Signal-to-noise assessment for diffusion tensor imaging with single data set and validation using a difference image method with data from a multicenter study

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Purpose: To describe a quantitative method for determination of SNR that extracts the local noise level using a single diffusion data set.

Methods: Brain data sets came from a multicenter study (eight sites; three MR vendors). Data acquisition protocol required $b = 0$, 700 s/mm^2 , $\text{fov} = 256 \times 256 \text{ mm}^2$, acquisition matrix size 128×128 , reconstruction matrix size 256×256 ; 30 gradient encoding directions and voxel size $2 \times 2 \times 2 \text{ mm}^3$. Regions-of-interest (ROI) were placed manually on the $b = 0$ image volume on transverse slices, and signal was recorded as the mean value of the ROI. The noise level from the ROI was evaluated using Fourier Transform based Butterworth high-pass filtering. Patients were divided into two groups, one for filter parameter optimization ($N = 17$) and one for validation ($N = 10$). Six white matter areas (the genu and splenium of corpus callosum, right and left centrum semiovale, right and left anterior corona radiata) were analyzed. The Bland–Altman method was used to compare the resulting SNR with that from the difference image method. The filter parameters were optimized for each brain area, and a set of “global” parameters was also obtained, which represent an average of all regions.

Results: The Bland–Altman analysis on the validation group using “global” filter parameters revealed that the 95% limits of agreement of percent bias between the SNR obtained with the new and the reference methods were -15.5% (median of the lower limit, range $[-24.1\%, -8.9\%]$) and 14.5% (median of the higher limits, range $[12.7\%, 18.0\%]$) for the 6 brain areas.

Conclusions: An FT-based high-pass filtering method can be used for local area SNR assessment using only one DTI data set. This method could be used to evaluate SNR for patient studies in a multicenter setting. © 2014 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4893195>]

Key words: SNR, quality control, diffusion tensor imaging, multicenter study

1. INTRODUCTION

Diffusion tensor imaging is sensitive to pathologic processes affecting white matter of the brain. To detect subtle changes, quantitative analysis of DTI metrics such as fractional anisotropy and axial and radial diffusivities are measured.^{1–3} However, these DTI metrics are subject to high uncertainties and bias caused by noise in the images.^{4–7} Seo *et al.* have reported SNR requirements for various anatomical areas of the brain and FA values for bias-free estimation of tensor metrics.⁸ Thus, documentation of adequate SNR is needed for accurate and reproducible measurements. This is especially important in a multicenter study, where the central data processing site bears the responsibility of quality control screening with little information on the performance of the MR scanners at each site on a day to day basis. DTI is commonly acquired with parallel imaging techniques using array head coils where the noise level is a function of spatial loca-

tions and cannot be assessed from background areas.^{9,10} SNR should be determined within the specific area of white matter under investigation as SNR measured at the periphery of the brain is not representative of that at the center. One valid approach for SNR evaluation in this situation is the difference image method where a noise image is obtained by taking the difference of two identically acquired images.^{11–13} However, this approach is not applicable if only one data set is available in a study. Therefore, the aims of this work are to develop a method based on high pass filtering in k-space for evaluating the noise level at localized brain areas in DTI using one data set only and to validate this approach using the difference method.

2. MATERIALS AND METHODS

Diffusion data sets collected in Child Oncology Group AALL06N1 study were used. Studies were stripped of

TABLE I. Patient information and group assignment.

