Localization Profile Correction for ERETIC based in vivo ^{1}H MRSI quantification

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Introduction

Magnetic resonance spectroscopic imaging (MRSI) enables the acquisition of quantitative metabolite distribution maps with internal water referencing (IWR) [1] being the current method of choice for signal normalization and determination of mM concentrations. IWR accounts for B_1^+ variations across the field of view but imposes problems when assessing diseases that lead to alteration of tissue water concentration [2] and relaxation behavior. ERETIC (Electrical REference To access Invivo Concentrations) has proven to be a reliable and accurate alternative for the quantification of metabolite concentrations *in vivo* in single voxel ^{1}H MRS [3] and an initial MRSI implementation has been presented previously [4]. ERETIC is independent of the disease state, automatically compensates for changes in coil loading conditions, receive gain settings and data processing and hence requires only a one time calibration against a high precision phantom. However, the combined effect of B_1^+ inhomogeneity across the volume of interest and slice profiles of the selective RF pulses used for localization create a localization profile that induces spatially varying metabolite intensities independent of physiological changes. This effect needs to be corrected for in case of ERETIC based MRSI quantification. Hence, ***in this work***, two localization profile correction methods for ERETIC based ^{1}H MRSI quantification are presented and cross-validated against IWR based ^{1}H MRSI.

Materials and Methods

Acquisition: In vivo and in vitro experiments were performed on a Philips Achieva 3T human MRI scanner (Philips Healthcare, Best, Netherlands) using a commercial transmit/receive birdcage proton coil with additional modifications to allow for ERETIC [3]. 2D MRSI (TR/TE: 2000/39ms) data were obtained from a 12 mm slice; 22 x 20 phases encoding steps over a FOV of 220 mm x 200 mm were applied. A VOI of 100 mm x 80 mm was preselected with PRESS, using the FREMEX05 RF pulse for excitation and the FMREF07 for refocusing. *In vitro* measurements were carried out in a spherical homogenous phantom containing brain metabolites. *In vivo* MRSI data were acquired in a healthy volunteer from an axial slice above the ventricles that included white matter of the centrum semiovale and gray matter along the interhemispheric fissure. Inner volume suppression was applied to avoid chemical shift displacement and render localization volumes consistent across all metabolites of interest. A T1-weigthed FFE image was acquired over a 36 mm slice centered at the MRSI slice position with an acquisition matrix of 220x200x9, (TR/TE 92/4.6ms) and used for tissue segmentation performed using SPM8. 3D actual flip angle maps were measured using the 3D AFI method [5]. The maps were recorded over a 108 mm wide stack with 9 slices centered at the MRSI slice and matching its FOV in the axial plane. In this way no slice profile corrections [6] had to be applied to the AFI maps itself. Resulting segmentation maps as well as flip angle maps were smoothed to the same effective resolution as the MRSI data, by convolving them with the PSF of the MRSI data. *Quantification:* All the spectra were eddy current and phase corrected and fitted using LCModel using simulated metabolite basis sets. The fitted resonance areas were corrected for relaxation attenuation and for partial volume effect due to CSF. IWR was carried out as described by Gasparovic et al. [7]. With ERETIC, the areas of the metabolite resonances are converted into concentrations by comparing them to an externally generated signal, that is inductively coupled into the receive coil [3]. *Localization profile correction (ACP and BSP):* To correct for the localization profile, the observable magnetization in every voxel under the given experimental conditions has to be estimated for a homogenous material. The correction of the metabolite/ERETIC ratio is then simply accomplished by division by the expected values for the observable magnetization. In this work these values are either calculated analytically (abbreviated *ACP* hereafter), using the formula from Moonen et al. [8] or by performing a Bloch simulation of the PRESS sequence with the relevant pulse and gradient waveforms (abbreviated *BSP*). In both cases the actual flip angles, from the measured AFI maps were used.

