DTI Quality Control Assessment via Error Estimation From Monte Carlo Simulations

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ABSTRACT

Diffusion Tensor Imaging (DTI) is currently the state of the art method for characterizing the microscopic tissue structure of white matter in normal or diseased brain in vivo. DTI is estimated from a series of Diffusion Weighted Imaging (DWI) volumes. DWIs suffer from a number of artifacts which mandate stringent Quality Control (QC) schemes to eliminate lower quality images for optimal tensor estimation. Conventionally, QC procedures exclude artifact-affected DWIs from subsequent computations leading to a cleaned, reduced set of DWIs, called DWI-QC. Often, a rejection threshold is heuristically/empirically chosen above which the entire DWI-QC data is rendered unacceptable and thus no DTI is computed. In this work, we have devised a more sophisticated, Monte-Carlo (MC) simulation based method for the assessment of resulting tensor properties. This allows for a consistent, error-based threshold definition in order to reject/accept the DWI-QC data. Specifically, we propose the estimation of two error metrics related to directional distribution bias of Fractional Anisotropy (FA) and the Principal Direction (PD). The bias is modeled from the DWI-QC gradient information and a Rician noise model incorporating the loss of signal due to the DWI exclusions. Our simulations further show that the estimated bias can be substantially different with respect to magnitude and directional distribution depending on the degree of spatial clustering of the excluded DWIs. Thus, determination of diffusion properties with minimal error requires an evenly distributed sampling of the gradient directions before and *after QC.*

Keywords: Diffusion Tensor Imaging, Quality Control and Monte Carlo Simulation.

1. INTRODUCTION

Diffusion tensor imaging (DTI) has become increasingly popular in the neuroimaging community due to its ability to non-invasively characterize the microscopic tissue structures of white matter in-vivo [1]. Diffusion of water molecules inside the white matter tissues can describe the interactions of molecules with many obstacles such as cell membranes, fibers and macro molecules. Understanding such interactions is vital for tractography of fiber bundles. In order to quantify the water diffusion within various brain tissues, a "diffusion coefficient" parameter is defined in DTI. The rate and directionality of diffusion are then extracted from this coefficient and represented by FA and PD measurements respectively. The diffusion coefficient is estimated from a set of Diffusion Weighted Images (DWIs) by using several non-collinear (at least 6) diffusion sensitizing *gradients* [2].

As theoretical work characterizing DTI grows, it is essential to increase its practical usability from a clinical environment perspective [3]. Inherently, DWI images suffer from a vast variety of artifacts as results of the acquisition sequence, magnet field strength, gradient amplitude, and "slew rate" as well as multichannel radio-frequency coils and parallel imaging [4]. Furthermore, the acquisition time for diffusion MRI is longer than conventional MRI due to the need for multiple acquisitions to obtain directionally encoded Diffusion Weighted Images (DWI). This leads to increased motion artifacts and reduced signal-to-noise ratio (SNR). Therefore, in a clinical environment, this imaging technique needs additional processes such as appropriate QC assessment methods to increase its practical usability.

The DWI-QC techniques aim to detect and correct these artifacts including inter/intra-slice intensity change [5], venetian blind [5], dropout signal intensities and vibration artifacts [6, 7] and eddy-current and motion artifacts [8, 5]; prior to tensor estimation. It is important to note that there are some pitfalls associated with these QC approaches [9] in the result

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of QC. The correction processes modify a configuration of gradient sampling from a scan either by changing the gradient's directions or excluding individual DWI's along a subset of the gradients due to artifacts. Nevertheless, no systematic studies have been performed to investigate the introduced bias after applying QC processes. In one of the few studies in this regard, Muller et al. [10] reported a relatively low change in FA due to excluded volumes in a subset of scans from the TrackHD study. The introduced bias allows making a decision whether the entire DWI-QC data is rendered unacceptable or acceptable. Often, a threshold level for DWI exclusion is considered above which the DWI-QC data is rendered unacceptable and thus no DTI is computed. This threshold is usually chosen heuristically and empirically and its value depends on the objectives of a particular study. However, such eliminative correction processes can produce uncorrelated bias in tensors properties such as FA and PD which is ignored by the existing empirical QC thresholds.

