Evaluation of SNR Performance and Utility of High Spatial and Angular Resolution Denoised 1mm3 Isotropic DTI of Entire Human Brain at 3.0 T

K. M. Hasan[1], K. Rodenacker[2], K. R. Hahn[2]

[1]Diagnostic and Interventional Imaging, University of Texas Medical Scool, Houston, Texas, United States, [2]Biomathematics & Biometrics, GSF-National Research Center for Environment and Health, Neuherberg, Bavaria, Germany

Introduction: Current DTI protocols use voxel sizes of (2-3 mm)^3 ~ 8-27 mm^3 or larger **[1]**. The choice of large voxels may enhance the signal-to-noise ratio in homogeneous regions but will exacerbate the effect of CSF in the voxel and partial volume averaging of CSF-gray-white matter boundaries **[2-3]**. Thus, the in vivo application of quantitative DTI methods to study the contributors to the healthy developing and diseased tissue anisotropy is clearly limited even on large compact structures such as the corpus callosum. In vivo studies of the healthy and diseased structures such as the prostate, cortex, cerebellum, optic nerve and spinal cord generally demand high spatial resolution **[4]**. Studies of the developing and aging cortex in Alzheimer's disease and multiple sclerosis where cortical lesions can be masked by dilution effects due to the suboptimal voxel sizes are expected to benefit from optimized DTI with high angular and spatial resolutions **[5]**. The signal-to-noise ratio is generally proportional to the voxel size (V), main magnetic filed (B_0) and increases as the square root of the total sampling time (i. e SNR~B_0*V*$\sqrt{NEX}$) **[6].** Thus, high spatial resolution DTI experiments are expected to be contaminated by the poor SNR ratios but can be compensated by increasing the main magnetic field and by using high angular sampling without replicated averaging. In this work, we validate the signal-to-noise performance of 1mm^3 human brain studies at 3.0 T in a clinical setup at isotropic 1mm^3 and using high angular resolution. The protocol uses a combination of multi-faceted, balanced and alternating polarity gradient with 42 directions distributed over the unit sphere **[7]** and a novel nonlinear spatial denoising procedure **[8]** to enhance the SNR without affecting the tissue boundaries. To test the utility of this true isotropic protocol, we demonstrate its ability to segment, map the callosal fibers, and quantify the effect of SNR- vs. anisotropy on selected white and gray matter regions.

Methods: DT MRI Acquisition: We have acquired entire brain data from consenting adults using a Philips 3.0 T Intera system using a SENSE receive head coil. The DT-MRI data were acquired using a single-shot spin echo diffusion sensitized EPI sequence with the balanced and alternating Icosa21 encoding scheme **[7]**, b=1000 smm^{-2}, TR=10 s , TE= 100 ms. To reduce EPI related image artifacts, we used a SENSE acceleration factor R=2. The slice thickness is 1mm, fov=25.6 cm and an acquisition matrix of 256x256 --without zero filling in k-space-- giving a true in plane voxel size of 1mm^3. The tensor encoding scheme is designed to minimize couplings between imaging, background and the large diffusion gradients used for encoding **[9]**. The scheme is designed and ordered to provide DTI-metrics from the same data set at different SNR levels, thus providing a simple method for DTI quality control **[7]**.

Data Processing and Analysis: Diffusion weighted data were distortion corrected using the mutual information maximization approach **[10].** The multi-pass non-linear denoising filter is applied on the diffusion encoded volumes as described in **Figure 1** and detailed elsewhere **[8]**. The DTI data processing, segmentation, analysis and fiber tracking are described elsewhere **[11,12].**

Results. Figure 2 demonstrates the effect of the nonlinear spatial filtering procedure applied on the noisy DW encoded. The computed DTI maps such as FA and the principal eigenvector maps are clearly denoised preserving white and gray matter boundaries. The entire data can be projected, rendered and fiber-tracked without any interpolation along any plane as shown in **Figure 3**. **Figure 3** also demonstrates the ability to segment out and fiber track the corpus callosum regions after denoising. Notice the ability to visualize the cortical gyrification after filtering. **Figure 4** compares the mean and SD placed in the cortical gray matter and the white matter of the splenium of the corpus callosum at different SNR levels by selecting different rotationally invariant icosahedral data subsets from the same data set. Notice the reduction in both estimated FA and its error as SNR increases confirming the well-known trend that noise overestimates anisotropy in gray matter **[1].** The FA-noise performance in the splenium is also predictable as noise in this highly organized structure would have reduced the anisotropy by roughening or overestimating the smallest eigenvalues and hence reducing the true FA, as shown in **Figure 3**.

