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Optimization of diffusion spectrum imaging and *q*-ball imaging on clinical MRI system

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Mapping complex crossing fibers using diffusion MRI techniques requires adequate angular precision and accuracy. Beyond diffusion tensor imaging (DTI), high angular resolution sampling schemes such as diffusion spectrum imaging (DSI) and *q*-ball imaging (QBI) were proposed to resolve crossing fibers. These schemes require hundreds of data approximately five to ten times more than DTI, offsetting their clinical feasibility. To facilitate its clinical application, optimum values of highest diffusion sensitivity (bmax) must be investigated under the constraint of scan time and gradient performance. In this study, simulation of human data sets and a following verification experiment were performed to investigate the optimum bmax of DSI and QBI. Four sampling schemes, two with high sampling number, i.e., DSI515 and QBI493, and two with low sampling number, i.e., DSI203 and QBI253, were compared. Deviation angle and angular dispersion were used to evaluate the precision and accuracy among different bmax of each scheme. The results indicated that the optimum bmax was a trade-off between SNR and angular resolution. At their own optimum bmax, the reduced sampling schemes yielded angular precision and accuracy comparable to the high sampling schemes. On our current 3 T system, the optimum bmax (s/mm^2) were 6500 for DSI515, 4000 for DSI203, 3000 for QBI493 and 2500 for QBI253. DSI was incrementally more accurate than QBI, but required a greater demand for gradient performance. In conclusion, our systematic study of optimum bmax in different sampling schemes and the consideration derived wherein could be helpful to determine optimum sampling schemes in other MRI systems.

Keywords: Diffusion MRI; Diffusion spectrum imaging; *q*-ball imaging; Optimum parameters

Introduction

Diffusion MRI has been widely used to assess the integrity of axonal fibers because of its unique ability to map fiber orientations *in vivo* (Le Bihan, 2003; Mori and van Zijl, 2002). To measure fiber orientation, diffusion tensor was proposed to estimate the probability distribution of water molecules using 3-dimensional (3-D) Gaussian approximation, from which the principal direction of the tensor was inferred to the fiber orientation (Basser et al., 1994; Pierpaoli et al., 1996). This method, called diffusion tensor imaging (DTI), can accurately define the fiber orientation of a voxel containing fibers with coherent directions, but cannot define directions of heterogeneous fibers presented with crossing or kissing patterns (Frank, 2001, 2002; Tuch et al., 2002; Wiegell et al., 2000). To address this problem, high angular resolution sampling schemes such as diffusion spectrum imaging (DSI) and *q*-ball imaging (QBI) were proposed to resolve local crossing fibers within each voxel (Gilbert et al., 2006a,b; Lin et al., 2003b; Schmahmann et al., 2007; Tuch, 2004; Tuch et al., 2003, 2005; Wedeen et al., 2005). Typically, these methods sample hundreds of data, approximately five to ten times more than DTI, offsetting its advantage in clinical applications (Hagmann et al., 2006; Khachaturian et al., 2007). Recently, diffusion MRI has been considered a potential tool to study abnormal connectivity of neural circuit in patients with neuropsychiatric disease (Ciccarelli et al., 2006; Ge et al., 2005; Jones et al., 2006; Kubicki et al., 2007). In addition, diffusion MRI and especially high *b*-value and angular resolution techniques are important to study normal and abnormal neural circuitry (Hagmann et al., 2007). It is a timely need to investigate the optimum setting of DSI and QBI for clinical scanners.

To perform DSI, we need hundreds of diffusion-attenuated images with variable directions and strengths of diffusion-sensitive gradients (Lin et al., 2003b; Wedeen et al., 2005). A spectral bandwidth (bmax) larger than 10,000 s/mm^2 is recommended to sample diffusion-encoding points over the 3-D *q*-space so that the probability density function (PDF) with sufficient resolution and field-of-view (FOV) can

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be obtained (Wedeen et al., 2005). High sampling number of DSI prolongs the scan time, making implementation of this method more susceptible to motion-induced errors (Jiang et al., 2002). Using high bmax poses a stringent challenge to the gradient performance in current clinical systems (Le Bihan et al., 2006). In addition, the high bmax used in clinical scanners resulted in low signal-to-noise ratio (SNR) due to prolonged TE and substantial diffusion-induced signal decay (Meca et al., 2004). Poor SNR affects the accuracy of PDF orientation and consequently the accuracy of fiber orientation. In order to overcome these limitations, one approach is to reduce the number of the diffusion-encoding gradients as well as the bmax of DSI. For example, by reducing the routine number of diffusion-encoding gradients from 515 to 203, the scan time can be reduced from approximately 1 h to 30 min. By lowering bmax, the maximum diffusion gradient strength can be reduced to secure gradient stability. Moreover, diffusion time and TE can be reduced to provide better SNR for the diffusion-weighted images.

More efficient than DSI, QBI samples data on a shell of a constant b-value in the q-space (Tuch, 2004; Tuch et al., 2003). Typically, its bmax and number of gradient encoding are approximately two- to three-fold lower than DSI, thus is considered more feasible in clinical applications. In QBI, orientation distribution function (ODF) along each radial direction is derived and the local fiber orientation can be inferred by the local maxima of ODF at each voxel.