In this work, we propose a simulation-based DTI QC to assess the resulting tensor properties from DWI-QC techniques. We define two error metrics based on the *directional distribution* of bias for FA and PD. These metrics can provide a promising benchmark for post-QC assessment of the remaining DWIs. In each iteration of MC, first, the true tensor is rotated randomly. Then, given the signal-to-noise ratio (SNR) level of choice, an appropriate Rician noise is added to the signal intensity along each gradient direction. These noisy signals are then used to compute the noisy tensor. The measurement error is computed as the difference between the true tensor and this noisy measured tensor. Similarly, diffusion parameters such as FA and PD are computed from the noisy tensor and compared to their true values. Based on our simulation results, we introduce rejection metrics (thresholds) with respect to magnitude and directional distribution of bias for FA and PD.

In experimental results, we applied our method on acquisition schemes and also individual scans post-QC. These results show that the proposed rejection metrics provide an effective assessment of post-QC individual scan and also acquisition protocols. Furthermore, our results confirm that higher degrees of uniformity in the sampling gradients results in lower overall bias. Thus, determination of diffusion properties with minimal error requires an evenly distributed gradient directions before and *after* QC. This method will be incorporated in our *DTIPrep* software, which is an open-source package[1], used for QC of DWI/DTI data.

2. METHOD

2.1 Tensor Simulation

The estimated diffusion tensor can be understood as a function of observed diffusion-weighted MR intensities via the Stejskal-Tanner equation:

$$S_i = S_0 \exp(-b\boldsymbol{g_i}\boldsymbol{D}\boldsymbol{g}_i^T),$$

where S_i is the ideal DWI magnitude, $\boldsymbol{g_i}$ is the ith gradient vector, $\boldsymbol{D}$ is the tensor matrix, b is a constant and S_0 is the baseline signal.

In our MC simulation, the true tensor has a fixed trace $Tr(\boldsymbol{D}) = 2.1\times10^{-3}mm^2/s$, which is a typical value for white matter. Then, the diagonal tensor is simulated with eigenvalues (λ_1, λ_2 and λ_3) computed from FA as follows:

$$\lambda_1 = \left(\frac{\mathrm{Tr}\,(\boldsymbol{D})}{\mathbf{3}}\right)\left(1 + \frac{2\mathrm{FA}}{\sqrt{3 - 2\mathrm{FA}^2}}\right)$$
$$\lambda_2 = \lambda_3 = \left(\frac{\mathrm{Tr}\,(\boldsymbol{D})}{\mathbf{3}}\right)\left(1 - \frac{\mathrm{FA}}{\sqrt{3 - 2\mathrm{FA}^2}}\right).$$

The simulations use a b-value of 1000 s/mm^2 and a baseline signal of 250. The chosen anisotropy level is 0.4 for adult

[1] http://www.nitrc.org/projects/dtiprep

data and smaller levels of anisotropy should be used for neonate data (0.3 or 0.25). A total 200,000 iterations are performed for the entire experimental results.

2.2 Noise Modeling

Diffusion weighted images are acquired by computing the magnitude of the Fourier transform of a measured k-space signal. The thermal noise associated with real and imaginary components of k-space are called Johnson noise and approximated by two zero-mean Gaussian noise generators (N_1 and N_2) with a standard deviation of σ. The noise in the magnitude signal is characterized by a Rician distribution as per following formula to arrive at biased S_i:

$$S_i' = \sqrt{(S_i + N_1)^2 + N_2^2}, \qquad N_1, N_2 \sim N(0, \sigma^2).$$

where S_i is the ideal DWI magnitude in the absence of noise and S_i' is the noisy DWI component given by MRI scanner. In our simulation results, the Rician noise level is chosen based on computed experimental SNR in images with no diffusion. Now, we can use noisy S_i' to compute the biased tensor. We have used the linear least-square method to estimate the noisy tensor.

