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Retrospective Correction of Bias in Diffusion Tensor Imaging Arising from Coil Combination Mode

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Abstract

Purpose—To quantify and retrospectively correct for systematic differences in diffusion tensor imaging (DTI) measurements due to differences in coil combination mode.

Background—Multi-channel coils are now standard among MRI systems. There are several options for combining signal from multiple coils during image reconstruction, including sum-of-squares (SOS) and adaptive combine (AC). This contribution examines the bias between SOS- and AC-derived measures of tissue microstructure and a strategy for limiting that bias.

Methods—Five healthy subjects were scanned under an institutional review board-approved protocol. Each set of raw image data was reconstructed twice—once with SOS and once with AC. The diffusion tensor was calculated from SOS- and AC-derived data by two algorithms—standard log-linear least squares and an approach that accounts for the impact of coil combination on signal statistics. Systematic differences between SOS and AC in terms of tissue microstructure (axial diffusivity, radial diffusivity, mean diffusivity and fractional anisotropy) were evaluated on a voxel-by-voxel basis.

Results—SOS-based tissue microstructure values are systematically lower than AC-based measures throughout the brain in each subject when using the standard tensor calculation method. The difference between SOS and AC can be virtually eliminated by taking into account the signal statistics associated with coil combination.

Conclusions—The impact of coil combination mode on diffusion tensor-based measures of tissue microstructure is statistically significant but can be corrected retrospectively. The ability to do so is expected to facilitate pooling of data among imaging protocols.

1. Introduction

The objective of this study is to quantify and retrospectively correct bias in diffusion tensor imaging (DTI) due to differences in coil combination mode. DTI provides quantitative measures of tissue microstructure that can be used to evaluate neurological disease. It is

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important to identify sources of variability in the measurement process to ensure that measurements reflect biological changes rather than instrumental factors. One potentially important factor is coil combination mode. Multi-channel coils are now common, but there are different options for combining the signal from the coils into an image. Sotiropoulos et al. demonstrated clear differences in DTI measures resulting from two coil combination modes: sum-of-squares (SOS) and SENSE-1 [1]. Differences were attributed to the systematically higher noise floor [2] associated with SOS. The difference in noise floor properties derives from the fact that SENSE-1 incorporates phase information from the coils while SOS does not.

Ideally, a DTI study will enforce uniformity in all aspects of image acquisition, including scanner hardware, pulse sequence parameters and image reconstruction algorithms. Unfortunately, this ideal cannot always be achieved. It is therefore necessary to determine how much of an impact differences make and develop corrections that can be applied retrospectively. Here, we focus on bias between DTI measurements taken with different coil combination modes, particularly SOS and adaptive combine (AC) [3]. Like SENSE-1, AC incorporates phase information but, unlike SENSE-1, AC is readily available in the standard DTI pulse sequence on Siemens platforms. With a button-click at the user interface, coil combination mode can be changed. The implications of such a change on DTI measures have not, to our knowledge, been examined closely.

In this contribution, we demonstrate that bias in tissue microstructure values can be substantial. We also demonstrate that, by accounting for the signal statistics, the bias can be reduced by an order of magnitude retrospectively. We expect that the approach described here will have practical use when pooling DTI data from acquisitions using different coil combination methods. Extensions of the work may facilitate pooling data from different scanners, an important consideration in the context of multicenter trials.

2. Material and Methods

2.1 Data Acquisition and On-Scanner Reconstruction

Under an internal review board-approved study, five healthy subjects were scanned on a 3 tesla Siemens Magnetom TIM Trio with a standard 12-channel head coil (Siemens Healthcare AG, Erlangen, Germany). A high angular resolution diffusion imaging [4] acquisition was acquired on each subject (51 2mm-thick axial slices with 256mm × 256 mm FOV, 128 × 128 matrix, twice-refocused spin echo twice-refocused spin echo [5] with TE = 92 msec, TR = 7800 msec, 71 noncollinear gradient directions with $b = 1000 \text{ sec/mm}^2$ and 8 $b = 0$ volumes, single-shot EPI readout with bandwidth of 1563 Hz/Pixel, partial fourier factor = 5/8). Raw data from each scan was reconstructed twice: once with SOS coil combination and another time with AC coil combination. Reconstruction with the AC coil combination was implemented directly on the scanner using the retro-recon feature. As the same raw data was used for each coil combination method, there is exact voxel-by-voxel correspondence between the SOS and AC images. No motion or eddy current distortion correction was applied. Such postprocessing would have eliminated the exact correspondence and would have modified the signal statistics.

