Sample of Level 3 Editing

Assessment of Reduced Encoding Diffusion Spectrum Imaging Implemented with a Bi-Gaussian Model Using Phantoms and Manganese-Enhanced Optic Tracts

Abstract

Diffusion spectrum imaging (DSI) can map complex fiber microstructures in tissues by characterizing their 3-D water diffusion spectra. However, a long acquisition time is required for adequate q-space sampling to completely reconstruct the 3-D diffusion probability density function (PDF). Furthermore, to achieve a high q- or b-value encoding for sufficient spatial resolution, the diffusion gradient duration and diffusion times are usually ~~enlarged~~ lengthened on a clinical scanner, ~~which~~ results~~ings~~ in a long echo time and low signal-to-noise ratio (SNR) of diffusion images. To bypass long acquisition times and ~~strong~~ strict gradient requirements, the reduced-encoding DSI with a bi-Gaussian diffusion model (RE-DSI) is presented in this study. The bi-Gaussian extrapolation kernel, ~~which is~~ based on the assumption of a bi-Gaussian diffusion signal curve~~s~~ across biological tissue~~s~~, is performed to fulfill a high q-value ~~request~~ requirement on the reduced-encoding scheme. ~~Both~~ The intersecting capillary~~ies~~ phantom model~~s~~ and the manganese-enhanced rat model~~s~~ ~~were~~ served as standards for accuracy assessment in RE-DSI. ~~, the~~ The errors of RE-DSI in defining fiber orientation were quantified

Comment [WL1]: CHECK:
"…served as standards" for what? I think you might mean they "served as standards for accuracy assessment in RE-DSI". This is used later in the article.

and the results were found to be close to the noise limit. Evidence~~s~~ from a human study demonstrated that RE-DSI significantly decreased the acquisition time~~s,~~ required to ~~meanwhile~~ resolve ~~d~~ complex neural fibers. The presented acquisition method facilitates the application ~~s~~ of DSI analysis on a clinical magnetic resonance imaging (MRI) system.

Keywords: diffusion spectrum imaging; phantom model; manganese-enhanced rat model

Introduction

Diffusion MRI has become an essential tool for contrast imaging ~~mechanism~~ of the ~~for~~ central nervous~~e~~ system. This~~,~~ has led to~~ and made~~ ~~a~~ significant improvement in clinical diagnosis. Further ~~progress~~advancement to the technique has been made with the ~~design~~introduction of diffusion tensor imaging (DTI) [1, 2],~~The technique makes further progress along with the design of diffusion tensor imaging (DTI) [1, 2], which is~~ a ~~feasible~~ valuable technique ~~for~~in identifying ~~to model~~ anisotropic diffusion as well as non-invasively ~~to~~ delineat~~e~~ing the principle orientations of white matter tracts ~~non-invasively~~ [3-5]. ~~.~~However, the assumption~~,~~ of a single Gaussian diffusion ~~compartment~~ component in the tensor model results in the ambiguous orientation~~s~~ of fibers in regions where they cross each other ~~containing crossing fibers~~ [6]. Thus,~~, it~~ with the typical resolution of a MRI, it may be ~~becomes intricate~~ difficult to interpret the complex neural connections between functional areas of ~~a~~the human brain~~ with under typical resolution of an MRI~~.

In recent years, various diffusion imaging strategies have been developed to improve the depiction of water diffusion and to resolve the intravoxel fiber orientations.~~.~~ Diffusion spectrum imaging (DSI) [7]~~,~~ for example, utilizes the 3-D spectra of water displacement~~s~~ to characterize the heterogeneity~~ities~~ of fiber architecture~~s~~. DSI ~~was~~is based on the~~Its~~ theory established ~~on~~ by the q-space imaging technique~~.,~~ ~~technique, which~~The theory describes the Fourier relationship

Comment [TK2]: CHECK:
Is this an appropriate word here? Are you saying that it is assumed that there is a single Gaussian diffusion component?

