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Numerical Simulations of Motion-Insensitive Diffusion Imaging Based on the Distant Dipolar Field Effects

Tao Lin^{1,2}, Huijun Sun¹, Zhong Chen^{1,3,*}, Rongyi You², and Jianhui Zhong^{3,*}

¹Department of Physics, State Key Laboratory of Physical Chemistry of Solid Surface, Xiamen University, Xiamen 361005, PR China

²Department of Physics, Jimei University, Xiamen 361021, PR China

³Department of Imaging Science, University of Rochester, Rochester, NY 14642, USA

⁴Department of Biochemistry and Biophysics, University of Rochester, Rochester, NY 14642, USA

Abstract

Diffusion weighting in MRI is commonly achieved with the pulsed-gradient spin-echo (PGSE) method. When combined with spin-warping image formation, this method often results in ghosts due to the sample's macroscopic motion. It has been shown experimentally (Kennedy and Zhong, MRM 2004;52:1–6) that these motion artifacts can be effectively eliminated by the distant dipolar field (DDF) method, which relies on the refocusing of spatially modulated transverse magnetization by the DDF within the sample itself. In this report, diffusion weighted images (DWIs) using both DDF and PGSE methods in the presence of macroscopic sample motion were simulated. Numerical simulation results quantify dependence of signals in DWI on several key motion parameters, and demonstrate that the DDF DWIs are much less sensitive to the macroscopic sample motion than the traditional PGSE DWIs. The results also show that the dipolar correlation distance (d_c) can alter contrast in DDF DWIs. The simulated results are in good agreement with the experimental results reported previously.

Keywords

DDF; motion; diffusion; image contrast; computer simulation

1. Introduction

The signals induced by dipolar couplings between distant spins can be analyzed with either the distant dipolar field (DDF) effect [1], or alternatively, with the theory of intermolecular multiple-quantum coherences (iMQC) [2]. Compared to conventional NMR signals, the signals originated from the DDF (or iMQC) contain some unique properties, the utility of which have been explored in a wide variety of applications, including contrast enhancement or novel contrast in MRI [3–5] and fMRI [6,7], suppression of inhomogeneous broadening [8,9], and measurements of magnetization structure [10–12].

* Authors to whom correspondence should be addressed. E-mail: chenz@xmu.edu.cn; jianhui.zhong@rochester.edu.

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Diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI) are noninvasive techniques and provide powerful tools for brain studies and brain diseases diagnoses [13-15], allowing *in vivo* mapping of the Brownian motion of water molecules that is influenced by tissue microstructures. Usually, diffusion weighting (DW) in both DWI and DTI is achieved with the use of the pulsed-gradient spin-echo (PGSE) method [16], where the image signal intensity depends on displacement of water molecules. Unfortunately, when combined with Fourier imaging where multiple phase encoding steps are used, these signals are also sensitive to macroscopic motion of the sample, often resulting in severe motion artifacts that hinder precise measurement and observation of DW signals. Although DWI or DTI based on single-shot methods such as EPI substantially eliminates the motion-related artifacts, severe susceptibility artifacts can prevent its use in some cases. It is noted that the NMR signal of a nucleus at a specific position originating from DDF is only correlated with the nearby nuclei intermingled on the correlation distance. Since the spatial scale of macroscopic susceptibility effects is generally much larger than the microscopic correlation distance (usually 10–1000 μm) in DDF experiments, macroscopic susceptibility effect should minimally affect the images generated by the DDF method. Moreover, we have previously discussed diffusion effects in DDF imaging when gradient pairs are applied during the evolution period [17]. However, Bowtell and coworkers first pointed out a unique diffusion-weighting process which occurs under the influence of the DDF during the detection period [18] which we will refer to as DDF-DWI. Recently, we demonstrated experimentally that DDF DWI can effectively suppress motion-induced artifacts with experiments in both phantoms and *in vivo* animal measurements [19].

In the work reported here, computer simulations for DWIs using both DDF and PGSE methods in the presence of macroscopic sample motion were performed. Simulated results quantify dependence of signals in DWI on motion parameters, and demonstrate that DDF DWIs contain fewer motion artifacts by virtue of their intrinsic insensitivity to the macroscopic sample motion, in agreement with the previous experimental results. In addition, the image contrast mechanism depending upon the dipolar correlation distance (d_c) in DDF DWIs was also simulated and discussed.

