Absolute Brain Temperature by ^{1}H MRS

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Introduction Knowledge of absolute brain temperature would be of clinical benefit in several brain pathologies, such as traumatic brain injury and stroke. Recently, ^{1}H MRS has been used for single-voxel (1,2) or multi-voxel (2,3) brain temperature measurements in man. Several calibration curves *in vitro* from metabolite phantoms (4,5) and *in vivo* (5,6) have been published for temperature dependent frequency difference between water and N-acetyl aspartate (NAA) (Δf), but not at higher field strengths used clinically (i.e. 3T). The relationship between Δf and temperature is derived by: T (^{o}C) = A + ΔfB. Compared to direct tissue measurement, ^{1}H MRS derived brain temperature is 0.5 ^{o}C lower (5). Given the temperature gradients (up to -1.2 ^{o}C) between surface and deep brain structures in the open skull preparations, the discrepancy between techniques (invasive measured *vs.* ^{1}H MRS) is likely to exceed 0.5 ^{o}C (5). This may be due to an additional factor in the equation: T (^{o}C) = A + B(Δf) + C, where C is a term for chemical and biophysical effects, as well as the influence of spectral characteristics, on Δf. The factors influencing precision of temperature measurement by ^{1}H MRS include spectral acquisition parameters, e.g. digital resolution, line width (LW) and line shape (2,3). In the present study we have calibrated Δf at 3T both in metabolite solution and *ex vivo* using a rat brain slice preparation. Brain temperature was determined by ^{1}H MRS in a group of healthy volunteers and compared to body temperature.

Methods In vitro calibration for Δf was performed in a temperature-controlled glass chamber from 32 to 44 ^{o}C using NAA and Cr solution (50 mM each) in phosphate buffered saline (PBS, pH 7.0) supplemented either with 0 or 75 μM $MnCl_2$. Δf calibration is given for NAA-water pair only. Rat brain slice preparation (thickness 350 μm, incubated in PBS) was used for *ex vivo* temperature calibration in the same chamber. ^{1}H MRS spectra from a volume of 30x18x18 mm^3 were acquired from the phantom with a Philips Achieva 3T scanner using a transmit/receive headcoil and a double spin echo method with the following parameters: TR 2000 ms, TE 60 ms, SW 1500 Hz, 2k data points, water suppression power set close to 70% of full signal suppression power. T_2 was estimated from data set acquired with TEs of 60, 90, 120 and 160 ms. Single voxel ^{1}H MRS spectra were acquired from healthy volunteers (6 males, aged 23 to 51 years) after obtaining informed consent. A 17x17x10 mm^3 voxel was positioned into three occipital lobe locations. Spectra were collected using a SENSE headcoil and the acquisition parameters as follows: TR 1600 ms, TE 60 ms, SW 1500 Hz, 2048 data points, NS 32, 4 dummy scans, 2 consecutive spectra, water suppression power set to about 50% of the power for full suppression of water signal. Ten minutes before entering the magnet, body temperature was measured in each subject at three sites; oral cavity, tympanum and skin overlying the course of the temporal artery using an infrared scanner (Exergen; MA, USA). These measurements were repeated immediately after the scanning session. Temperature in the scanning suite was 21.4±0.1 ^{o}C. FIDs were processed offline by exponential functions corresponding to 0.3-2.0 Hz line-broadening before Fourier transformation. Lorenzian lines were fitted using the software obtained from MRSTools Inc (Kuopio, Finland).

Results The calibration curves for temperature dependency of Δf are shown (Fig. 1). T_2 for water was >1000 and 280 ms in 0 and 75 μM $MnCl_2$ containing phantom, respectively. Table 1 shows the coefficients in the linear regression equation T (^{o}C) = A + B(Δf). Importantly, these curves differ statistically from each other ($p<0.001$), which supports the argument for the relationship between temperature and Δf as follows: T (^{o}C)= A + B(Δf) + C. The coefficients A, B and C obtained by fitting the results from phantoms and brain slice preparations to the latter equation are: A = 308.31 ^{o}C, B = -102.53 ^{o}C/ppm, and C varying as follows: -0.19 ^{o}C (NAA phantom + 0 μM $MnCl_2$), 0.48 ^{o}C (NAA phantom + 75 μM $MnCl_2$) and 0.24 ^{o}C (brain slices). The RMS errors for these three curves using both calibration procedures were 0.165 ^{o}C and 0.174 ^{o}C, which are almost identical**,** but the latter method includes one fitted parameter less**.** The average Δf and brain temperatures in three occipital brain volumes are shown (Table 2). The body temperature was 36.6±0.3 ^{o}C before and 36.8±0.1 ^{o}C after the MR scans (not significant). These values and the temperatures from Table 2 indicate that the brain was ~0.4 – 0.6 ^{o}C cooler than the body temperature. SDs of the temperature values from human brain ^{1}H MRS data increased exponentially when the LW of NAA exceeded 12 Hz. This is in agreement with a previous study using simulated data (2), and places LW limit for precise frequency determination.

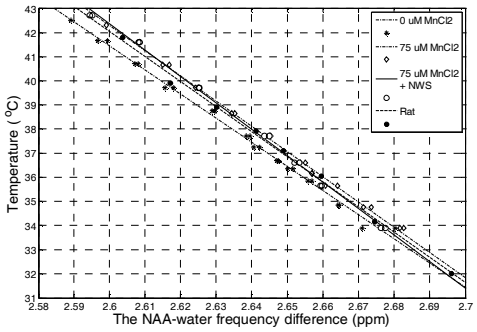

Fig.1. Calibration curves for phantoms and rat brain slices

TABLE 1. Coefficients for the temperature calibration

PHANTOM	Coef A	SD	Coef B	SD
NAA	301.66	4.22	-100.08	1.60
NAA + $MnCl_2$	314.05	3.48	-104.52	1.32
NAA + $MnCl_2$ (no water supp)	327.19	4.43	-109.55	1.68
Brain Slices	312.08	6.75	-103.86	2.55

TABLE 2. Δf and brain temperatures in human brain volumes

BRAIN VOLUME	Δf	SD	Temp (no term C)	SD	Temp (with term C)	SD
VOL #1	2.656	0.0057	36.14	0.60	36.15	0.5
VOL #2	2.656	0.0033	36.19	0.35	36.19	0.3
VOL #3	2.658	0.0142	35.96	1.48	35.96	1.4

Conclusions The calibration data for Δf and temperature relationship indicate that the influences of the chemical environment and spectral characteristics are small and consequently, the relationship follows the equation: T (^{o}C) = A + B(Δf) + C. The proposed relationship will give accurate temperature dependence for Δf owing to elimination of effects by chemical environment. Our results show that there is no systematic variation in the brain temperature between the sites scanned and that the mean absolute temperature in the occipital brain may be lower than that determined from the three body sites. Our data also places requirements for LWs for spectral quality for precise Δf determination.

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