Group	Number and gender	Age (years)	Scanner used in study
Entire cohort	27 (15 females)	Minimum = 5; maximum = 20; mean $\pm$ S.D. = 13.0 ± 4.3	17 Philips; 8 GE; 2 Siemens
Optimization group	17 (9 females)	Minimum = 6; maximum = 0; mean $\pm$ S.D. = 13.1 ± 4.1	11 Philips; 5 GE; 1 Siemens
Validation group	10 (6 females)	Minimum = 5; maximum = 20; mean $\pm$ S.D. = 13.0 ± 5.0	6 Philips; 3 GE; 1 Siemens

identifying data, and the investigation was HIPAA compliant. This was a multicenter study of neurocognitive function in children treated with methotrexate for acute lymphoblastic leukemia. The patients had no known significant neurodevelopmental disability unrelated to cancer diagnosis. These patients may have had normal or moderately decreased fractional anisotropy in cerebral white matter.¹⁴ The DTI protocol required scans to be done on a 1.5 T scanner, $2 \times 2 \times 2$ mm³ isotropic acquisition voxel, $b = 0$ and 700 s/mm², the “Jones30” diffusion encoding scheme¹⁵ with $b = 0$ volume acquired 5 times and averaged, fov = 256 mm, TR/TE = 8292/100 ms, parallel imaging with an acceleration factor of 2. The DTI scan was repeated three times without signal averaging and saved as three separate data sets. Images were received in DICOM format and were identified by a COG number and MRI study date. The DICOM DTI images were converted to the data format of one vendor and were linearly registered against the $b = 0$ volume of one acquisition on an offline computer.¹⁶ The SNR analyses were performed with internally developed software written in IDL 8.2 (Exelis VIS, www.exelisvis.com).

Data came from eight sites involving three major MRI vendors (one Siemens sites, four GE sites, and three Philips sites) that were compliant to the imaging protocol. Patients were divided into two groups, one for method optimization and one for validation. Table I contains details of patient gender and age, group division, and distribution among MRI scanners.

We evaluated the SNR in six white matter areas: the genu and splenium of corpus callosum (GCC and SCC), right and left centrum semiovale (CS), and right and left anterior corona radiata (ACR). The fractional anisotropy at the GCC was of interest for the COG AALL06N1 study, and the FA findings of this area are frequently reported in the literature. The centrum semiovale contains several important white matter tracts including the superior longitudinal fasciculus, corticospinal, and corticopontine tracts. The ACR is an area of crossing fibers. The GCC typically has an area of 100 mm² on one transverse slice for adults, corresponding to 25 acquisition voxels. The noise level measured from 25 independent voxels, e.g., from data of a single diffusion direction or $b = 0$ image, has poor reproducibility due to the low voxel count with the 95% confident interval from 72% to 128% of the true value based our Monte Carlo simulation assuming random Gaussian noise. More robust and reproducible noise level estimations can be obtained by analyzing diffusion weighted images, particularly for high angular resolution diffusion imaging, due to the large number of image volumes. In addition, areas across multiple adjacent slices were combined to form a single ROI for the SNR analysis to further increase the statistical power

(two slices were combined for centrum semiovale and four slices for all other areas). The ROIs were manually drawn on the $b = 0$ image volume (Fig. 1). The noise level for the ROI was estimated with both a difference image method and a single data set method.

2.A. Difference image method

Three difference images were calculated by pairwise subtraction of the three data sets for each patient. We call the pair of image sets with the least residual signal as image set 1 and set 2, and only these data were used for subsequent analyses. The noise variance of the diffusion weighted subtraction image within the ROI was calculated for all encoding directions, and an average noise variance $V_{\text{noise_diff}}$ was then obtained. The final SNR for the image set 1 or 2 is given by

$$\text{SNR}_{\text{diff}} = \frac{\sqrt{2} \cdot S_0}{\sqrt{V_{\text{noise_diff}}}}, \quad (1)$$

where S_0 is the average signal of the ROI in the $b = 0$ image volume.