2.3 Rotation Simulation

We have embedded a rotation procedure in the Monte Carlo simulation where the original diagonal tensor $\boldsymbol{D}$ is rotated to predetermined uniformly distributed points on a sphere. The method that selects random points from uniform distributions of latitude and longitude will fail, since latitudes have different circumference and cause differential area varying. Thus, the picked points are inordinately numerous near the poles and sparse at the equator. In order to select uniform points in a sphere, first we have generated uniformly distributed points on a sphere using Cook et. al. [3] theorem; If φ and u are random variables with uniform distribution such that, $0 \le \varphi \le 2\pi$, $-1 \le u \le 1$, then the following coordinates point to uniformly distributed points on the surface of a sphere:

$$\begin{aligned} x &= \sqrt{1-u^2}\cos\varphi\ , \\ y &= \sqrt{1-u^2}\sin\varphi\ , \\ z &= u\ . \end{aligned}$$

Our rotation algorithm follows two steps: (1) we rotate the tensor around its principal direction by a random angle $[0, 2\pi]$ and (2) we rotate the tensor by the angle between its principal direction and the vector represented by the mentioned point around their cross product. The first step of the rotation can be removed if we assume that $\lambda_2 = \lambda_3$. Fig. (1-a) demonstrates the rotation steps and its concept.

2.4 Error Criteria

We have introduced two error metrics associated with FA and PD measurements for evaluating differences between the simulated (noise-free) and estimated tensor (noisy) after uniformly rotating the tensor. We have defined error-based directional distributions implemented by quasi-uniform icosahedron subdivision, in which the triangular faces of an icosahedron are linearly or recursively subdivided into smaller triangles whose vertices are projected to the unit sphere. The vertices of the icosahedron subdivision are binning PDs from the simulated tensors using nearest-based algorithm; and express the error values. The angle between the simulated principal direction and the estimated principal direction is computed as the error associated with the PD. The difference between the true FA value and the estimated FA value is assigned as the error of FA measurement. After finishing MC iterations, each vertex carries two error lists. Fig. (1-b) shows the directional distribution implementation of error-metrics in the icosahedron subdivision system. The spherical histogram of the error metrics shows whether there are non-random patterns in error distributions (see Fig. 2 and Fig. 3). If the error histogram follows uniform distribution, it means that the given gradients sampling does not introduce bias in tensor estimation and likewise DTI statistical analysis. It is noted that to evaluate FA error, it is required to use a measurement to support the non-linear domain of FA. Thus, the mean-square-error measurement cannot be appropriate. Assuming that a large enough number of MC iterations are considered, we computed median-square-error between the given noise-free tensor and the estimated noisy tensor.

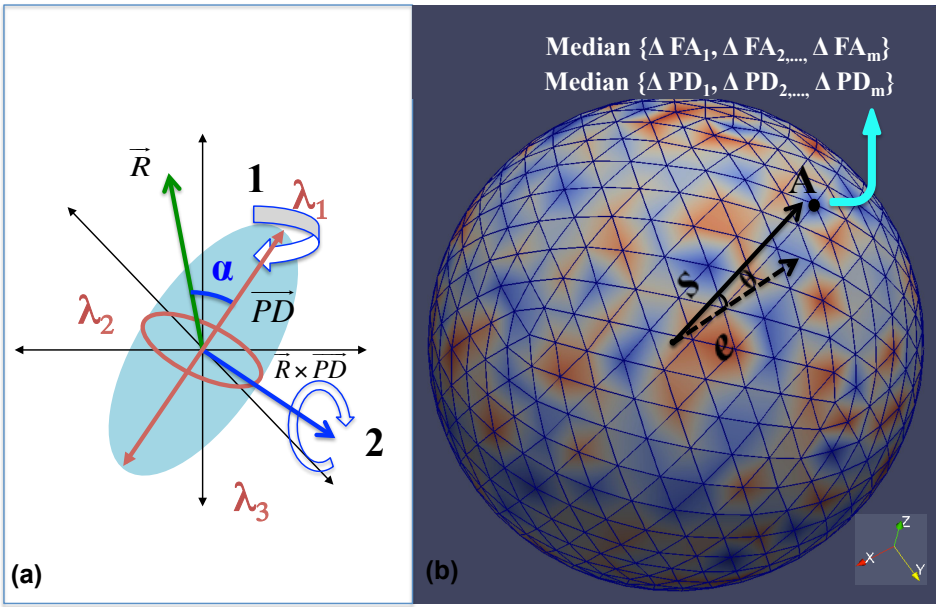

Figure 1: (a) the uniform rotation of a tensor steps (**1** and **2**). (b) the directional distribution implementation of error metrics using quasi-uniform icosahedron subdivision. The simulated principal direction ($\vec{s}$) is binned in vertex *A* using nearest-vertex based binning. The angle between the simulated principal direction and the estimated principal direction ($\vec{e}$) is computed ($\theta \in [0,\pi/2]$) as an error associated with the PD binned in vertex *A*.

