Voxel Based Relaxometry

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Synopsis: The standard procedure for analysis of T2 relaxometry data uses manually drawn regions of interest. This approach is subject to criticism due to its subjective nature and because of the variability introduced in grey matter regions by partial voluming with CSF. This study aims to tackle these issues by a two-fold approach. An improved fitting procedure is used that takes account of CSF contamination in grey matter. Statistical analysis was then carried out with a methodology akin to voxel based morphometry. This approach is tested in a study comparing controls and patients with temporal lobe epilepsy.

Introduction: T2 relaxometry has been established as a reliable tool for the assessment of tissue signal change in conditions such as temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) (1). The acquisition of a T2 map is commonly carried out in the clinical context with a CPMG multi-echo sequence (with 2 or more echoes). Data analysis is usually carried out by manual placement of regions of interest (ROIs) over predefined areas of anatomy. However, this approach suffers from intra- and inter-operator variability. Moreover, reproducible placement of ROIs in grey matter (GM) regions such as the hippocampus is difficult due to the close proximity of CSF in surrounding ventricles and sulci. The T2 of CSF is an approximately 25 times that of tissue and even a small degree of CSF contamination will artefactually increase the T2 value. Through-slice partial voluming of GM with CSF will further decrease the accuracy and reproducibility of the results. This study introduces an alternative method of analysis that aims to overcome these problems by a two-fold approach. Firstly, the CSF contribution to the voxel T2 measurement is minimised by an alternative fitting procedure. Secondly, a modification of the voxel based morphometry (VBM) technique is used to carry out the statistical analysis of the relaxation data in a more objective manner.

Methods: All experiments were performed on a GE 3T LX scanner. The T2 mapping sequence was a standard CPMG multi-echo sequence (8 echoes, maximum echo time, TE\text{max}=231\text{ms}, TR=4\text{sec}, slice thickness=6/1.5\text{mm}, 256\times128, FOV=24\text{cm}, 10 slices, scan time, T_{\text{scan}}=6.5\text{min}).

Fitting procedure: In order to take account of the consequences of partial voluming with CSF, the standard mono-exponential decay curve fit was modified to include a baseline component i.e. \( M(t) = M(0)\exp(-TE/T2)+k \) where \( k \) is the baseline level. The fit takes advantage of the duration of the T2 time of CSF relative to the maximum echo time of the T2 mapping sequence (231ms vs approx. 2000ms). In GM voxels that typically contain a CSF component (<30% by volume), the contribution of CSF to the signal decay can be well described by a baseline (see Fig. 1(a) for a GM ROI, the T2 value is 99ms and 75ms for regular and modified fits respectively). In white matter (WM) regions, the fitted baseline should be close to zero and the fit will be unaffected. Image fitting was carried out with code written in IDL using an optimized curve fitting routine (mpcurvefit, CMarkwardt, MCW, WI, USA).

Statistical analysis: VBM is an automated whole-brain image analysis technique that enables voxel-by-voxel comparison of structural and morphological changes (2). In order to analyse the T2 data with a similar approach (voxel based relaxometry, VBR), the relaxation maps were spatially normalised in SPM to standard space using a template from multiple high-resolution T2-weighted scans collected in our laboratory. Since the T2 maps have relatively poor tissue contrast, this step was carried out via initial spatial normalisation of the T2-weighted images (3rd echo, TE=87ms). The normalisation parameters were then applied to the T2 maps. The images were smoothed with a 5mm kernel. The grouped subject data sets could then be compared by simple statistical analysis. A 2-sample t-test was carried out in SPM for the comparison of the relaxation times of controls (n=25) and a group of TLE patient (left HS: n=5, right HS: n=5). Statistical parametric maps of the test were displayed at the desired level of statistical significance.

Results: The T2 maps from the modified fitting procedure (Fig. 1(c)) had a visibly “cleaner” appearance than regular fit maps (Fig. 1(b)) and the CSF is less apparent. The T2 values in WM were unaffected by the fit but the T2 of GM was reduced by 5-20% with a corresponding improvement of the \( R^2 \) of the fit in these areas. Voxels that were dominated by CSF such as the ventricles were still apparent since the slow exponential decay of T2 then dominates the signal behaviour. However, these voxels are not of clinical interest. The VBR results of the controls vs right-HS patients analysis is shown in Fig. 2 (t+ve patient-control, p=0.001 uncorrected). The increased signal in the right hippocampus and in other areas indicates the utility of the method.

Discussion & Conclusions: The VBR analysis is not biased to a particular structure and provides an even-handed and comprehensive assessment of T2 differences through the brain volume. The combination of modified fitting and statistical analysis procedures described in this study has attempted to remove a significant component of the subjectivity of relaxometry data analysis. The spatial normalisation step of the T2 maps in VBR corresponds to the same step in VBM but may be more valid since it is not the geometry of the images that is subsequently tested. The results of the TLE study provide important evidence of pathological tissue change within the hippocampus of TLE patients. This confirms the findings of previous ROI analyses but without the remaining doubt that the measured T2 change may be a consequence of increased CSF partial volume effects due to atrophy.