Comment [WL3]: CHECK:
I think you mean “a single Gaussian diffusion component” not “a single Gaussian diffusion compartment”.

between echo signal attenuation and the probability density function (PDF) ~~–~~of the displacement of water molecule~~s~~ ~~displacements~~ with the prerequisite of a narrow pulse approximation [8-10]. The DSI technique ~~was~~has been used ~~in~~to map the ~~mapping~~ tissue architecture of biological systems ~~DSI has shown its capability of mapping tissues architectures in biological systems~~ [7, 11]; specifically, it ~~,~~ provid~~ing~~ed the intravoxel compartment scales of ~~the~~ neural fibers [12], thus allowing ~~and interpreting the~~ physiological and structural conditions of ~~the~~ neural tissues to be interpreted. In addition, 3-D tractography and comparative segmentation of human brain structures have been identified based on DSI and the proceeding orientation distribution function (ODF) [13].~~–~~

Notwithstanding the utility of DSI, a complete reconstruction of the diffusion PDF requires 515 q-value encoding points distributed on a Cartesian lattice across 3-D q-space. This involves long acquisition times as well as adequate~~–~~ ~~–~~q~~–~~values for sufficient resolution. Since the available gradient strength in clinical systems are limited, t~~T~~he latter requirement is achieved by prolonging the diffusion gradient duration (δ) and the diffusion time (Δ) ~~since the available gradient strength in clinical systems is limited~~. Unfortunately, this ~~would accompany~~ leads to a long echo time (TE) and a decline in the SNR~~–~~ ~~level~~ due to a severe T2 decay in ~~an~~the echo

Comment [WL4]: CHECK:
Do you mean “intravoxel component” here instead of “intravoxel compartment?” This follows on throughout the article, do you mean “compartment” or “component”?

Comment [TK5]: CHECK:
This sentence is confusing. It seems you are saying that tractography and comparative segmentation of brain structures were identified with DSI. Then you talk about what appears to be another technique, ODF. However, it is not clear how this technique is related to DSI or was it just another technique used in conjunction with DSI? Consider rewording to clarify. Also, if ODF is another technique (in addition to DSI), which has been helpful in reconstructing tissue structure, it may be good to point that out. At the moment, it doesn’t quite tie into the rest of the paragraph but just appears all of a sudden at the end.

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Comment [TK6]: CHECK:
The meaning of this portion of the sentence is not clear.

Comment [TK7]: CHECK:
Consider not using the word “adequate”. Perhaps use ‘large quantities of’ if that is appropriate.

planar imaging (EPI) sequence. As a consequence of this, ~~The~~ angular accuracy and discrimination ~~would be~~are ~~–~~unavoidably diminished ~~– as a consequence –~~[11]. ~~Both t~~The lengthy acquisition time~~s~~, ~~cost~~ and the requirements of the gradient system~~,~~ ~~request~~ have ~~retarded~~hindered the further application~~s~~ of DSI on clinical scanners. These limitations basically stem~~s~~ from the need to exhaustively sample on a 3-D Cartesian sampling lattice.

A hemispheric encoding scheme (half-q-DSI) ~~could~~ can be applied to halve the scan time in DSI since the ~~the~~ diffusion contrast is positive and spherical~~l~~ (and thus~~y~~ symmetrical) [7, 14]. However, uncorrected cross-term interaction~~s~~s between diffusion and imaging gradients might result in the ~~a misunderstanding~~misinterpretation of the q-space analysis and inaccurate ODFs in half-q-DSI [15, 16]. Instead of a Cartesian lattice, a body-centered cubic lattice (~~BBC~~BCC) sampling scheme ~~is~~was proposed to ~~gain~~ improve the imaging efficiency of DSI by 30% [17]. Another non-Cartesian q-space encoding scheme, ~~H~~hybrid diffusion imaging (HYDI), ~~was~~has also been employed for DSI-PDF reconstruction. This scheme ~~was~~ comprises~~d~~ of five concentric spherical shells and may be applied to multiple types of diffusion analysi~~s~~s [18]. ~~, which is flexible for multiple diffusion analyses, employs a non-Cartesian q-space encoding scheme comprising five concentric spherical shells for DSI-PDF reconstruction.~~ Although it ~~was~~is possible to shorten the ~~the~~ acquisition times ~~could be shortened~~ with ~~all of~~ the ~~above~~ q-space

Comment [TK8]: CHECK:
This sentence seems repetitive. You've already talked about the sampling requirements of DSI and the inherent problems with it, and mentioned how because of these problems, DSI is not used in clinical imaging systems. Thus, you may consider deleting this sentence or reworking it into the paragraph elsewhere.

