High Precision Calibration of MRS Thermometry using Validated Temperature Standards

E. Vescovo[1], A. Levick[2], S. Zhao[1], G. Machin[2], C. Childs[3], T. Rainey[3], and S. Williams[1]
[1]Imaging Science and Biomedical Engineering, The University of Manchester, Manchester, Greater Manchester, United Kingdom, [2]Temperature Group, National Physical Laboratory, Teddington, Middlesex, United Kingdom, [3]Brain Injury Research Group, The University of Manchester, Manchester, Greater Manchester, United Kingdom

Introduction: Knowledge of brain temperature is important clinically because of recent interest in the relationship between inflammation, raised temperature and neurological outcome following conditions such as stroke and traumatic brain injury, as well as the potential benefits of therapeutic hypothermia for neuroprotection. MRS can measure the internal temperature of the brain; it relies on the linear relationship between the resonance frequency of water in the tissue and temperature. The absolute temperature is obtained by measuring the chemical shift of water relative to a reference compound such as N-Acetylaspartate (NAA). To convert the frequency difference into temperature, a particular calibration curve is used [1]. Currently used calibration curves, though accurate for measuring temperature differences, still have relatively large uncertainties in absolute temperature measurements. Our contention is that this is due to inadequate temperature control and/or inaccurate temperature standards used when constructing the curves. In this study fixed-point validation phantoms and a water circulating phantom are used to calibrate MRS thermometry, providing stable reference sources of accurately known temperature, traceable back to the primary International Temperature Scale 1990 (ITS-90) as realised at the UK National Physical Laboratory.. The water-circulating phantom is also used to investigate the effect of pH and ionic strength on the relationship between ^{1}H frequency and temperature.

Methods: Spherical glass temperature-reference phantoms were used, providing stable sources of accurately known temperature. The phantoms are comprised of two concentric glass spheres: the inner one contains the phantom mixture to be measured by MRS , while the outer one contains a substance with a known temperature stable to within 0.1°C. The substances were freezing organic fixed-point materials or temperature controlled circulating water. The organic fixed-point materials were diphenyl ether (freezing at 26.3°C) and ethylene carbonate (freezing at 35.8 °C). The water circulating phantom was used in a temperature range of 20 –45°C. The MRS phantom contained 25 mM NAA in 20 mM phosphate buffer with the pH adjusted to between 6.5 and 7.5.

For data acquisition of the fixed-points, once the organic compounds had achieved their freezing temperature, the phantoms were introduced into the magnet bore and left to stand until the inner materials reached thermal equilibrium with the fixed-point materials. For the water circulating phantom, the water was piped to the phantom via insulated plastic tubing from a temperature-controlled water-bath, kept in the control room. Using this phantom, the pH and ionic strength of the mixture were changed by addition of sodium hydroxide solution or sodium chloride to analyse the influence of these parameters on ^{1}H frequency. All measurements were carried out using a 1.5 T Philips *Intera* scanner. A series of 10 single-voxel spectra were recorded for each sample at each temperature using single voxel PRESS localization (TR/TE/Nx =3000/100/16, 15x15x15 mm volume) from which the chemical shift of water (δ_{H2O}) and NAA (δ_{NAA}) are measured. During acquisition, temperature (T_{FO}) was monitored using a fluoroptic probe (Luxtron 790), previously calibrated with respect to a standard platinum resistance thermometer..

Results: The frequency differences ($\Delta=\delta_{H2O}-\delta_{NAA}$) were estimated, and the mean and standard deviations (SD) were calculated for each series. Fig.1 compares the mean Δ measured by MRS thermometry using both methods (fixed point and circulating water bath) with the T_{FO}.

The figure also shows the variation of Δ with ionic strength at two fixed temperatures (25.1°C and 44.8°C) and the relative fit line for two points with the same ionic strength variation. Variation of pH between 6.5 and 7.5 did not affect Δ.

