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Minimum SNR and acquisition for bias-free estimation of fractional anisotropy in diffusion tensor imaging — a comparison of two analytical techniques and field strengths

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Abstract

Although it is known that low signal-to-noise ratio (SNR) can affect tensor metrics, few studies reporting disease or treatment effects on fractional anisotropy (FA) report SNR; the implicit assumption is that SNR is adequate. However, the level at which low SNR causes bias in FA may vary with tissue FA, field strength and analytical methodology. We determined the SNR thresholds at 1.5 T vs. 3 T in regions of white matter (WM) with different FA and compared FA derived using manual region-of-interest (ROI) analysis to tract-based spatial statistics (TBSS), an operator-independent whole-brain analysis tool. Using ROI analysis, SNR thresholds on our hardware–software magnetic resonance platforms were 25 at 1.5 T and 20 at 3 T in the callosal genu (CG), 40 at 1.5 and 3 T in the anterior corona radiata (ACR), and 50 at 1.5 T and 70 at 3 T in the putamen (PUT). Using TBSS, SNR thresholds were 20 at 1.5 T and 3 T in the CG, and 35 at 1.5 T and 40 at 3 T in the ACR. Below these thresholds, the mean FA increased logarithmically, and the standard deviations widened. Achieving bias-free SNR in the PUT required at least nine acquisitions at 1.5 T and six acquisitions at 3 T. In the CG and ACR, bias-free SNR was achieved with at least three acquisitions at 1.5 T and one acquisition at 3 T. Using diffusion tensor imaging (DTI) to study regions of low FA, e.g., basal ganglia, cerebral cortex, and WM in the abnormal brain, SNR should be documented. SNR thresholds below which FA is biased varied with the analytical technique, inherent tissue FA and field strength. Studies using DTI to study WM injury should document that bias-free SNR has been achieved in the region of the brain being studied as part of quality control.

Keywords: Diffusion tensor imaging; SNR threshold; Bias-free FA; Manual ROI analysis; Tract-based spatial statistics

1. Introduction

Diffusion tensor imaging (DTI) provides information about white matter (WM) microstructure and integrity not possible with conventional magnetic resonance (MR) imaging [1–3]. Numerous studies have reported alterations in diffusion tensor metrics with disease states which, when affecting the cerebral WM, usually cause fractional anisotropy (FA) to fall [4,5].

Prospective studies using DTI as a potential biomarker for disease or response to therapy are often conducted at multiple centers or at a single institution on different MR platforms at different times. Whether tensor data acquired at different field strengths at different sites can be compared continues to be debated. Problems with reproducibility of FA measurements have led to calls for standardization of sequence parameters, although less attention has been paid to quality control issues which may also impact the reproducibility of FA measurements.

DTI is most often acquired with parallel imaging to decrease scan time and motion. Moreover, the noise within accelerated images is nonhomogeneous with higher signal

Abbreviations: ACR, anterior corona radiata; CG, callosal genu; DTI, diffusion tensor imaging; FA, fractional anisotropy; g-factor, geometric factor; PRIDE, Philips Research Image Development Environment; PUT, putamen; ROI, region of interest; SD, standard deviation; SNR, signal-to-noise ratio; TBSS, tract-based spatial statistics; WM, white matter.

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peripherally and noise centrally [6–9]. Signal-to-noise ratio (SNR) levels are not routinely reported despite previous reports suggesting that low SNR causes a bias in FA which may vary with the inherent FA of the region of brain being studied, field strength, hardware and software, subject age, head size, location within the brain and numerous other technical factors [10–14].

Different methodologies and software platforms are used to quantitatively assess FA and the individual diffusivities; manual region-of-interest (ROI) analysis is performed on tensor data in native space and is one of the most commonly used operator-dependent techniques, while tract-based spatial statistics (TBSS) is a widely used operator-independent methodology which facilitates cross-sectional and longitudinal comparison of spatially normalized tensor data from large numbers or groups of subjects. There are few studies reporting direct comparison between tensor metrics derived using manual ROI analysis vs. TBSS.

