Measuring diffusion tensor parameters in the human hippocampus: region of interest placement

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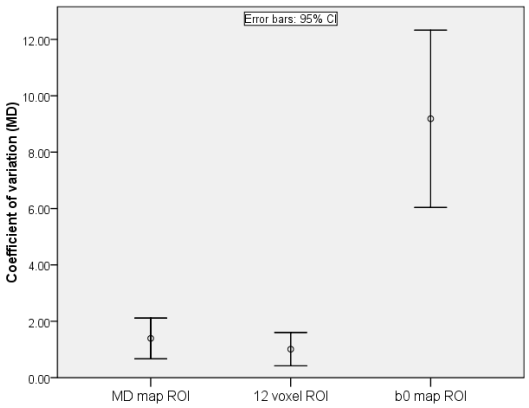
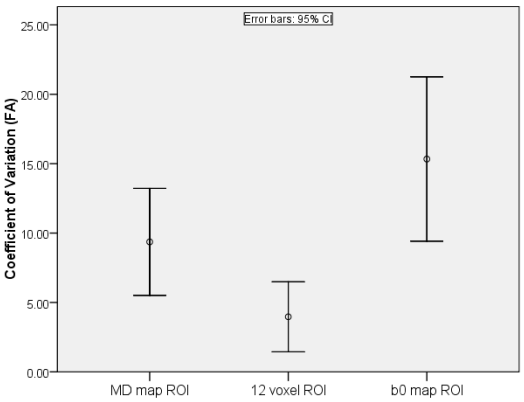
Introduction: Diffusion tensor imaging (DTI) is increasingly being used in the evaluation of hippocampal abnormalities in patients with epilepsy by measuring mean diffusivity (MD) and/or fractional anisotropy (FA). This is commonly achieved by using a region of interest (ROI) based approach. Some studies using this approach have found significantly decreased hippocampal FA in patients with temporal lobe epilepsy whereas others have not. Part of this may be due to differences in methodology as there is no widely accepted gold standard for either DTI sequences or ROI placement. Since inter/intra observer variability of up to 15% is reported with FA measurements it is important to have as consistent and precise a technique as possible so that any inherent inaccuracy can be minimised. As part of our work investigating diffusion changes in the human hippocampus following convulsive status epilepticus, we designed the following series of experiments to evaluate if there was an optimum method of ROI placement within the hippocampus.

Graph 1: Comparison of CoV (MD) for 3 methods of ROI placement



Graph 2: Comparison of CoV (FA) for 3 methods of ROI placement



	CoV MD	CoV FA
MD map ROI	0.014	0.094
Fixed size ROI	0.010	0.040
b0 map ROI	0.091	0.153

Table 1: Mean coefficient of variance for MD and FA measurements by method

Methods: Twenty scans were randomly selected from an existing database of patients and controls. Each of these patients had DTI on a 1.5T scanner (Siemens Avanto; TR/TE, 6300/89; Matrix 96x96; b = 1000 s/mm^2; in-plane resolution 2.5x2.5mm; slice thickness 2.5mm with no gap). Diffusion gradients were applied along 20 optimized non-collinear directions with 3 averages being performed. The diffusion sequences were then combined to produce b_0, MD and FA maps on a voxel by voxel basis using a custom MATLAB script.

A number of different methods of ROI placement were trialled, using the software package MRIcroN to visualise the hippocampus in 3 orthogonal planes and to define the ROI:
1) Using the MD map to draw an ROI containing all voxels thought to be within the hippocampus
2) Using a fixed-size ROI placed within the hippocampus on the MD map. This was varied between 1 and 27 voxels in size. (Figure 1)
3) Using the b0 (T2-weighted) map to draw an ROI containing all voxels thought to be within the hippocampus

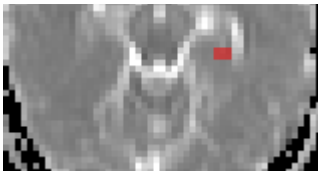
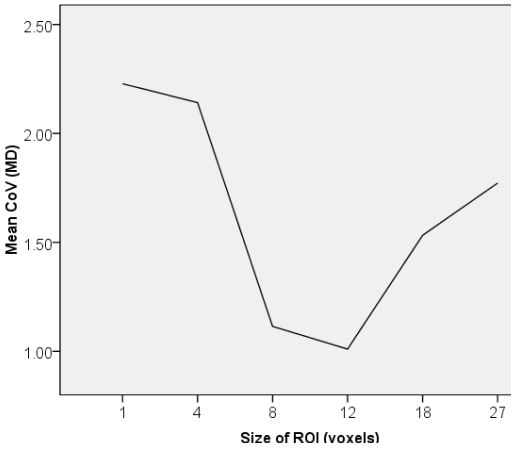


Figure 1: MD map showing12 voxel ROI in cross-section

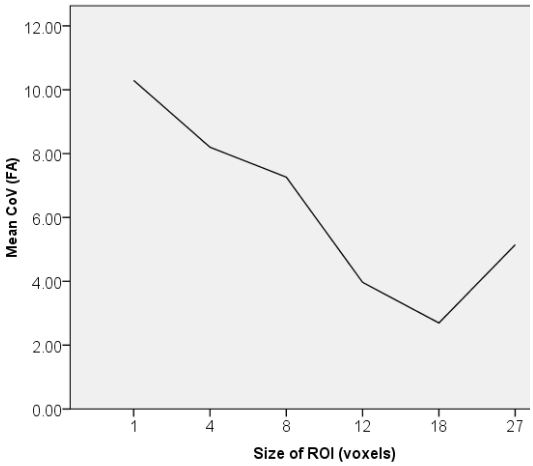
Each method was used on each scan for both left and right hippocampi and then repeated a minimum of 48 hours later. Repetition was performed blind to the results of the first run. MD and FA values were then calculated for each of the ROIs and used to calculate a mean value and coefficient of variation (CoV) for each method in each hippocampus.

Results: The fixed size ROI of 12 voxels (3x2x2) had a significantly lower CoV compared to the b0 map ROI for both MD ($p < 0.001$) and FA measurements ($p = 0.001$). It also had a significantly lower CoV than the MD map ROI for FA measurements ($p = 0.019$) (graphs 1 & 2) but not for MD measurements. When we compared different sizes of ROI, although there were no significant differences between 8, 12 and 18 voxel ROIs, there was a clear optimum at 12 voxels for MD measurements (graph 3) and 18 voxels for FA measurements (graph 4).

Graph 3: Coefficient of variation for MD versus size of R



Graph 4: Coefficient of variation (FA) versus size of ROI



Discussion: Imprecision in MD and FA measurements can arise from a number of sources, of which the simplest to control is ROI placement. It is important that the ROI can be consistently and accurately placed within the hippocampus and that partial volume effects are minimised. Hence although the hippocampus measures some 2x1cm in cross-section at its largest, it is likely that the optimal ROI size is smaller than that, especially at the low resolution typical of DTI. We have shown that using a small fixed size ROI improves precision and that it is possible to optimise the size of this ROI for a given set of scanning parameters. It is likely that the optimum ROI size is dependent on the assumed size of the structure of interest in the study population as well as the voxel size of the acquired DTI. We suggest that this simple analysis would be useful to other groups working with ROI based DTI analysis of the hippocampus in order to maximise the power of their study to detect underlying differences.