Development of Particle-Based Imaging and MRI Contrast Agents

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Over the last few decades, magnetic resonance imaging (MRI) has been used as a noninvasive diagnostic tool by which internal organs, tumors, and structures can be resolved. Analogous to nuclear magnetic resonance spectrometry, MRI measures a change in an applied magnetic field as water molecules relax to their nuclear ground state; spatially resolving this information produces an MRI image. Commercial MRI contrast agents, such as Magnevist®, alter the relaxation of water molecules thereby enhancing the image's contrast. While these commercial agents are indeed effective, the challenge remains to design complexes with increased hydration numbers (q) and optimized water exchange rates without sacrificing chelate stability. Additionally, the retention time of these commercial agents in vivo is relatively short.

Our group is focused on designing new ligand architectures that optimize these parameters such as Gd^{+3} chelating ligands as well as peptides with specific affinities for binding metal ions from the lanthanide series. These species are immobilized on mesoporous silica nanoparticles, for site-specific targeting. These silica particles, which have a large internal porosity, can be chemically functionalized for specific applications. In this project, their extensive internal surface area allows many MRI contrast agents to be attached to the surface, leading to very large per particle relaxivities. This effect that can be further enhanced by surface rehydroxylation. Additional modification of the external surface mesoporous silica can add separate functionality; for example, efforts have been made towards synthesizing a particle that targets mesothelioma cells by employing a cell-specific antibody. Equipped with an MRI contrast agent, these particles have a long lifespan in the circulatory system, and accumulate in malignant tumors. Overall, the specific aim of this project is to develop particles to probe the treatment of tissues and tumors in vivo.