Contrast agents in Magnetic Resonance imaging: The new challenges regarding toxicity and increased safety

M. M. Ribeiro[1], A. Coelho[1]

[1]H&TRC- Health & Technology Research Center, ESTeSL- Escola Superior de Tecnologia da Saúde, Instituto Politécnico de Lisboa, Lisbon, Portugal

The Magnetic Resonance Imaging (MRI) provides images of any part of the body with multiplanar spatial location and is currently a widespread used imaging method in the clinical diagnostic routine. Indeed, MRI provides better soft tissue contrast than the other imaging methods and can better differentiate fat, water, muscle, and other soft tissues. The first MRI contrast agent to be used was ferric chloride in 1981. Over the past 3 decades, many contrast agents have been developed for use in clinical practice and some of them were withdrawn due to safety conditions. The justified use of gadolinium-based contrast agents (GBCAs) carries some risks, including side effects such as allergic reactions and nephrogenic systemic fibrosis (NSF). The Gadolinium related toxicity has been documented for at least 10 years, with potentially life-threatening disease recognized in 1997 in 15 dialyzed patients. The MRI contrast agents include T1-weighted (T1W) and T2-weighted contrast agents. Since its image signal increases the positive contrast, gadolinium (Gd) chelates as (T1W) contrast agents, dominate the current market of MRI. The current scientific evidence, from the last 4 years, recognizes a concentration-dependent deposition of gadolinium in the brain of the post-mortem human or animalmainly through thehigh signal intensities in the globus pallidus and dentate nucleus on T1Wimages, demonstrating roundly the residual deposition of gadolinium T1-hyperintensity in anatomical areas, raising new concerns on the safety of GBCAs. Since 2017 the International Society of Magnetic Resonance in Medicine (ISMRM) Safety Committee, the US Food and Drug Administration (FDA) and The Pharmacovigilance Risk Assessment Committee (PRAC) produced many recommendations and some restrictions on the use of linear gadolinium agents, giving preference to these contrast agents only for liver scans in low concentrations. From this recommendation some types oflinear agents were suspended and replaced by more stable and appropriate gadolinium agents known as macrocyclic agents, like gadoteric acid, gadobutrol, and gadoteridol.Regarding that problem, with the focus on the research of new contrast agents, new-typed nano-scaled T1W MRI contrast agents have been designed to overcome the draw-back of clinical gadolinium agents. So, due to the better biocompatibility compared with the Gd-chelates, magnetic iron oxide nanoparticles (MIONs) have been increasing attention as MRI contrast agents. So, due to the better biocompatibility compared with the Gd-chelates, MIONs have attracted increased attention as MRI contrast agents.

- The recently emerged exceedingly small MIONs (ES-MIONs) are promising to overcome the disadvantages of the Gd-chelate-based T1W contrast agents and MION-based T2W contrast agents because they have good biocompatibility and can be used as T1W contrast agents. Compared with the commercial gadolinium agents, nano-scaled gadolinium-based inorganic agents exhibit excellent T1W MR performance with good biocompatibility. Furthermore, these nanoparticles can be easily conjugated with biomolecules making a multifunctional nanoplatform based on gadolinium nanocomposites that can be apply for multimodal imaging and therapy.Other options are the biomedical applications of MXene-based nanoplatforms by exploring further functionalization strategies and also provide a novel and efficient theranostic nanoplatform that successfully constructed a novel superparamagnetic MXene-based theranostic nanoplatform based on tantalum carbide (Ta4C3) MXene.With this presentation the authors propose to explain and highlight the most recent progress and challenges in the synthesis and modifications of paramagnetic contrast agents showing the currently, newer and more reliable MRI agents, capable of targeting specific organs, tumours and other diseases, with greater specificity.