Comment [TK9]: CHECK:
Are you trying to say that the cross-term interactions would not be corrected (uncorrected) or that they would not be correct (incorrect).

Comment [WL10]: CHECK:
You don't use this term anywhere else, so there is no need for an abbreviation.

Comment [TK11]: CHECK:
You don't use this term anywhere else, sothere is no need for an abbreviation.

sampling strategies described above, the ~~need~~requirement ~~for~~of a large number of~~high~~ q-values to preserve adequate spatial resolution~~ acquisitions~~ could not be omitted~~ to preserve adequate spatial resolution~~.

Another category of diffusion imaging techniques~~methods~~ utilizes an encoding scheme formed by a single spherical shell with a constant diffusion weighting~~,~~ as opposed to ~~a~~the 3-D Cartesian lattice with multiple diffusion weightings. These techniques include high angular resolution diffusion imaging (HARDI) [19, 20], q-ball imaging (QBI) [21, 22], persistent angular structure MRI (PAS-MRI) [23], fiber orientation estimation~~ed~~ using continuous axially symmetrical tensors (FORECAST) [24], diffusion orientation transformation (DOT) [25], and spherical deconvolution methods [26, 27]. These approaches provide information on the orientation~~directional information~~ of complex neural fiber networks~~s~~ within a ~~a feasible~~ reasonable scan ~~–~~time and may be~~for~~ routinely implemented. ~~implementation.~~ The substantial~~ly~~ increase in imaging efficiency mainly results from the fewer number~~s~~ of diffusion~~–~~-weighted images (DWIs) ~~needed~~ required for data analysis. In addition, the shortened TEs following on a moderate b~~–~~-value could enhance the SNR of DWIs. These conditions~~,~~ however, may be insufficient to characterize the 3-D diffusion function that is derived from ~~the~~ multiple q-value diffusion measurements, and would thus ~~would~~ be unable to ~~For~~ infer~~ring~~ ~~tissue~~ microstructural

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Field Code Changed

Comment [TK12]: CHECK: Would it be appropriate to say: 'estimation of fiber orientation using continuous axially symmetrical tensors'?

Comment [WL13]: CHECK:
The abbreviations used in this sentence (eg. HARDI, QBI, PAS-MRI) are not needed as the terms are only used here and nowhere else in the paper.

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Field Code Changed

Comment [WL14]: CHECK:
Do you mean "are routinely implemented" or only "may be routinely implemented"? "May be" indicates that they are not currently routinely implemented but "may be".

Comment [TK15]: CHECK: 'following a moderate b value' OR 'followed by a moderate b value' would make more sense. If neither of those fits, consider revising that part of the sentence. Perhaps 'following' is not an appropriate word choice here.

Comment [WL16]: CHECK:
Do you mean "can enhance" or "could ... [1]

Comment [WL17]: CHECK:
Refer to previous comment on "may be".

tissue ~~conditions~~shape and orientations.

~~, however, they might be insufficient to characterize the 3-D diffusion function derived from the multiple q-values diffusion measurements.~~

In this study, it is proposed that ~~the~~ reduced-encoding DSI ~~implemented~~ complemented with a bi-Gaussian model (RE-DSI), ~~is proposed~~be used to trim down the drawbacks of DSI ~~as well as~~while ~~to~~ retaining q-space information. In RE-DSI, a reduced Cartesian sampling scheme, where high q-value acquisitions are omitted, is used to bypass long acquisition times and gradient system demands in DSI. To achieve sufficient resolution ~~for~~ to ~~resolving~~ ~~determining~~determine the ~~fiber~~ orientation~~s~~ of fibers, the 1-D bi-Gaussian model ~~fitting is performed on~~is applied to the sampled data at low q-space to regain all diffusion signals at high q-space. Previous studies on animal and human brains have demonstrated that diffusion-attenuated curves ~~could~~ can be characterized as a bi-exponential function [28-31]. Accordingly, we hypothesized that the diffusion signal attenuation along each radial direction in q-space was a bi-Gaussian function. ~~The~~ This assumption is similar to ~~with~~ that used in the DOT technique [25]~~,~~ which ~~straightforwardly~~ directly converts the diffusivity function into displacement probabilities at a particular distance away from the origin, while RE-DSI tends to reconstruct a diffusion PDF from q-space signals.