Discussion and Conclusions: In this work we demonstrated the feasibility of 1mm^3 isotropic and denoised DTI at 3.0 T using high angular resolution noisy measurements. We have shown examples demonstrating compact white matter fiber tracking, automatic DTI-based tissue segmentation of structures such as the corpus callosum after nonlinear filtering, and the ability to project and render the DTI data without further interpolation. We predict that this protocol applied on systems at high magnetic fields, parallel imaging, large gradient systems and efficient sampling will make noisy entire human brain acquisition at 1mm^3 feasible. The acquisition and processing strategy used here may also be extremely useful for mapping delicate structures such as the optic nerve, spinal cord, and cortex in pathologies such as AD and MS where cortical thinning and cortical lesions are notoriously challenging to visualize and localize using MRI**[5].** The combination of this acquisition-processing strategy with fluid attenuation preparation (DTI-FLAIR) and high-b factors will enhance the accuracy of the estimated metrics in the different diffusion compartments in applications where CSF contamination is problematic. The efficiency and advantage of such protocols are clearly to reduce total imaging time, improve accuracy and specificity as temporal multiplexing and averaging may be substituted with such spatial denoising approaches. This approach time efficiency will facilitate imaging uncooperative subjects such as children and the elderly.

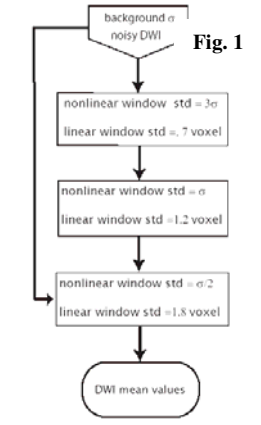


Fig. 1

←**Figure 1**.The spatial denoising of DWI volumes involves the iteration of three nonlinear Gaussian filters; the widths of the filt-windows are given by their standard deviations. In the last iteration the iterated filter weights are applied to the noisy data

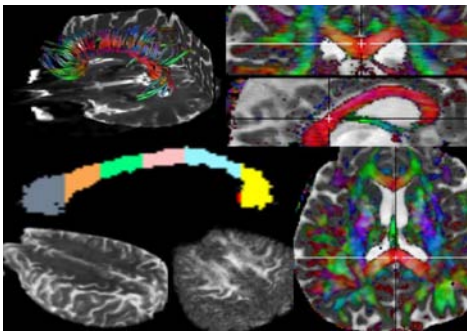
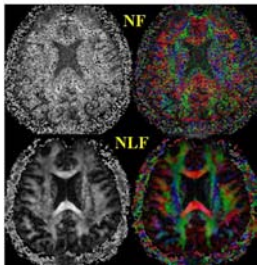


Figure 3. (**above**) shows the ability to fiber -track, DT_ data segment structures using denoised 1mm^3 dat project and render data directly without interpolation.



←**Figure 2 (left)** compares FA and the FA modulated principal vector map before and after spatial denoising

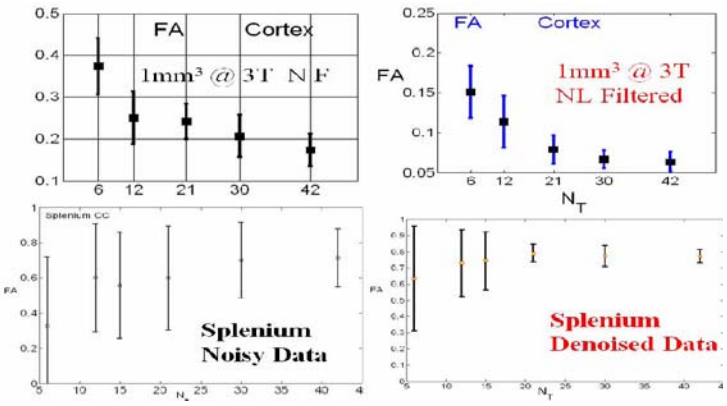


Figure 4. ROI mean and SD Plots testing the SNR performance of FA as function of encoding in the cortex and splenium using the noisy (NF) and non-linear filtered data.

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