2.B. Single data set method

The noise level of the ROI in each diffusion weighted image volume was obtained with the following steps. Each amplitude image slice containing the ROI was first transformed to the k -space domain with a matrix size of 256×256 . The central 128×128 subarray of the k -space contained the

FIG. 1. ROIs for SNR assessment were manually traced on $b = 0$ images to include white matter only. (a) ROIs for right and left ACR, GCC, and SCC. Each ROI combined image pixels from four adjacent slices. Slices at different levels may be used for these ROIs in one patient. (b) ROIs for right and left CS. Each ROI combined image pixels from two adjacent slices.

acquired data before zero-filling. Because the brain structures within the ROI are smooth, we assumed that the signal is distributed in the center of k -space, and noise could be evaluated from the peripheries of k -space. A high pass Butterworth filter¹⁷ was then applied in k -space

$$F(k_x, k_y) = \frac{F_0}{\sqrt{1 + (k_c^2 / (k_x^2 + k_y^2))^n}}. \quad (2)$$

Here $k_x = (2\pi/\text{fov}) \cdot i$, $k_y = (2\pi/\text{fov}) \cdot j$ ($i, j = -127, -126, \dots, 128$), n and k_c are the order and cut-off value of the filter, respectively; F_0 is a normalization factor accounting for the loss of noise from the central area caused by the application of the filter. Theoretically, F_0 should be chosen such that the average value of $F(k_x, k_y)^2$ over the k -space is one. This will ensure that the total noise variance remains the same after filtering for uniform noise distribution in k -space. In reality, however, F_0 can be adjusted to obtain the best agreement between the single set method and the reference SNR measurement. The filtered k -space data were then inversely Fourier Transformed back to image space, and an amplitude noise image was obtained. The noise variance within the ROI was calculated. This procedure was repeated for all diffusion encoding directions, and an average noise variance V_{noise} was obtained. Finally, the SNR of the ROI was given by

$$\text{SNR}_{\text{single set}} = \frac{0.655 \cdot S_0}{\sqrt{V_{\text{noise}}}}, \quad (3)$$

where S_0 is the average signal of the ROI in the $b = 0$ image volume, and 0.655 is a correction factor because the noise follows a Rayleigh distribution after our processing.¹⁸ In this work, the single data set method was only used on diffusion weighted images. For $b = 0$ volume, the filter did not remove the CSF signal, which is bright and not limited to the vicinity of k -space center.

2.C. Statistical analysis and filter optimization

The difference between the single data set and the difference image approaches were evaluated using the Bland–Altman method,¹⁹ where we used the percent difference SNR and average SNR as the vertical and horizontal axis

$$\Delta_{\text{SNR}} \% = \frac{2 \cdot (\text{SNR}_{\text{single set}} - \text{SNR}_{\text{diff}})}{(\text{SNR}_{\text{single set}} + \text{SNR}_{\text{diff}})} \cdot 100\%$$

$$\text{AV}_{\text{SNR}} = (\text{SNR}_{\text{single set}} + \text{SNR}_{\text{diff}})/2. \quad (4)$$

For each ROI the parameters of the Butterworth filter, k_c and n were varied in searching for the minimum standard deviation of $\Delta_{\text{SNR}} \%$ of the whole optimization group. F_0 was adjusted so that the group mean of $\Delta_{\text{SNR}} \%$ is below 0.05%. Results of Bland–Altman analysis were reported in terms of 95% limits of agreement (mean $\pm 1.96 \cdot \text{SD}$, assuming a Gaussian distribution).

Based on the optimal results of all ROIs, the weighted average values of F_0 , k_c , and n were calculated as “global” optimal values, which were tested for all ROIs. The $1/(\text{S.D. of } \Delta_{\text{SNR}} \%)^2$ of each area from the optimization group was used

as weighting for the average, and $\log(n)$ was used in calculating the average n value.

2.D. Phantom studies

Phantom studies were conducted to compare the SNR obtained from the difference image method and the high-pass filtering method. An ACR head phantom was scanned on a Philips 1.5 T Achieva MRI scanner using the patient study protocol. Nine circular ROIs with a diameter of 30 mm were evaluated, each consisting of identical areas across four consecutive slices from the uniform section of the phantom near and at ACR Slice 7.²⁰ There was one ROI at the center of the slice and the other 8 ROIs uniformly distributed on a circle 55 mm from the center. Data from two different days were combined for statistical analysis. Similar to the study on patient data, noise was assessed from diffusion weighted images only.

