Emerging Applications of Magnetic Nanoparticles for MRI Contrast: Positive T1 Contrast at Low Field and "Color" Contrast at High Field

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Magnetic resonance imaging (MRI) is a non-invasive technique that produces three-dimensional images of human anatomy, making it a powerful tool for neuroimaging. MR images can be enhanced using contrast agents, which are exogenous magnetic materials that interact with resonant protons in tissue and modify image characteristics. Iron oxide-based magnetic nanoparticles (MNPs) have long been researched as MRI contrast agents and are usually thought of as negative contrast agents because they dephase signal from water protons, resulting in a region of decreased signal on an MR image. However, new technological advancements related to low field MRI scanners and, separately, microfabrication of MNP constructs, have created new opportunities for contrast generation that move beyond negative contrast. In this talk, I will describe new pathways for MNP-based MRI contrast using low field MRI and, also, "color" contrast with magnetic microstructures.

First, I will describe possibilities for using MNPs as positive contrast agents with low field MRI (LF-MRI). LF-MRI scanners require less infrastructure than traditional MRI scanners and can be wheeled next to a patient's bedside, creating revolutionary possibilities for point-of-care neuroimaging. While MNPs can be used as T1 contrast agents for clinical and high field MRI, the MNPs need to be specially synthesized with sizes of 3 nm or smaller to minimize proton dephasing effects. Here, I will discuss using FDA-approved contrast agents, like ferumoxytol, as well as commercially available iron oxide MNPs with sizes of 5 nm to 16 nm for positive T1 contrast at low field. I will present experiments using an FDA-approved 64 mT neuroimaging scanner to evaluate the potential of MNPs as contrast agents for LF-MRI. At 64 mT, MNPs show enhanced longitudinal relaxivity (r_1) and reduced transverse relaxivity (r_2) compared to 3 T. Moreover, MNPs have a size-dependent r_1 that is up to 8x larger than a common Gd-based contrast agent (Gd-BOPTA), suggesting that MNPs may outperform traditional T1 agents at lower fields [1]. These properties lead to enhanced T1 contrast at 64 mT for MNP-based contrast agents compared to conventional clinical field strength.

Secondly, I will describe how hollow cylinder shaped MNP-polymer microparticles can be used as radio frequency (RF) multispectral MRI contrast agents at high magnetic fields (9.4 T). Multispectral, or "color" contrast is a unique form of contrast that uses three-dimensional magnetic microstructures to produce a distinct frequency readout [2]. I will describe a new way for producing MNP-polymer microparticles which generate spectral shifts which are tens of times larger than familiar NMR chemical shifts, providing an RF-identifier that is spectrally distinct from the environment. These contrast agents can also be used as biosensors by using shape reconfigurable "smart" hydrogels that expand or shrink in response to environmental conditions. The change in shape causes a corresponding shift in the proton resonance, producing an MRI-addressable readout of the microenvironment. I will discuss proof-of-principle experiments where pH changes are detected via multispectral contrast using shape reconfigurable microparticles.

[1] S. D. Oberdick et al., *Scientific Reports*, 13, 11520 (2023).
[2] G. Zabow et al., *Nature* 453, 1058 (2008)