Although QBI and DSI with reduced bmax and encoding number are potentially advantageous for reducing scan time and improving gradient stability, insufficient sampling rate and inadequate bmax over the q-space may lead to inaccurately estimating fiber orientations. For DSI, insufficient sampling rate within the 3-D q-space may result in aliasing in the PDF profile. On the other hand, inadequate bmax may result in truncation in Fourier transform, causing a ringing artifact to PDF (Wedeen et al., 2005). As for QBI, it is known that the resolution of ODF depends on the bmax. Accordingly, reduced bmax may degrade the angular resolution of QBI (Tuch, 2004). All the above problems may lead to inaccurately estimating local fiber orientation. Therefore, a systematic study on how to determine the optimum bmax and encoding number for clinical application is needed.

To facilitate clinical application, it is necessary to investigate optimum values of bmax under the constraint of scan time and gradient performance on current clinical system. Thus, the purpose of this study is to determine the optimum sampling scheme for DSI and QBI obtained from 3 T clinical system. In either DSI or QBI, one scheme with a higher encoding number (approximately 500) and one with a lower encoding number (approximately 200) were studied. For each scheme, the precision and accuracy of fiber orientation were quantified and compared between different bmax values. Since it is exhausting to perform all the experiments on clinical system, simulation from human data sets was first performed to determine the optimum parameters. Based on the simulation results, selective ranges of optimum bmax for each sampling scheme were decided for the verification study. Finally, the combined effects of gradient number and bmax on the angular resolution of DSI and QBI were discussed and the strategy of determining optimum sampling schemes on clinical scanners was recommended.

Materials and methods

Diffusion spectrum imaging (DSI) and q-ball imaging (QBI)

The concept of DSI is based on the Fourier relationship between the attenuated echo signal in q-space $E(q)$ and the probability density function (PDF) of water molecular diffusion $P_s(r)$

$$E(q) = \int P_s(R, \Delta)\exp(i2\pi qR)\mathrm{d}R, \tag{1}$$

where R is the relative displacement of water molecular diffusion during the diffusion time (Callaghan, 1991). Based on this relationship, 3-D Fourier transform of the echo signal over the q-space yields the 3-D PDF (Wedeen et al., 2005). In practice, the diffusion spectrum is reconstructed by applying the 3-D discrete Fourier transform to the grid q-space data $E(q)$. For each voxel, the attenuated echo signals are filled into the 3-D Cartesian coordinate space ($17\times17\times17$) according to their respective position vectors. As suggested by Wedeen et al. (2005), a Hanning window is used to smooth the attenuated echo signal to prevent the truncation artifact. In our analysis, the Hanning window with a raised cosine function, $h(r)=0.5\times\cos(2\pi r/17)$, was applied for all the DSI schemes. After 3-D Fourier transform applied on $E(q)$, a discrete 3-D PDF space can be derived in a 3-D Cartesian coordinate space ($17\times17\times17$). In order to characterize the magnitude of directional diffusion probability, orientation distribution function (ODF) was then calculated based on the following definition. The definition of the ODF in the direction of the unit vector $\mathbf{u}$ for DSI is

$$\mathrm{ODF}(\mathbf{u}) = \int_0^{r_{\max}} P_s(r\mathbf{u})r^2\mathrm{d}r. \tag{2}$$

This approach can be viewed as a weighted radial summation of P_s and the local fiber orientations were inferred by the orientations of the local maxima of ODF (Lin et al., 2003b; Wedeen et al., 2005).

QBI is reconstructed based on the relationship of the interested ODF vector and its orthogonal plane projected onto the acquired q-space data, so-called Funk–Radon transform (Tuch, 2004; Tuch et al., 2003, 2005). The ODF was directly calculated from the attenuated echo signal on a shell in the q-space with a fixed b-value based on the Funk-Radon transform approach. The detailed procedures of QBI reconstruction can be found in Tuch's papers, and were described very briefly here. It bypasses the computation of PDF and estimates ODF and local fiber orientations directly. To derive ODF in a desired direction, the circular integral is performed along the equator whose plane is perpendicular to this particular ODF direction based on the following equation:

$$\mathrm{ODF}(\mathbf{u}) = \frac{1}{Z}\int_{q\perp\mathbf{u}} E(q, \Delta)\mathrm{d}q, \tag{3}$$

where $\mathbf{u}$ is the unit vector for the desired ODF direction and Z is the normalization constant. In practice, the signals on the equator have to be interpolated and the interpolation kernel width (σ) closely affects the accuracy of the ODF estimation. According to Tuch's simulation results, we performed QBI reconstruction using $\sigma=5°$ to achieve a trade-off between the accuracy and stability (Tuch, 2004). To further improve ODF accuracy, appropriate smoothing function was applied to the estimated ODF. To simplify the comparison, a simple average smoothing function with the same smoothing window was performed to post-process the QBI data. For both DSI and QBI, ODF within each voxel was reconstructed to 162 radial directions pointing at the vertices of regular triangular mesh on the unit sphere surface. Reconstruction of DSI and QBI data was performed using an in-house program written in MATLAB 7.0 (The Mathworks, Natick, MA, USA).