The purposes of this study were (a) to determine, using a single human phantom, the effect of field strength on SNR in clinical DTI and (b) the thresholds below which further decreases in SNR bias FA in different regions of the brain; (c) to compare the thresholds for SNR derived using manual ROI analysis and TBSS; and (d) to select the minimum number of acquisitions for the SNR thresholds at different field strengths.

2. Materials and methods

2.1. Imaging protocol and data acquisition

All tensor data were derived from a single normal adult male volunteer. DTI was performed at 1.5 T (Intera R11, Philips Healthcare Systems) and 3 T (Achieva R2.6, Philips Medical Systems, Cleveland, OH, USA) with eight-channel sensitivity encoding (SENSE) head coils. A total of 15 DTI data sets were acquired at each field strength using multislice single-shot echo-planar imaging; field of view=256×256 mm^2; 128×128 matrix size (reconstructed to 256×256); 2×2×2 mm^3 voxel size; 42 slices; repetition time/echo time (ms)=6218/100 at 1.5 T and 4344/74 at 3 T; *b*-value=1000 s/mm^2; SENSE factor=2 and 30 gradient encoding directions [15]. Each DTI data set consisted of 30 diffusion-weighted (DW) images and five $b=0$ images. An average of 5 $b=0$ images was taken to increase SNR. Fifteen acquisitions were averaged as complex images to decrease bias in the resulting high-SNR data set and to obtain a baseline tensor data set to which incremental noise was added as described below.

2.2. Image postprocessing

DTI data sets were registered and averaged using the Philips Research Image Development Environment (PRIDE) with affine transformation for the correction of eddy current distortion and motion artifacts.

2.3. SNR calculation and simulation

SNR was determined in the average of 5 $b=0$ images using software written in IDL 6.1 (IDL Research Systems Inc., Boulder, CO, USA) because SNR in DW images varies with different gradient encoding directions even though the same ROI is selected. Mean signal intensity and noise (=the standard deviation of pixel intensity) were assessed from the average and subtraction of two magnitude images of consecutive acquisitions, respectively. The SNR was calculated as the mean pixel intensity divided by the standard deviation of pixel intensity in the same ROI as follows [16,17]:

$$SNR = \sqrt{2} \times \frac{S}{\sigma},$$

where S=mean pixel intensity in the average image and σ=standard deviation (SD) of pixel intensity in the difference image.

After 14 pairs of the difference image and the average image were obtained from the 15 tensor data sets, 14 SNRs were obtained. SNR as a function of the number of acquisitions was calculated by multiplying the mean of the 14 SNRs by the square root of the number of acquisitions. Gaussian complex random noise with a mean of zero, a standard deviation of one and magnitude scaled to the desired root mean squared noise level was increasingly added to the maximum SNR tensor data set to create 10 simulated tensor data sets with each discrete noise level. FA was measured on each of the 10 DTI data sets by choosing the same ROI and the FA derived from 10 manual ROIs which were placed by a single observer. This process was repeated with incremental noise levels.

2.4. FA analysis

2.4.1. Manual ROI-based analysis

Using PRIDE, a single observer repeatedly manually placed ROIs on the callosal genu (CG), representing a region with high FA in a region of the coil known to have higher noise; the anterior corona radiata (ACR), a region of intermediate FA in a region of the coil with lower noise; and the putamen (PUT), a region of low FA in a region of the coil with relatively high noise in Fig. 1(A–C) [6–9]. Placement of each ROI was repeated on the 15 acquisition tensor data until SD of the FA for each measurement was <10%; the average of three FA measurements was considered representative of FA for each region. The ROI was then stored and used for all data sets with different SNR.

2.4.2. TBSS analysis

FSL (FMRIB Software Library, FMRIB, Oxford, UK) was used to estimate diffusion tensor eigenvectors and eigenvalues and to generate FA images. All FA images were aligned to the standard FA image data using nonlinear registration and affine transformed into MNI152 (Montreal Neurological Institute) space. The mean FA image was used