In the Pursuit of Intra-Voxel Fiber Orientations: Comparison of Compressed Sensing DTI and Q-Ball MRI

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Introduction: Diffusion tensor imaging (DTI) is widely used to characterize tissue micro-architecture and brain connectivity. DTI suffers serious limitations in regions of crossing fibers because traditional tensor techniques cannot represent multiple, independent intra-voxel orientations. One fruitful approach to resolve this problem has been to acquire more detailed information through additional scans at higher diffusion sensitization (e.g., q-ball imaging [1]). Yet, scan time, signal-to-noise ratio (SNR), and hardware constraints limit widespread adaptation of these methods in clinical research. With Crossing Fiber Angular Resolution of Intra-voxel structure (CFARI) [2, 3], we characterize regions of crossing fibers using data acquired with traditional DTI protocols (i.e., low b-value, low angular resolution: ≤30 directions). CFARI is based on the premise of compressed sensing, i.e., exact estimation is possible with limited data using sparse models. Here, we compare q-ball and CFARI intra-voxel structure estimation using simulated and *in vivo* crossing fibers using traditional DTI data and a typical q-ball protocol [4]. CFARI reliability using DTI data exceeds that of q-ball using data from a more sophistical q-ball acquisition. The improvements with CFARI increase when both methods are allowed to use the full data from a q-ball acquisition.

Methods: Simulations were conducted with a crossing fiber model: Tensors of two fibers (fractional anisotropy=0.7, mean diffusivity=$1\text{x}10^{-3}$ mm^2/s) were randomly selected to cross between 45º and 90º for 1,000 Monte Carlo simulations. For visual comparison, two bundles of fibers crossing at 90º were simulated in an isotropic background. For each simulation, synthetic observations with Rician noise were simulated with an SNR of 15:1, 25:1, and 40:1 (on an unweighted reference) for a DTI and q-ball protocol. For an *in vivo* study, a healthy volunteer (M, 20 y/o) was scanned on a Philips 3T Achieva system with an eight channel head coil. Two traditional DTI acquisitions were acquired (each scan 4 min 4 s: 30 directions, b=700 s/mm^2, 5 averaged reference scans, SS-EPI, TR/TE=6410/69 ms) along with a standard q-ball sequence (31 min 27 s: 99 directions, b=3000 s/mm^2, 3 sets of 5 averaged reference scans, SS-EPI, TR/TE=15348/77 ms). All scans achieved axial whole brain coverage (65x2.2 mm slices) with in plane resolution of 0.94^2 mm (212^2 mm FOV, 96^2 matrix, SNR 15-20:1). Q-Ball and CFARI analyses were performed for simulated and *in vivo* datasets: (1) individual DTI acquisitions (30 dir.), (2) on pairs of DTI acquisitions (2x30 dir.), and (3) on q-ball acquisitions (99 dir.).

Analysis: For *in vivo* data, motion compensation and eddy current distortion correction were performed prior to analysis with JIST-CATNAP [5]. In the q-ball analysis, a regularized 6th order spherical harmonic fit was estimated Analytical Q-Ball with Laplace–Beltrami regularization with the recommended regularization term of 0.006 [4]. Intra-voxel orientations chosen as local maxima of the spherical harmonic estimate projected to a discrete basis set of 289 directions as described in [4]. The non-negative version of CFARI (CFARI+) was employed [3]. In CFARI+, each voxel was modeled as a finite mixture of discrete and independent compartments. The observed signal, S_k, along the k^{th} diffusion weighting direction (g_k) is determined by the exponential mixture model, $S_k = S_0 \sum_i^N f_i e^{-b\, g_k^T \mathrm{D}_i g_k} + \eta$ where S_0 is a noise-free reference signal in the absence of diffusion weighting, N is the number of possible compartments (tensors) within each voxel, f_i is the (unknown) mixture component for each compartment, D_i is the tensor associated with the i^{th} compartment, and η is a noise term that follows a Rician distribution. It is assumed that the *reconstruction basis* $\{\mathrm{D}_i\}$ — i.e., the set of possible diffusion tensors that may comprise a voxel — is fixed and known (herein, fractional anisotropy=0.7, mean diffusivity=1 mm^2/s, 253 orientations). CFARI+ mixture fractions were determined with the compressed sensing criteria, $f = \text{argmin}_{f:f_i\in[0,\infty)} \|\mathrm{S}f - y\|_{L2} + \beta\|f\|_{L1}$, where β (here, 1) is a strictly positive *sparsity regularization parameter* and f_i are restricted to be non-negative. All analyses were performed with open source tools developed as part of the Java Image Science Toolkit (JIST, http://www.nitrc.org/projects/jist/).

