highly comparable uses as compared to the conventional ferrofluid for sale; however have enhanced functionality in Imaging and reaction.

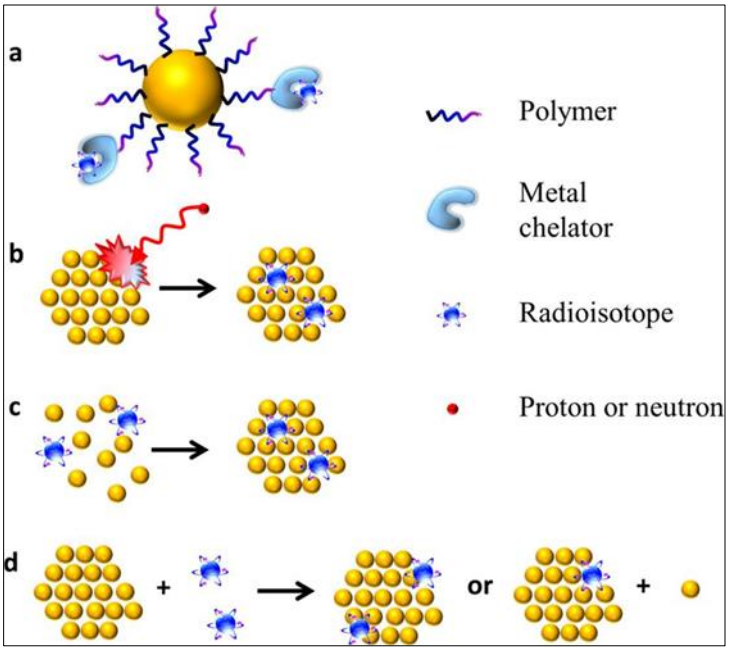

Figure 1 Four approaches for radiolabelling NPs. This Figure is reproduced from a literature review produced by Sun et al

Iron oxide nanoparticles have a natural contrast, which the addition of radionuclides can enhance and hence allow PET imaging. To take advantage of the superparamagnetism characters of Fe_3O_4 NPs, it is apparently applicable to label

radionuclides onto the surfaces of Fe_3O_4 NPs using a facile method and then applying isotopic Imaging [3]. This allows scientists and doctors to track the migration and find traces of the artificially injected substances or nanoparticles in an in-vivo environment. This is a common kind of labelling technique for Fe_3O_4 NPs. Since Fe_3O_4 NPs are isolated, the OH- on the surface can coordinate with the radioisotopes to form chelates with the preparation of labelled Fe_3O_4. Positron emission tomography with label-incorporated radioactivity will confine the specific cells in a PET image. Fe_3O_4 NPs possess superparamagnetic properties, so the labelled region produces heavy contrast on the isotopic Imaging of the monitored location, which may serve to validate the position and demonstrate the orientation of the artificers in the monitored area.

4. Principles and Instrumentation of PET Imaging

The Principles of PET Imaging Positron emission tomography is one of the most distinguished molecular imaging methods; it is characterized by high resolution and spatial characteristics, as well as the ability to apply radioisotopes emitted in the body to be detected noninvasively and quantitatively. In the case of a radiopharmaceutical, it is given to the body usually through an injection, and then the radiotracer, which contains endogenous radioisotope precursors, discharges charged particles in which a positron is most common with the help of spontaneous decay [6]. Different from gamma rays generated by radioactive isotopes, which have no physical bond with the body, the positron can cause the annihilation reaction interaction with the electrons in and around the site where the positron has been emitted within the body and generate two gamma rays of 511 keV travelling in opposite directions the scanner picked each up. Finally, the position of each pair of coincidences is determined, and those above are used to reconstruct the images and make them into three-dimensional form.

The current PET is one of the most prominent molecular imaging techniques that is used in clinical as well as various other preclinical studies. Some of the usefulness include that it can identify and meas- ure radiolabeled radionuclides in organisms without incising the total body. This chapter is going to continue with the PET imaging instrumentation and the pattern investigations imaging methods, and the major characteristics of the iron oxide nanomaterial as the PET radiolabeling agents will be introduced and expounded.

5. Pros and Cons of Applying Iron Oxide Nanoparticles in Imaging with Positron Emission Tomography

The applications of iron oxide nanoparticles as agents for PET imaging have some specific advantages over the other imaging modalities for the same purpose, which is discussed below. Still, there are some challenges, too, which have been explained in this review. The PAT principals of high-resolution molecular and cellular imaging of biological processes in vivo can be done through biocompatible multimodal nanoparticles which have incorporated elements like 64Cu, 89Zr, 68Ga, 124I, 18F and 11C either through chelators or radiolabeling of the nanoparticle surface or; iron oxide nanoparticles can be synthesized directly by the incorporation of 64Cu, 89Zr [7]. These modified or unmodified iron oxide nanoparticles may further be conjugated with other targeting modalities like antibodies/ peptides/small molecules/ aptamers. Specific to the required application, other attributes like size, shape charges and characteristics of the surface where the particles are deposited can also be selected.

