Title

Gd-Free MRI Contrast Agents Based on Mn-Porphyrin: Limitations and Opportunities of Classic Paramagnetic Relaxation Model

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Abstract

Current clinical MRI contrast agents (CAs) are predominantly based on gadolinium (Gd3+) complexes. With a high paramagnetic dipole moment, relatively long electron relaxation time, and a large ionic radius to form stable multidentate chelate, Gd3+ has been a preferred and obvious choice for the development of MRI CAs. The NMR paramagnetic relaxation enhancement properties of Gd T1 agents have been well studied, as summarized in the classic Solomon, Bloembergen and Morgan (SBM) model. Challenges remain however, since conventional Gd-chelates exhibit lower-than-anticipated T1 relaxivity, especially at high clinical field of 3T, and sub-optimal stability, restricting the applications for future targeted molecular or cellular imaging. In this talk, I will present our efforts on the development of Gd-free CAs based on Mn3+-porphyrin (MnP). Despite the fact Mn3+ has only 4 unpaired electrons, in contrast to 7 for Gd3+ and 5 for Mn2+, rationally designed MnPs could achieve higher T1 relaxivity, especially at high clinic fields. Furthermore, as synthetic metal-ligand complex, MnP is remarkably more stable against metal dissociation or transmetallation in vitro and in vivo, even though Mn3+ is a relatively small metal ion. I will highlight our challenges to use the existing relaxation model to interpret these desirable yet “abnormal” behaviors of MnP as potentially better MRI T1 agent. Finally, the advantages of MnP for constructing next generation molecular/cellular imaging probes, will be summarized.

Author Biography

Xiao-an Zhang received his B.S. degree in medicinal chemistry from Shanghai Medical University (now merged with Fudan University), China. He obtained Ph.D. degree in chemistry with a Summa cum laude from Universität Basel, Switzerland. Before he moved to Canada, he was a joint postdoctoral fellow in the department of chemistry and McGovern institute for brain research at MIT (Boston, USA). Currently he is an associate professor jointly appointed in the Department of Chemistry, Department of Physical and Environmental Sciences and Department of Biological Sciences at the University of Toronto, Scarborough campus. His current research interest is to develop chemical probes for biomedical imaging, especially MRI, as well as “green” catalysts for clean and renewable energy.