MRI active nanoparticles: towards a future of metal-free contrast agents

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Magnetic Resonance Imaging (MRI) is a reliable, non-invasive imaging method commonly used for clinical diagnosis. However, despite the technique itself being harmless, most of the contrast agents (CAs) used to enhance the contrast are based on Gadolinium complexes[1] with toxic Gd^{3+} ions, which have recently been found to accumulate in the patient's body[2]. As several Gd-based complexes have been withdrawn from the market due to safety concerns, the need of finding suitable alternatives has become essential.

Organic radicals[3] can be potential alternatives to those metal-based, but their lower T_1 relaxivity provides a weaker contrast when compared with their metallic counterparts.

In our group we have previously succeeded on anchoring those organic radicals into macromolecules known as dendrimers, overcoming their lower contrast with a high density of radicals in each nanoparticle[4].

In this work, we present the different types of metal-free CAs developed by our group. The systems are based on highly stable and monodisperse nanoparticles, either mono or multimolecular, that contain an organic radical synthesized in our lab, which despite itself not being water-soluble, together with the nanoparticle form a non-toxic and water-compatible system with high contrast.

Results on *In Vitro* and *In Vivo* tests show these systems as promising models for the future of contrast agents both by contrast strength and biocompatibility.

References

[1] Caravan, P., Ellison, J.J., McMurry, T.J., Lauffer, R.B., Chem Rev., 99 (1999), 2293–2352.
[2] Rogosnitzky, M., Branch, S., BioMetals, 29 (2016), 365–376.
[3] Brasch, R.C., London, D.A., Wesbey, G.E., Tozer, T.N., Nitecki, D.E., Williams, R.D., Doemeny, J., Tuck, L.D., Lallemand, D.P., Radiology, 147 (1983), 773–779.
[4] a) Zhang, S., Lloveras, V., Lope-Piedrafita, S., Calero-Pérez, P., Wu, S., Candiota, A.P., Vidal-Gancedo, J., Biomacromolecules, 23 (2022), 2767–2777. b) Wu, Y., Lloveras, V., Lope-Piedrafita, S., Mulero-Acevedo, M., Candiota, A.P., Vidal-Gancedo, J. Acta Biomater., 192 (2025), 461-472.

Figures

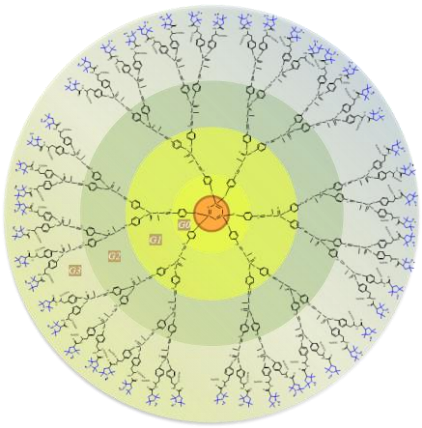

Figure 1. Radical dendrimer [4a].

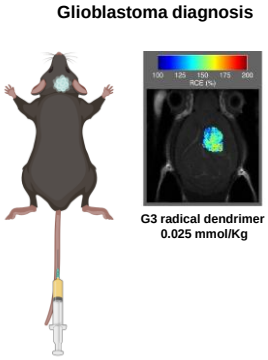

Figure 2. Color-code scale for relative contrast enhancement (RCE) of GL261 glioblastoma tumour-bearing mice with intravenous administration of the radical dendrimer (0.025 mmol/kg, 60 min).[4a]

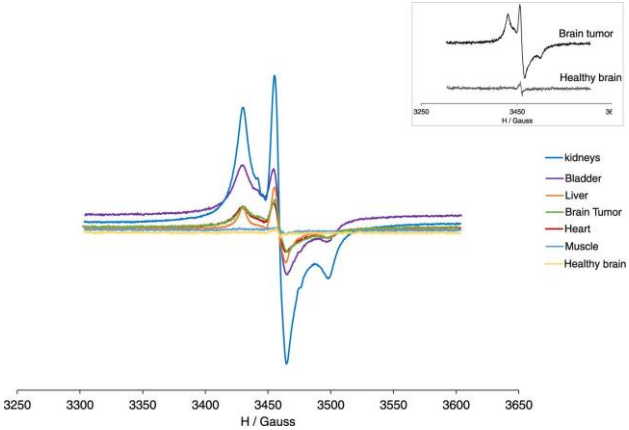

Figure 3. EPR spectra of kidneys, bladder, liver, heart, muscle, brain tumor, and contralateral healthy brain from GL261-tumor-bearing mice after 15 h of 0.025 mmol/kg administration of MRI active nanoparticles [4a].