Optimization of Lipid Nanoparticles Embedding Gd(III)-Chelating Lipids via DoE approach for Enhanced MRI Contrast and Safety

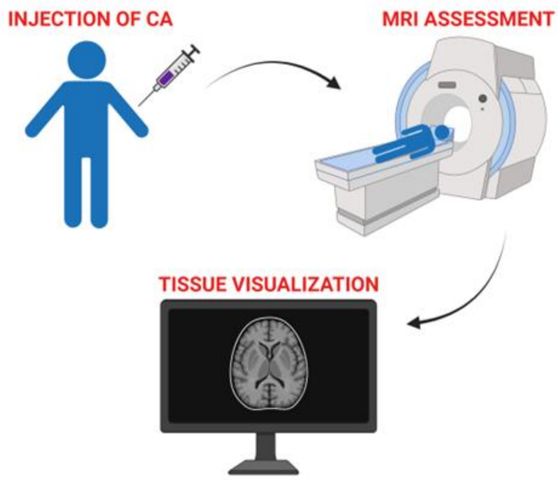
Nowadays, medicine has increasingly advanced diagnostic technologies that allow precise examination of the body's internal structures. One of the most important diagnostic tools in this field is the Magnetic Resonance Imaging (MRI) technique.

How does MRI work?

MRI uses strong magnets and radio waves to obtain detailed images of the body's interior. During the test, the patient is placed inside a cylindrical MRI machine, which generates a magnetic field that is safe for the test subject. Hydrogen protons in the patient's body respond to this field, and when subjected to pulses of radio waves, emit characteristic signals. These signals are then analyzed and transformed into spatial images of an area of the body, giving information about tissue changes. MRI imaging is an important tool for detecting tumors and their metastases, for observing the brain and nervous system, and for assessing cardiovascular function, among others. In addition, defined needs for MR imaging itself include: higher resolution (higher field, parallel imaging), increased sensitivity and specificity, simultaneous diagnostic imaging and therapy, including personalized imaging, and multimodal imaging capabilities (e.g., PET/MRI, MRI/IR, MRI/FOI). Combining the anatomical resolution of MRI with the sensitivity of optical imaging may prove to be a good technique for finding and quantifying the size of tumors, particularly tumors or metastases too small to be detected by MRI.

Contrast agents (CAs), brightening the mysteries of diagnostic imaging

The use of CAs leads to changes in the behavior of hydrogen protons in the body, resulting in increased sensitivity in MR imaging of specific tissues or organs. The most commonly used contrast agents in MRI are based on gadolinium compounds Gd(III), whose magnetic properties result in contrast enhancement on the acquired images, by brightening them. Unfortunately, Gd(III), by accumulating in organs such as the brain and kidneys, can be toxic. Over the past four decades, many contrast agents have been developed for use in clinical practice, and some have even been withdrawn for safety reasons. Researchers around the world is conducting numerous studies on new contrast agents that are equally effective, including those that exploit the potential of nanotechnology and nanoparticles.



Project objective: Contrast agents based on lipid nanoparticles

The current challenge in the design of new contrast agents is the search for new paramagnetic Gd(III)-based CAs or their substitutes, whose low concentration (micromolar or even submicromolar) would make it possible to achieve the desired contrast with a low risk of systemic toxicity. As mentioned above, Gd(III) is toxic, so it is administered to the body as a so-called „chelate”. Such a compound has greater durability, helps reduce toxicity, which can provide more effective treatment and increase patient safety. An innovative approach in the design of Gd(III) ion-based contrast agents is the use of high-molecular-weight Gd(III) chelating lipids and their combination with lipid nanocarriers. The proposed self-organized structures appear to offer a large charge of coordinated Gd(III) ions, and their extensive water channels can enable efficient water exchange between the inner and outer spheres surrounding the Gd(III) ions, resulting in better relaxation. The high relaxivity of r_1 is necessary due to the low sensitivity of magnetic resonance. The above advantages allow us to conclude that the proposed GMO-lipid nanoparticles enriched with Gd(III)-chelating lipids may be promising new contrast agents for MR imaging, and thus a new type of nanocarrier for further development of multifunctional systems combining diagnostics and therapy.