3. RESULTS

3.A. Patient data study

The received DTI data may have minor deviations of the acquisition parameters such as the use of a 32 direction encoding scheme, slightly thicker slices (up to 2.4 mm), and slightly smaller FOV (250 mm). These minor inconsistencies with the protocol did not lead to exclusion of the data. Table II lists the median and range of SNR for each brain area that was studied. Information on the ROI size is also included.

In general, a wide range of filter parameters yields reasonable results. Figure 2 shows the optimization of k_c and n for the GCC. Table II also lists the optimal filter parameters and the resulting limits of agreement for each brain area that we studied. The column on the far right lists the average filter parameters and the resulting limits of agreement (LOA) for each area. Figure 3 shows the Bland–Altman plot comparing $\text{SNR}_{\text{single set}}$ and SNR_{diff} at GCC using locally optimal and globally averaged filter parameters for both the optimization group and the validation group.

3.B. Phantom study

For ROIs on phantom DTI images, SNR_{diff} ranged from 23.3 to 37.7, with a median value of 35.9. The optimal filter parameters were $k_c = 10 \cdot (2\pi/\text{fov})$, $n = 100$, and $F_0 = 1.062$, yielding 95% limits of agreement of percent difference SNR from -7.7% to 7.7% using the Bland–Altman method. Using the globally optimized parameters in Table II from patient data, the 95% limits of agreement were -3.2% to 16.4% .

4. DISCUSSION

SNR assessment is important if quantitative measurement of DTI metrics is performed. Regional image noise is usually measured using the difference image of two data sets.

TABLE II. ROI pixel count, filter parameters, and the agreement between $\text{SNR}_{\text{single set}}$ and SNR_{diff} for the optimization group.

Area and group	SNR_{diff} (median, [range])	ROI pixel count (mean $\pm$ SD)	ROI specific filter optimization		Averaged filter optimization ($k_c = 24.8$, ^a $n = 3.1$, $F_0 = 1.136$)
			k_c , ^a n , F_0	95% LOA	95% LOA
GCC,OG	8.7, [5.5, 12.5]	634 $\pm$ 113	27.5, 3, 1.164	− 14.5%, 14.5%	− 16.7%, 12.9%
GCC,VG	9.5, [5.0, 14.1]	684 $\pm$ 84	27.5, 3, 1.164	− 14.2%, 16.1%	− 15.7%, 14.5%
SCC,OG	9.5, [7.3, 11.1]	823 $\pm$ 180	30, 1, 1.170	− 16.4%, − 16.4%	− 19.5%, 15.1%
SCC,VG	9.8, [7.9, 12.2]	865 $\pm$ 176	30, 1, 1.170	− 24.4%, 15.8%	− 24.1%, 12.7%
Lt-CS,OG	11.2, [8.2, 14.2]	1717 $\pm$ 366	17.5, 5, 1.050	− 12.4%, 12.4%	− 10.2%, 15.4%
Lt-CS,VG	12.4, [7.6, 16.7]	1634 $\pm$ 373	17.5, 5, 1.050	− 13.4%, 10.6%	− 8.9%, 13.1%
Rt-CS,OG	11.3, [8.3, 14.6]	1741 $\pm$ 306	25, 2, 1.156	− 12.9%, 12.9%	− 12.3%, 13.7%
Rt-CS,VG	11.9, [6.9, 15.8]	1579 $\pm$ 363	25, 2, 1.156	− 15.2%, 17.7%	− 13.8%, 18.0%
Lt-ACR,OG	12.0, [6.9, 18.1]	874 $\pm$ 163	22.5, 10, 1.093	− 16.9%, 16.9%	− 15.8%, 18.2%
Lt-ACR,VG	11.4, [5.4, 18.8]	887 $\pm$ 226	22.5, 10, 1.093	− 17.3%, 13.7%	− 15.2%, 14.4%
Rt-ACR,OG	12.2, [6.3, 20.7]	930 $\pm$ 203	30, 3, 1.217	− 15.8%, 15.8%	− 18.2%, 14.2%
Rt-ACR,VG	11.0, [6.6, 19.5]	885 $\pm$ 143	30, 3, 1.217	− 16.4%, 18.8%	− 18.5%, 17.2%