Results: Simulations illustrated that CFARI with traditional DTI data was able to recover intra-voxel structure with higher fidelity than q-ball imaging (Table 1: 9.1º versus 12.7º at SNR 25:1) and the CFARI estimates were far superior when CFARI used the full q-ball data (Table 1: 5º versus 12.7º at SNR 25:1). Figure 1 provides a visual comparison of the crossing fiber model. Figure 2 shows a representative *in vivo* coronal section where corpus callosum fibers cross the internal capsule. The left subplot indicates the region of interest shown. The right subplot shows the normalized spherical harmonic q-ball projection. In this figure, the crossing fibers are visually more apparent with CFARI than with q-ball analysis. Note that repeated observations of typical DTI data (8 min 8 s) can be used to improve CFARI estimates in less time than a full q-ball sequence (31 min 27 s), but the additional low b-value scans do not substantively improve q-ball estimates in either simulation or *in vivo*.

Discussion: CFARI is robust to the regularization constant and choice of basis model [3], and, here we shown that estimated mixture directions can be determined with greater precision that traditional q-ball analysis using only 13% of the scan time. We note that CFARI makes no attempt to model the full richness of the orientation distribution functions possible with q-ball analysis; rather CFARI directly extracts "dominant" orientation contributions and is able to do so with far less information. The q-ball error metrics are disconcertingly high, yet are consistent with the 12-16º error reported in Table 5 of [4] for a biological phantom. Visually, q-ball contains additional information than local maxima (right subplot) and it seems possible to use the representation to find other definitions of mixture components, yet, as shown herein, this information is not well-captured by local maxima. In summary, CFARI enables evaluation of intra-voxel structure (e.g., for advanced fiber tracking and tissue classification) in studies that have hitherto been limited to tensor analysis due to scan time availability or others limitations on acquiring a full q-ball dataset.

References: [1] D. S. Tuch, "Q-ball imaging," MRM, 52(6), 1358-72 (2004). [2] B. A. Landman, et al. CDMRI Workshop at MICCAI, New York, NY (2008). [3] B. A. Landman, et al. SPIE Medical Imaging, San Diego, CA (2010). [4] M. Descoteaux MRM 58:497–510 (2007). [5] B. A. Landman, ISMRM (2009)

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Table 1. Estimation Error in a (Tensor) Crossing Fiber Model

		Simulated Reference SNR		
Protocol	**Method**	**15:1**	**25:1**	**40:1**
Traditional DTI (4 min)	**CFARI**	13.2±6.3º	9.1±4.1º	6.9±2.5º
30 direction, b-value 700 s/mm^2	**Q-Ball**	22.7±9.7º	20.2±8.8º	18.9±8.7º
Traditional DTI (8 min)	**CFARI**	10.6±4.8º	7.5±3.0º	6.0±1.8º
2 rep x 30 direction, b-value 700 s/mm^2	**Q-Ball**	20.4±9.1º	19.2±8.9º	18.4±8.9º
Q-Ball HARDI Sequence (31 min)	**CFARI**	10.2±3.5º	5.0±1.1º	4.7±1.1º
99 directions, b-value 3000 s/mm^2	**Q-Ball**	19.8±10.9º	12.7±9.3º	9.8±7.1º

Error shown in degrees ± standard deviation at indicated SNR.

Fig. 1. Crossing Fiber Model with CFARI and Q-Ball

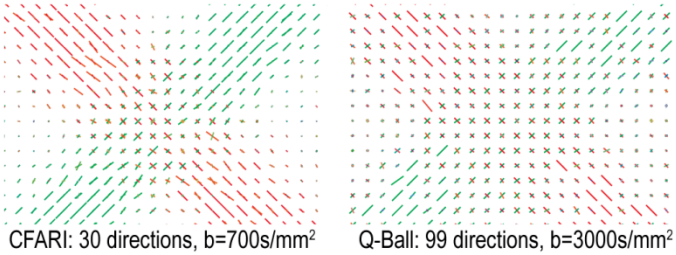

Fig. 2. Comparison of CFARI and Q-Ball Intra-Voxel Directions