Water-Referenced Metabolite Normalization for MR Spectroscopic Imaging

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INTRODUCTION: The analysis of in vivo MRS data using metabolite ratios is known to be limited by the lack of a single metabolite signal can be reliably used as a reference; therefore quantitation or normalization to "institutional" units is preferred. For this purpose, signal normalization using the tissue water signal has been recommended for single voxel MRS (1), being readily implemented and having acceptable precision, while the phantom replacement method (2) has been widely applied for MR Spectroscopic Imaging (MRSI). In the choice of method, considerations include difficulties associated with changes of tissue water content and mismatch between the intensity correction functions from the phantom and the object under study, which occurs at higher field strengths (≥3T). In this report is described a normalization method for brain 1H MRSI data using tissue-water. The method requires only the conventional MRI measurement typically done as part of every MRSI study.

METHODS: A signal normalization procedure must correct for spatially-dependent signal variations, account for the tissue volume contributing to the MRSI signal, and scale the data relative to a known reference. In this study, this is achieved using the internal brain water signal derived from a proton density MRI and convolved by the MRSI spatial response function, *srf*, to obtain a reference image corresponding to 100% water at each MRSI voxel. Firstly, the acquired proton density MRI is processed using tissue segmentation of coregistered T1 and (optional) T2 weighted images to calculate an image equivalent to 100% water distribution across the brain, as:

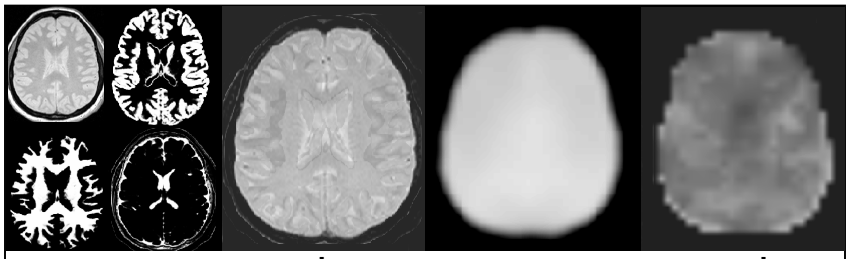
$$I_{H2O} = I \cdot \left(F_{CSF} / \delta_{CSF} + F_{WM} / \delta_{WM} + F_{GM} / \delta_{GM} \right)$$

Where I is the proton density image, F_{CSF}, F_{WM}, and F_{GM} are the tissue fraction content of each voxel obtained from segmentation, and δ_{CSF}, δ_{GM} and δ_{WM} are the relative water content for CSF, gray, and white matter, initially taken to be 0.98, 0.82 and 0.73 respectively. Additional processing includes correction of the proton density MRI for incomplete relaxation based on literature T1 values for each tissue type; adjustment of the relative water content for GM and WM to minimize intensity variation over the resultant image; and edge-preserving smoothing of I_{H2O} to diminish effects of classification errors. I_{H2O} is then convolved by *srf* and the fitted metabolite signal at each voxel normalized by:

$$Met_{Norm} = K_{MRI/MRSI} \cdot Met_{Raw} / I_{H2O} \cdot Gain_{MRI/MRSI}$$

where $Gain_{MRI/MRSI}$ accounts for differences of the receiver gain used for the MRI and MRSI measurements and K is the MRI/MRSI signal intensity ratio per unit of metabolite concentration (in mM) obtained from a calibration measurement for the same acquisition and processing protocol. The result is normalized to institutional units only and does not include correction for spin relaxation terms.

RESULTS AND DISCUSSION: Example images are shown in the following Figure. In (b) it can be seen that the initial conversion to a 100% water equivalent image still contains some local image intensity variations due to small differences in water content or relaxation times for different brain regions, however, these are removed by the subsequent image smoothing and convolution operations.



Example images showing: (a) Proton density MRI and tissue segmentation results; (b) Initial water reference image at MRI resolution; (c) Smoothed reference image result at SI resolution; (d) Normalized NAA image.

The proposed normalization method requires no additional measurements and is conveniently incorporated into any MRSI protocol. Limitations include potential errors due to normal regional variations of tissue water density and relaxation rates and in regions of pathology; however, these may be diminished by the more sophisticated processing methods, including brain region identification and data interpolation over regions of pathology.

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REFERENCES: 1) S.F. Keevil, *et al.*, Magn Reson Imag 16:1093 (1998). 2) B.J. Soher, *et al.*, Magn Reson Med 35: 356 (1996).