Published in final edited form as:

J Magn Reson. 2012 August ; 221: 24–31. doi:10.1016/j.jmr.2012.04.010.

A Spin Echo Sequence with a Single-Sided Bipolar Diffusion Gradient Pulse to Obtain Snapshot Diffusion Weighted Images in Moving Media

R. Z. Freidlin^{a,*}, J. W. Kakareka^a, T. J. Pohida^a, M. E. Komlosh^b, and P. J. Basser^b

^aDivision of Computational Bioscience, Center for Information Technology, National Institutes of Health, Bethesda, Maryland, United States

^bSection on Tissue Biophysics and Biomimetics, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland, United States

Abstract

In vivo MRI data can be corrupted by motion. Motion artifacts are particularly troublesome in Diffusion Weighted MRI (DWI), since the MR signal attenuation due to Brownian motion can be much less than the signal loss due to dephasing from other types of complex tissue motion, which can significantly degrade the estimation of self-diffusion coefficients, diffusion tensors, etc. This paper describes a snapshot DWI sequence, which utilizes a novel single-sided bipolar diffusion sensitizing gradient pulse within a spin echo sequence. The proposed method shortens the diffusion time by applying a single refocused bipolar diffusion gradient on one side of a refocusing RF pulse, instead of a set of diffusion sensitizing gradients, separated by a refocusing RF pulse, while reducing the impact of magnetic field inhomogeneity by using a spin echo sequence. A novel MRI phantom that can exhibit a range of complex motions was designed to demonstrate the robustness of the proposed DWI sequence.

Keywords

Motion Artifacts; DWI; DTI; Heart; Spinal Cord; Diffusion; MRI

1. Introduction

Motion artifacts are a serious confound for *in vivo* phase contrast and amplitude MRI studies. In phase contrast MRI motion causes phase offsets and ghosting in phase maps, distorting measured displacement profiles, and velocity maps. In amplitude MRI, intravoxel motion velocity distributions and shearing motion lead to signal loss. For example, in diffusion MRI, velocity shear within a voxel causes signal attenuation that appears like

*Corresponding author: raisa@helix.nih.gov (R. Z. Freidlin).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

diffusion (pseudo-diffusion) but is not caused by Brownian motion[1]. The brainstem and spinal cord move significantly during the cardiac cycle, and are particularly troublesome to image. Although DTI data has been collected in human and animal hearts[2, 3, 4, 5, 6, 7, 8], reproducible DTI in the beating heart still remains an illusive goal. Whole body diffusion MRI is becoming increasingly important with the recognition that one can detect and possibly stage tumors using diffusion MRI[9]. However, significant motion in the abdomen and gut can hamper the interpretation of DWI data in these soft tissues.

Moreover, there are a number of promising High Angular Resolution Diffusion Imaging (HARDI)[10] sequences that can provide additional information about tissue microstructure and microarchitecture, which are also based on acquiring a large number of DWIs. In these methods, the tissue occupying each voxel is presumed to be the same in each DWI. However, this assumption can seldom be satisfied with existing DWI methods. This is one reason why HARDI-based methods have been applied largely to relatively slowly moving organs and tissue, like the brain, and not more generally, particularly to the beating heart. A snapshot DWI sequence would address these and other important needs within the imaging community.

We have also developed an MR phantom capable of controlling the motion of a specimen that can be used to test a DWI sequence's sensitivity to complex motion. Generally, it has been difficult to compare and contrast different motion control strategies in MRI and to reliably produce and reproduce different motion artifacts and assess their relative severity. An important development would be a controllable MRI phantom that can exhibit a range of complex motions to test the susceptibility of MRI sequences to various motion artifacts and evaluate the efficacy of different correction strategies to mitigate them.