3. EXPERIMENTAL RESULTS

3.1 Acquisition Protocols Bias Analysis

Based on the MC simulation, the proposed error metrics allow DTI-based analysis studies to select the best gradient sampling scheme for image acquisition; and robust estimation of anisotropy and PD orientation. Fig. (2, a-c) shows three different schemes with different levels of uniformity: a quasi-uniform distribution with 42 gradients [4], Phillips 32-direction non-uniform, and a uniform icosahedron-distribution with 6 gradients. The MC simulation results show estimated bias distribution in the PD (Fig. 2, d-f) and FA (Fig.2, g-i). A high clustering pattern in error distribution of FA and PD in the non-uniform 32-gradient scheme is observed, although the number of gradients is larger than a uniform 6-gradient scheme. The ugly fact is that the Phillips scheme has been used in DTI analysis studies published in many prestigious journals [5]. On the other hand, the quasi-uniform 42-scheme conveys highly satisfactory results in both metrics of FA and PD.

3.2 Scan-specific Bias Analysis

The proposed error metrics associated with FA and PD measurements are also used to quantify the introduced bias after applying quality control processes for individual and group scans. As a quality control process, scans end up with a modified configuration of gradient sampling. The modification is caused by correction methods via changing gradient directions (such as eddy motion correction [5,8]) or excluding a set of gradients affected by artifacts (such as vibration artifacts [7]) and changing the gradients distribution on a scan-specific basis. A different gradient distribution means a different degree of uniformity and therefore a different amount of expected bias in the diffusion properties estimated from the scan. In our experiment, we chose two scans acquired by the same protocol. The acquisition protocol employs seven b = 0 and 42 gradient directions quasi-uniformly spaced with single *b-value* = 1100 s/mm^2 at a resolution of 2 isotropic. The scans were processed for quality control including gradients exclusion affected by slice-wise and gradient-wise intensity disruption, vibration artifact and eddy current, head motion correction and noise filtering. Fig. 3 shows the estimated error merits for these scans with different uniformity level of sampling in the survived gradient directions. One

