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Contrast Agents for Magnetic Resonance Imaging (MRI) for the Diagnosis of Tumors

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Abstract

The MRI contrast agents for tumour diagnosis are the main topic of this review. As longitudinal relaxation time (T1) and transverse relaxation time (T2) MRI contrast agents, several low molecular weights Gd3+-based complexes and dextran-coated super paramagnetic iron oxide (SPIO) nanoparticles have been employed to diagnose clinical tumours. New kinds of chelates for T1 MRI contrast agents and combinations of low molecular weight T1 MRI contrast agents with various kinds of carriers have been researched to further increase the sensitivity of MRI. The formation of secure coating layers of SPIO and unique super paramagnetic particles with greater relativity values have been investigated using a variety of materials. To enhance the capacity of both T1 and T2 contrast agents to target tumour, many types of ligands have been used. Furthermore, MRI contrast agents for tumour metabolism detection were investigated.

Keywords: Tumor Diagnosis; Magnetic resonance imaging; Magnetic nanoparticles; Tumor-associated bacteria

Introduction

Noninvasive imaging techniques make it simple and relatively safe to diagnose diseases and characterise their underlying pathologies. Included in these methods are nuclear imaging modalities including positron emission tomography (PET), single photon emission computed tomography (SPECT), computed tomography (CT), optical imaging (OI), ultrasound (US), and magnetic resonance imaging (MRI). Each of them offers unique advantages on its own, as well as drawbacks that must be taken into account in the context of the study's objectives. Because of its inherent high spatial resolution, deep tissue penetration, and three-dimensional anatomical information, MRI is frequently used. As a result, it is frequently used in clinics to determine the diagnosis and prognosis of a variety of medical situations.

Despite this, MRI has a limited sensitivity that must be addressed with the use of exogenous contrast agents that reduce the relaxation times of bulk water. Contrast agents facilitate multimodal imaging in addition to improving picture contrast. Based on the operational mode, they can be divided into two types. Shortening longitudinal relaxation times and brightening the accumulation region are two effects of T1, also known as positive contrast agents. In contrast, T2, or negative contrast agents, reduce transversal relaxation times and make the immediate and surrounding area darker. Several formulations, ranging from metal complexes to nanoparticles, have been used as MRI contrast agents. The majority of these formulations are based on the usage of strongly paramagnetic ions like Gd3+, Mn2+, and Fe3+ [1].

To lessen the related toxicity of the free metal ion, they are typically used as coordination complexes with acyclic or cyclic chelate agents. Paramagnetic metallic complexes have issues because of their rapid excretion, despite the fact that these chemical agents have been used extensively. The high synthesis demand and potential for unfavourable side reactions limit the utilisation of low molecular weight lanthanide complexes in terms of targeting and adding additional imaging modalities. These factors have caused research on paramagnetic contrast agents to concentrate on the creation of Nano particle forms over the past few years.

Compared to conventional coordination complexes, paramagnetic nanoparticles have a number of advantages. Size and form, as well as composition, are easily adjustable. Geometric local density effects produce significantly greater T1 and/or T2 relax metric values than the comparable coordination complexes, which increase magnetic properties. The accompanying pharmacokinetics may be controlled, which also allows for longer blood circulation times. The reticuloendothelial system (RES), which is activated by macrophages like Kupffer cells and generates uptake from the bloodstream to the liver and spleen, is ultimately responsible for clearing most Nano particulate platforms. The size of the nanoparticle and its chemical coating affect the rate of this opsonisation process [2].

Nanoparticles with a diameter of less than 5-7 nm can pass through the kidney glomerulus, causing rapid excretion through the urine. The RES pathway allows for the excretion of larger particles with kinetics that are regulated by surface chemistry. The protein corona that forms on these particles during circulation is crucial for this and can be managed, for instance, by pegylation or a polymer coating, to maximise blood circulation time. This directly affects MRI acquisition, as a longer acquisition period improves "picture quality" by increasing the signal-to-noise ratio. The high surface-to-volume ratio of nanoparticles, which allows for a high ligand (protein, antibody, and peptide) payload as well as tuneable and possibly accessible internal volume, is another crucial aspect of their application. These characteristics allow for medication combinations that enable simultaneous theranostic therapy-targeted imaging-based diagnosis followed by treatment tailored to the patient's condition [3].

A few of the numerous methods that have been employed to create paramagnetic nanoparticles for MRI will be discussed here. One of two synthetic approaches is typically used: either (1)

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creating nanoparticles with the paramagnetic ion integrated into the nanostructured framework or (2) post functionalizing the particles with a lanthanide coordination complex. The synthesis of stoichiometric or nonstoichiometric nanoparticles of metal oxides, such as Gd2O3, MnO, Mn3O4, Dy2O3, or -Fe2O3, has formed the foundation of the first strategy. This method also uses nanoparticles such as NaGdF4, KGdF4, -NaDyF4, NiFe2O4, and ZnFe2O4. The second method uses a variety of nanoparticle scaffolds as supports (including silicon, gold, micelles, polymers, and semiconducting quantum dots), which are then doped with DTPA, DOTA, or derivatives. The creation of Gd3+, Mn2+, Dy3+, and Ho3+ nanoparticles and their usage in biomedicine as contrast agents for MRI and multimodal imaging are the main topics of this paper [4].

