The Feasibility of Diffusion Tensor Imaging for the Human Brain at 1 mm^3 Resolution

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Introduction Experiments with high b-values, small voxel sizes or low field strengths are characterized by low signal-to-noise ratios (SNR) close to the noise floor. For SNR<4, the noise of measured diffusion weighted images (DWI) follows approximately the Rician statistics with biased mean values, SNR dependend variance and skewness, which has large impact on the statistical properties of the DTI metrics derived from the DWIs. The influence of Rician statistics is studied for the rank=2 tensor model by Monte Carlo Simulations (MCS) and real data applications. We find especially for the tensor eigenvalues and for derived variables, e.g. mean diffusivity (MD) or fractional anisotropy (FA), a strong influence of the Rician bias, the main directions are essentially distorted by the higher moments. Based on these MCS-results a denoising method is proposed. It is validated by a gold standard model of the brain. Finally, the method is applied to human brain measurements with 1x1x1 mm^3 voxels acquired with 6, 15 and 21 multi-faceted icosahedral diffusion gradients, providing three tensor estimates with different noise level from the same data set [**1**].

Methods and Materials A) Single voxel MCS for cigar and lense shaped diffusion were performed, FA was respectively 0.8 and 0.5. The SNRs averaged over all gradient directions were approximately 2.2, corresponding SNR for the reference signal (b=0) was 4.2. Twelve icosahedral designs were applied in the simulations, ranging from 6 to 126 gradients [**2**]. **B)** The proposed denoising method proceeds in three steps: a) perform NEX experiments to reduce the noise level in the DWIs by averaging, b) apply a nonlinear spatial filter [**3**] to the averaged DWIs to increase the effective number of replications NEX_effective = NEX * n_filter , c) perform a bias correction bc to the estimated mean DWIs which is similar to the Rician bias correction but avoids the singular slope close to the noise floor. Validation of this method relies on a measured clinical data set, which was, after postprocessing, used as gold standard, and was affected with different artificial high noise levels. **C)** The small voxel experiment was performed on a consented normal volunteer (F40y) with a GE 1.5 MRI scanner using a dual spin echo prepared diffusion sequence with ramp sampling and fat suppression. The field of view is 256 mm^2 with a data matrix of 256x256 pixels, a total of 28 contiguous axial sections covering corpus callosum were selected from a sagittal scout localizer. The b factor is 1400 s mm^{-2}, TR=4.5 seconds and TE=82 ms, the number of replication was NEX=4, the DWIs were averaged within the scanner, gradients are specified above [**1**, **2**].

Results A) The MCS were performed for NEX=1,5, and 30, for NEX=30 also bc was applied. Main results are: An appreciable impact of the Rician bias on the tensor eigenvalues is apparent. Increasing NEX or the number of gradients does not eliminate this eigenvalue bias. The variables MD and FA show similar features. Correcting the DWIs by bc improves the situation considerably, the relative bias in the eigenvalues, MD and FA reduces to <5% and reduces further for NEX>30 for all gradient numbers applied. **B)** The denoising method was applied to the gold standard via 6 icosahedral gradients, for different NEX and low SNRs. The results fit well to those of A), indicating that the spatial filter is a convenient substitute for voxelwise DWI averaging. For NEX=7 and averaged SNR=2.6 postprocessing achieved NEX_effective =45 and averaged SNR=17.5. Again the importance of bc was verified, e.g. the fraction of voxels for MD with relative deviation below 10% from the model without noise increased from 48% for filtered data to 95% for data filtered and bias corrected, and similar for FA from 41% to 48%. **C)** Application of the denoising method to the small voxel experiment with averaged SNR below 3 is illustrated in Fig. 1 and 2. The FA maps in Fig. 1 improve from left to right with respect to spatial coherence and contrast. This is supported by the global FA distributions for 28 slices, right panels, where the lowest panel indicates maximum contrast. In general, the experiment with 6 gradients is essentially improved by the use of 15 gradients, but further improvement for 21 gradients is small. The global MD distributions after application of the denoising method and AIR-registration peak for all gradients at .00083 mm^2 s^{-1}. Main diffusion directions around corpus callosum in Fig. 2 demonstrate the high resolution capacity of small voxel experiments necessary for tracking of small fiber bundles.

Discussion and Outlook Due to scanner instabilities, loading effects etc., the basic assumption of Rician statistics is only an approximation. However, the method showed in all real data applications a high robustness. A more realistic bc may be constructed by experimental modelling [**4**]. Also spatial filtering can only approximate averaging of ideal experimental replications, the presently used filter was successfully tested and applied in numerous DTI applications under clinical conditions [**5**]. The main part of the method is independend of a specific tensor model and can be regarded as a realization of the statistical Delta Method [**6**]. Therefore, the method may be convenient for any DTI model, when derived from DWIs.

Fig. 1:

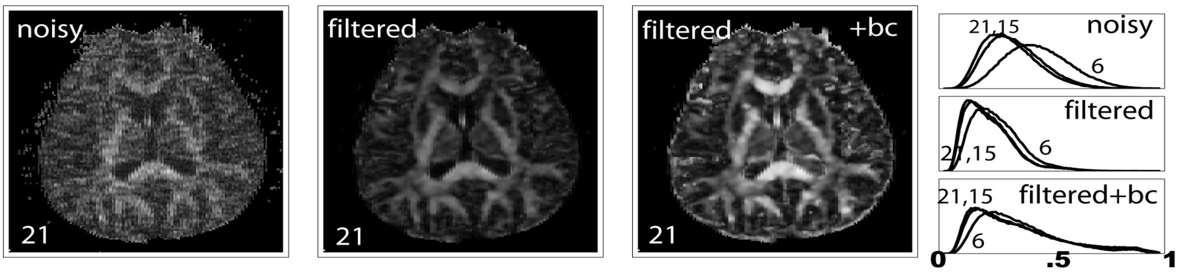

Fig. 2:

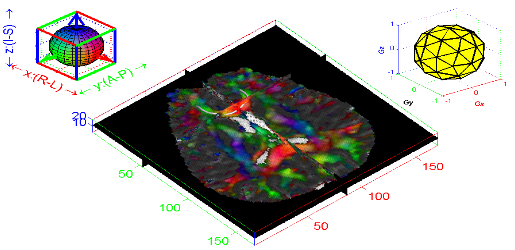

Fig.1 Axial FA maps for 21 gradients and global FA distributions for 6, 15 and 21 gradients calculated from small voxel data. Axial slices, **noisy** : FA from averaged DWIs, NEX=4, **filtered** : spatial filtering applied to averaged DWIs, **filtered+bc** : bc applied to filtered DWIs. Right panels: FA distributions for 28 slices, labels like in axial slices.
Fig. 2 A demonstration of fiber tracking of 1 mm^3 data after denoising (**filtered+bc**) and image registration. The view shows the fronto-callosal fibers in overlay of [main directions x FA x MD] and encoding scheme.

References: **[1]** Hasan K et al, Magn Reson Med (2003), 50, 589-598. **[2]** Hasan K et al, J Magn Reson Im (2001), 13(5), 769-780. [**3**] Hahn K R et al, A novel denoising technique for very noisy DTI data, Proc. ISMRM12 (2003), Kyoto, 1208. [**4**] Dietrich et al, Magn Reson Med (2001), 45, 448-453. [**5**] Heim S et al, Magn Reson Med (2004), 52, 582-589. **[6]** Lehmann E L, Elements of large sample theory, Springer, New York, 1999.