Cerebral temperature mapping by self-referenced proton spectroscopic imaging thermometry

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Background: Cerebral hypothermia shows promise as a cerebroprotective therapy in newborn infants suspected of exposure to perinatal hypoxia-ischaemia[1]. In order to determine an optimal, safe strategy for attaining brain hypothermia, a non-invasive means of measuring regional cerebral temperature is required. To a good approximation the proton (^{1}H) chemical shift of water (δ_{H20}) is linearly dependent on temperature. Determination of the difference between δ_{H20} and the chemical shift of temperature-stable reference metabolites in non-water-suppressed single-voxel ^{1}H-spectra has allowed the accurate estimate of absolute local temperature *in vivo*[2,3]. In this work we demonstrate, to our knowledge for the first time, that non-water suppressed 2D proton spectroscopic imaging (^{1}H-MRSI) may be used to obtain two dimensional maps of absolute cerebral temperature.

Methods: *In vivo* data were acquired from the brains of newborn piglets studied at 7 Tesla. In 3 animals cerebral hypothermia was induced by step-wise whole-body cooling maintained by means of a thermally regulated water-mattress. In 3 piglets selective head cooling was obtained by the application of a water-filled plastic "cooling cap" proximal to the animals' scalp. ^{1}H-MRSI thermometry results were corroborated with simultaneous invasive measurements obtained with a surgically inserted fibre-optic probe (Luxtron) and rectal temperature was determined with a thermistor. Non-water suppressed ^{1}H–MRSI data were acquired from a coronal slice (thickness 4 mm, TE 45 ms, TR 3000 ms, 16x16 voxels, FOV 5 cm, 2048 complex points per FID, BW 4khz) using a 6cm x 4cm elliptical surface coil positioned above the parietal lobes. Manual slice selective shimming was performed. Suppression of out-of-volume lipids was not required in these experiments. MRSI data sets were processed using in-house software: following mild spatial apodization and FFT, for each voxel separate water and metabolite spectra were obtained from the single non-water suppressed spectrum using a convolution-difference method. The chemical shift difference between the water peak and that of n-acetylaspartate (NAA) was obtained by calculating the cross-correlation between these two spectra[4]. This chemical shift difference was converted to absolute temperature using a calibration previously obtained from single voxel measurements. Analysis proceeded in a semi-automatic manner, voxels yielding non-analyzable spectra (due to poor line shape or SNR) being rejected manually. Temperature data were interpolated from the original 16 x16 voxel data to 256 x 256 pixel maps using a Gaussian kernel.

Results: Figure 1 shows representative temperature maps from (A) a piglet subject to whole-body hypothermia and (B) a different animal in which topical "cap-cooling" was employed. In the first case, cerebral temperature was approximately uniform and close in value to the rectal temperature. In the second case, marked temperature gradients between the cortex and deep-brain regions were evident. MRSI Temperature values were consistent with invasive measurements.

Discussion: Non-invasive maps of cerebral temperature distribution have been obtained. This method will enable the relative efficacy of clinically viable brain-cooling strategies to be investigated. The advantage of this self-referenced method is that absolute temperature is obtained in a single measurement. The alternative proton resonant frequency (PRF) phase-difference mapping approach[5] only provides temperature *differences* between two separate image acquisitions. Our method is potentially applicable to human neonates enrolled in clinical trials of therapeutic cerebral hypothermia, and other applications where the determination of cerebral temperature distributions is required.

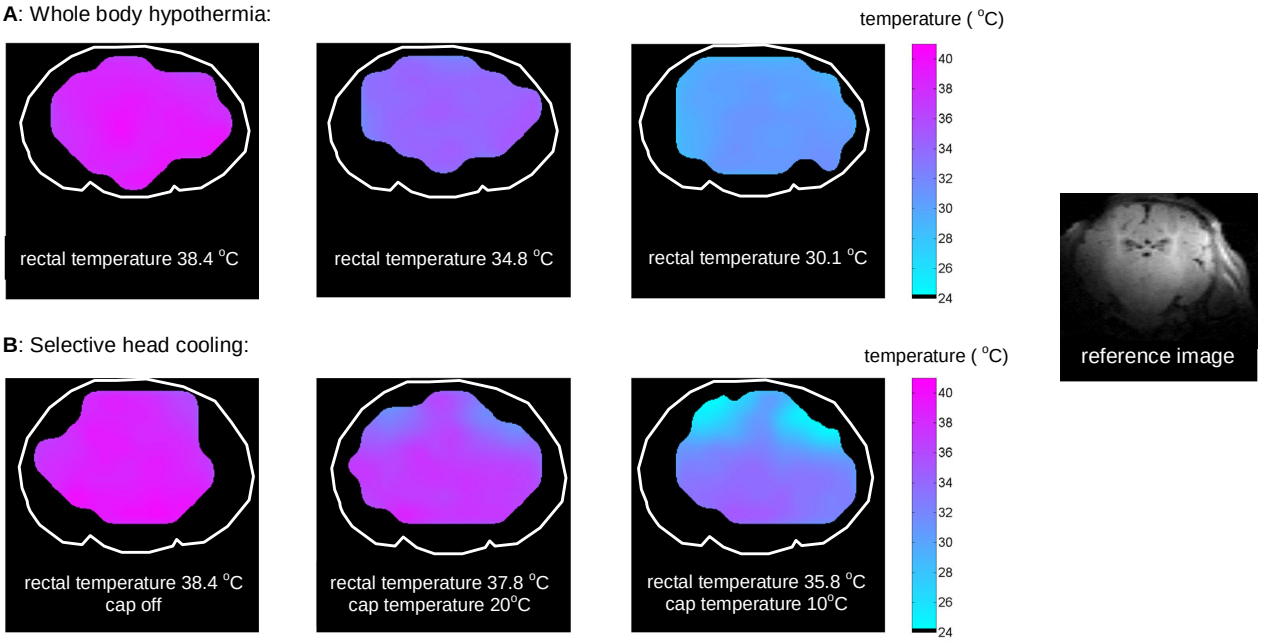

Figure 1. *In vivo* self-referenced coronal MRSI cerebral temperature maps from newborn piglets. The white line indicates the cerebral boundary. MRSI voxels located at the edge of the brain did not yield valid temperature values due to magnetic susceptibility induced line-broadening or inadequate SNR. The data was interpolated to yield smooth temperature maps. A representative FLAIR reference image is shown at the right.

References:

1. Wyatt et al. Acta-Paediatr. 86:1029, 1997 **2.** Cady et al., Magn. Reson. Med. 33:862, 1995; **3.** Corbett et al. J-Cereb-Blood-Flow-Metab. 17: 363, 1997 **4.** Thornton et al. Proc ISMRM 2003, 263 **5.** De-Poorter et al. Magn-Reson-Med 33: 74, 1995.