Materials and Methods

As research subjects, 67 meningioma patients who had been surgically and pathologically diagnosed in a hospital between July 2018 and March 2020 and whose T2WI of pathological type had an obvious low signal were chosen. There were 27 women and 40 men. The range of ages was 21 to 78, with a mean age of 47.67. The patient's headache, nausea, dizziness, blurred vision, and other symptoms were clinical signs. All participants in the study completed an informed consent form, and the trial process had been approved by the hospital's ethics committee [5].

Spin echo (SE) and tuber spin echo (TSE) sequences were used in an axial, sagittal, and coronal imaging procedure on a PHILIPS-produced MRI scanner. T1WI (TR/TE 420 ms/20 ms), T2WI (TR/TE 4200 ms/90 ms), layer thickness of 5.0 mm, layer interval of 1.0 mm, matrix of 256 256, field of view (FOV) of 22 cm 22 cm, sagittal and coronal layer thickness of 5.0 mm, and layer interval of 1.0 mm were the scanning settings. Gadopentetic acid (GD-DTPA) was intravenously given into all patients for enhanced scanning. All MRI imaging findings were examined and evaluated by 2 senior imaging diagnostic experts using the blinded method.

The surgically removed tumour tissue samples were preserved in 4% paraformaldehyde for 24 hours. Leaching of paraffin and conventional dehydration were completed. Sections were divided by 3 to 4 m after embedding. The sections were dewaxed, submerged in a gradient of xylene, and then stained with hematoxylin. 0.4% eosin was applied for staining after rinsing. Slices were sealed after being made transparent with xylene so that pathological alterations caused by various forms of HE staining could be seen [6].

Immunohistochemistry was used to find out how much Ki67, VEGF, and P73 protein was present in tumour tissues. As primary antibodies, Ki67, VEGF, and P73 antibodies were used. Routine procedures were followed for the immunohistochemical procedures. With a light microscope, the expression of the proteins Ki67, VEGF, and P73 in tumour tissues was investigated. Positive results included brown or brownish yellow staining of the cytoplasm or nucleus. The results were sorted into three groups based on how much the colourant stained the surface: Negative means that the cytoplasm or nucleus are not stained; weak positive means that they are stained a light brownish yellow; and sng positive means that they are stained a dark brownish yellow [7].

Discussion

Due to the wide variation in tissue structure, meningioma has a number of subtypes. The most common types of meningiomas, according to widespread consensus, are the fibrous, syncytial cell, psammomatous, transitional, haemangioma, meningeal melanoma, secretory, lymphoplasmacytic, metaplastic, clear cell, and atypia types. Due to the multiplicity of subtypes, meningioma patients' MRI imaging features and pathological underpinnings are very varied. The majority of transitional meningioma tumours are oval or quasicircular, while a few include lobules. Confounding signals are commonly visible in the T2WI of MRI images. According to studies, the tissue of transitional meningiomas contained areas of hyaline degeneration, thick fibrous structures, and necrotic patches. As a result, hierarchical mixed signals in MRI images are caused by the variety of meningeal tissues. This result was comparable to that seen in individuals with transitional meningiomas who had calcification and low signal in their T1WI, T2WI, and enhancement. Patients with fibrous meningiomas typically have oval- or round-shaped tumours. T1WI and T2WI typically display equal or weak signal in patients' MRI scans. The T2WI signal is low in patients with fibrous meningiomas because there is significant calcification and collagen-dimensional hyaline alteration [8].

The most notable aspect of MRI imaging of psammomatous type meningiomas tumours is the prevalence of calcification. While T1WI and T2WI both have double-low signals, T2WI typically exhibits erratic signals. The shape of the melanoma was consistent, and there was no apparent edoema surrounding the tumour. High signal on T1WI and low signal on T2WI were visible on the MRI imaging. The findings revealed that VEGF and Ki67 and P73 were both strongly expressed in transitional meningiomas, with VEGF being mostly present in the cytoplasm and P73 and Ki67 being primarily expressed in the nucleus [9].

In comparison to comparable proteins in fibrous meningiomas, the high expression of VEGF protein and mRNA in meningeal melanoma was noticeably higher. The MRI score of peritumoral edoema was found to be strongly linked with Ki67 expression. The histological grade of meningioma, tumour cell differentiation, and VEGF were all found to be closely associated to the angiogenesis of meningiomas. Meningeal melanoma's elevated VEGF expression suggested that the tumour had a robust invasion. Researchers discovered a strikingly strong correlation between the expression of the P73 protein and peritumoral edoema, which suggests that patients with transitional meningiomas will experience edoema. In line with the findings of this paper, it was discovered that certain patients with transitional meningioma will exhibit moderate edoema [10].

Conclusions

Magnetic contrast agents demonstrate their value as useful tools for a variety of powerful MRI applications. Despite the widespread use of conventional paramagnetic coordination complexes, little can be done to manage their pharmacokinetics, biodistribution, thermodynamic stability, or imaging potency. Developing nanoparticles conjugated with paramagnetic ions with a degree of control over composition, size, and shape is possible using a wide range of readily available synthetic techniques. This encourages simple management of pharmacokinetics, biodistribution, and stability. At high levels of local loading, associated paramagnet hydration, water exchange kinetics, or residence lifespan can all be controlled. They are much more interesting because they can easily be combined with different imaging techniques and use multivalent vectors on quite large particle surfaces. These constructions have been used in the administration of drugs, photodynamic therapy, and sonodynamic therapy, as well as targeted multimodal molecular imaging of cancer, cardiovascular, and neurological illnesses. The

chemical diversity here is expected to have a significant impact during the next ten years.

Acknowledgement

None

Conflicts of Interest

None

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