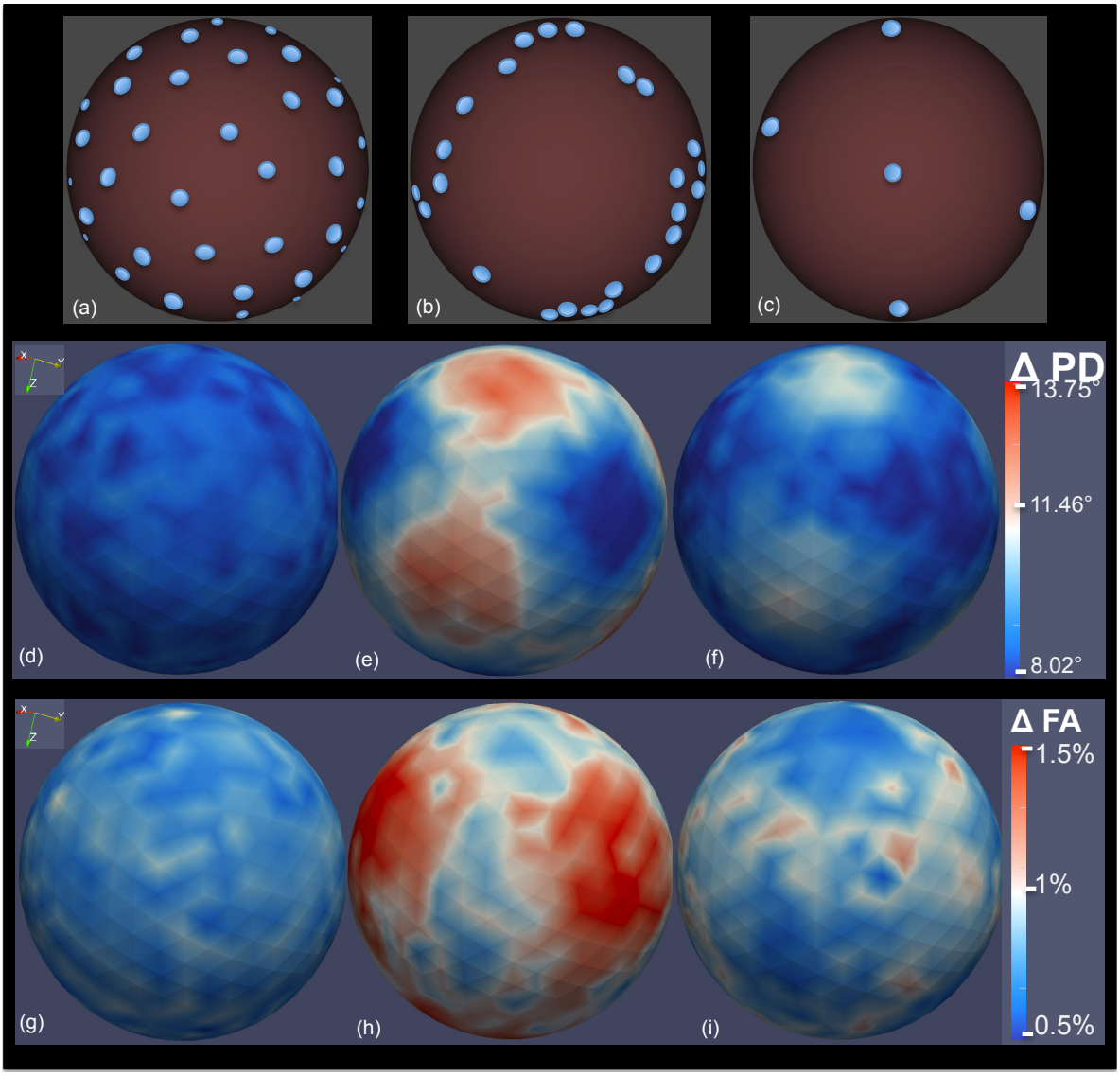

Figure 2: Bias analysis of different DWI schemes via MC simulation. (a-c) Gradient direction distribution for 3 acquisition schemes: 42-direction quasi-uniform, Phillips 32-direction non-uniform, and 6-direction uniform. (d- f) Estimated error distribution in PD computation. (g-i) Estimated error distribution in FA computation as a percentage of true FA. Number of iteration 200,000, true FA value of 0.4 and SNR = 10.

scan displayed various intensity artifacts; the QC processes excluded 20% of the gradient directions (Fig. 3a). The second scan shows a moderate vibration artifact where also 20% of the gradient directions were removed during QC. However, the gradient directions, removed due to the vibration artifact, were mostly clustered along a single plane (Fig. 3b). The bias analysis shows that the non-uniform distribution of the remaining gradients leads to a strong bias in the estimation of both the PD (Fig. 3c) and the FA (Fig. 3d). It is shown that the scan with clustered exclusions in gradient directions suffers more bias-related patterns in the directional error distribution of FA and PD.

3.3 Rejection Metrics

Knowing the propagated bias of estimated tensor properties as rejection metrics of individual post-QC scans helps DTI studies to avoid unexpected and inconsistent results during analysis. Depending on the application and study targets, we

introduced two rejection metrics defined by the 90th percentile of our proposed error distributions of FA and PD. In an anisotropy-based analysis such as Tract-Based Spatial Statistics (TBSS) [6] applications, rejection threshold from FA error distribution is 1% (see Fig. 3-d). On the other hand, in tractography-based analysis, the rejection threshold mainly depends on error distribution of PD and is set as 10° (see Fig. 3-c). This interpretation is also important for selecting the appropriate acquisition scheme protocol. For example, while the uniform 6-gradient scheme may not be an attractive choice for studies based on tractography, it could be used for studies based on the analysis of tissue anisotropy properties (see Fig. 2-f,i). On the other hand, for both tractography and anisotropy studies, the quasi-uniform 42-scheme would be the best scheme, (see Fig. 2-g,d) and the non-uniform 32-scheme would be the worst among the compared schemes (see Fig. 2-e,h).

