A novel bootstrap approach for reducing noise-induced error in DTI-based measurements of muscle architecture

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Background Diffusion tensor- (DT-) MR imaging studies can characterize skeletal muscle fiber architecture and can assess muscle damage and pathology [1-3]. A significant challenge to DT-MRI is noise, which has been shown to dramatically affect the estimation of diffusion parameters used in interpretation of the diffusion data [4]. The random nature of this noise, and the existence of diffusion encoding direction-specific artifacts including eddy currents, means that the data from some diffusion encoding directions may be more corrupt than those from other directions. Excluding these data from the estimation of the diffusion tensor (**D**) may improve the estimates of key diffusion tensor indices such as the orientation of the first eigenvector, but the manual selection of corrupted data is time consuming and subjective. The purpose of this study was to determine whether or not an automated method, based on bootstrap resampling of a subset of the diffusion-encoding data, could improve the estimation of the orientation of the first eigenvector of **D**.

Methods *Simulation* Similar to the approach in [4], a model tissue containing "true" or known diffusion properties was simulated. A T_2-weighted image was calculated assuming full longitudinal relaxation, TE=50 ms, and T_2=35 ms. The true eigenvector (**E**) and eigenvalue (Λ) matrices were defined as

$$E = \begin{bmatrix} 0 & 0 & 1 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \end{bmatrix}, \quad \Lambda = \begin{bmatrix} 0.0021 & 0 & 0 \\ 0 & 0.0016 & 0 \\ 0 & 0 & 0.0013 \end{bmatrix},$$

where the units for Λ are mm^2/s. **D** was calculated for each element of the simulated image from $\mathbf{D}=\mathbf{E}\Lambda\mathbf{E}^T$, where $\mathbf{E}^T$ is the transpose of **E**. To generate noise-free diffusion-weighted images, the signal was calculated for each of the diffusion directions from **D**, a *b*-value of 500 s/mm^2, and a diffusion-weighting matrix having 15 directions corresponding to those used in the human MR scan protocols described below. Artificial noise was added to the diffusion images corresponding to a signal-to-noise ratio (SNR) of 40 in the T_2-weighted image; 1500 independent noise realizations were performed. **D** was estimated from the noisy data using the full 15 diffusion directions and all combinations of 14 (of the available 15) directions. Eigenvector and eigenvalue matrices were obtained by diagonalization of **D**, and the eigenvalues were magnitude-sorted. Because the fractional anisotropy (FA) is a very noise-sensitive measurement, the subset of 14 diffusion-encoding directions producing the FA value that was closest to the median value for all possible combinations of 14 directions was chosen as the "optimal" estimate of **D**. To determine if **D** was better estimated from the full 15 diffusion directions or from the optimal combination of 14 directions, we compared the average apparent diffusion coefficient (ADC), fractional anisotropy (FA), and angle of deviation (AD) between the principal eigenvector of the noise-corrupted images and the true principal eigenvector. To eliminate edge effects from noise, we eroded the image before calculating descriptive statistics. To characterize the variability in the measures, the standard deviation (SD) was calculated. Also, the coefficient of variation (CV) was determined as CV=100*SD/mean.

Muscle data application Written, informed consent was obtained from two subjects prior to their participation in the study. A Philips Achieva 3T MR scanner, 8-element phased array torso coil, and a pair of 14x17 cm flexible surface coils were used to obtain all MR data. Diffusion-weighted data were acquired in 15 directions (12 axial slices from the mid-calf; voxel size=1.5 x 1.5 x 6 mm^3; TR=4000 ms; TE=46 ms; b-value=485 s/mm^2). Using the same approach described for the simulations above, both the full 15 diffusion directions and all combinations of the 14 diffusion directions were used to calculate diffusion parameters over an elliptical ROI (51 voxels/slice) drawn in the medial gastrocnemius muscle. Since no "true" diffusion characteristics are known for the human subjects, we determined the ROI $\mathbf{D}_{AVG}$ by averaging the signal over the ROI for the T_2-weighted image and all 15 of the diffusion directions, and then estimating $\mathbf{D}_{AVG}$ using weighted least squares. This $\mathbf{D}_{AVG}$ was used to estimate the mean muscle fiber orientation over the entire ROI. When D is estimated for individual voxels, voxel-specific differences in the orientation will exist because of true biological variation in fiber orientation and because of noise. We calculated the AD between the principal eigenvector determined for each voxel from the real data (using either 15 or 14 diffusion directions) and the ROI average "true" eigenvector. A reduction in the variability of the AD would indicate that the effect of noise was reduced and that the resulting AD was closer to the true biological variability. To characterize the variability in the AD, the standard deviation (SD) of the AD was calculated.

Results *Simulation* The SD of the AD of the principal eigenvector calculated from the noise-corrupted images from the true principal eigenvector was smaller for the diffusion tensor calculated from the optimal 14 directions than for the diffusion tensor calculated from the full 15 diffusion directions, suggesting that this method improves estimation of diffusion parameters from noise-corrupted images (Table 1). In addition, the CV for FA is smaller for the diffusion tensor calculated from the 14 best directions than that calculated from the full 15 directions, and the apparent diffusion coefficient was identical, whether 14 or 15 directions were used to calculate the diffusion tensor.

Table 1. Diffusion parameters estimated from the noisy simulated images, using diffusion-weighted signals from all 15 directions or from the optimal subset of 14 directions. Presented are the means of the 1500 independent noise realizations.

SD of AD (°)		CV for FA		ADC (mm^2/s)	
15 directions	Optimal 14 directions	15 directions	Optimal 14 directions	15 directions	Optimal 14 directions
5.36	4.18	17.02	16.78	0.0019	0.0019

Muscle data application The CV of the AD of the ROI for the full 15 directions is commensurate with that for the optimal set of 14 diffusion directions for both subjects (Figure 1). However, using the best 14 diffusion directions to calculate the diffusion parameters eliminates spurious results that occur in the diffusion analysis using the full 15 directions.

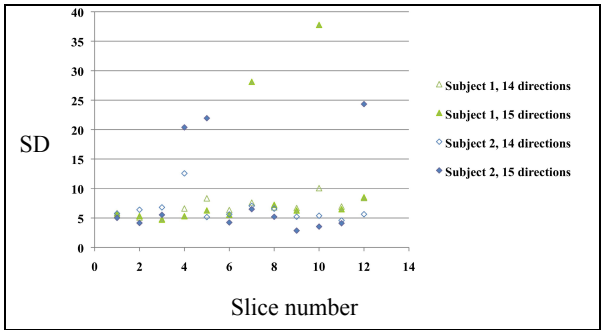

Figure 1. Standard deviation (SD) of the angle of deviation between the predicted principal eigenvector and the "true" principal eigenvector calculated from the average signal over the ROI.

Conclusion This novel approach of identifying and using the best 14 diffusion directions for calculation of the diffusion tensor and associated diffusion parameters has been demonstrated on simulated images and implemented in real DT-MR data sets. This heuristic reduces the effects of noise-induced errors in principal eigenvector calculations, which may otherwise obfuscate interpretation of DT-MR data in skeletal muscle.

References

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