

## Combining Registration and Outlier Rejection in Preterm DTI Data

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**Introduction:** In the processing of DTI data, a common correction step is registration of volumes that are misaligned due to eddy current distortions and patient motion<sup>1,2</sup>. Robust estimators have also been used to deal with outlier data which cannot otherwise be corrected<sup>1,3</sup>. However, it is not clear which of these two operations should be performed first. In a previous investigation of DTI processing in very preterm neonates<sup>4</sup>, we showed that detection and replacement of outliers prior to inter-volume registration improved tensor goodness-of-fit. Two shortcomings were observed in this approach: 1) fitting the data points prior to registration could result in false outliers being detected due to misaligned data; and 2) replacing an outlier with an interpolated value, in order to support subsequent registration, may be inaccurate when many outliers are clustered together. This proposed method addresses these two issues as well as incorporating inter-slice motion correction.

**Subjects:** DTI data from 15 premature neonates (mean gestational age at birth 28.1, at scan 29.5 weeks) presenting normal radiological findings were selected from a larger cohort involved in a longitudinal multi-modal MRI study. Subjects were recruited from the neonatal intensive care unit with parental consent and in compliance with hospital ethics. No sedation was administered.

**Imaging:** Images were acquired on a GE 1.5T system (Signa Excite HD) using a third party MR compatible incubator and head coil (Advanced Imaging Research, Cleveland, USA). Twice refocused spin echo planar DTI<sup>5</sup> was acquired using: 2D axial oblique slices, FOV=205mm, with 1.6 mm cubic voxels. TR/TE/FA=15s/85ms/90°. 3 non-diffusion and 15 non-collinear diffusion weighted volumes with b=700 s/mm<sup>2</sup> were acquired.

**Processing:** DTI data was processed with three different pipelines:

*Pipeline 0:* A tensor model was estimated from uncorrected data using a non-linear least squares fit<sup>6</sup>.

*Pipeline 1:* To correct for inter-slice motion, each slice in the diffusion weighted volumes was rigidly aligned<sup>7</sup> to the corresponding slice on the average of all 15 diffusion weighted volumes. The resulting corrected volumes underwent inter-volume, affine registration<sup>7</sup> to mitigate inter-volume motion and eddy currents. The diffusion tensor was then estimated using RESTORE<sup>3,6</sup> to reject outliers.

*Pipeline 2:* Inter-slice and inter-volume transformations were calculated, as in pipeline 1. Resampling and robust tensor estimation were then performed  $S \times V$  times (where S is number of slices and V is number of diffusion weighted volumes) to detect outliers. In each iteration, one slice in one volume was used as the target for registration so that it would not be resampled. After outliers had been detected for every slice in each volume, outliers were replaced with values computed from the estimated diffusion tensor for those voxels. These modified data were then registered slice-wise and volume-wise using the initially calculated transformations, then fit to a tensor using a non-linear least squares fit<sup>6</sup>.

**Analysis:** For each pipeline the residual,  $R_i$ , for each diffusion weighted data was calculated as  $S_{D,i}/S_0 - \exp(-b \cdot \bar{g}_i \cdot \hat{D} \bar{g}_i^T)$  where  $\bar{g}_i$  is the diffusion gradient vector,  $\hat{D}$  is the tensor estimate,  $S_{D,i}$  and  $S_0$  are the diffusion and non-diffusion weighted signals. Voxelwise normalized mean square residuals (NMSR) were calculated as  $\frac{1}{9 - n_o} \sum_{i=1}^{15} \frac{R_i^2}{\sigma_{D,i}^2/S_0^2 + \sigma_0^2 S_{D,i}^2/S_0^4}$ , where  $\sigma_{D,i}$  and

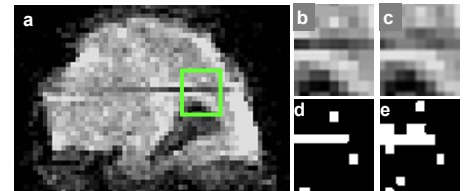
$\sigma_0$  are the estimated standard deviations of background noise in the diffusion and non-diffusion weighted images, and  $n_o$  is the number of outliers occurring at that voxel. For pipelines 1 and 2,  $\sigma_{D,i}$  was corrected for the effects of interpolation using the method described in [8].

**Results:** Both methods rejected 3% to 12% of voxels, depending on the data quality. Pipeline 2 consistently removed fewer voxels. Figure 1a shows a diffusion weighted volume with a corrupted slice. Using pipeline 2, outliers are detected on that slice (1d) and replaced, while in pipeline 1, the corrupted data are resampled by registration (1c), and corrupted data spreads, causing more outliers to be detected (1e). Figure 2 shows the averaged NMSR histograms for the three pipelines. Histograms for individual subjects showed similar results. Both pipelines 1 and 2 show a reduction in high NMSR values, though pipeline 2 presents smaller NMSR values than pipeline 1.

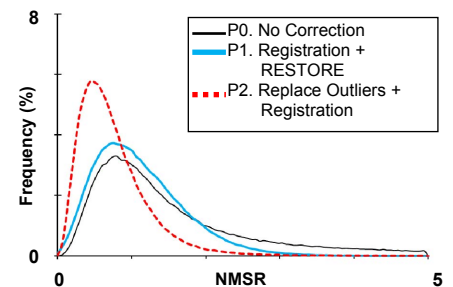
**Discussion and Conclusions:** Using the proposed pipeline 2, outliers are found in raw, uninterpolated data, with all other data aligned to it. Any detected outliers are replaced by a datum derived from the tensor model in that voxel. This prevents corrupted regions from spreading to adjacent voxels (as per Figure 1), which prevents added noise or data loss, in cases where the interpolated outlier corrupts multiple voxels. It also avoids the unsatisfactory situation of estimating outliers by computing a tensor from misaligned data. While the present study analyzes specific pipelines for our preterm data, this method can be generalized to any pipeline involving both outlier rejection and registration based corrections.

### References:

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**Fig 1.** a) DTI volume affected by outliers b) detail c) after registration based corrections d) outliers detected using pipeline 2 e) outliers detected using pipeline 1. Note the increase of outliers in e.



**Fig 2.** Normalized mean residual histogram for 3 pipelines. Pipeline 2 shows largest reduction in model residuals