4. DISCUSION AND CONCLUSION

In this paper, we proposed a simulation-based DTI QC approach that defines rejection/acceptance thresholds for individual post-QC scans via assessing the propagated bias of tensor properties from remaining QCed DWIs. Based on our MC simulation, the bias is estimated by finding the error-difference between simulated and estimated tensor properties associated with FA and PD measurements. Then, two error metrics were defined with respect to the directional distribution of bias for these measurements. According to our results, the rejection threshold is 1% from the FA bias distribution for FA-based applications and up to 10° from PD bias distribution for tractography-based studies. Furthermore, our experimental results demonstrated that determination of diffusion properties with minimal error requires an evenly distributed sampling of the gradient directions (DWIs) before and *after QC*.

While there are other approaches for deriving the samples on the sphere, such as the electrostatic repulsion model [15], the exact distribution of these bins is not crucial to the work, since they are merely used as histogram bins for understanding the proper rejection/acceptance thresholds; in this sense, any approximately even distribution of the samples is adequate. The icosahedron subdivision method is faster and has more straightforward implementation and therefore it is more suitable for our aims.

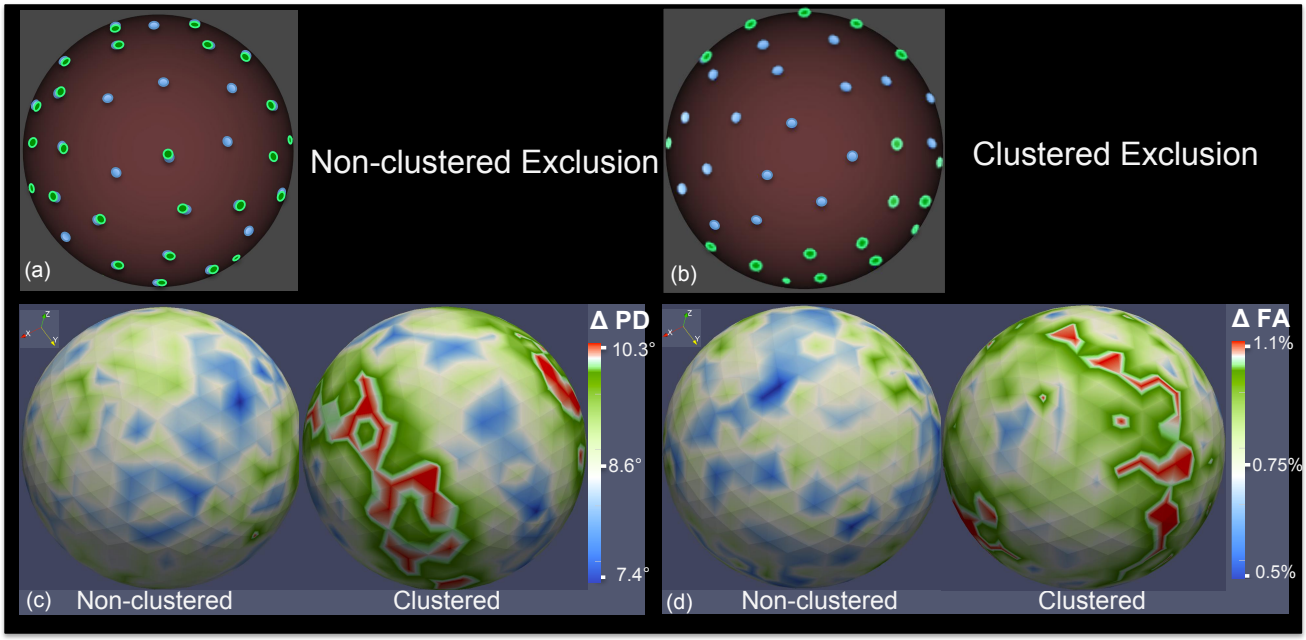

Figure 3: Scan-specific bias analysis via MC simulation. **(a-b)** The gradient direction distribution after excluding 20% of the total number of gradients due to artifacts, in two configurations: non-clustered and clustered exclusion (blue: excluded gradients, green: included gradients). **(c)** Estimated error distribution of PD computation given the gradient sampling schemes in (a) and (b). **(d)** Estimated error distribution in FA computation, shown as percentage of true FA. MC simulation was performed for 200,000 iterations for this experiment, with a true FA value of 0.4 and SNR = 10.

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