Absolute internal thermometry in MRI test-objects using ^{1}H-MRS to 50milli-degree level precision

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Aim: To develop internal self-referenced thermometry for test-objects, with sufficient precision to eliminate errors arising from the temperature dependence of quantitative MR parameters

Introduction: Long-term clinical studies require the use of test-objects with stable properties (1). Many MR properties (e.g. T_1, T_2, D, MT) are temperature dependent with temperature coefficients of about 2-3%/ ^{o}C. Thus for consistent quality assurance (QA) results, temperature should ideally be known to within 0.3^{o}C (1). The linear dependence of the proton (^{1}H) chemical shift (σ) of water relative to that of temperature-stable reference species (such as N-acetylaspartate (NAA)) has allowed the determination of absolute temperature *in-vivo* using ^{1}H-MRS (2). Relative to NAA, water chemical shift in piglet brain depended linearly on temperature from 30ºC to 40ºC: temperature T=286.9-94.0 σ ºC (2). In contrast to other NMR thermometry techniques such as T_1 measurement, the method potentially yields absolute, rather than relative (to a reference measurement at 37˚C), temperature values. Potential reference compounds were evaluated using criteria such as the compound-water chemical shift, proton molarity, solubility, stability, biohazard, pH dependence of the chemical shift, intrinsic T_2 (i.e. linewidth), and cost, and the NMR reference standard DSS (sodium 2,2-dimethyl-2-silapentane-5-sulfonate) was found to be most suitable. ^{1}H-MRS chemical shift measurements of water with respect to DSS were fitted to a linear model, demonstrating that absolute internal thermometry could be developed for test objects. The reproducibility of temperature measurements using this method was also investigated, using repeated measurements at a single temperature.

Methods: ***1. Calibration:*** ^{1}H-MRS PRESS spectra without water suppression were acquired on a 1.5T GE Signa scanner (General Electrics Medical Systems, Milwaukee, WI, USA), with TR=3s, TE=30ms, 96 averages in groups of 8 NEX, voxel-of-interest (VOI) size 2.3cmx2.0cmx1.5cm (total acquisition time per spectrum 4:48 mins). A 60mM (i.e. 13.10 g/L) concentration DSS solution (in a phosphate buffer solution, pH neutral) was contained in a small plastic bottle held within a phenolic foam thermally insulating cylinder (thermal time constant to within 1.0°C~10-20hrs (P. S.l Tofts, unpublished data)), enabling the aqueous solution to be imaged at a known temperature, remaining constant for the duration of the experiment. ^{1}H-MRS chemical shift measurements of water with respect to DSS were performed at 5 temperature points (13°C-36°C) in a random order (solution temperatures were measured using a K-type thermocouple, ensuring that no temperature change took place during the scanning process). At each temperature, 2 acquisitions were made (without repositioning, shimming or other prescan adjustments between measurements). The water-DSS σ difference was estimated in the frequency domain after time domain fitting using jMRUI software (3). The standard deviation (SD) of the signed difference between repeated measurements was used to estimate the SD of a single σ measurement (4), and linear regression was used to determine the relationship between relative σ and T.

2. Reproducibility: The purpose of this experiment was to characterise the reproducibility of measurements under conditions of stable temperature, with a realistic setup procedure before each repeated data collection. 10 acquisitions were performed from a 250mM (i.e. 54.58 g/L) concentration DSS solution (again, in the phosphate buffer solution) in a 39ml volume plastic container, submerged in a cylindrical water bath (volume 250ml, diameter 60mm x height 145mm), at room temperature. Again, the insulating cylinder was used to ensure that the temperature remained constant throughout the experiment. The number of averages was varied (in a random order), and in each of the 5 cases the SD (with voxel re-positioning and shimming for each of the 10 acquisitions) was estimated.

Results: ***1. Calibration:*** Linear regression yielded the relationship T=485.39-96.21σ (± 0.25)ºC (13°≤T≤36 ºC) (see Figure 1). The error bars reflect the estimated SD for a single measurement, found to be just 0.13˚C. This gives a minimum detectable temperature difference (defined to be the 95% confidence limit (CL) i.e. 1.95*SD) of 0.25ºC, which is artificially large, since it includes a potential contribution from temperature variations (due to the large temperature difference between the scanner bore and the samples).

2. Reproducibility: Interestingly, the SDs did not exhibit the expected proportionality to (no. of averages)$^{-1/2}$ (see Figure 2), indicating the presence of additional variations other than thermal noise. The software resolution is ~0.015ºC; therefore this is unlikely to be a limiting factor. Other possible contributing factors include voxel repositioning and shimming. Here the pooled SD of just 0.050(±0.007)°C is quoted, since we assume that noise is not the limiting factor in the reproducibility of temperature measurements. The error bars represent the 95% CL in estimating the reproducibility of temperature measurements, with the uncertainty (s_{SD}) calculated using the relation: s_{SD}=SD/√2(n-1), where n=no. of samples (n=10 in each case).

Figure 1: Temperature (T) as a function of water-DSS chemical shift (σ)

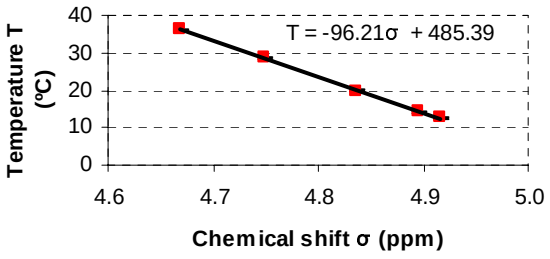
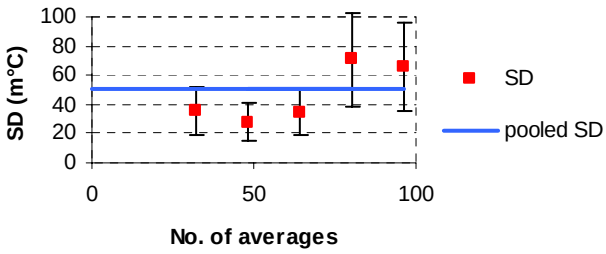


Figure 2: SD as a function of the number of averages



Discussion and Conclusions:

1. Internal thermometry to within 0.3°C in phantoms using the DSS-water σ is realistic. The minimum detectable temperature difference (95% CL) with voxel repositioning and shimming between scans is 0.10^{o}C. This estimate of reproducibility is the relevant one, since the effect of possible temperature fluctuations was removed.
2. The use of an insulating 'enclosure' significantly reduced variation due to scanner bore temperature fluctuations, improving the repeatability of temperature measurements.
3. Small, highly concentrated reference compound samples could be inserted into existing phantoms to enable internal thermometry.
4. Optimisation of acquisition parameters and spectral processing strategies (5) may improve precision.

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