2.2 Theory

The noncentral-chi (ncX) probability distribution describes signal from a multi-coil system using SOS coil combination:

$$p(M|A, \sigma, n) = \left(\frac{A}{\sigma^2}\right) \left(\frac{M}{A}\right)^n \exp\left(-\frac{(M-A)^2}{2\sigma^2}\right) \left[\exp\left(-\frac{MA}{\sigma^2}\right) I_{n-1}\left(\frac{MA}{\sigma^2}\right)\right]. \quad (1)$$

Each of n coil elements contributes noiseless signal of amplitude A and gaussian noise with standard deviation σ . M is the measured combined magnitude signal. I_{n-1} is a modified Bessel function of the first kind of order $n-1$ [6]. The expression has been rearranged slightly from the form in Constantinides et al. [6] to improve numerical stability. For a single coil, $n = 1$, eqn. 1 becomes a Rician distribution. In regions of background, with zero signal amplitude, $A = 0$, the distribution becomes central chi (cX) which in turn becomes a Rayleigh distribution for a single coil. For phase-sensitive coil combination such as SENSE-1 and AC, the signal statistics are expected show Rician behavior, Rayleigh in background, as if there were a single coil [1].

An important consequence of the ncX probability distribution is that the noise floor and measurements of the diffusion tensor depend on the number of coil elements. Rectification of noise by sum-of-squares signal combination results in the minimum detectable signal, the noise floor, being larger than zero [2]. This places a limit on sensitivity to small signals. As DTI requires accurate measurement of small signals, the noise floor also places limits on the accuracy of DTI. The first moment of the ncX probability distribution [6] at zero signal amplitude, $A = 0$, is the value of the noise floor for SOS coil combination:

$$\langle M \rangle = \frac{1 \cdot 3 \cdot 5 \cdots (2n-1)}{2^{n-1}(n-1)!} \sigma \sqrt{\frac{\pi}{2}} \quad (2)$$

Inspection of this expression numerically shows that $\langle M \rangle \propto \sqrt{n}$. All other things being equal, the more coil elements, the higher the noise floor. Diffusivity values, the eigenvalues of the diffusion tensor, become systematically lower as the noise floor becomes higher, a fact that can be inferred from fig. 2 of Jones et al. [2]. The noise floor may negate the signal-to-noise ratio advantage offered by multichannel coils if SOS coil combination is used. The signal statistics for AC coil combination acts if there were only one coil. As a result, the noise floor is expected to be lower for AC than for SOS. Diffusivity values derived from SOS signal will be systematically lower than those derived from AC signal. There will be bias between diffusion tensor measures derived from SOS and from AC coil combine. We will quantify this bias on a voxel-by-voxel basis for, for example, axial diffusivity (AD) as:

$$\text{bias}_{AD}^{LLSQ} = \frac{AD_{AC}^{LLSQ} - AD_{SOS}^{LLSQ}}{\left(\left(AD_{AC}^{LLSQ} + AD_{SOS}^{LLSQ}\right)/2\right)} \quad (3)$$

where LLSQ refers to the fact that the diffusion tensor from which AD was derived was calculated with a standard linear least-squares (LLSQ) algorithm. Similar measures of bias for radial diffusivity (RD), mean diffusivity (MD) and fractional anisotropy (FA) will also be examined (bias_{RD}^{LLSQ} , bias_{MD}^{LLSQ} , bias_{FA}^{LLSQ}).

