Contribution of Cardiac Pulsation to Variability of Tractography Results

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Background: There are several sources of perturbation to diffusion weighted (DW) imaging including Gaussian RF noise, rigid body patient motion and eddy current distortions. While uncertainty due to RF noise has been incorporated into tractography algorithms and motion /eddy current distortion schemes exist, a further source of variability is the local displacement and distension of tissue[1] °ccurring mainly during systole in the cardiac cycle. Notably, a non-exhaustive review of recent tractography papers reveals that the use of cardiac gating is by no means widespread, with at least a dozen studies using non-gated acquisitions. While the effect of pulsation on mean diffusivity and anisotropy measurements has been reported previously, its effect on estimates of fiber orientation and tractography results have not. We were particularly interested in the potential confound of pulsation on assessment of 'connectivity'. By using the bootstrap technique to examine DT-MRI data acquired at different phases in the cardiac cycle (delays after the QRS peak), we examined, for the first time, the intra- and inter-delay variability of both deterministic tractography results and of the confidence one can assign to tracking results.

Methods: Acquisition: Whole brain DT-MRI data were acquired from healthy volunteers on a GE LX 1.5 T system with 50 mT m^{-1} gradients, using a gated single-shot EPI sequence. DW data were acquired at 9 trigger delays (100 ms increments starting at 20ms after the onset of the R-wave), using the dual-gradient scheme[2]. For each delay, 8 complete volumes were collected, such that 8 × (1@b=0 + 6@b=1100smm^{-2}) = 56 images were acquired at each slice location. Details of the acquisition and correction of residual subject motion and eddy current induced distortion are described in detail elsewhere[1,3]. Bootstrap Tractography: Based on previous reports of the effects of cardiac pulsation on DT-MRI data[1], we focused our attention primarily on the genu of corpus callosum, fornix and cerebellar peduncles which we hypothesized *a priori* would exhibit most marked delay-dependent tracking results, together with other tracts (e.g., cingulum and SLF) which we hypothesized to be less affected. For each delay, 1000 bootstrapped volumes were generated (each containing 14 images per slice location, from which to estimate the tensor), and tracking initiated from seedpoints within the tracts of interest using an approach detailed in (4). The resulting trajectories were subsequently binned to voxel grid locations to form 'visitation maps'[5] in which the value assigned to each voxel represents the percentage of the 1000 bootstrapped tracts, launched from the seedpoint, that pass through it. e.g., if all 1000 bootstrapped tracts pass through a voxel, it is assigned a visitation count of 100%. Maximum intensity projections (MIPs) of these data were computed and overlaid on FA maps for visualization. Further, for each delay, the number of voxels with visitation counts greater than a fixed threshold (incremented from 2.5% to 95%) was computed to generate plots of tract-volume *vs.* confidence.

Results and Discussion: Figure 1 shows typical results obtained in the genu and fornix. The former are particularly concerning for un-gated tractography studies – particularly those that attempt to infer connectivity between two regions through the number of tracts passing between them, or by assigning a 'confidence' to the pathway. Clearly, assessments of 'inter-hemispheric connectivity' would be highly variable - with almost no connectivity established between the two hemispheres with a cardiac delay of 120 ms, (peak systolic brain pulsation). Across the remaining time points, the visitation maps are largely comparable. These observations are also reflected by the close overlaps of the volume *vs.* threshold plots for the diastolic time points, but the 'outlier' profile for the 120 ms delay. The plots indicate that, for a given confidence threshold, the volume of the genu is lower during systole, but largely constant across the remaining time points