2. Background

2.1. Conventional Stejskal-Tanner DWI Sequences

The most common method for sensitizing magnitude MRI data to the effects of water diffusion is by incorporating the Stejskal-Tanner pulsed gradient NMR sequence into a spin-echo (PGSE) MRI sequence[11, 12, 13, 14]. Specifically, the spin echo is formed by applying a 90° RF pulse followed by a 180° RF pulse. Diffusion weighting is obtained by applying a pair of identical unipolar gradient pulses around the slice selective 180° RF pulse (Fig. 1a). These unipolar diffusion-sensitizing gradients induce diffusion-related signal attenuation in tissues as described in Eq. 1. Signal attenuation caused by phase dispersion from diffusion or the random motion of incoherently moving spins enables one to estimate the water diffusivity in each voxel, using:

$$S(b)=S(0)e^{-bD}, \quad (1)$$

where $S(b)$ is the observed signal, $S(0)$ is a signal in the absence of the diffusion-sensitizing gradients, D is the apparent diffusion coefficient (ADC), and b is given by:

$$b=\gamma^2 G^2 \delta^2 \left[\Delta - \frac{\delta}{3} \right], \quad (2)$$

where G is the magnitude of the diffusion gradient pulse with duration δ , and diffusion time [15].

Meanwhile, coherently moving spins (bulk motion in which there is a uniform velocity) produce a constant phase shift[16] in the Stejskal-Tanner pulsed field gradient (PFG) SE sequence:

$$S(\sigma)_v = S(\sigma) e^{-i2\pi\sigma}, \quad (3)$$

where σ is a function of the gradient strength, G , the diffusion timing parameters, δ , and Δ ; velocity, v , and is calculated according to:

$$\sigma = \gamma G \delta \Delta v. \quad (4)$$

It can be seen from Eq. 4 that in the presence of motion as the diffusion time, Δ , gets longer, it is less likely for the family of spins tagged by the first diffusion-sensitizing gradient, which corresponds to a particular anatomical location, to be refocused by the second one, since the tissue has moved, thus introducing a constant phase shift.

2.2. Motion correction strategies for obtaining DWIs in moving media

A number of techniques have been proposed to minimize signal attenuation due to bulk motion during DWI acquisition.

A Gradient Echo MRI sequence, a special case of the Stejskal-Tanner pulse sequence, consists of a single bipolar gradient block played out after the 90° RF pulse, where the interval between diffusion-sensitizing gradients, Δ , is set to δ (Fig. 1b). Since the duration of the diffusion-sensitizing gradients, in general, is shorter than the diffusion time ($\delta < \Delta$), the effect of coherently moving spins is reduced, compared to the conventional PGSE sequence. The b -value for a single bipolar gradient is given in Eq. 5[17]:

$$b = \frac{2}{3} \gamma^2 G^2 \delta^3, \quad (5)$$

and the velocity sensitive phase variable in Eq. 3 reduces to:

$$\sigma = \gamma G \delta^2 v \quad (6)$$

However, despite a shorter echo time and the reduced effect of the diffusion time, this technique is highly sensitive to magnetic field inhomogeneity, and suffers from a significant signal loss due to a shorter T_2^* relaxation time.

In their work, Hong and Dixon[18] demonstrated how replacing the unipolar diffusion-sensitizing gradients in the conventional Stejskal-Tanner with two bipolar diffusion-sensitizing gradient blocks (Fig. 1c) decreases spin dephasing due to magnetic field inhomogeneity, as well as reducing sensitivity to bulk motion. The b -value for the two consecutive bipolar diffusion-sensitizing gradient blocks is:

$$b = \frac{4}{3} \gamma^2 G^2 \delta^3. \quad (7)$$

Although, the bipolar diffusion-sensitizing (BP) sequence appears to be useful for compensating for the coherently moving spins and is cross-term free in regards to the imaging gradients, in real experiments it is impossible to reduce the times between two consecutive bipolar gradients to δ , due to the duration of the 180° RF pulse, as well as the duration of the crushers on both sides of the slice selective refocusing RF pulse. Once again, this sequence suffers from a prolonged time between two consecutive bipolar gradients and the possibility that the medium has moved between the application of the two diffusion gradient pulse blocks.

It is important to note that the effect of the reversed bipolar-sensitizing gradients[18] is similar to the PGSE sequence, since it is not free of cross-term caused by imaging gradients. Hong and Dixon[18] showed that in the presence of such cross-terms the error in the diffusion coefficient calculations is increased.