^a k_c in units of $(2\pi/\text{fov})$; LOA = limits of agreement; GCC = Genu of corpus callosum; OG = optimization group; VG = validation group; SCC = splenium of corpus callosum; CS = centrum semiovale; ACR = anterior corona radiata; Lt = left; Rt = right.

However, in many studies, only one data set is available especially in high angular resolution studies²¹ or Q-ball imaging.²² Therefore, an alternative method not based on the difference of two data sets is desirable, and this work fills this gap in the method of image quality control for DTI.

An area of interest for SNR assessment can be small (e.g., in the case of genu of corpus callosum), and the noise level quantified using only the $b = 0$ image will have large variances. Therefore, we used diffusion weighted images to improve the statistical power and reliability of the noise estimation. We assumed that the noise level is the same for both $b = 0$ and diffusion weighted images,²³ despite the fact that signal levels are very different. This assumption was verified by our phantom study. Furthermore, the SNR of Eqs. (1) and (3) did not include the effects of signal averaging of the $b = 0$ image volume within each data set, which was performed during the data acquisition from the multicen-

ter study. Therefore, if the $b = 0$ image is acquired 5 times and then averaged in the pulse sequence, such as being specified in our study protocol and considered by Seo *et al.*,⁸ the values presented here will need to be multiplied by $\sqrt{5}$ to obtain the actual SNR of the $b = 0$ image.

Our patient data were acquired from scanners of different vendors using different parallel image reconstruction algorithms. Our results showed the k-space filtering method is applicable to this mixed group. Table II revealed that the SNR of the patient data has a variability of a factor of 2–3 within each brain area. The variability of regional SNR across patients highlighted the importance of quality assessment of the patient data in a multicenter study. Our single data set method can be used for SNR assessment when single data sets only are available. However, even in this situation, it is advisable to collect some duplicated images for optimization of filter parameters for a particular pulse sequence or patient population. If this is not possible, or if the DTI protocol is similar to what we used here, the globally averaged parameters in Table II could be used for crude SNR estimates and for SNR comparison of different data sets.

There are potential complications in validating the single data set SNR measurement method using the difference image method for brain DTI. It is known that diffusion weighted images are prone to physiological noise arising from local tissue motion where signal from certain pixels may drastically drop out.²⁴ Physiological noise is large, unpredictable and unreproducible. Consequently, the noise in a single data set and in the subtracted images from two data sets can be quite different. Therefore, disagreements between the single image set method and the difference image method are expected for diffusion weighted images even if the former works perfectly. For example, it is known that the SCC is an area with particularly large physiology noise and prone to artifacts on DTI.²⁵ The results from our study are consistent with this physiological observation in that larger SNR discrepancies were found in this brain area.

FIG. 2. The optimal k_c and n for the Butterworth filter at GCC were determined on the optimization group consisting of 17 patients. Here, n is the order of the filter; k_c is the cutoff spatial frequency in units of $(2\pi/\text{fov})$. The minimum SD of $\Delta\text{SNR}\%$ (7.4%) was found at $n = 3$, $k_c = 27.5$.

FIG. 3. Bland–Altman plots for GCC: (a) filter parameters were locally optimized for the optimization group; (b) globally averaged filter parameters were used on the optimization group; (c) locally optimized filter parameters were used for the validation group; (d) globally averaged filter parameters were used on the validation group.

5. CONCLUSION

A method for SNR assessment of white matter on diffusion tensor imaging is described, which does not require difference images. The method was validated using the difference image method on patient data from multiple sites and multiple vendors.

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