2.3 Retrospective Reduction of Bias

This contribution examines whether or not we can retrospectively reduce the bias. The LLSQ algorithm used to calculate the tensor from the image data implicitly assumes that image noise follows a gaussian distribution and is independent from the signal. These assumptions are not strictly true when the ncX probability distribution holds. We therefore examine the impact on bias when we take the ncX probability distribution into account when calculating the diffusion tensor. To do so, we find, on a voxel-by-voxel basis, the diffusion tensor that maximizes the joint probability distribution:

$$\max_D \prod_{i=1}^N p(M_i | A_i(D), \sigma, n) \quad (4)$$

There are N measurements, M_i , for each voxel. For example, the data acquired in this study has 71 diffusion-weighted acquisitions and eight $b=0$ acquisitions, giving $N = 79$. We model the noise-free signal amplitude for each measurement,

$$A_i(D) = S_0 \exp(Db_i) \quad (5)$$

as that predicted by the diffusion tensor model with diffusion tensor D where b_i is the row of the b -matrix that pertains to the signal A_i and S_0 is the signal intensity without diffusion weighting [7]. In each voxel, we find the diffusion tensor that minimizes the negative of the logarithm of the joint probability distribution in eqn. 4 using the MATLAB function *fminsearch* (MATLAB Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States). From these values of the diffusion tensor, we calculate the eigenvalues and then the metrics of tissue integrity (AD, RD, MD and FA). The calculation is repeated for data from SOS coil combination and AC coil combination, resulting in measures of bias for the fit based on the ncX probability distribution (bias_{AD}^{ncX} , bias_{RD}^{ncX} , bias_{MD}^{ncX} , bias_{FA}^{ncX}).

In the fit based on the ncX probability distribution, values for the noise parameter, σ , and the effective number of coils, n , must be determined. We set these parameters by fitting background signal to the central-chi distribution (eqn. 1, with $A=0$). Aja-Fernandez et al. [8] introduced the use of effective coil number to account for correlations among coil elements. Ideally, the coil sensitivity profiles are mutually independent, in which case the effective number of coils is the same as the physical number of coils for SOS. Deviation from the ideal leads to lower effective coil number. For phase sensitive coil combination such as SENSE or AC, the effective number of coils is ideally 1. We select background by applying a robust range threshold [9] to the $b=0$ images, selecting voxels among the $b=0$ images with intensity below the threshold and then eliminate outliers by applying cutoffs at the 1st and 99th percentiles. We then fit a normalized histogram of background signal intensities to the

central-chi distribution using the MATLAB function *nlinfit*. The parameters are initialized using the moment expressions derived Aja-Fernandez et al. [10]. The resulting values of noise parameter, σ , and the effective number of coils, n , are then used in the fit based on the ncX probability distribution.

To test the hypothesis that accounting for signal statistics can reduce bias between SOS and AC coil combination in DTI, we examine voxel-by-voxel differences in bias of metrics of tissue integrity. If accounting for signal statistics limits bias, we expect bias associated with the ncX algorithm to be significantly smaller than bias associated with the standard algorithm. For example, we expect $\text{bias}_{AD}^{\text{ncX}} < \text{bias}_{AD}^{\text{LLSQ}}$.

3. Results

Analysis of signal in the background illustrates differences between SOS and AC coil combination in terms of signal statistics. Figure 1 shows histograms of signal from background of SOS and AC reconstructions from the same subject along with fits to the central-chi distribution. The underlying noise parameter is similar between SOS and AC, with the mean $\pm$ standard deviation of values across all subjects being $\sigma_{\text{SOS}} = 14.4 \pm 0.6$ and $\sigma_{\text{AC}} = 14.8 \pm 0.8$. However, the measured intensity of background signal is clearly higher for SOS than for AC, as is apparent from inspection of the histograms in figure 1.