2. Theories and methods

DWI signals were simulated with three-dimensional integration calculations on the time evolution of magnetization governed by the nonlinear Bloch equations. The time evolution of the magnetization vector of each volume element is given by [20]:

$$\begin{aligned} \frac{\partial \mathbf{M}(\mathbf{r}, t)}{\partial t} = & \gamma \mathbf{M}(\mathbf{r}) \times \left\{ \frac{\Delta\omega}{\gamma} \hat{\mathbf{z}} + \mathbf{G}(\hat{\mathbf{s}} \cdot \mathbf{r}) \hat{\mathbf{z}} \right\} + \mathbf{B}_d(\mathbf{r}) \\ & - \frac{M_x(\mathbf{r})\hat{\mathbf{x}} + M_y(\mathbf{r})\hat{\mathbf{y}}}{T_2(\mathbf{r})} + \frac{M_0(\mathbf{r}) - M_z(\mathbf{r})}{T_1(\mathbf{r})} \hat{\mathbf{z}} + D_T \nabla^2 \mathbf{M}(\mathbf{r}, t), \end{aligned} \quad (1)$$

where γ is the magnetogyric ratio; $\hat{\mathbf{x}}$, $\hat{\mathbf{y}}$, and $\hat{\mathbf{z}}$ are unit vectors along coordinate axes; $\hat{\mathbf{s}}$ is the unit vector along the gradient direction applied for modulating the dipolar field, and $G(\hat{\mathbf{s}} \cdot \mathbf{r})$ is strength of the gradient along the $\hat{\mathbf{s}}$ direction at the position $\mathbf{r}$. Ignoring radiation damping effect, Eq. (1) includes some terms correlated only to local magnetization such as chemical shift ($\Delta\omega$), longitudinal relaxation (T_1), transverse relaxation (T_2), gradient field ($G(\hat{\mathbf{s}} \cdot \mathbf{r})$), and introduces other terms that are nonlocal in real space such as DDF ($\mathbf{B}_d$) and translational self-diffusion ($D_T \nabla^2 \mathbf{M}$). The complete expression for the DDF is given by

$$\mathbf{B}_d(\mathbf{r}) = \frac{\mu_0}{4\pi} \int d^3 \mathbf{r}' \frac{1 - 3 \cos^2 \theta}{2 |\mathbf{r} - \mathbf{r}'|^3} \left[3 M_z(\mathbf{r}') \hat{\mathbf{z}} - \mathbf{M}(\mathbf{r}') \right], \quad (2)$$

where $\theta_{rr'}$ is the angle between the interspin vector $\mathbf{r}-\mathbf{r}'$ and the main magnetic field. Equation (2) can be simplified in the Fourier space (k -space) as:

$$\mathbf{B}_d(\mathbf{k}) = \frac{\mu_0}{6} \left[3(\hat{\mathbf{k}} \cdot \hat{\mathbf{z}})^2 - 1 \right] \left[3M_z(\mathbf{k})\hat{\mathbf{z}} - \mathbf{M}(\mathbf{k}) \right]. \quad (3)$$

Similarly, the calculation of the bulk diffusion operator $D_T \nabla^2$ is reduced to multiplication by $-D_T k^2$ in the Fourier space. Consequently, to boost operational efficiency, the DDF and diffusion terms were computed directly in k -space for calculating Eq. (1), which was integrated from $t = 0$ to t_{final} with a fifth-order Cash-Karp Runge-Kutta formulism [21]. Based on estimation of truncation errors, the step size during time evolution was adjusted after balancing the calculation speed and needed numerical accuracy [22].

In addition, to describe the effects of motion, a Fourier imaging process was also simulated. In most previous reports, only single image periods were applied to simulate 3D structured samples [21-23]. The final image was formed by directly sampling the magnitude of the transverse magnetization at the center of the spin echo and summed along z , the slice thickness direction. This simulation approach substantially reduces calculation time when the distribution of the initial magnetization in the sample is known. However, to study motion-induced distortions and ghosts which are closely related to the Fourier imaging method, it is indispensable to introduce the simulations of phase-encode and frequency-encode gradients and perform the needed periodic repetition of an imaging sequence.