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Comment [TK18]: CHECK: Throughout the paper, you refer to high q-values. However, it is not clear what you mean by that. Is it many q-values? Or, a high value of q? It would be helpful if this term was explained more clearly early on in the paper to avoid confusion.

Comment [TK19]: CHECK:
Do you mean 'regain' or 'retain'?

The performance of RE-DSI in terms of clearly defining the orientations of ~~coherent and~~ heterogeneous ~~fiber orientations~~fibers ~~is~~was assessed using the capillary phantom model~~s~~ and the manganese-enhanced (ME) rat model~~s~~., B~~b~~oth of ~~which~~ these models have been previously utilized to validate the DTI and DSI ~~methods~~techniques [5, 11]. The magnetic resonance (MR) images of capillary phantoms and the ME rat optic tract~~s~~ ~~were~~ served as the standard for the ~~the~~ measurement of angular uncertainties in RE-DSI. The results show~~ed~~ that the ~~consequential~~ resulting PDF profiles and ODF patterns reconstructed by RE-DSI were comparable ~~with~~ to ~~that~~those ~~by~~achieved by DSI. The merits of RE-DSI in a clinical environment are twofold: (a) the scan time can be remarkably shortened to a half or a quarter of its original time; and (b) DWIs can be acquired with better SNR under limited gradient intensity. To demonstrate the clinical ~~the~~ feasibility of ~~,~~RE-DSI, this technique ~~–~~was performed on a healthy subject at the end of this study.

Comment [WL20]: CHECK:
This is the first time “MR” is used apart from “MRI”. I assume it stands for “magnetic resonance”.

Comment [TK21]: CHECK:
Consider revising. Suggestions: ‘DWIs can be acquired with a limited gradient intensity, leading to a better SNR’ OR ‘better SNR allows for acquisition of DWIs under limited gradient intensity’

Materials and Methods

Reduced-Encoding Scheme

In DSI, the q-space sampling scheme consists of 515 diffusion wave vectors (q), where q = γgδ/2π (γ: gyromagnetic ratio, g: gradient vector, δ: duration of diffusion gradient), placed on a Cartesian lattice within a sphere that has a radius of ~~the sphere of~~ five lattice units ~~in radius~~ [7]. The framework of the q-space acquisition scheme in RE-DSI is the same as ~~with~~ that ~~in~~ of DSI~~,~~ except that the encoding wave vectors are within a radius of ~~four~~ three or ~~three~~ four lattice units. The final~~resultant~~ encoding numbers are 257 and 123, respectively. ~~.~~

Bi-Gaussian Model

The bi-Gaussian model assumption in RE-DSI~~–~~ ~~is~~was established according to several studies on bi-exponential analyses of high b-value diffusion data [28-31]. The bi-exponential diffusion model, also called the ~~or so-called~~ two-~~-~~compartment model, ascribes the contribution of MR signal attenuation to the weighted sum of fast and slow water diffusion. The general formula is shown as follows [32]:

fitting of~~on~~ undersampl~~ing~~ed data. The slightly increased error~~s~~ of 4.70° ± 3.51° for the case of 45° crossing in RE-DSI ~~[~~123~~]~~ ~~might~~may have result~~ed~~ from fewer q-space acquisitions.

Comment [TK22]: CHECK:
This sentence doesn't tie into the rest of the paragraph well enough and thus appears to be making a statement unrelated to the paragraph. Perhaps state what the encoding numbers are in reference to more clearly.

Comment [TK23]: CHECK:
Consider revising to: 'Assumption of the bi-Gaussian model in RE-DSI…'

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Comment [TK24]: CHECK:
This sentence does not appear tied to the rest of the paragraph. Consider first suggesting that there was an increase in errors, and then explaining why, rather than combining both of those concepts into one sentence.

Page 6: [1] Comment [WL16] William Ling 2008/2/7 11:29:00 PM

CHECK:

Do you mean “can enhance” or “could enhance”? If they always enhance it, use “can enhance”.