Another interesting approach to shorten the diffusion time is the Oscillating gradient Spin Echo sequence[19] (OGSE). As shown in Fig. 1d), OGSE is similar to a conventional BP sequence, where the bipolar diffusion-sensitizing gradients are replaced by sinusoidally oscillating gradients with number of cycles, n , with period T (each cycle behaves like a bipolar gradient). The b -value for an oscillating gradient is calculated according to Eq. 8:

$$b = \frac{3}{4} \gamma^2 G^2 \frac{\delta^3}{\pi^2 n^2}, \quad (8)$$

where δ is a duration of the gradient pulse and n is a number of cycles. As the conventional BP sequence, OGSE has the same shortcoming, i.e., a prolonged time between two consecutive oscillating gradients. Thus, it is not suitable in the presence of complex motion.

Cardiac and respiratory triggering techniques[20, 21] are relatively successful for suppressing artifacts arising from such quasi-periodic bulk motion as cardiac and cerebrospinal fluid pulsation, and respiratory motion. However, triggering is not as effective for remedying motion artifacts in DWIs of cardiac tissue itself and/or spinal cord, due to uncertainty of the organ's position after each cardiac cycle.

Other motion-remediation approaches are based on navigator echo correction[22, 23], where phase correction is performed during post-processing. Once again, such approaches are not efficient for cardiac and spinal imaging due to a number of assumptions about tissue location during acquisition. Thus, the most efficient and logical time to reduce the influence of coherently moving spins is during the acquisition itself.

3. Theory

3.1. Single-sided Bipolar Gradient Spin Echo DWI sequences

In this work we propose a novel idea of applying only one bipolar diffusion-sensitizing gradient (Fig. 1e), rather than two on both sides of the slice selective 180° RF pulse in the Spin Echo DWI sequence. This approach minimizes the effect of the magnetic field inhomogeneity one observes in the Gradient Echo DWI sequence, and reduces the influence of the coherently moving spins by shortening the time between consecutive diffusion-sensitizing gradients. Although commonly used bipolar DW sequences have a diffusion time, Δ , set to the duration of the diffusion-sensitizing pulse, δ , the time between consecutive bipolar diffusion-sensitizing gradients in the moving media causes motion artifacts. Since the diffusion-sensitizing gradients are the leading source of phase dispersion, it is extremely important to minimize the impact of dephasing due to bulk motion not just during, but especially in between these gradients. These new single-sided bipolar spin echo (SS-BPSE) DWI sequences utilize minimum diffusion gradient separation, while reducing signal attenuation due to T_2^* relaxation.

As in the case of the Gradient Echo sequence, b -values are calculated according to Eq. 5. For other than the rectangular shaped diffusion-sensitizing gradients, the calculations of b -values or b -matrices[24] have to be modified according to the shape of the pulses[25].

Although applying a single bipolar gradient block significantly reduces the diffusion weighting as compared to the conventional “two-sided” bipolar or unipolar diffusion-sensitizing sequences, it is still possible using current clinical gradient hardware to generate b -values adequate for cardiac tissue ($b \approx 400 \text{ s/mm}^2$)[7] and spinal cord DWI ($b \approx 500 \text{ s/mm}^2$)[26].

Another major advantage of the bipolar diffusion-sensitizing waveform is elimination of the residual eddy currents[17]. Since the lobes of this gradient are of opposite polarity, eddy currents are largely refocussed.

4. Materials and Methods

4.1. Rotating MRI Phantom

A Bruker Rheo-NMR[27] unit consists of an MR compatible rotating shaft driven by an integrated stepper motor/controller unit that imparts a continuous angular motion to a “cone and plate” or Couette flow cell within a Micro2.5 microscopy probe (25mm solenoid coil). We cannibalized this apparatus, replacing the motor and controller unit so that the shaft and fixture can exhibit arbitrarily rotational complex, jerky motions. A custom module allows the user to prescribe arbitrary shaft rotation waveforms based on a trigger input, including motionless periods. A combination of rotational acceleration and motionless periods (pause in rotation) during each cycle simulates jerky motions in the heart. Another important feature of this apparatus is that this complex motion can be triggered to the acquisition of the MRI sequence. We also developed specialized fixtures to hold different tissues to be scanned, see Fig. 2. The specimen holder allows for a tissue plug to be inserted.

