Improved Calibration of Tm-Chleates for use in MR Thermometry

Michael A. Boss[1]

[1]*National Institute of Standards and Technology, Boulder, CO, United States*

Purpose: The need for in situ MR-compatible temperature measurements has driven research into MR thermometry. Cyclen-based thulium chelates can be used as highly sensitive chemical shift thermometers. Previous studies have indicated that the chemical shifts of residues on the chelate exhibit a linear dependence on temperature [1-3]. This research was conducted to determine the linearity of the temperature-dependence of Tm-chelates for use in MR thermometry as applied to in vivo and phantom studies.

Methods: 20 mM solutions Tm-DOTMA and Tm-DOTA were prepared in D_2O and pipetted into 5 mm NMR tubes, to which was added a small amount of DSS to serve as a 0 ppm reference. A fiber-optic (FO) thermometer was inserted into the NMR tube so that the sensing element was lined up with the center of the RF coil when placed in a 7 T NMR magnet. Temperature-regulated N_2 gas was passed over the sample while in the magnet, and the temperature tracked with the FO thermometer until thermal equilibrium was attained. NMR spectra were collected ten times at each temperature sampled from 5-45 °C, while the temperature of the samples was simultaneously monitored and recorded by the FO probe. 3 T MRI images of 4 mL phantoms containing Tm-DOTMA and Tm-DOTA in H_2O and D_2O were acquired at the water resonance and at the methyl resonance of Tm-DOTMA, while monitored with the FO thermometer.

Results: The H4 and H5 peaks of Tm-DOTA, and the methyl peak of Tm-DOTMA in the NMR spectra were fit, and the center frequency of each peak recorded relative to DSS for each temperature. The center frequencies of the 10 acquisitions at each temperature were averaged, and plotted versus temperature (Fig. 1). Chemical shifts had standard deviations of less than 0.006 ppm, and temperatures were held constant during NMR data acquisition to within .012 °C. Data were fit using linear and inverse quadratic functions. Images of the phantoms were acquired at water resonance in a 3 T MRI scanner (Fig. 2). Images using the methyl residue of Tm-DOTMA were acquired at a frequency 14147 Hz below that of water, or -110.8 ppm (-105.4 ppm relative to DSS). This correlates with a temperature of 24.2 °C using the inverse quadratic calibration curve. The fiber optic probe recorded a temperature of 24.2 °C during image acquisition. The linear calibration over the whole range of temperature yielded a temperature of 24.7 °C from this chemical shift; the linear calibration over body temperature yielded a temperature of 23.5 °C.

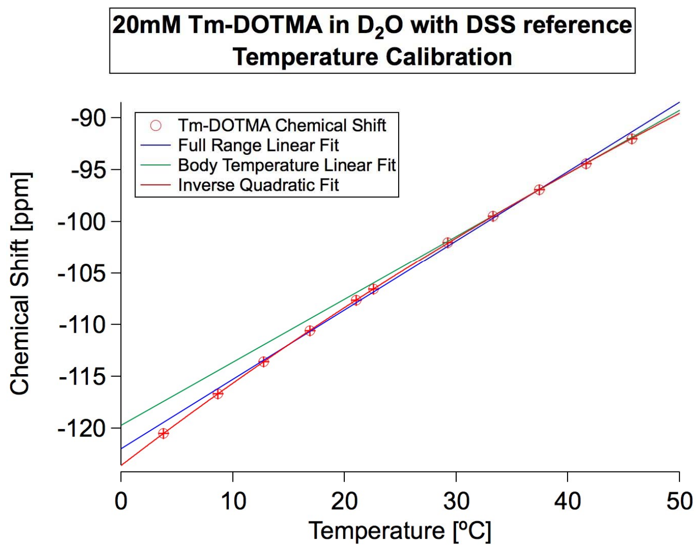

Figure 1: Chemical shift of the methyl residue of Tm-DOTMA relative to DSS as a function of temperature. Two linear fits are shown: one over the full range of sampled temperatures (blue), and another that is fit to only the 5 high temperature points (green). An inverse quadratic fit was used to generate the red calibration curve, which best fits the data.

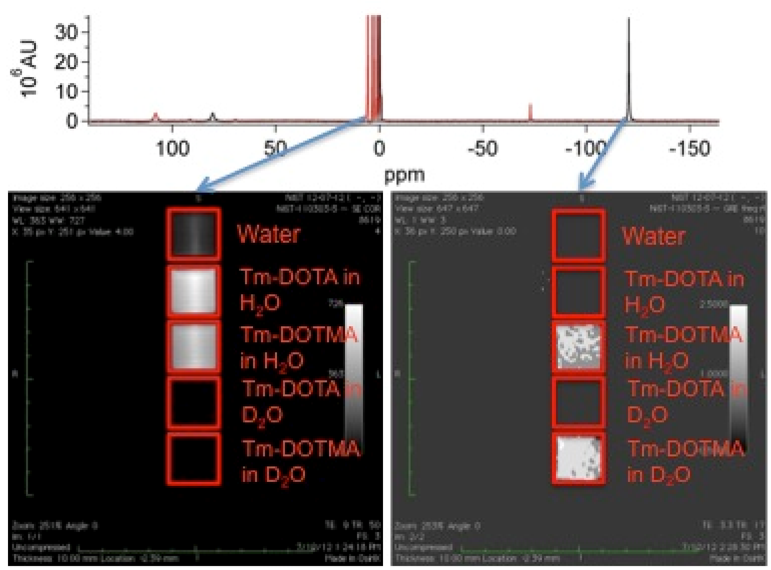

Figure 2: (Top) Example NMR spectrum of Tm-DOTMA in D_2O with DSS reference. (Bottom left) 3 T image of Tm-chelate phantoms acquired at water resonance. (Bottom right) 3 T image taken 14147 Hz below the water resonance, corresponding to the Tm-DOTMA methyl resonance. This frequency corresponds to a temperature of 24.2 °C, when using an inverse quadratic calibration fit, in agreement with a fiber optic probe used to monitor temperature during imaging. Linear calibrations resulted in large errors of 0.5 °C or larger.

Discussion: An inverse quadratic fit best fit the NMR data. It was found that linear fits to data points near body temperature led to deviations greater than 1 °C at room temperature from the inverse quadratic fit. A linear fit performed over the entire temperature range still resulted in disagreement on the order of 0.5 °C. The MRI data reflected these deviations at 24.2 °C as the linear fits yielded errors on the order of over 0.5 °C. This error is exacerbated at lower temperatures (~20 °C) found in many scanner rooms.

Conclusions: Use of a linear calibration can result in significant errors when using Tm-DOTMA as a chemical shift MR thermometer. This has important implications in temperature monitoring where a high degree of accuracy is required, such as in thermometry as applied to diffusion phantoms. An inverse quadratic function provided a superior fit.

References: [1] CS Zuo et al., J. Mag. Reson. **151**:101-106 (2001), [2] SK Hekmatyar et al., Mag. Reson. Med. **53**:294-303 (2005), [3] JR James et al., Mag. Reson. Med. **62**:550-556 (2009)