Comparison of Parametric and Nonparametric Probabilistic White Matter Tractography Methods

M. Lazar[1], A. L. Alexander[1]

[1]The Waisman Center, University of Wisconsin, Madison, WI, United States

Introduction: White matter tractography is a noninvasive method for estimating white matter connectivity pathways using diffusion tensor imaging (DTI) data. Experimental noise may induce errors in the measured fiber directions and reduce the accuracy and precision of the estimated white matter trajectories. Several probabilistic tractography methods have been previously proposed to account for the uncertainty in the local fiber direction estimation. Probabilistic methods can be largely categorized in two groups, the parametric methods that assume certain models of dispersion in the fiber direction (1-4), and the nonparametric methods that estimate the uncertainty from data itself without any model assumption (5, 6). The nonparametric methods are based on bootstrap statistical resampling methods and use as a sampling pool a set of multiple (repeated) diffusion-weighted measurements. The advantage of bootstrap methods lies in intrinsically accounting for sources of noise that are not easily modeled (e.g., physiologic, scanner instabilities, etc.). However, they require long acquisition times, and are computationally intensive. Both parametric and nonparametric methods have been used to investigate white matter connectivity in the human brain (5-7). Yet, to date there has been no direct comparison of the parametric and nonparametric tractography methods. The goal of this study was to compare the performances of the parametric random vector perturbation (RAVE) algorithm (4) against a nonparametric bootstrap tractography (BOOT-TRAC) algorithm (5).

Methods: DTI images were acquired for two volunteers using a diffusion-weighted spin-echo EPI sequence with cardiac gating on a 3T Signa MRI scanner. Diffusion-weighted images were obtained for 12 uniformly distributed diffusion-encoding directions. A constant diffusion weighting of 1000 s/mm^2 was used for all diffusion-weighted images. Other imaging parameters included an image acquisition matrix of 120×120 and a field of view of 240×240 mm^2. The reconstructed 2D images were zero-filled interpolated to a 256×256 image matrix resulting in a voxel size of 0.9375x0.9375x3 mm^3. The acquisition time for a single DTI set for a brain volume was roughly 2.6–3.25 min. The acquisition was repeated 8 times for subsequent bootstrap analyses, resulting in a total imaging time of approximately 30 min.

The diffusion-weighted images were first corrected for bulk motion and eddy current distortions using a two-dimensional affine registration algorithm in AIR (8). EPI image distortions from B0 inhomogeneities were then corrected using a field map estimated from two gradient echo images using the fugue software program in the FSL software tools library. Each of the eight diffusion-weighted image volumes was corrected using the same field map. Misregistration between image volumes was assessed by taking the difference between image volumes and was deemed negligible. <u>BOOT-TRAC</u>: Bootstrap methods use repeated random sampling with replacement from a set of measurements to generate estimates of the underlying statistical distributions of the measurements. A bootstrap trajectory is generated from bootstrap estimates of the diffusion-weighted values at each voxel along the trajectory, obtained by randomly choosing subsets of the 8 measurements set and averaging them (with the subset size, N_{av}, varying from 1 to 8). The process is repeated until a distribution of 1000 trajectories is obtained for each seed point. The bootstrap algorithm used here is described in detail in (5). <u>RAVE Tractography</u>: RAVE algorithm generates a distribution of possible propagation directions at each step along the trajectory by
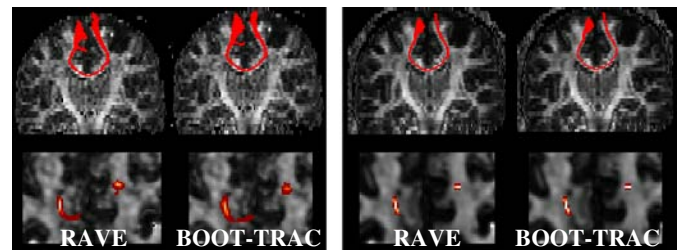

