'Time-Series' Analysis of the Diffusion Weighted Signal as a Model-Free Approach to Segmenting Tissue

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INTRODUCTION: An active area in diffusion-weighted MRI (DW-MRI) research is tissue classification based on diffusion-derived similarity metrics. Wiegell et al.[1], for example, identified the thalamic nuclei based on local similarity of the diffusion tensor. Ziyan and Tuch[2] performed similar analysis, making use of eigenvector information. Behrens et al.[3] have also segmented the thalamic nuclei by investigating the cortical connectivity. A general disadvantage of most current DW-MRI clustering techniques, however, is their reliance on the tensor model which is ill-posed in areas of fibre-crossing and branching. Unfortunately, it is unclear how model-free techniques, such as q-Ball[4] and DSI[5] may be used to cluster data. In this work we propose a novel approach for clustering DW-MRI data by treating the series of diffusion-weighted signals acquired with varied diffusion-encoding gradient amplitude and/or direction as a pseudo "time" series. With the assumption that the wave-form of this time-series is characteristic of tissue structure, voxels containing like tissue (shape and orientation) will have maximally correlated time series. We refer to our approach as MADCOWS (Model-less Analysis of Diffusion by Correlation Of Weighted Signals).

METHODS: ACQUISITION Data were acquired on a GE 1.5T Scanner with 40mT/m gradients using an optimized and peripherally gated multi-slice EPI sequence with 7 B = 0 images and 64 images with B = 1200 s/mm^2, with gradients isotropically distributed in space.[6] ANALYSIS: As proof-of-concept, the right and left thalamus were manually segmented from the acquired 3D T_2-weighted image and this mask applied to the DW-MRI data. An agglomerative clustering approach based on time-series correlation was then used in which local connectivity was either forced (voxels were only clustered if they touched) or not (voxels were clustered based *only* on correlation) to divide the right and left thalamus into 16 primary nuclei. To determine which two groups of voxels (A and B) to merge into a single cluster at each step, the correlation between each member of A with each member of B was calculated and the minimum value was taken as correlation between groups A and B. The two groups with max, correlation were merged at each step.

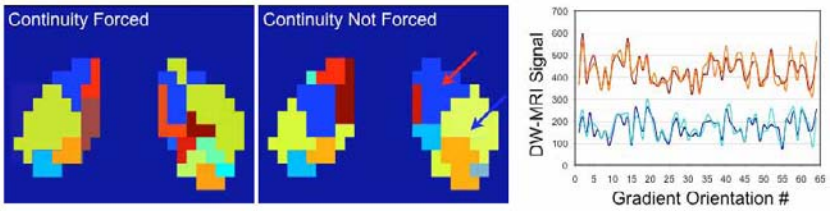

Figure 1: Comparison of segmentation results obtained using the continuity criterion (left) and not (middle). On the right we show pseudo time-series from two distinct clusters.

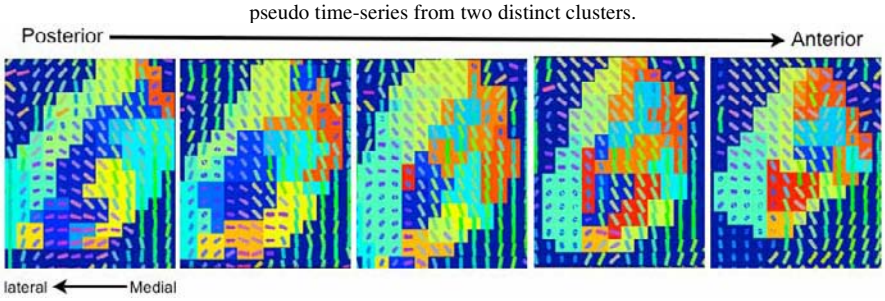

Figure 2: Successive slices through the segmented left thalamus with overlayed tubes aligned with the principle eigenvector.

RESULTS / DISCUSSION: Representative slices through the right and left thalamus segmentation results are shown in Fig. 1 for both the forced and unforced continuity cases. General agreement is noted across the right and left hemispheres in both sets of results. The slight discrepancy between the right and left hemispheres may be the result of a subtle tilt of the volunteer's head. Good agreement is also noted between the forced and unforced continuity results. It can be argued that a continuity criterion is necessary since the thalamic nuclei themselves are continuous structures. That similar results are obtained without the inclusion of this criterion, however, attests to the robustness of the approach. Also shown in Fig. 2 are representative diffusion time-series plots taken from two cluster regions (shown by the coloured arrows). As can be seen, the blue-coloured time-series (corresponding to the cluster identified by the blue arrow) show strong correlation, as do the two red-coloured curves. However, the red and blue curves have much lower correlation. Figure 2 shows a series of successive slices through the left thalamus segmentation with overlayed DEC tubes oriented along the principle eigenvector. In general we note that the eigenvector orientation is consistent within similarly classified voxels, with sharp distinctions observed at some boundaries. Boundaries are also detected at other locations, presumably where ε_1 does a poor job of characterizing the tissue.

CONCLUSION: We have demonstrated a novel technique for clustering voxels by applying a time-series analysis framework - similar to that employed in fMRI studies - to the diffusion-weighted signals. The primary advantage of the approach is the lack of reliance on the tensor model (or any model for that matter). Further, knowledge of the magnitude, nor direction, of the diffusion-encoding gradients is unnecessary, it is only important that each voxel was treated with the same encoding scheme. The method is also robust in the presence of B_0 and B_1 inhomogeneities, as although these effects will affect the amplitude diffusion-weighed signal, they will act as a constant scalar and therefore have little affect on the correlation between local voxels. A disadvantage of any clustering algorithm is the need to know *a priori* the number of cluster one seeks. In the case of the described approach, a correlation threshold may be used to determine when to terminate clustering or, alternatively, the correlation at each step can be monitored with the Gap-statistic[7] used to determine the optimum number of clusters for the data.

REFERENCES: [1] Wiegell MR *et al.* Neuroimage 19:391-401 (2003), [2] Ziyan U *et al.* Proc ISMRM 625 (2005), [3] Behrens TE *et al.* Nat Neurosci 6:750-757 (2003), [4] Tuch DS MRM 52:1358-1372 (2004), [5] Wedeen VJ *et al.* MRM 24 (2005), [6] Jones DK *et al.* MRM 42:515-525 (1999), [7] Tibshirani R *et al.* J Royal Stat Soc 63:411-423 (2001).