Susceptibility effects can be minimized by potting the specimen in perfluoropolyether oil (“Fomblin”). The fixture itself is constructed from ULTEM, a susceptibility matched plastic.

4.2. Excised Pig Spinal Cord DTI Experiments

To test whether the proposed SS-BPSE PFG MRI sequence reduces motion artifacts in moving media as compared to the PGSE and BP sequences, we obtained different DWI data from the same excised pig spinal cord fixed with 4% paraformaldehyde solution. Prior to DWI data collection, the spinal cord was washed in phosphate-buffered saline (PBS) doped with Gd-DTPA. Gadolinium was used to decrease the T_1 relaxation time of the spinal cord tissue. The sample was imaged in the modified “cone and place” cell from the RheoNMR cell kit filled with Fomblin, within a vertical-bore 7T Bruker (Germany) scanner fitted with Micro2.5 microscopy probe (25mm solenoid coil) with 1450 mT/m 3-axis gradients (Fig. 2). The common parameters for PGSE, conventional BP, and SS-BPSE sequences include repetition time (TR) = 800ms, bandwidth = 100kHz, field-of-view (FOV) = 20×20 mm, matrix = 64×64 with a 1-mm thick axial slice. PGSE echo time (TE) was set to 26ms, while both BP and SS-BPSE had TE set to 37ms. One DWI per slice was acquired with $b \approx 0$ s/mm², followed by 21 DWIs with $b = 1200$ s/mm². DWIs were acquired: 1) without rotation and 2) with rotation at 1Hz and 15ms motor pause. The diffusion gradient duration, δ , was 8ms and the gradient separation, Δ , was 10.2ms for PGSE and $\delta = 8$ ms and $\Delta = 8$ ms for conventional BP and SS-BPSE, respectively. The same diffusion-sensitizing gradient duration was chosen in order to show the impact of separation (duration of 180° RF pulse and spoilers around it) between unipolar and bipolar gradients in PGSE and BP sequences, respectively. Although reducing a diffusion gradient duration for PGSE and BP sequence decreases the diffusion time, this separation remains constant.

At each voxel location in the raw image, the apparent diffusion tensor, $\hat{\mathbf{D}}$, was estimated from the acquired DWIs and tensor-derived parameters, such as the eigenvectors or principal directions, ε_1 , ε_2 , and ε_3 , and the corresponding eigenvalues or principal diffusivities, λ_1 , λ_2 , and λ_3 , were estimated[28]. These were passed to parsimonious model selection[29] and multivariate hypothesis testing clustering[30] algorithms.

5. Results

5.1. Comparison of SS-BPSE with PGSE and Conventional BP

As can be seen in Fig. 3, the results were highly consistent for all three evaluated sequences for the stationary sample of the excised pig spinal cord, although the SNR was better for PGSE sequences due to a shorter echo time. For this particular sample, the average fractional anisotropy, FA , in white matter was around 0.48, while trace of the diffusion tensor, Tr , was approximately 1.3×10^{-3} mm²/sec. However, for the rotating sample, results obtained with the BP sequence (Fig. 4b) were quite different from the results obtained with PGSE and SS-BPSE (Fig. 4a and c, respectively), i.e., $FA \approx 0.71$ and $Tr \approx 4.5 \times 10^{-3}$ mm²/sec for the BP sequence, while for both PGSE and SS-BPSE $FA \approx 0.49$ and $Tr \approx 1.3 \times 10^{-3}$ mm²/sec.

Although results for the rotating sample obtained with PGSE and SS-BPSE sequences appear to be similar, after further examination of the individual DWIs (the examples of the

DWIs for one direction are given in Figs. 5a, b, and c for stationary, and d, e, and f for rotating samples, respectively), it becomes clear that motion artifacts are more pronounced in PGSE images (Fig. 5d) compared to SS-BPSE images (Fig. 5f).

