1H MRS temperature calibrations in tissue-equivalent gel phantoms show dependence on macromolecular concentration

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Introduction: In-vivo 1H MRS has been used as a non-invasive probe of temperature through the observed linear dependence of the water chemical shift on temperature in the physiologically relevant range [1]. Using a suitable calibration and internal reference metabolite peaks that are insensitive to temperature variations but account for static magnetic field variations, absolute temperature measurements are possible. However, such measurements are potentially subject to other contributions to water chemical shift from fast magnetization and/or chemical exchange effects that are dependent on factors such as macromolecular contents, molecular dynamics, microstructure, and pH. Previous water chemical shift vs temperature calibration studies have been carried out in animal models and various test solutions containing a combination of metabolites, ionic salts and protein solutions. These studies have shown significant variations in calibration constants. However, few if any studies have addressed the effect of tissue microstructure on such temperature calibrations in tissue-equivalent gel phantoms. In this study a series of tissue-like phantoms consisting of a carrageenan gel matrix containing appropriate metabolite solutions have been constructed and used to test the effects of macromolecular concentration and dynamics on temperature measurements using 1H MRS.

Method: Four phantoms were constructed separately by heating and stirring 3% by weight of carrageenan followed by 0%, 0.5%, 0.5% and 1% by weight of agarose, respectively, in 500 ml of de-ionised water until fully dissolved. While the solutions were cooling, 25 mM of n-acetyl aspartate (NAA) and 20 mM of creatine (Cr) were added in powder form. Finally, 0.1% of Gd-DOTA was added as a T_1 modifier. An additional 1.5 l test object was constructed using 0.5% agarose concentration with smaller concentrations of Cr and lactate (Lac) to investigate uniformity of the metabolite concentration and reproducibility of the water chemical shift measurement. Single-voxel (SV) MRS (PRESS, TR 1500ms, 2x2x2 cm^3, NSA 32) was repeated 3 times within the same session at 3 different locations within the 1.5 l test object at short (30ms) and long (135ms) TE and on 2 separate occasions on a 3 T Siemens Verio MRI scanner. To investigate the effect of agarose concentration on the water chemical shift and its temperature dependence, the four 750 ml phantoms were placed together within the multichannel head RF coil of a 3 T Siemens Verio scanner. A thermocouple device was used to measure the temperature of each test object outside of the scanner bore at a depth of 5 cm below the surface to coincide with the MRS voxel placement prior to the initial measurement at room temperature and before and after each subsequent MRS measurement. The phantoms were then heated in a microwave oven to approximately 40 deg C and the temperature of each was measured using the thermocouple before re-placing in the scanner followed by repeated SV MRS measurements during the cooling process interspersed with thermocouple temperature readings. Spectra were processed and analysed using jMRUI and AMARES to fit Lorentzian lineshapes to the water, Cr and NAA peaks. Least squares fitting was used to estimate the coefficients of water chemical shift as a function of temperature and their standard errors (S.E.).

Results: The room temperature measurements of water chemical shift relative to Cr and NAA were highly reproducible with between scan and between session variability of less than 0.005 ppm. Measurements at different locations within the 1.5 l phantom also showed showed only small variations. All calibrations of chemical shift as a function of temperature showed a strong linear relationship with $R^2 > 0.97$. Table 1 shows that the correlation coefficients are approximately 0.01 ppm/°C, in agreement with the literature. However, there is a significant linear relationship between the temperature coefficients of the chemical shift and the agarose concentration ($P < 0.05$).

Table 1. Water chemical shift relative to Cr and NAA vs temperature for phantoms with different agarose concentrations

Agarose concentration	δ(H2O-Cr) ppm/°C		δ(H2O-NAA) ppm/°C		Mean coeff. (ppm/°C)
	Coeff.	S.E.	Coeff.	S.E.	
0%	-0.00916	0.00074	-0.00883	0.00077	-0.00899
0.5%	-0.00978	0.00049	-0.00974	0.00050	-0.00976
0.5%	-0.00980	0.00079	-0.00936	0.00068	-0.00958
1.0%	-0.01126	0.00044	-0.01143	0.00055	-0.01135

Conclusions: This study suggests that macromolecular concentration and tissue microstructure may play an important role in water chemical shift measurements and these factors should be taken into account in calibrations for ^{1}H MRS thermometry. Further investigation of water chemical shift measurements as a probe of fast exchange effects for tissue characterisation is required.

REFERENCES:

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