The following simulation experiments were performed. First, in order to verify the authenticity of the acquired iDQC signal, simulations of iDQC imaging for human brain, using the DDF DWI sequence shown in Fig. 1b with a simple (x , $-x$) phase cycling applied to the first $\pi/2$ RF pulse, were performed with the correlation gradient applied along four different directions: z -axis, x -axis, y -axis, and magic angle (54.7°). A $56 \times 56 \times 24$ 3D sample was formed by replicating 2D magnetization intensity matrix of a single 56×56 T_1 -weighted MR image of the human brain 24 times along the third dimension (slice thickness). The dataset was further expanded into a $64 \times 64 \times 32$ simulation region, with 4 pixels of zero-padding inserted at the edges of the sample to prevent anomalous edge effects [22]. As is well known, an important property of iDQC is the overall scaling of the signal intensity by a factor of $3\cos^2\theta-1$, where θ is the angle between the main magnetic field (B_0) and the correlation gradient direction. Based on this property, it is expected that intensity of the iDQC signal with the correlation gradient along the z -axis is twice as large as that with the correlation gradient along x - or y -axis, and is zero when the gradient is along the magic angle. It should be noted that only the M_0 value from the original T1W image for every pixel was used into a solution to Eq (1), and the differences in T_1 , T_2 and D in different pixels in this image were not considered during simulations.

Second, to investigate DWI characteristics influenced by the sample macroscopic motion, a sample of simple geometry was used for simulation. The sample shown in Fig. 2 is a large cylinder bounded by $30 \times 30 \times 24$ grid points inside a $64 \times 64 \times 32$ point array (the distance between two adjacent points is $20 \mu\text{m}$). The physical parameters for the cylinder were: magnetization density $M_0 = 0.023 \text{ A/m}$, $T_1 = 1 \text{ s}$, $T_2 = 0.1 \text{ s}$, diffusion coefficient $D_T = 0$, and chemical shift $\Delta\omega = 0$. Magnetization $M_0 = 0$ for points surrounding the sample (empty space). A smaller cylinder (shaded, $10 \times 10 \times 24$ grid points) with identical parameters but a different diffusion coefficient, $D_T = 3.0 \times 10^{-9} \text{ m}^2/\text{s}$ is inside the larger cylinder. The pulse sequences used in simulation were the standard PGSE DWI sequence in Fig. 1a and DDF DWI sequence in Fig. 1b. The parameters of PGSE DWI sequence were: $\Delta = 26 \text{ ms}$, $\delta_D = 1 \text{ ms}$, $G_D = 30 \text{ G/cm}$ (the diffusion weighting factor $b = \gamma^2 G_D^2 \delta_D^2 (\Delta - \delta_D/3) \approx 165 \text{ s/mm}^2$, the diffusion gradient G_D was along the z direction). To achieve an equivalent diffusion weighting ($\sim 40\%$ signal reduction) [19], the parameters of DDF DWI sequence were: $TE = 80 \text{ ms}$, $d_c = \pi/\gamma G_c \delta_c = 60 \mu\text{m}$ ($b = \pi^2 TE/d_c^2 \approx 220 \text{ s/mm}^2$, the correlation gradient G_c was along the z direction). During the course

of imaging with these two pulse sequences ($TR = 3.5$ s), the sample was assumed to move periodically along the z axis following a sine velocity function, mimicking the motions such as heartbeat or breathing in the human. Two motion modes were simulated, one with the motion frequency constant (1.25 Hz) while the maximum motion amplitude was 0.65, 0.75, and 0.85 mm respectively; the other with the motion amplitude constant (0.75 mm for PGSE DWI and 1.5 mm for DDF DWI) while the motion frequency was 1.25, 1.58, and 2.10 Hz respectively. In addition, to mimic the abnormal heartbeat of the patients with heart fault, random motion mode was also simulated, where the motion frequency in each image periods varied from 1.25 Hz to 2.10 Hz randomly, and the amplitude varied from 1 mm to 2.5 mm randomly.