Figure 1 RAVE and BOOT-TRAC distributions for a seed point situated in the body of corpus callosum, for N_{av}=1 (left image) and N_{av}=8 (right image). Top row: fiber distributions projected onto coronal FA maps. Bottom row: Fiber density shown in the same axial cross-section for all cases.
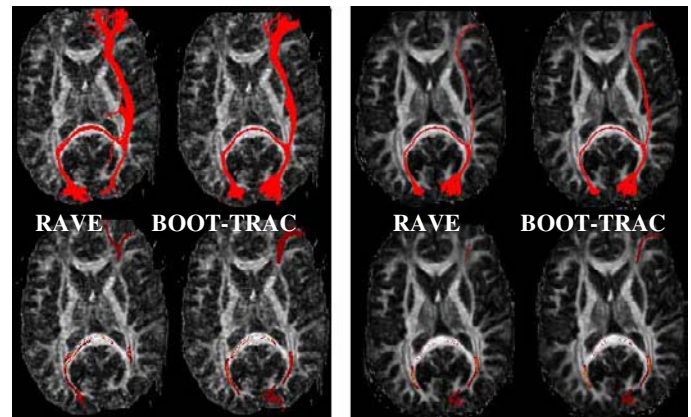
perturbing the local tensor major eigenvector (4). Initially, the tensor in the measurement frame, D, is diagonalized into the tensor frame, D_0. A perturbed direction e_1 is obtained by randomly generating normally distributed y and z offsets with mean zero and standard deviation proportional to ratio of the ellipsoid length along the corresponding axes and the length along the x axis: $y = \alpha \cdot (N(0, \lambda_2/\lambda_1)^{n/2})$ and $z = \alpha \cdot (N(0, \lambda_3/\lambda_1)^{n/2})$, where α is a proportionality factor. The perturbed vector is rotated back to the measurement frame and used as local propagation direction by the fiber-tracking algorithm. A trajectory is obtained by starting at the seed point and propagating along "perturbed" directions at each step. As in bootstrap tractography, the process is repeated to obtain a distribution of trajectories. "Reference" trajectories are obtained for each seed point from the diffusion data set given by the average of all measurements.

Results: The BOOT-TRAC and RAVE algorithms were compared for several seed points. We investigated the behavior for data sets of different SNR (obtained by averaging a different number of measurements, e.g., N_{av}=1-8). Comparative images of the fiber distributions obtained using the two algorithms are presented in Figures 1 and 2 for representative cases and for two noise levels (corresponding to 1 and 8 averages, respectively). Tract density at each voxel was calculated and was given by the number of trajectories intersecting the voxel divided by the total number of trajectories. The tract density is shown in Figures 1 and 2 (bottom rows) using a modified hot temperature color map (with high tract density indicated by white and low density by dark red). A RAVE "n" parameter with a value of 2 has been found to generate distributions comparable with the BOOT-TRAC results. The parameter α was chosen empirically for each SNR, and was found to increase slightly with decreasing SNR (0.12 to 0.24).

Discussion: The RAVE algorithm appears to generate fiber distributions similar to the BOOT-TRAC algorithm for trajectories situated in homogeneous white matter regions. Distributions might differ for highly diverging branches, with this situation more likely to occur at low SNRs. In diverging cases, the RAVE algorithm appears to indicate the same "branching points" as BOOT-TRAC. These preliminary results indicate that RAVE might be a viable substitute for the BOOT-TRAC tractography in cases when multiple measurements of the diffusion-weighted images are not available or are difficult to obtain (e.g., for clinical applications where imaging time is a concern).

Figure 2 RAVE and BOOT-TRAC distributions for a seed point situated in the splenium of corpus callosum, for N_{av}=1 (left image) and N_{av}=8 (right image). Top row: fiber distributions projected on axial FA maps. Bottom row: Fiber density shown in the same axial cross-section for all cases.

References: **1.** Parker et al. J Magn Reson Imaging. 2003 18:242. **2.** Behrens et al. Magn Reson Med. 2003;50:1077. **3.** Hagmann et al. Neuroimage. 2003 19:545. **4.**Lazar et al. Proc. of 10th ISMRM Annual Meeting, Honolulu, 2002, p. 539. **5.** Lazar et al. Neuroimage 2005;24:524. **6.** Jones et al. Magn Reson Med. 2005;53:1143. **7.** Parker et al. Neuroimage. 2005;24:656. **8.**Woods et al. J. Comput. Assist Tomogr. 1998, 22, 141.