Results

The results from the *in vitro* measurement are presented in Fig. 1. Obtained water/ERETIC ratios in the VOI are shown without any correction for the localization profile (1B) and with the two corrections proposed in this work (1C, 1D). Fig. 1E shows the difference between the Cho/water and Cho/ERETIC ratios, when ERETIC is corrected with *BSP*. The coefficient of variation of the ratios over the voxels in the pass band of the regarding RF pulses are 3.3 % for the Cho/water, 4.88 % for Cho/ERETIC with *ACP*, 4.95 % for Cho/ERETIC with *BSP* and 8.8 % for Cho/ERETIC without corrections for the localization profile. From the *in vivo* measurements the calculated Cr/ERETIC ratios with *BSP* correction are shown and compared with the Cr/water ratios in Fig. 2.
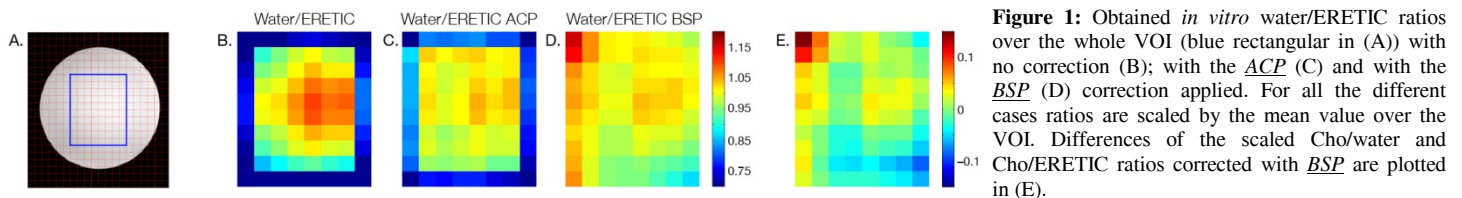

Figure 1: Obtained *in vitro* water/ERETIC ratios over the whole VOI (blue rectangular in (A)) with no correction (B); with the *ACP* (C) and with the *BSP* (D) correction applied. For all the different cases ratios are scaled by the mean value over the VOI. Differences of the scaled Cho/water and Cho/ERETIC ratios corrected with *BSP* are plotted in (E).
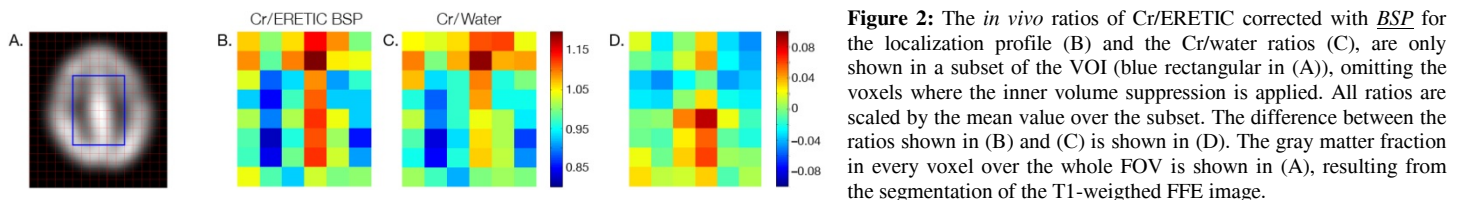

Figure 2: The *in vivo* ratios of Cr/ERETIC corrected with *BSP* for the localization profile (B) and the Cr/water ratios (C), are only shown in a subset of the VOI (blue rectangular in (A)), omitting the voxels where the inner volume suppression is applied. All ratios are scaled by the mean value over the subset. The difference between the ratios shown in (B) and (C) is shown in (D). The gray matter fraction in every voxel over the whole FOV is shown in (A), resulting from the segmentation of the T1-weigthed FFE image.

Discussion

ERETIC can only be a reliable quantification method for MRSI, when an appropriate localization profile correction is applied. As demonstrated by homogeneous phantom metabolite/ERETIC maps and low coefficients of variation both the *ACP* and the *BSP* localization profile correction method compensate the metabolite intensity variations in the region of the PRESS volume that corresponds to the pass band of the regarding RF pulses. In contrast, the *BSP* localization profile correction is clearly superior at the border of the PRESS volumes, which correspond to the transition bandwidth of the RF pulses used for localization. Remaining inconsistencies in the corner of the PRESS volume where the transition bandwidth of multiple RF pulses overlap result most likely from spectral fitting errors due to very low metabolite signal intensities. Another source of errors are inaccuracies in the flip angle maps. In vivo Cr/water maps and Cr/ERETIC maps with *BSP* localization profile correction are highly similar and reflect the expected higher Cr concentration in the grey matter along the interhemispheric fissure in comparison to adjacent white matter voxels. **In conclusion**, *BSP* localization profile corrected, ERETIC based ^{1}H MRSI quantification represents a reliable method for signal normalization and determination of mM concentrations.

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