T_2^{CSF} pitfalls using water as internal reference for metabolite quantification

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Introduction

The unsupressed water signal is often used as an internal reference for metabolite quantification in ^{1}H-MRS. The water signal arises from different compartments of the human brain (brain matter BM and cerebral spinal fluid CSF) with large differences of T_2 relaxation times between BM and CSF.

Bi-exponential fitting of T_2 relaxation times can be used to calculate the water signal at TE = 0ms. The knowledge of these T_2 relaxation times is crucial to obtain reliable results. In principle the T_2 times can be determined with imaging and spectroscopy methods. Additionally, there are several publications reporting T_2s with a large range of results (T_2^{CSF} = 110-2000ms) [1-5]. Helms [5] suggested that there is a dependency of the water T_2 fit on the voxel's CSF partition. In this study we wanted to compare the results obtainable for T_2^{CSF} with different methods in a typical MRS-Voxel in the anterior cingulated gyrus.

Methods

Unsupressed water spectra and MRI-T2maps from 23 subjects were obtained on a 3T clinical MR system (TIM Trio, Siemens, Erlangen).

We conducted two T_2 measurements for an anterior cingulate single voxel MRS location (size: 5.4ml, see Fig. 1). First, we used a PRESS sequence without water suppression with six echo times (TE = 30, 80, 276, 552, 1000, 1500 ms) with a repetition time of TR = 10s. Quantification of the decaying water signal was done with LCModel. Bi-exponential models were fitted to the MRS water signals based on the assumption that the VOI consists solely of BM and CSF. A T_1-weighted isotropic 1m^3 3D MPRage data set was used to determine the compartment-fraction by SPM5 (SegSpec [6]). The exponential functions were weighted by this voxel compartment-fraction and the proton density of BM and CSF in comparison with pure water.

Formula: $M_0*((GM_{spm}*81+WM_{spm}*71)*\exp(-TE/T_2^{BM})+CSF_{spm}*98*\exp(-TE/T_2^{CSF}))$.

To investigate the influence from T_1, number of obtained echoes and Voxel position, we additionally acquired spectra from a single subject from two VOI locations: an additional VOI was placed in a ventricle. In this experiment both VOIs were examined with two different repetition times (TR = 10s and TR = 30s) to identify a possible T_1 relaxation effect and with 14 echo times (TE_{min} = 30ms, TE_{max} = 1500ms).

Second, we acquired high resolution (1x1x3mm) T2maps using a multiecho imaging sequence, with 31 echoes, (TE_{min} = 30ms, TE_{max} = 930ms, ΔTE = 30ms) consisting of 5 slices covering the same volume as the MRS VOI. The multiecho images were fitted by a mono-exponential function and masked by the segmented MRS volume. Mean T_2 values for each tissue class were calculated. Only voxels which SPM classified with 100% probability to contain solely BM or CSF were analyzed

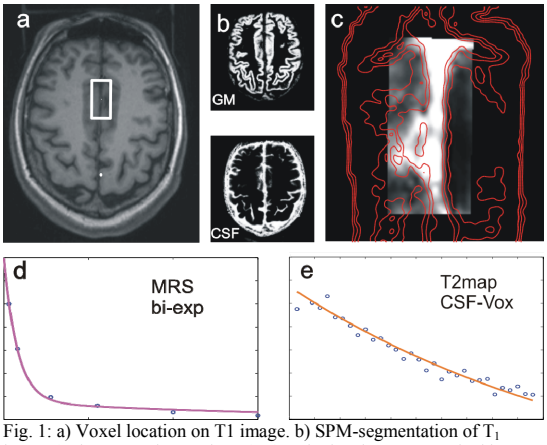

Fig. 1: a) Voxel location on T1 image. b) SPM-segmentation of T_1 image (only GM and CSF shown). c) Calculated T2map masked by MRS-voxel overlaid with GM-contour. d) Bi-exponential fit to MRS data. e) Mono-exponential fit to CSF-Voxel.