The diffusion-weighting mechanism of DDF DWI is very different from that of conventional PGSE DWI, with d_c and TE determining the amount of diffusion weighting instead of G_D , δ_D and Δ . To study this unique mechanism, a set of simulations reflecting image contrast with different d_c and TE were performed in the absence of motion. The 3D sample used is the same in the structure and magnetization distribution as for the above simulation shown in Fig. 2, but it has a bigger size than the former. The small cylinder consisting of $16 \times 16 \times 48$ grid points is located at the center of the large cylinder of $48 \times 48 \times 48$ point array. The large cylinder is zero-padded with 8 pixels on each side of it to form a $64 \times 64 \times 64$ simulation region (the side length $L_x = L_y = L_z = 1.28$ mm). Except $D_T = 0.8 \times 10^{-9}$ m²/s for the large cylinder and $D_T = 3.0 \times 10^{-9}$ m²/s for the inner, small cylinder, other physical parameters were retained, and the same DDF DWI sequence shown in Fig. 1b was used. The correlation gradient G_c was along z direction. The parameters were in the range 60–160 μ m for d_c and 50–200 ms for TE .

The program used for the study was written in Matlab 7.0 (Mathworks, MA, USA), and all simulations were performed on an AMD Athlon (tm) XP 2800+ PC with 512MB of memories. The computational time varied from 30 to 65 hours depending on the sample size, number of time steps (or truncation errors), and the intrinsic physical parameter, including chemical shift and diffusion coefficient distributions among others.

3. Results

In Fig. 3a-d, simulated iDQC images of a human brain obtained with correlation gradients along z -axis (parallel to the main static magnetic field B_0), x -axis, y -axis and the magic angle direction are shown respectively. As expected, excluding a slight leakage of the residual SQC signal at the edges of the images (as will be discussed later in the text), the overall signal intensity is approximately half when correlation gradients are along the direction perpendicular to B_0 (Fig. 3b-c) compared to the image with the gradients along B_0 (Fig. 3a), and signal approaches zero when the gradients are at the magic angle (Fig. 3d), in good agreement with the important property of iMQC (the signal $\propto 3\cos^2\theta - 1$).

From Fig. 4, it can be calculated that the diffusion weighting results in $\sim 40\%$ signal reduction in the centric area compared to the rest of areas ($D_T = 0$) around it in both motion-free DDF and PGSE DWIs. When the motion frequency is constant, the motion artifacts along the phase-encoding (PE) direction increase with the increasing amplitude of the sample motion (Fig. 5). In the PGSE DWIs (Fig. 5a-c), the ghosts are so strong that the primary image is hardly distinguishable from them. On the other hand, the motion artifacts in the DDF DWIs (Fig. 5d-f) are barely observable. Similarly, when the motion amplitude is constant and the motion frequency increases, motion artifacts in the DDF DWIs are much less pronounced than in the PGSE DWIs, even though the motion amplitude of the sample for DDF DWIs is twice that for PGSE DWIs in these simulations (Fig. 6). The simulated results in Fig. 7 show, when the motion frequency and amplitude were both random, compared to the PGSE DWIs, motion artifacts in the DDF DWIs are much reduced, demonstrating further the advantage of the DDF method.

Figure 8 demonstrates that, in DDF DWIs, image contrast changes due to molecular diffusion under the DDF with different d_c and TE in the absence of motion. If SI_{out} and SI_{in} stand for the signal intensities of the large and small cylinders respectively, the image contrast is defined as $|SI_{out} - SI_{in}| / (SI_{out} + SI_{in})$. Figure 9 shows the region-of-interest (ROI) analysis of the image contrast changes in Fig. 7, where the solid lines represent the simulation results and the dashed are calculated from the model described by [18,24,25]

$$S = S_0 e^{-\frac{(\tau + TE)/T_2}{2} \cdot \frac{1 - e^{-\left(2D\pi^2/d_c^2 + 1/T_1\right)TE}}{2D\pi^2/d_c^2 + 1/T_1}} \cdot e^{-2D\pi^2/d_c^2 \left(\Delta_c - \delta_c/3\right)} \quad (4)$$

From these results we can see that, for the imaging areas containing different diffusion coefficients, image contrast will increase when TE increases; furthermore, when TE is constant, the image contrast will be markedly enhanced with decrease of the correlation distance d_c .