For the radiolabeled iron oxide nanomaterials for molecular and cellular PET imaging, there are several rational: First, a vast enhancement of performance has been made on stability in monocrystalline iron oxide nanoparticles that existed on the scale of ultrasmall (5–10 nm) to medium size (30–40 nm) with controlled physical and biochemistry characteristics. Several strategies have been described to incorporate chelators for attaching radioisotope labels to the nanoparticle surface or other methods for integrating the radioactivity during the synthesis of the iron oxide nanoparticles. Second, the performance of PET/MRI or PET/optical imaging can be realized with radiolabeled iron oxide nanomaterials for in vivo and ex vivo high-resolution cellular imaging and for tracking labelled cells and understanding the investigation of various biochemical processes. Third, these materials are non-toxic, chemically stable, and environmentally benign and they are already included in clinical uses [8]. Therefore, the synthesis of radiolabeled iron oxide nanomaterials is a major achievement in molecular and cellular PET imaging. These monocrystalline iron oxide nanoparticles or other nanomaterials engineered here are tiny in size, varying from ultrasmall to medium-sized, and possess greater stability with specifically designed physical and biochemical characteristics.

They allow the achievement of PET/MRI or PET/optical imaging, both for in vivo and ex vivo use through, for instance, chelators for radioisotope attachment or integrating radioactivity at the time of synthesis. Notably, these nanomaterials are biocompatible, chemically inert, and eco-friendly; some are even used for clinical purposes. Also, they provide high-resolution images of cells, and the ability to follow labelled cells adds to understanding biochemical pathways. In

conclusion, radiolabeled iron oxide nanomaterials have great potential to become a new generation of diagnostic imaging agents, and they have a bright future in improving biomedical research and clinical applications.

6. The Preclinical And Clinical Studies Using Radiolabeled Iron Oxide Nanoparticles

In the last decade more and more studies started to focus on the clinical use of iron oxide nanoparticles (IONPs), especially for targeted molecular imaging and stem cell labeling. The main issues that are related to the clinical application of IONP labelling have been to define the type of signal obtained from newly differentiated cells apart from other resident cells, especially in diseases and or in response to an acute challenge [9]. In an attempt to overcome these difficulties, we have designed a new bimodal IONP template, which enables the visualization of the labelled cells by MRI and the visualization of the radiolabeled component used in positron emission tomographic imaging. Interestingly, the inclusion of a radiolabeled component made it possible to get image resolution at single-cell bases. In this report, we outline the procedure for radiolabeling and then provide details on the preclinical process, starting from the synthesis of the IONP and its incorporation from synthesis through to the PET/ CT imaging and the routes of administration used in the project, followed by a summary of the subsequent first in man clinical trial.

7. Future Development and New Trends to PES Imaging with Iron Oxide Nanoparticles

Some of the difficulties are aimed at the further evolution of the processes of creating safe and efficient nanomaterials using the 52Mn label in the future, mainly due to the long half-life of 52Mn in comparison with other isotopes. Its daughter radionuclides should be shielded temporarily, and its lesions bring this necessity into focus [10]. The other acknowledged related new trends for PET imaging with the aid of the iron oxide nanomaterials labelled 52Mn are available in the area of imaging agents. It is the application of the photoacoustic/magnetic resonance multimodal imaging method. This will augment the outcome of PET imaging and also make the locked-in tumor radiotherapy a lot of efficient with the help of 52Mn labeled multi-functionality iron oxide nanomaterial. Other trends could be using the beneficial properties of the hybrid nanomaterials in highly efficient photothermal therapy and have initiated corresponding research, proudly within melanoma bio-tissue place research. Each of these trends not only emphasizes the necessity of non-cytotoxic iron oxide nanomaterials but also can define further tendencies in advancement and, at the same time, contribute to further investigation and development.

Similarly, it is seen in this review that several vital aspects of using PET imaging, such as having a high spatial resolution, good sensitivity, deep penetration, and short diffusion distance, make PET imaging of significant necessity. Like 18F, 89Zr, and 64Cu, it is useful in isotope and semiconductor labelling. The use of 52Mn in PET does not create long-lived positron emitters as other dominating PET radioisotopes do, and 52Mn can show similar bone metabolism to 99mTc, creating a perfect opportunity for theranostic couples. Its usage and development, particularly into fused nano-structured material, is of great value to today's cancer, gene, immunology and radiotherapy.

8. Conclusion and Implications for Research and Clinical Practice

Applying copper-64 as a radiolabeling in diagnosis has brought a drastic change in nuclear medicine, especially in imaging cancerous tissues using different methods like PET, CT and SPECT. This radioactive isotope is chosen because of the kind of β+ decay and its energy spectrum, which is more powerful for imaging.At pH 6. 0, copper-64 is present mostly as Cu(II) and, therefore, is favourable for the radiolabeling of the catechol-based targeting probes. This equilibrium, however, gets disturbed at a pH of seven. 4, present in normal and slightly acidified cancer tissues, prefers Cu(II) to Cu(I). This pH sensitivity is very important in designing the specific imaging agents since it facilitates their accumulation in diseased but not healthy tissue.

