

# Non-uniform diffusion encoding directions schemes to minimize fiber direction uncertainty in skeletal muscle DTI

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**Introduction:** Recent studies employing diffusion MRI to characterize skeletal muscle and perform muscle fiber tractography have shown the need to minimize fiber directional uncertainty [1]. Dominated by the inherently low SNR of muscle diffusion MRI and the low anisotropy of muscle fibers, Monte Carlo studies suggest that tensor orientation estimates may vary up to 10% in a typical DTI experiment [2]. In the brain, it has previously been demonstrated that directional uncertainty also depends upon the magnitude of diffusion weighting and the distribution of directional measurements [3]. When the dominant orientation of white matter is known *a priori*, it is possible to further reduce the uncertainty of different metrics of the diffusion tensor (trace, fractional anisotropy or primary eigenvector orientation) through non-uniform distribution of diffusion encodings [4-7]. Specifically, diffusion encoding schemes using directions in an angular band around the fiber orientation can minimize the direction uncertainty [5]. In this work, we propose a novel approach for increasing the precision of tensor directional estimates in skeletal muscle, for which a dominant fiber orientation is characteristic in the extremities (Fig. 1a). Results from computer simulations and preliminary *in vivo* experiments are presented, showing that fiber directional uncertainty can be reduced by up to 37%, which might have implications in improving the precision of DTI-based skeletal muscle biomechanical models.

**Materials and Methods:** We used an analytical formulation for distributing points on a hemisphere together with a recently developed framework for error propagation in DTI [9,10] to minimize the mean area of the elliptical cone of uncertainty (COU). Simulations and calculation of optimized directions was performed using MATLAB. A uniform distribution of directional measurements of diffusion  $\Xi$  was first at 30 non-collinear points on the hemisphere using a 3D spiral trajectory [8] (Fig. 1b). A compression transform  $T$  is then defined so that the directions are limited to an angular band between two zenith angles, parameterized by the tilt angle of the band  $\theta_0$  and the thickness of the band  $\Delta\theta$ . The optimal transformation is defined as the one that minimizes the area of COU [9,10], as constrained by an assumed dominant orientation and dispersion around this orientation. The optimized non uniform diffusion encoding scheme is defined by applying the transformation  $T$  on  $\Xi$  to derive the optimized scheme  $\Xi' = T(\Xi)$  (Fig 1c).

**Simulations:** Muscle fibers were assumed to have zenith angle following a Rayleigh distribution with parameter=10° and azimuth angle following a uniform distribution, resulting in a population of fibers within a cone around the Z axis. Simulated tensor parameters were  $\lambda_1/\lambda_2/\lambda_3 = 2.0/1.4/1.2 \cdot 10^{-9} \text{ m}^2/\text{s}$  and SNR=60 for the  $b=0$  signal, corresponding to a typical *in vivo* experiment [2].

**In vivo measurements:** An eight-channel lower extremity coil was used to scan the left calf muscle of one healthy volunteer on a 3 T full-body GE scanner. Diffusion-weighted images were acquired using a single-shot diffusion-weighted stimulated-echo EPI sequence [11] with the following parameters: TR/TE=2000/52 ms, FOV=20x20 cm<sup>2</sup>, slice thickness=10 mm, acquisition matrix=64x40 (5/8 partial phase encoding),  $N_{ex}=10$ , 6 slices,  $\delta=15$  ms,  $\Delta=40$  ms,  $g=3$  G/cm,  $b=541 \text{ s}/\text{mm}^2$ . The acquisition was repeated twice: once with the standard uniform diffusion encoding scheme  $\Xi$  and once with the optimized non-uniform diffusion encoding scheme  $\Xi'$ .

**Results: Simulations:** Fig 1c. shows the optimized 30-directions scheme ( $\theta_0=44^\circ$ ,  $\Delta\theta=57^\circ$ ). Simulations are also performed for the two schemes to compute the elliptical cone of uncertainty as a function of the angle  $\theta_1$  between the fiber and the Z axis. The optimized scheme results in a decrease in the area of the COU up to 37% (Fig. 2a). Figs. 2b and 2c show the effect of the directions scheme on the major and minor axes of the elliptical COU.

**In vivo results:** Bootstrap resampling is performed for the signal in an ROI of the tibialis anterior (TA) muscle (Fig. 3a). 200 samples are formed from the 30-directions data (with 5 acquisitions averaged). The cone of uncertainty is constructed based on the projection of the primary eigenvector of the bootstrap samples on the plane defined by the mean secondary and tertiary eigenvectors (Figs. 3b and 3c) [12]. The optimized directions scheme leads to a decrease in the area of the elliptical COU by 12%.