4. Discussion

The simulated overall iDQC image intensities for the human brain with different correlation gradient directions (Fig. 3) agree well with a fundamental property of iMQC (the signal $\propto 3\cos_2\theta - 1$), thus verifying the authenticity of the acquired signals due to the DDF and the validity of our simulation codes. It was noted, however, that the signal intensity at the edges of brain images (one or two voxels) in Fig. 3b-c did not fall, and instead increased a little compared to the image in Fig. 3a. Besides calculation errors resulted from the limited number of grid points used in simulation, one possible reason is that for small field of view studies (as the simulation work here), where the imaging gradients are relatively strong, some cancellation of the correlation gradient can occur if the latter is too weak. This causes a gradient-recall of the SQC echoes. A simple (x, -x) phase cycling applied to the first $\pi/2$ RF pulse of the DDF DWI sequence cancels most of the contamination but not completely [23]. These effects however do not affect the overall simulated image intensity since the residual SQC signal is small. Using computer simulations, we succeed in verifying the authenticity of the iMQC signals from a 3D structured sample, which can not be achieved by previously reported simulation methods [21-23], and the simulation method used here will benefit designs of new iMQC imaging pulse sequences in the future.

It is well known that motion-induced phase shift causes appearance of ghosts along the PE direction in the Fourier MR imaging. Our simulated results confirm that, with the equivalent diffusion weighting, DDF DWIs have much less severe artifacts resulted from sample motion than PGSE DWIs. As pointed out by Kennedy and Zhong [19], this is because the refocusing effect of modulated magnetization in DDF DWI comes from the DDF carried within the sample, not the external gradient field produced by gradient coils as in conventional PGSE DWI. In DDF DWI, during the detection period following the coherence selection gradients, the DDF induces a phase shift, $\phi_d(r_i) = \gamma \int_0^{TE} B_d(r_i, t) dt$, which makes the previously dephased magnetization gradually refocused. It is clear that the phase shift depends only on r_i , the position of spin i within the sample relative to the sample itself. So the phase shift of the final refocused signal is only influenced by molecular displacements, which comes into being with diffusion weighting, not by the sample motion which may bring unwanted artifacts. In other words, the macroscopic motion does not alter the phase shift due to the DDF inside the sample, and thus does not interfere with signal formation. On the other hand, in PGSE DWI, the phase shift, $\phi_i = G_D \delta_D \cdot \Delta z_i$, depends on the spin displacement Δz_i relative to the gradient coils outside the sample during the time interval Δ between diffusion weighting gradients, and under this condition molecular diffusion within the sample and macroscopic motion of the entire sample are indistinguishable. So motion-induced phase shift variation in each step during

Fourier imaging often causes severe motion artifacts that hinder the true DWI signals to be precisely observed.

There are still some residual motion artifacts in DDF DWIs arising from conventional diffusion weighting due to separation of the coherence selection gradients [19,24]. Our simulations confirm that motion artifacts increase when the time interval Δ_c between coherence gradients increases (data not shown). So for all simulations of DDF DWIs mentioned above in this paper, the delay has been kept to a minimum to restrain artifacts to the greatest extent, as the same care should be taken in practical applications.

Since motion-induced phase changes are the main source of ghost artifacts in the Fourier imaging methods, motion in all directions causes similar effects but mostly manifested as ghosts (displaced intensities) in the phase-encode direction. In the conventional DWI motion along the DW gradient direction is more severe for artifacts. In our DDF DWI implementation, theoretically the only source of motion artifacts comes from the residual DW due to the correlation gradients. Since they are applied along the slice-selection direction, the potential artifact is the most severe. Our simulation suggests that even in this case the artifacts are much reduced in comparison to the conventional DWI. If the geometry of the phantom is more complicated, such as without axial geometry or with various sizes along the motion direction, another artifact (spins in different geometry are included in the final image) will occur. However this will cause signal intensity variations, not ghost artifacts as we analyzed in the article.

We noted that the NMR signal from one nucleus at a specific position originating from DDF is only correlated with the nearby nucleus intermingled on the correlation distance. Since the scale of spatial dependence for macroscopic susceptibility effects is usually much larger than the correlation distance in DDF experiments, one of our own works shows that macroscopic susceptibility effect can be largely eliminated in some DDF imaging method [26].

