

**Educational Course:** Molecular & Cellular Imaging: From Bench to the Bed  
**Time & Date:** 9:30 am, Sunday April 21, 2013  
**Speaker:** Marty Pagel, PhD  
Director, Small Animal Medical Imaging Services  
Associate Professor of Biomedical Engineering,  
Chemistry & Biochemistry, and Medical Imaging  
University of Arizona Cancer Center  
University of Arizona  
1515 N Campbell Ave.  
Tucson, AZ 85724-5024  
Tel: (520)-404-7049  
Email: mpagel@u.arizona.edu

**Title:** Switching & Sensing: The Design and Application of Responsive MRI Contrast Agents for Molecular Imaging

**Highlights:**

- Review the six physicochemical phenomena that can be used to design responsive MRI contrast agents.
- Investigate examples of how responsive agents can detect enzyme activity, reporter gene expression, metabolites, metal ions, hypoxia, pH, redox state, and temperature.
- Evaluate practical challenges for detecting or measuring biomarkers with responsive MRI contrast agents.

**Target Audience:** Researchers focused on MRI contrast agents for molecular imaging

**Outcome/Objectives:** To develop a comprehensive foundation for designing responsive MRI contrast agents that qualitatively detect or quantitatively measure enzyme activity, reporter gene expression, metabolites, metal ions, hypoxia, pH, redox state, and temperature. To evaluate practical challenges for detecting or measuring biomarkers with responsive MRI contrast agents.

**Abstract**

This presentation will focus on MR contrast agents that are responsive to a change in physiological environment. The response mechanisms are dependent on six physicochemical phenomena, including the accessibility of water to the agent, rotational tumbling time, proton exchange rate, electron spin state, MR frequency, or local field inhomogeneities caused by the agent. These phenomena can be affected by the physiological environment, including changes in enzyme activities, transcription & translation of nucleic acid genes, and concentrations of proteins, metabolites, metal ions, hypoxia, pH, redox state, and temperature. Examples will be presented that show how each of these conditions of a physiological environment affect one or more of the six physicochemical phenomena, leading to a detectable change in MR image contrast.

A total of 52 examples of responsive MRI contrast agents were reported by 2007, as catalogued in a review published in early 2008 [1]. This presentation will update this review by listing the examples reported between 2007 and 2012. These examples will demonstrate the variety and creativity of different approaches used to design responsive MRI contrast agents. These examples will be grouped according to their response biomarker, so that the advantages and disadvantages of various responsive agents can be compared for detecting each biomarker.

Finally, the challenges for practical implementation of responsive contrast agents for in vivo studies will be presented. These challenges include "MRI engineering design" criteria including spatial resolution, temporal resolution, SNR and CNR, and considerations for image processing. These challenges also include "biomedical" criteria including sensitivity and specificity for assessing the physiological environment, and qualitative detection vs. quantitative measurement of physiological conditions.

References:

1. Yoo B, Pagel MD. An overview of responsive MRI contrast agents for molecular imaging. *Front. Bioscience*, 2008, 13:1733-1752.