## Bias in Diffusion Tensor Tissue Integrity Measures Due to Sum of Squares Reconstruction: Characterization and Retrospective Correction

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TARGET AUDIENCE: Researchers using diffusion tensor imaging (DTI) to characterize tissue integrity.

PURPOSE: To quantify and correct bias in DTI measures of tissue integrity associated with Sum of squares (SOS) reconstruction of multi-coil images. Measures of tissue integrity derived from the diffusion tensor (e.g., longitudinal and transverse diffusivity (LD, TD)) can be biased by noise <sup>1</sup>, particularly with the Rician noise floor from magnitude reconstruction resulting from SOS. We quantify the bias in tissue integrity measurements due to SOS by comparison with another reconstruction algorithm, known to have a lower noise floor, adaptive combine (AC). We demonstrate that a simple correction due to Gudbjartsson and Patz (GP)<sup>2</sup> dramatically reduces the bias.

METHODS: DTI was acquired from five subjects under an internal review board-approved protocol. All images were acquired on a Siemens 3T Tim Trio with a standard 12-channel head coil (Siemens Medical Solutions, Erlangen). Data were acquired at 2mm and 2.5mm isotropic resolution with the same set of diffusion gradients (71 directions with b=1000sec/mm<sup>2</sup>, 8 b=0). Each dataset was reconstructed with SOS and subsequently reconstructed again by AC using the retro-recon feature implemented on the imaging host. The GP correction was applied to the SOS data. Thus, the same imaging data were reconstructed in three ways: with SOS, AC and SOS followed by the GP correction (SOS-GP). The diffusion tensor and tissue integrity measures were then calculated with standard algorithms<sup>3</sup>. Bias is characterized on a voxel-by-voxel basis with respect to values derived from AC reconstruction. For example, bias in LD calculated with SOS-GP is defined as  $bias(LD_{SOS-GP}) \equiv (LD_{SOS-GP} - LD_{AC})/LD_{AC}$ .



RESULTS: Figure 1 illustrates the bias in tissue integrity measures.  $bias(LD_{SOS})$  is pronounced in regions with high anisotropy such as splenium (fig 1a, arrow).  $bias(TD_{SOS})$  is less pronounced overall (fig 1d), but particularly in regions of high anisotropy (fig 1d, arrow). The GP correction effectively reduces bias for both LD and TD (fig 1b, 1e). Figure 2 illustrates the impact of the GP correction across all data by showing distributions of bias in LD from all subjects and 2mm data. The GP correction reduces bias by a factor of 7. Similar reductions were found for TD and for 2.5mm data.

DISCUSSION: This work focuses on the influence of SOS reconstruction on tissue integrity measurements and a simple correction that can be applied retrospectively. Intuitively, the Rician noise floor produces an upward bias in low signal values, diminishing attenuation due to diffusion-weighting gradients and overall downward bias in diffusivity values, particularly large

diffusivities found mostly among LD. Previous work has focused on bias in fiber orientations<sup>4</sup> and amelioration by SENSE reconstruction<sup>5</sup>, which can typically be implemented only prospectively. The GP correction reduces bias substantially, is easy to implement, and can be



Figure 2. Histograms of bias( $LD_{SOS}$ ) (solid blue) and bias( $LD_{SOS-GP}$ ) (dashed red)

applied retrospectively. A more comprehensive approach has been developed<sup>6</sup> but requires computationally intensive nonlinear optimization that, in our experience, does not always converge. As a practical note, the default reconstruction switched from AC to SOS due to a software upgrade on our scanner, necessitating the implementation of a retrospective correction.

CONCLUSION: SOS introduces substantial bias in tissue microstructure measurements, particularly in LD. A simple correction ameliorates this bias and can be effective for retrospective analysis.

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