Detection and Characterization of Europium based PARACEST Contrast Agents

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Introduction

Paramagnetic Chemical Exchange Saturation Transfer (PARACEST) utilizes an RF pulse to saturate a small pool of bound protons at the chemical shift induced by the paramagnetic lanthanide complexes. Exchange between this saturated proton pool and free protons in bulk water results in decreased signal from bulk water. This type of contrast has been shown to have wide uses including the detection of small molecules (1,2), temperature (3), and pH(4). Sensitivity to small concentrations of PARACEST agent would be useful to increase the potential for these and other studies. This abstract investigates the detection of a europium based PARACEST agent from 100mM down to 0.4mM. The results demonstrate contrast generation at 14.6T for various pH’s and temperatures.

Experimental

Phantoms of the europium complex (Eu-DOTA-4AmC; Macrocyclics) in water were imaged at the AMRIS facility on the 14.6 T instrument using spinecho and gradient recall echo magnetization transfer sequences. The CEST image was generated from the difference between two images, one with a positive offset value and the other with the negative offset value. Each individual image utilized a presaturation pulse consisting of 2000 3-lobe sinc or Gaussian pulses lasting 1 ms for a total irradiation time of two seconds. The offset value from bulk water for each set of images was varied between 0 and ±100 ppm.

Results and Discussion

Imaging results show a percent contrast of 85%, with a resulting contrast to noise ratio (CNR) of 80 at the highest concentrations. The lowest concentrations resulted in a 2% contrast, with a CNR of 3. The results of the pH imaging illustrate a shift in the location of the optimal presaturation offset as a function of pH. The pH imaging also indicates a difference in magnitude of contrast at a given offset for different pH values, in agreement with previous studies (4). Contrast generation was achieved at pH’s of 3, 7, and 10, but not at 13. The lack of contrast at the pH of 13 may suggest a pH dependant chemical change that prohibits the CEST in extremely basic conditions. CEST spectra from temperature studies indicate contrast generation potential at all tested temperatures ranging from 14°C and 38°C (287 and 312 K). The CEST spectra also show an increase in contrast generation at the lower temperatures. They illustrate a broader width of useful presaturation offsets at the higher temperatures, and a shift of the optimal offset with temperature. These results agree with previously documented effects of temperature on PARACEST agents (2), and are consistent with expectations of chemical exchange as a function of temperature.

Conclusions

The overall results of this study show that at magnetic field strengths of at least 14.6 T, this PARACEST agent can generate contrast in a variety of pH and temperature environments, at concentrations down to 0.4mM.

Acknowledgements

All data were collected at the AMRIS facility of the NHMFL, at the University of Florida McKnight Brain Institute, Gainesville, FL. Eu-DOTA-4AmC was obtained from Macrocyclics, in Dallas, TX.

References