The effective number of coils reveals interesting properties. The physical number of coils is 12. However, the effective number of coils for SOS is less, with the mean $\pm$ standard deviation of values across all subjects being $n_{\text{SOS}} = 3.76 \pm 0.07$, indicating that the sensitivity profiles of the coils overlap considerably. The effective number of coils for AC is $n_{\text{AC}} = 1.03 \pm 0.01$, indicating that the signal statistics for AC are those expected from SENSE-1 reconstruction.

Bias shows clear patterns across the brain. Figure 2 illustrates bias from LLSQ and ncX tensor fits in one slice of one subject. Bias between SOS- and AC-derived tissue integrity measures are clearly lower when using the ncX fit approach, particularly in regions of high anisotropy, such as splenium.

Whole-brain histograms demonstrate that accounting for noise floor effects dramatically reduces bias throughout the brain. The central value of bias is close to zero when accounting for the noise floor for AD, RD, MD and FA (fig. 3, red histograms). Bias is clearly larger when using a standard LLSQ fit (fig. 3, blue histograms).

Accounting for noise floor effects dramatically reduces bias throughout the brain in all subjects. To characterize the bias in each subject, we take the median value across all voxels. Use of the median accounts for the skew distribution that is apparent in figure 3. The mean and standard deviation, across subjects, of these across-brain medians is shown in Table 1. Bias when taking into account the ncX probability distribution is an order of magnitude times lower than when using the standard LLSQ approach.

4. Discussion

DTI provides quantitative measures of tissue microstructure that have been widely used to assess neurological disease. This contribution has shown that differences in coil combination mode can introduce significant bias among such measures. However, bias can be limited retrospectively to a great extent by taking into account the statistical properties associated with the noise floor. Bias due to coil combination mode can be particularly insidious. While a change in hardware, such as a different head coil, is easy to notice, a change in coil combination can be asserted by a single mouse click on the user interface of the scanner or by an automated software patch. Ultimately, such bias can mask important biological effects or introduce false effects. For example, when pooling data across sites, one site may have acquired data using SOS coil combination while another may have acquired data using AC coil combination. Even if all other aspects of the pulse sequences and image reconstruction are identical, there will be a systematic, site-dependent difference in DTI-based parameters. This difference can introduce variance that reduces the statistical power of the measurement. As another example, in a longitudinal study, an inadvertent switch from SOS to AC coil combination in the middle of the study can introduce a false change in measures at the time of the switch. Ideally, coil combination mode should be the same across all scans in a study. Unfortunately, it is not always possible to do so. It is therefore necessary to develop retrospective correction methods. We have shown that accounting for the statistics associated with coil combination can limit bias between AC and SOS coil combine methods in retrospective analysis.

We have demonstrated that the impact on diffusion tensor parameters is statistically significant given the conditions of the coil combination method. The size of the effect will depend on the SNR of the measurement. For the SNR levels of this measurement (~16 in white matter for the $b=0$ scans), the bias between tensor parameters derived from the two coil combination modes is several percent, as illustrated in fig. 3. Bias will be larger at lower SNR, a situation that may arise from using higher spatial resolution, higher diffusion weighting or a combination of the two.

We also demonstrated that statistics of adaptive combine act as if the effective number of coils is 1. The noise floor for the same signal is lower with adaptive combine than with sum-of-squares coil combination. Previous work addressing the noise floor advocated the use of SENSE with acceleration factor of 1 as an alternative to sum-of-squares coil combination to limit the impact of noise floor bias [1]. This work suggests that adaptive combine is a practical alternative.

There are a number of limitations to this study. Use of a single pair of values for the noise parameter and effective number of coils across the entire image volume may not be valid. Aja-Fernandez et al. demonstrated that parallel imaging can introduce variation in these parameters across the field of view [11]. Accounting for such variation requires information about image reconstruction parameters that are not typically provided to the user. Retrospective correction would either require enough foresight to gather these parameters or to develop new approaches that do not require such parameters. A related point is the estimation of the noise parameter and effective number of coils, here calculated from signal

background. In certain applications, such as body imaging or reduced field of view imaging of the brain, there may not be any background to make this estimation. Other approaches have been proposed and may be more generically useful [10].

