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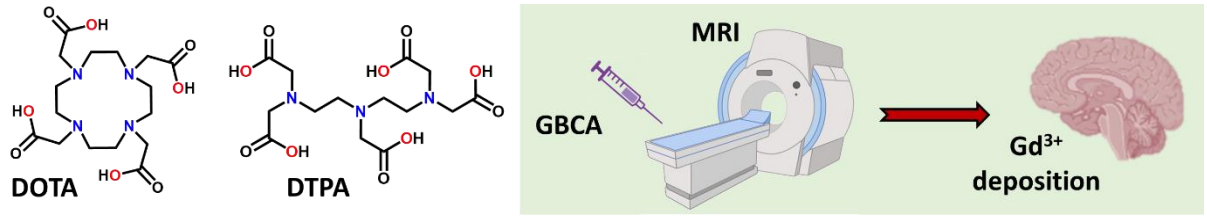
Stability of MRI contrast agents in physiological-like conditions

Nowadays, about 40% of magnetic resonance imaging (MRI) scans are performed through the administration of Gd^{3+}-based contrast agents (GBCA), which allow enhanced sensitivity and diagnostic efficacy. GBCAs are thermodynamically stable and kinetically inert Gd^{3+}-complexes with linear and cyclic polyaminocarboxylate ligands such as DTPA and DOTA (Figure).[1]
Despite their high stability, growing evidence has recently shown that Gd^{3+} can form deposits in the central nervous system.[2,3] However, the mechanism by which toxic Gd^{3+} is released from GBCAs is not yet understood.



Hence, the aim of this internship is to explore the potential chemical pathways that can lead to Gd^{3+} release in the body. In particular, *in vitro* studies will be performed in order to assess the stability of different GBCAs in physiological-like conditions, i.e. in the presence of the main physiological competitors found in the bloodstream or in the synaptic cleft. These include metal ions such as Cu^{2+} and Zn^{2+}, which could displace Gd^{3+} via trans-metallation of the CA, as well as anions such as phosphate, bicarbonate and glutamate and pH drop. Reactions will be followed via a variety of spectroscopic techniques, including UV-vis absorption, fluorescence, nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR). Fast kinetics measurements using stopped-flow methods are also foreseen. Based on these measurements, structure-property relationships will be drawn by comparing the resistance to Gd^{3+} dissociation of different GBCAs.

References

1. Wahsner, J., Gale, E. M., Rodríguez-Rodríguez, A. & Caravan, P. Chemistry of MRI Contrast Agents: Current Challenges and New Frontiers. *Chem. Rev.* **119**, 957–1057 (2019).
2. Guo, B. J., Yang, Z. L. & Zhang, L. J. Gadolinium Deposition in Brain: Current Scientific Evidence and Future Perspectives. *Front. Mol. Neurosci.* **11**, 335 (2018).
3. Kromrey, M. L. *et al.* Intracerebral gadolinium deposition following blood–brain barrier disturbance in two different mouse models. *Sci. Rep.* **13**, 10164 (2023).