Results

According to the results of image segmentation the examined voxel had a CSF-fraction ranging from 20% to 69%. The bi-exponential fit to the MRS data revealed lower T_2^{CSF} values but similar T_2^{BM} compared to the T2map fits (Fig. 2). An explorative plot of T_2^{CSF} over CSF content shows a strong dependency for both methods of the evaluated T_2^{CSF} values on the CSF content calculated by the Segmentation algorithm (Fig. 3). The single experiment, where spectra from a VOI with a CSF-fraction of 88% were acquired, indicated that the T_2 relaxation time of CSF is at least 1530ms. We found neither a difference in T_2 times for TR = 10s compared to TR = 30s, which excludes a T_1 effect, nor for the higher number of TEs acquired (14 vs. 6).

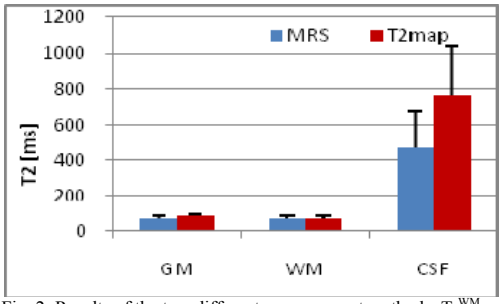

Fig. 2: Results of the two different measurement methods. T_2^{WM} and T_2^{GM} of the MRS method have the same value and are identical to T_2^{BM}.

Discussion

Partial volume seems to have a major effect on the T_2-estimations leading to better values for the high-resolution T2maps. Nevertheless, the map results still have a strong dependency on the global CSF content. There could be two possible reasons for the discrepancies in the measured T_2 times. 1st: T_2^{CSF} actually changes in restricted volumes over different brain areas. 2nd: The T_1-weighted image based tissue segmentation algorithm largely overestimates the CSF content. To investigate this we used a hypothetical signal decay with the assumption of a T_2^{CSF} of 1730ms [5], T_2^{WM} = 71ms and T_2^{GM} = 83ms, randomizing over a wide range of tissue contents we fitted the simulated data with different over- and underestimations of the CSF-compartment. An overestimation of CSF by a factor of about 2.86 could best fit our experimental data (Fig. 3). 3rd: An unknown mechanism or additional compartment, which influences the fitted T_2 times and mainly takes effect in partial volume. However, our simulated data showed that signals from myelin water or an additional intermediate component cause an opposite effect.

Although the use of tissue segmentation from T_1-weighted images for partial volume calculation in MRS metabolite quantifications seems adequate so far, the method is unsatisfactory for the quantification of T_2^{CSF}. The bi-exponential fitting procedure exhibits major variances if used in the presence of significant and intra-individually varying amounts of CSF in the voxel. This has direct impacts on the absolute quantification of brain metabolites when water scaling is used. The discrepancy in the measurement of T_2^{CSF} in different brain areas needs some further investigation with high resolution T2maps, avoiding partial volume.

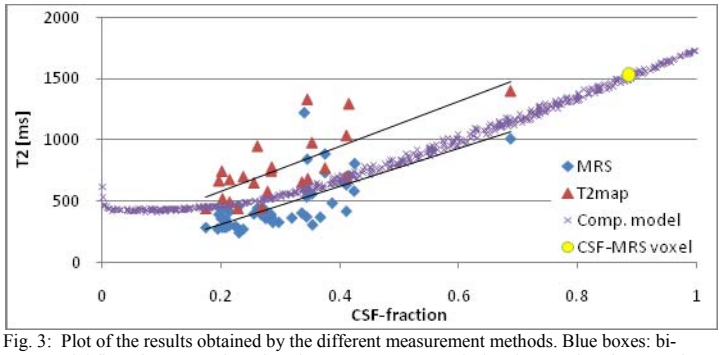

Fig. 3: Plot of the results obtained by the different measurement methods. Blue boxes: bi-exponential fit to the 6 TE point relaxation measurement. Red triangles: results of T2mapping. Yellow circle: data of the single experiment. Purple crosses: findings of the simulation by lowering the signal of CSF by a factor of 2.86;

References

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