Another limitation of this study is that it assumes that the implementation of the adaptive combine algorithm is that of Walsh et al. [3]. In reality, the implementation may differ in substantial ways that are difficult to determine because of the proprietary nature of the reconstruction code. However, the typical user neither has access to the reconstruction code nor is at liberty to make modifications to the code to make it align with expectations. The approach here does appear to limit bias despite the lack of detailed information about the reconstruction implementation. However, this study is limited to examination on a single imaging platform. Further validation will be required to determine if the approach is effective generally.

There are a number of alternative approaches that have not been examined. Jones accounted for noise floor effects by introducing an ad-hoc constant parameter representing the noise floor [2]. Koay et al. [12] developed a framework for mapping ncX signal statistics to a Gaussian distribution. The ncX distribution can also be used to denoise images [13]. The deviation of signal statistics from the ncX distribution due to postprocessing steps such as corrections for motion, eddy current distortion and susceptibility distortion has also been considered [14]. Modification of the image reconstruction can also render the signal statistics as gaussian, thereby eliminating the need for retrospective correction [15]. Comparison of the general applicability of these methods to the diffusion tensor and to higher order models is beyond the scope of this contribution.

5. Conclusions

We have demonstrated that differences in coil combination mode can introduce differences in measurements of the diffusion tensor. Uniformity among acquisitions in coil combination should therefore be considered when setting up a study. However, we have also shown that retrospective correction methods are able to limit the impact of coil combination mode. We expect use of these methods to be valuable when pooling data across sites, a situation in which there may be limited control over the type of coil combination mode used.

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Highlights

- Coil combination is a key step in image reconstruction from multichannel coils.
- Bias in diffusion tensor imaging due to coil combination is quantified.
- Substantial reduction in bias can be achieved retrospectively.
- Limiting bias is expected to enable effective pooling of data.

Figure 1.

Normalized histograms of background signal from A) sum of squares (SOS) and B) adaptive combine (AC) coil combination modes from the same raw data from one subject. Fits to the central-chi distribution (red lines) yield noise parameters of $\sigma_{SOS} = 14.9$ and $\sigma_{AC} = 15.3$ with effective number of coils $n_{SOS} = 3.72$ and $n_{AC} = 1.03$.

Figure 2.

Maps of bias between SOS- and AC-derived tissue integrity parameters. Gray-scale maps (first column) show spatial variation of tissue integrity parameters (axial diffusivity (AD), radial diffusivity (RD), mean diffusivity (MD) and fractional anisotropy (FA)). Color maps show absolute value of bias, defined in eqn. 3. Bias is lower when the noncentral chi probability distribution (ncX) is taken into account when calculating the diffusion tensor than when using a standard log-linear least squares (LLSQ) fit.

Figure 3.

Histograms of bias measured across the entire brain in one subject for A) axial diffusivity (AD), B) radial diffusivity (RD), C) mean diffusivity (MD) and D) fractional anisotropy (FA). Blue histograms represent bias between adaptive combine (AC)-derived and sum of squares (SOS)-derived measures calculated with standard linear least-squares (LLSQ). Red histograms represent bias between AC-derived and SOS-derived measures calculated accounting for noise floor effects.

Table 1

Bias between SOS- and AC-derived tissue integrity parameters calculated using standard log-linear least squares ($\text{bias}^{\text{LLSQ}}$) and after taking the noise floor into account with the noncentral-chi distribution (bias^{ncX}). The mean (standard deviation) across subjects of whole-brain median values is shown.

	AD	RD	MD	FA
$\text{bias}^{\text{LLSQ}}$	0.026 (0.003)	0.016 (0.002)	0.021 (0.003)	0.025 (0.002)
bias^{ncX}	-0.0014 (0.0004)	-0.0011 (0.0003)	-0.0012 (0.0003)	-0.0089 (0.0004)