Micellar nanoparticles and SPIO loaded with copper-64 are used in these imaging applications. These nanoparticles are stable, biocompatible, and can host both the configuration types, core (SPIO) and core/shell (micellar), which, in turn, help in escalating the targeting specificity and image quality.Cycling copper-64 with 1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA) and carbohydrates allows the copper-64 BET to emit β+ and β- radiation. This hetero-functional chelation chemistry is very important because radiolabeling is integrated and needs to be carried out efficiently with minimal effects on product quality while at the same time having a very short half-life, thus a shelf life of only 12 hours in the case of copper-64. 7 hours.

The radiolabeling process has been especially emphasized because the physical decay copper-64 shortens the reaction time and results in an offline radiolabeling process compatible with targeting molecules' shelf lives—for instance, the 34CB-TEG-Cy5. 510-COOH/ZHER2:2891 Affibody molecules need a technique that would quickly achieve a

concentration of radiolabeling within a small-time frame. Depending on the nature of the nanoparticles, their constitution differs regarding their application possibilities in vivo. The creation of copper-64-labelled nanoparticles for diagnostic imaging is an outstanding example of how complex, interdisciplinary concepts of chemistry and nanotechnology can promote medical advancement. These advancements enhance the diagnosis and description of malignant tissues and CI use in a more clinical perspective that defines personalized medicine where targeting and visualization of tissues are critical. Continuous advancements are made to these technologies to improve their sensitivity, specificity, and utility in cancer diagnosis and assessment of response to treatment.

Compliance with ethical standards

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References

[1] National Academies of Sciences, E., Division, H. and M., Services, B. on H. C., & Techniques, C. on I. N. or I. D. or E. (2023, May 1). Overview of Selected Techniques for Diagnosing and Evaluating Patients. Www.ncbi.nlm.nih.gov; National Academies Press (US). https://www.ncbi.nlm.nih.gov/books/NBK593686/

[2] Kapoor, M., & Kasi, A. (2022, October 3). PET Scanning. PubMed; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK559089/

[3] Montiel Schneider, M. G., Martín, M. J., Otarola, J., Vakarelska, E., Simeonov, V., Lassalle, V., & Nedyalkova, M. (2022b). Biomedical Applications of Iron Oxide Nanoparticles: Current Insights Progress and Perspectives. Pharmaceutics, 14(1), 204. https://doi.org/10.3390/pharmaceutics14010204

[4] Vargas-Ortiz, J. R., Gonzalez, C., & Esquivel, K. (2022). Magnetic Iron Nanoparticles: Synthesis, Surface Enhancements, and Biological Challenges. Processes, 10(11), 2282. https://doi.org/10.3390/pr10112282

[5] Khalid, K., Tan, X., Mohd Zaid, H. F., Tao, Y., Lye Chew, C., Chu, D.-T., Lam, M. K., Ho, Y.-C., Lim, J. W., & Chin Wei, L. (2020). Advanced in developmental organic and inorganic nanomaterial: a review. Bioengineered, 11(1), 328–355. https://doi.org/10.1080/21655979.2020.1736240

[6] Rong, J., Haider, A., Jeppesen, T. E., Josephson, L., & Liang, S. H. (2023). Radiochemistry for positron emission tomography. Nature Communications, 14(1). https://doi.org/10.1038/s41467-023-36377-4

[7] Creţu, B. E.-B., Dodi, G., Shavandi, A., Gardikiotis, I., Şerban, I. L., & Balan, V. (2021). Imaging Constructs: The Rise of Iron Oxide Nanoparticles. Molecules, 26(11), 3437. https://doi.org/10.3390/molecules26113437

[8] Karageorgou, M.-A., Bouziotis, P., Stiliaris, E., & Stamopoulos, D. (2023). Radiolabeled Iron Oxide Nanoparticles as Dual Modality Contrast Agents in SPECT/MRI and PET/MRI. Nanomaterials, 13(3), 503. https://doi.org/10.3390/nano13030503

[9] Xie, W., Guo, Z., Gao, F., Gao, Q., Wang, D., Liaw, B., Cai, Q., Sun, X., Wang, X., & Zhao, L. (2018). Shape-, size- and structure-controlled synthesis and biocompatibility of iron oxide nanoparticles for magnetic theranostics. Theranostics, 8(12), 3284–3307. https://doi.org/10.7150/thno.25220

[10] Poletto, G., Evangelista, L., Venturini, F., Gramegna, F., Seno, F., Moro, S., Vettor, R., Realdon, N., & Cecchin, D. (2022). Nanoparticles and Radioisotopes: A Long Story in a Nutshell. Pharmaceutics, 14(10), 2024. https://doi.org/10.3390/pharmaceutics14102024