Using the covariance matrix we can calculate the uncertainty in temperature measurement due to random errors in the calibration curve as SD<0.1°C. Temperatures estimated using the literature calibration curve [1] did not agree with T_{FO} with an increased deviation of the literature calibration curve from the circulating phantom curve at the highest temperature (45°C).

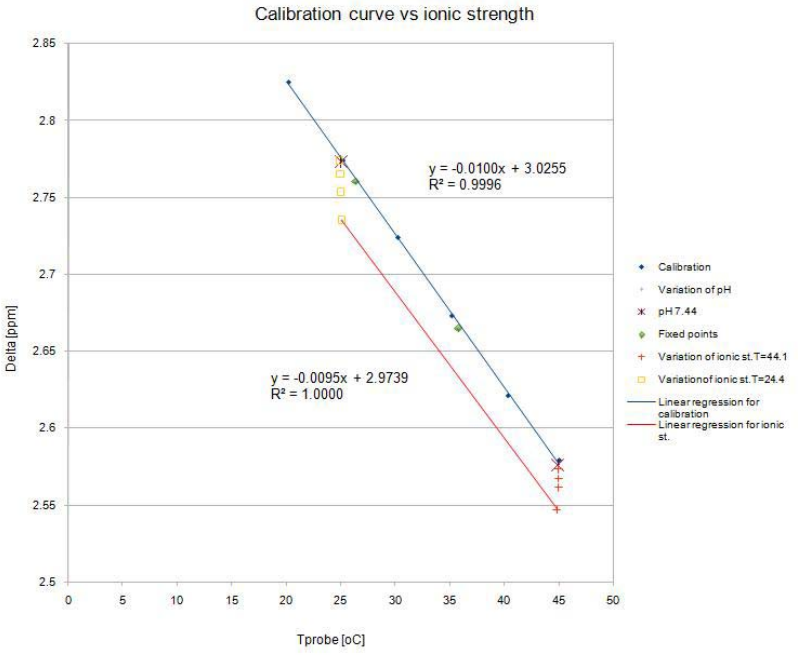

Fig.1 *Frequency differences Δ versus probe temperature T_{FO}. The blue line is obtained from the water circulating data (T_{FO} range : 20.2 °C - 45.1 °C, SD of mean delta in the order of 10^{-4}), this is a very good fit with R^2=0.9996. The green rhombs are from fixed-point experiments while the yellow squares at 25.1 °C and the orange crosses at 44.8 °C show the variation of Δ accordingly with the variation of the ionic strength. The red trend line is obtained using points of same values of ionic strength.*

Conclusion: The data showed good stability and very good reproducibility in Δ between the two signals, reflecting both the excellent magnetic field homogeneity (NAA and water linewidths <1.5 Hz) and the temperature stability achieved. The probe temperature measurements are consistent with the known freezing points of the organic compounds and with the temperature measured in the water bath. Variation of ionic strength affected the intercept of the fit but not the slope, as exemplified in Fig.1 by the parallel red and blue trend lines. Ionic strength is the most likely cause of the difference between this calibration curve and literature curves [1,2]. Establishing uncertainties in temperature measurement due to errors in the calibration is difficult without access to the raw data, but it can be estimated from publications as SD>0.5°C [1,2]. Temperature estimated using our curve has a much lower uncertainty than this (SD<0.1°C), because of excellent temperature stability so that absolute temperature measurements should be possible with higher precision than currently possible.

In future work we will use physiological intracellular ionic strength in the phantom and investigate the effect of macromolecule binding and water exchange.

Acknowledgements: DIUS NMS Programme For Materials & Thermal Metrology (2007-2010).
EC Marie Curie project FAST fellows. The staff at WTCRF for use of the imaging facilities.

Reference: [1] Zhu et al. Magnetic Resonance in Medicine 2008; 60:536-541. [2] Corbett et al. J Neurochem 1995;64:1224-30