It is known that the transverse magnetization dephased by the coherence selection gradients is gradually refocused during TE by the DDF, which results from spatially modulated z -magnetization established by the first coherence selection gradient and the second $\pi/3$ RF pulse. During TE the iDQC signal first gradually rises under the refocusing effect of the DDF, the amplitude of which at a particular location depends mainly upon the surrounding magnetization found within the correlation distance d_c (or the half-wavelength) [27]. It then rises more slowly because of the attenuation of DDF effect and T_2 relaxation decay with the increasing evolution time, and finally reaches a maximum with a balance between the DDF and the T_2 relaxation. After this “balance point” the signal begins to decay with the dominant T_2 relaxation. During this course of signal formation, when the diffusion distance $\sigma = \sqrt{2 \cdot D_T \cdot TE}$ is on the order of d_c , displacements of the spins tend to spoil the spatially-modulated magnetization, resulting in destruction of the dipolar field and, consequently, the growth of the signal is halted [18,19, 24]. The amount of signal attenuation due to diffusion weighting depends on the diffusion coefficient D_T , the echo time TE , and the dipolar correlation distance d_c . Besides TE which evidently affect diffusion weighting, d_c also has influence upon image contrast. In DDF DWI, for the same TE , regions with larger D_T have more pronounced diffusion effect which will destroy the DDF more rapidly, resulting in more attenuation of the signal (the “balance point” appears at an earlier TE with a reduced signal maximum). As d_c is reduced (the effect is equivalent to σ increase), the diffusion effect becomes more prominent, and therefore the signal difference will be amplified by the larger diffusion weighting, resulting in a more pronounced enhancement of the image contrast.

The simulated results of DDF DWIs shown in Fig. 7 and Fig. 8 reflect the above trends of the image contrast variation based on molecular diffusion under the DDF. The simulation results

(solid lines) agree well with the theoretical predictions (dashed lines) especially when TE is small, but when TE increases the errors increase accordingly. The errors may result from the limited number of grid points in simulation and/or limitation of the presented theoretical model.

Taking advantage of the unique property that the DW signal due to the distant dipolar field effect is insensitive to the macroscopic motion of sample, one may find the use of the DDF DWI method in motion-prone regions such as heart, lungs, and abdomen, as well as brain imaging for patients with Parkinson' disease or other motion-disorders.

5. Conclusions

In this article, properties of diffusion-weighted MRI based on the distant dipolar field were investigated. The simulations quantify dependence of DDF and conventional DWI on motion parameters, and the results confirm that compared to traditional PGSE DWIs with the equivalent diffusion weighting, DDF DWIs are much less sensitive to the macroscopic sample motion, thus having fewer motion artifacts. This technique is expected to facilitate the use of DWI for motion-prone objects such as heart, lungs, and abdomen, as well as brain scans for patients with motion disorders. Furthermore, our simulations verify that DDF DWIs with a varying dipolar correlation distance can alter contrast in images, which can be used to probe microscopic structures of materials or tissues with different diffusion coefficients.

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Fig. 1.

(a) PGSE DWI pulse sequence; (b) DDF DWI pulse sequence. A simple (x, -x) phase cycling was applied to the first $\pi/2$ RF pulse to eliminate single quantum contamination.

Fig. 2.
Sample used in simulation. The region of simulation is the dashed box, and the shaded, small cylinder contains different diffusion coefficient from the large cylinder surrounding it.

Fig. 3. Simulated iDQC images for a human brain with different correlation gradient directions: (a) z-axis (b) x-axis, (c) y-axis, (d) magic angle.

Fig. 4. Motion-free PGSE DWIs (a) and DDF DWIs (b). The signal of the centric areas is reduced ~40% due to diffusion when the sample is immobile.

Fig. 5. (a)~(c): PGSE DWIs and (d)~(f): DDF DWIs with motion. The motion frequency is 1.25 Hz and the motion amplitudes of the sample are 0.65 mm (a, d), 0.75 mm (b, e), and 0.85 mm (c, f), respectively. “↑”denotes the phase-encoding direction.

Fig. 6. (a)~(c): PGSE DWIs and (d)~(f): DDF DWIs with motion. The motion amplitude is constant (0.75 mm for PGSE DWIs, 1.5 mm for DDF DWIs), and the motion frequencies are 1.25 Hz (a, d), 1.58 Hz (b, e), and 2.10 Hz (c, f), respectively. “↑” denotes the phase-encoding direction.

Fig. 7. (a) PGSE DWIs with motion and (b) DDF DWIs with motion. The motion frequency in each image periods varied from 1.25 Hz to 2.10 Hz, and the motion amplitude varied from 1 mm to 2.5 mm randomly.

Fig. 8. Simulated DDF DWIs for different d_c and TE in the absence of motion. All images were normalized to their maximum intensity to show the relative contrast changes.

Fig. 9. Region-of-interest (ROI) analysis of the image contrast changes in Fig. 8. The solid lines represent the simulation results, and the dashed are from theory calculations.