An accurate calibration of MRS thermometry at 3T

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Purpose: To investigate the effect of varying protein and ionic concentrations on the water chemical shift temperature calibration at 3T using Magnetic Resonance Spectroscopy (MRS) with accurate temperature methods.

Introduction: MRS can be used as a non-invasive temperature by probe measuring the chemical shift difference between water and a reference metabolite [1]. The water chemical shift is linearly dependent on temperature and calibration curves are used to get absolute temperature measurements [2]. However, various slope and intercept values for different test samples at different magnetic field strengths have been reported in the literature [3], reducing the confidence in accurate thermometry using MRS. A recent systematic investigation of the effects of ionic strength, pH, buffer solution and a single protein concentration has been performed on a 1.5T clinical scanner [4]. In this study, phantom solutions were used to mimic the ionic strength of neuronal cells and protein concentration of the area of interest, for example childhood tumours compared to healthy tissue. By measuring the temperature of the solution while performing MRS a temperature calibration curve can be created. To ensure absolute confidence the temperature calibration curve should be demonstrably traceable to ITS-90 (international temperature scale of 1990), most easily achieved through traceability to national standards. The National Physical Laboratory (NPL), are the UK's national metrology institute responsible for maintaining and disseminating the temperature scale in the UK and have provided world leading temperature equipment. This study aims to compare the calibration obtained by Vescovo et al [4], using the same equipment from the NPL on a 3T clinical scanner, and investigate the effect of variable protein concentrations.

Methods: Temperature fixed point artefacts (high purity organic solutions providing known temperature reference source when undergoing a phase change), water circulation artefacts (providing controllable variable temperature sources) and a fibre optic thermometer (Luxtron) were used. Four pH normalised solutions have so far been investigated with 25mM NAA used as the reference metabolite (Table 1), including phosphate buffer, two concentrations of the bovine serum albumin (BSA) protein and a NaCl/KCl mixture used to approximate the ionic concentration within a neuronal cell. Each solution was placed in the inner core of a two-compartment spherical glass phantom. The outer core contained the fixed-point temperature organic solution or temperature controlled circulating water to provide the different temperature points. The temperature range was 21-42^{o}C and on average three temperature points were measured per solution. Solutions were scanned with a 3T Phillips Achieva using single voxel MRS (PRESS TR/TE/NSA = 2000ms/100ms/32, 15x15x15mm Voxel) with no water suppression, repeated six times per temperature point. The temperature was measured periodically during the MRS acquisitions using a fibre optic probe, with the tip placed immediately adjacent to the MRS sampled volume, with an estimated uncertainty of 0.06^{o}C (k = 2, 95% confidence). Solution temperatures were stable to $\pm$0.02^{o}C and $\pm$0.05^{o}C for the fixed point and water circulation, respectively during each MRS measurement. The spectra were processed offline using jMRUI. The water peak chemical shift was calculated by modelling the water peak using HSVD [5] and the NAA chemical shift was obtained by fitting with the AMARES tool [6] after removal of the water peak, allowing the water-NAA shift (Δ) to be calculated by subtraction. The Δ values were plotted against temperature and fits in Microsoft Excel used to give linear equation and correlation coefficients.

Results & Discussion: The temperature calibration curves changed with ionic and protein concentration (Table 1). There is good agreement between these calibrations at 3T and those done at 1.5T using the same apparatus, with very similar slope and intercept values obtained for the neuronal cell ionic solution. However, the calibration coefficients for the ionic control solution are different, which could be due to the decreased phosphate buffer concentration used here. The protein calibrations indicate a linear dependence of water PRF on protein concentration, where the values for 10% BSA in the Vescovo et al study fit linearly between the values for 5% and 15% BSA (R^2=0.99). Overall, the results show that water chemical shift at a given temperature decreases with ionic concentration and increases with protein concentration. This agrees with the theory of weakening of the hydrogen bonds with increased ionic strength and increased water-amide fast proton exchange with increased protein concentration.

Table 1: Linear fit results from the different solutions compared to Vescovo et al showing slope (α), intercept (β), linear fit (R^2) and water-NAA shift at body temperature (Δ at 37^{0}C).

Phantom solution	α	T=$\alpha\Delta+\beta$ β	R^2	Δ at 37^{0}C (ppm)
Ionic control (water,25mM NAA, 10mM phosphate buffer)	-104.32	313.44	0.9886	2.654
Neuronal cell ionic concentration (water. 83mM KCL, 26mM NaCl, 25mM NAA)	-101.09	303.86	-	2.640
BSA 5% w/v, 25mM NAA, 10mM phosphate buffer)	-86.35	266.99	0.9972	2.663
BSA 15% w/v (as above)	-120.57	361.22	0.9559	2.689
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Ionic control control (water,25mM NAA, 20mM phosphate buffer)	-99.7	301.6	0.99959	2.654
Neuronal cell ionic concentration (water. 83mM KCL, 26mM NaCl, 25mM NAA)	-100.85	303.56	0.99933	2.643
BSA 10% w/v (25mM NAA, 20mM phosphate buffer)	-105.81	320.25	-	2.677

Conclusion: This study indicates that MRS thermometry calibration curves are consistent between 1.5T and 3T scanners and depend strongly on protein concentration. This dependence, along with the ionic strength, should be considered in both therapeutic and diagnostic applications of MRS thermometry. Further investigation into the dependence of water chemical shift temperature calibrations on variations in macromolecular content and microstructure present in tumours, and on using creatine and choline as reference metabolites will be conducted.

References: [1] Cady EB, et al. Magn Reson Med 1995; 33: 862-867. [2] Hindman et al. J.Chem. Phys. 1966;44:4582. [3] Davies et al. Abstract 1769 ISMRM 2011. [4] Vescovo et al. NMR Biomed. (online pub. 07Sep2012) [5] Vanhamme L. et al. J Magn Res 1997;129: 35-43. [6] Barkhuijsen, H et al. J Magn Reson 1985;61: 465-481.