**Discussion and Conclusion:** The present optimization framework uses analytical error propagation formulas instead of Monte Carlo simulations to accelerate the formation of optimized diffusion directions schemes. The presented examination of the COU with the optimized scheme in the *in vivo* data did not take into account the effect of other sources of noise, other than thermal noise, such as motion. The analysis of the *in vivo* data also focused on the TA muscle, which is known to have a low pennation angle (around 10°). Therefore, further work would be required towards establishing diffusion schemes with improved noise properties for multiple muscle groups and understanding the effect of the optimized schemes in the diffusion anisotropy metrics. However, the present preliminary results show that optimized diffusion directions schemes can minimize the cone of uncertainty in DTI of skeletal muscles with *a priori* known preferential orientation.

**References:** [1] Heemskerk et al, MRM 61: 467-472, 2009, [2] Damon et al, MRM 60: 934-944, 2008, [3] Jones et al, MRM 515-525, 1999, [4] Peng et al, MRI 25: 147-153, 2007, [5] Yanasak et al, MICCAI 2008, p. 866-873, [6] Gao et al, Neuroimage 44: 729-741, 2009, [7] Majumdar et al, ISMRM 2009, p. 3513, [8] Wong et al, MRM 32: 778-784, 1994, [9] Koay et al, IEEE TMI 26: 1017-1034, 2007, [10] Koay et al, IEEE TMI 27: 834-846, 2008, [11] Karampinos et al, ABME in press, [12] Jeong et al, MRM 60: 1408-1421, 2008.

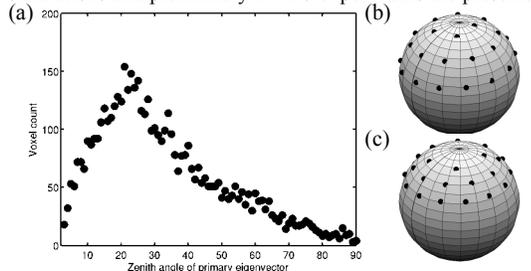


Fig. 1: (a) Histogram of the zenith angle of the primary eigenvector from a calf muscle DTI dataset (64x64 matrix, 6 slices), and (b-c) 30 diffusion encoding directions schemes: (b) standard uniform scheme  $\Xi$ , and (c) optimized non-uniform scheme  $\Xi'$ .

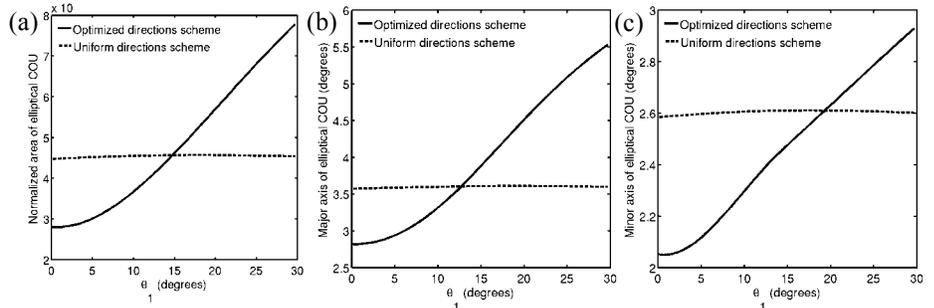


Fig. 2: Metrics of fiber uncertainty as a function of the angle between the fiber and the Z axis for the optimized and the uniform directions schemes: (a) normalized area, (b) major axis, and (c) minor axis of elliptical COU.

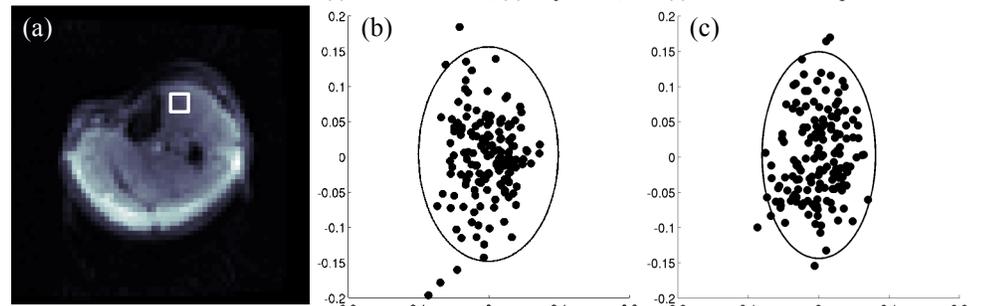


Fig. 3: Fiber orientation uncertainty in TA muscle: (a) ROI position in  $b=0$  image, and (b-c) comparison of the elliptical cone of uncertainty for the uniform (b) and the optimized directions (c) schemes.