Gadolinium-Phosphate Complexes with Large Relaxivities Immobilized on Silica Particles for Magnetic Resonance Imaging (MRI)

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Most of the clinically available MRI contrast agents are based on complexes of Gd(III) ions with a polyaminocarboxylate scaffold, such as $[Gd(dtpa)]^-$ (dtpa = diethylenetriamine pentaacetic acid). Porous particles are attractive substrates for the immobilization of MRI contrast agents, because the particles can be modified with biomolecules to target specific tissues in vivo, leading to new applications in therapy and multimodal imaging. Moreover, particle-based MRI contrast agents have proven to be more sensitive, due to decreased molecular tumbling rates, and per-particle relaxivities can be quite large due to the large number of complexes that can be immobilized. In this study, we immobilized a phosphate-based ligand (imido diphosphate, "NP_2") onto nanoporous silica microparticles and studied their relaxivities as a function of pore diameter. We found that the r_1 and r_2 relaxivity parameters were significantly higher than for $[Gd(dtpa)]^-$ or the related complex, $[Gd(dota)]^-$; in some cases, we measured a 3 – 5 fold increase in these parameters relative to the free Gd complexes. Per-particles relaxivities were on the order of 10^7 $mM^{-1}s^{-1}$. These data indicate that $Gd(NP_2)$ complexes are particularly promising in particle-based MRI techniques.