Analyzing the contribution of cardiac pulsation to the variability of quantities derived from the diffusion tensor

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Synopsis: We analyze the contributions of cardiac-pulsation to the variability in estimates of diffusion tensor quantities in the human brain. We identify two contributions to variability arising from cardiac pulsation, namely (i) mis-registration of different structures and (ii) non-uniform intra-voxel motion (e.g. stretch and shear of the tissue), and propose a novel approach for differentiating them.

Introduction: Pulsations during the cardiac cycle cause significant brain motion, with peak velocities of 1-2 mm/s and displacements in the order of 1 mm[1]. Macroscopically, this motion cannot be considered a simple rigid-body motion as different brain regions have velocity and displacement profiles that differ in magnitude, direction, and time course. Occasionally, non-gated diffusion weighted echo planar images (DW-EPI) show severe signal attenuation in the brain parenchyma suggesting that cardiac pulsation itself induces intravoxel incoherent motion of the spins. Indeed, previous studies[2-4] have demonstrated the benefit of gating such studies, and that the best acquisition window occurs during diastole. However, these studies have been limited to uni-directional DW-EPIs and apparent diffusion coefficients measurements. Here, for the first time, we investigate the effects of cardiac pulsation on *tensor*-derived quantities including the trace, anisotropy indices, and the eigenvectors.

Theory: Both mis-registration and intra-voxel incoherent motion induced by cardiac pulsation, should lead to increased variance in the distribution of trace values ($Tr(\mathbf{D})$) obtained at different points in the cardiac cycle. However, while mis-registration may cause both under- and over-estimation of $Tr(\mathbf{D})$, the pseudo-diffusion effect of increased intra-voxel incoherent motion can only lead to over-estimation. Since the latter will always lead to increased positive skewness of the distribution of $Tr(\mathbf{D})$, we propose that by analyzing both the variance and the skewness of the distribution, $\mathbf{S}(Tr(\mathbf{D}))$, one can differentiate between these sources of variability in $Tr(\mathbf{D})$.

Methods: *Acquisition:* Simultaneous ECG and pulse oxymeter measurements were performed in 15 subjects to characterize the delay between the onset of the R wave and the onset of the plethysmographic wave. ECG-gated DT-MRI data sets were acquired with 2 x 2 x 4 mm resolution, using the gradient scheme proposed elsewhere[4] and b = 1100 s/mm^2. For each subject, we acquired 18 whole brain DT-MRI datasets with 9 different trigger delays (100ms increments starting at 20 ms after the onset of the R wave).
Data Processing: For each subject, all volumes were corrected for eddy current distortion and rigid-body brain motion using the approach of Rohde *et al.*[5], during which the 18 data-sets were also co-registered with themselves, and then the tensor ($\mathbf{D}$), $Tr(\mathbf{D})$, fractional anisotropy (FA) and eigenvectors were computed. Visual inspection of images of these variables was used to determine the temporo-spatial pattern of the artifacts. For each voxel, the coefficient of variation, (CoV = SD/Mean) and the skewness of the distribution of Tr ($\mathbf{D}$) over the 9 trigger delays were computed. (N.B. The theory concerning the skewness outlined above does not apply to anisotropy and tensor-derived quantities other than $Tr(\mathbf{D})$ and so only the SD was determined for these quantities). The analysis was then repeated for the volumes acquired with trigger delays > 220 ms (diastolic phase).

Results / Discussion: (i) The pulse wave delay was found to have low variability (mean ±sd = 249±17 ms) over a wide range of heart rates (66 ± 14 bpm), suggesting peripheral pulse trigger values can be reliably converted to ECG trigger values via the equation: ECG trigger Peripheral pulse trigger + 250 ms; **(ii)** The magnitude and spatial extent of pulsation artifacts was greatest at 120 ms after the R wave. Significant artifacts were observed in all tensor-derived parameters, being most pronounced in the cerebellar peduncles, anterior portions of the cerebellum (Fig 1), and the middle portion of the genu of the corpus callosum; **(iii)** Whole brain analysis of the distribution of CoV of $Tr(\mathbf{D})$ and $\mathbf{S}(Tr(\mathbf{D}))$ revealed a significant deviation from normality when all time points where included. However, this deviation from normality virtually disappeared when the systolic time-points (120ms and 220ms) were excluded (Fig 2). Although the variability of $Tr(\mathbf{D})$ was relatively homogeneous throughout the brain in diastole, diffusion anisotropy and eigenvectors still showed high variability in subcortical white matter regions. **(iv)** Interestingly, regions of high CoV of $Tr(\mathbf{D})$ and regions of high positive $\mathbf{S}(Tr(\mathbf{D}))$ did not completely superimpose, indicating that mis-registration and intra-voxel tissue deformation affect different regions of the brain.

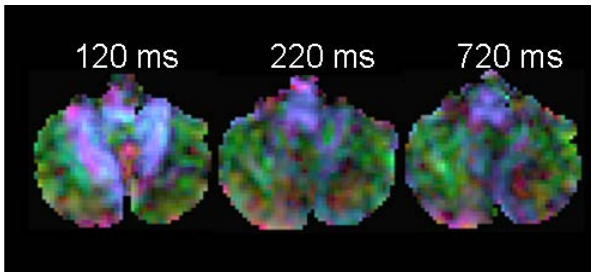

Fig 1: Color fiber orientation[7] maps acquired at different points in the cardiac cycle. Significant artifacts are seen at 120ms in the medial ventral portion of the cerebellum. These are diminished after 220 ms

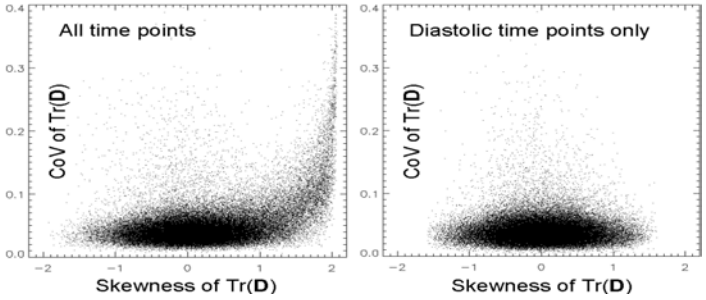

Fig 2: Plot of CoV of Tr($\mathbf{D}$) *vs* Skewness of Tr($\mathbf{D}$) for the whole brain of a representative subject.

Conclusion: The results of this study will help in the interpretation of the complex motion of brain parenchyma during the cardiac cycle and will help in developing strategies to remediate cardiac-induced artifacts in clinical diffusion tensor MRI studies.

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