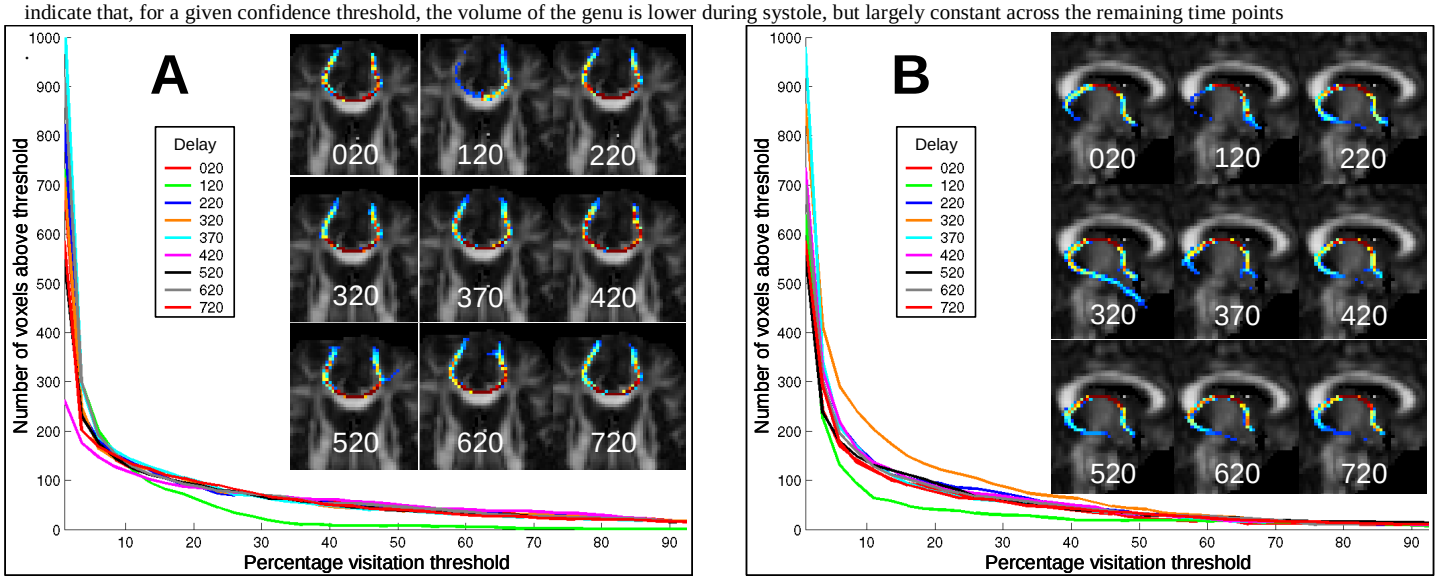

Figure 1. Results obtained for **A**. Genu of corpus callosum and **B**. Fornix. The plots show the number of voxels with visitation counts above a given threshold, data acquired at nine different points in the cardiac cycle (units = ms). The insets show the visitation maps obtained at the same time points

In the body of the fornix, (where the seedpoint was placed), both the intra- and inter-delay reproducibility are high. However, reconstructions of other parts of the structure are more variable on an inter-delay basis. The most pronounced effect is the extremely low visitation count in the posterior segment (*crura* and *fimbria*) at a cardiac delay of 120 ms (systolic peak). Again, the profiles of volume *vs.* percentage threshold indicate that for any given confidence level, the volume of brain assigned as 'fornix' will be less during systole than during the diastolic plateau. More interestingly, even during the diastolic phase, there are inter-delay variations in the reproducibility of the tract reconstructions. Note the more complete reconstruction of the fimbrial extension of the fornix towards the hippocampus at a delay of 320 ms, which is again reflected in the profiles of volume *vs.* visitation threshold, i.e. for a given threshold, the volume assigned to fornix is invariably larger. Based on our initial observations, the inter-delay variability during the diastolic plateau seems to be more marked in regions where the visitation count is generally low across all delays, suggesting that these structures are more difficult to track and more sensitive to slight perturbations of the tissue, such as the minor perturbations occurring during the diastolic plateau. This effect is not as noticeable in regions where the visitation count is high across time delays, such as in the genu, where the volume *vs* visitation thresholds overlap more closely. In other tracts, such as the cingulum (result not shown here), the visitation maps are closely matched across all time points, and the volume *vs.* visitation threshold plots are virtually superimposed thereby indicating that not all tracts require the acquisition to be gated. We are currently performing a systematic study of which tracts are likely to be most affected by cardiac pulsation and we are focusing on the curious variability in tracking results obtained during the diastolic time points.

Conclusions: Our results clearly show the importance of gating the acquisition of diffusion weighted data for fiber tractography studies. Deterministic tractography studies performed with non-gated acquisitions run a real risk of false-negatives, while probabilistic approaches may erroneously assign low 'likelihood' to a connection simply as a result of cardiac pulsatility. Our result further suggest that gating must be performed not only to avoid systole, but that even within diastole, the trigger delays for acquisition may need to be carefully selected in order to obtain reliable tractography results.

References: 1). Pierpaoli *et al.* ISMRM 2003, p.70; 2). Davis *et al.* ISMRM 1993, p. 289; 3). Rohde *et al. MRM* 2004; **51:**103; 4). Catani *et al. NeuroImage* 2002 **17**:103; 5). Jones *et al.* ISMRM 2004; p1276.