Furthermore, evaluation of the Direction Encoded Color maps[31] shows that the result obtained with PGSE (Figs. 6a and 6d) and BP sequences (Figs. 6b and 6e) are not consistent between stationary and rotating experiments. Alternatively, the SS-BPSE sequence produces compatible results for both stationary and rotating experiments (Figs. 6c and 6f), respectively).

Figs. 7a) and b) show clusters of homogeneous tissue obtained from the measured DTI field maps obtained with PGSE and SS-BPSE sequences for the stationary sample. As can be seen, both sequences produced consistent results in white matter. However, in the rotating experiment, due to averaging caused by motion, the clustering algorithm fails to distinguish white and gray matter in the spinal cord (Fig. 7c). The SS-BPSE sequence successfully separates white and gray matter (Fig. 7d); however, there are slight variations in the degree of homogeneity in white matter (the different colors within the white matter identify three separate clusters).

6. Discussion

In this work we show that in the presence of complex motion, the SS-BPSE sequence outperforms both PGSE and the conventional BP sequences. Especially poor performance of the conventional BP sequence in the presence of jerky motion can be explained by the fact that this sequence is flow compensating only. In other words, if tissue experiences different types of motion (stopping and starting) during the bipolar gradients applied before and after the 180° RF pulse, dephasing can lead to a significant signal loss along some diffusion-sensitizing directions (Fig. 5e). As has been mentioned before, the same b-value for all three sequences was achieved by varying the strength of the diffusion gradient, rather than its duration. In the presence of jerky motion, varying the duration of the diffusion gradients instead of their amplitudes did not achieve a significant improvement for the PGSE and the conventional BP sequences compared to SS-BPSE. This can be attributed to an insufficient duration reduction, since for the PGSE and the conventional BP sequences the durations could be reduced only by ~14% and ~20% compared to SS-BPSE, respectively. Such reduction is not sufficient for minimizing jerky motion artifacts when the two diffusion-sensitizing gradients, either unipolar or bipolar, are separated by the refocusing 180° RF pulse with spoilers around it. The advantages of SS-BPSE are especially pronounced as resolution is reduced since velocity shear within a voxel is more pronounced as the voxel size increases[1]. It is important to note that PGSE has better *SNR* due to shorter TE and requires less diffusion gradient strength to achieve diffusion weighting comparable to SS-BPSE and conventional BP.

This new DWI sequence is potentially useful in many application areas. Clearly, there is a need to perform diffusion MRI studies in the beating heart; this goal has been illusive since the invention of diffusion MRI. DTI in the beating heart will enable the assessment of muscle fiber structure and architectural organization in the heart wall as well as the

acquisition of mean ADC estimates in cardiac muscle tissue. The mean ADC could be calculated from the estimated diffusion tensor itself, from several ADCs obtained in an isotropically organized DWI acquisition, or by using an isotropically weighted DWI sequence. This information should be useful in identifying abnormal or ischemic areas of the heart.

Increasingly, there are reports of intravoxel incoherent motion (IVIM)[32] in living tissues, particularly in highly perfused tissues like kidney[33] and liver[34]. IVIM effects have been reported in b -value ranges of 0 to approximately 100 sec/mm². Some of the observed IVIM effect may be due to complex organ and tissue motion and deformations in addition to the presumed capillary and extracellular fluid flow assumed in the IVIM theory. This new DWI acquisition framework may reduce this artifactual contribution to the IVIM effect, and allow a closer examination of the IVIM perfusion effects if they exist.

Another area of intense interest in the neuroimaging community is the assessment of spinal cord and the brainstem. It is extremely challenging to obtain DWIs in these structures owing to the significant side-to-side “whip” of the spinal cord and the plunging motion of the brainstem. We expect that the ability to measure of diffusion rapidly will improve the assessment of these important structures.

There are clearly several potential embodiments of this DWI sequence that have advantages for particular applications. The diffusion spectroscopic SE sequence could be used as an NMR prefilter prior to the application of an MRI block. The diffusion gradient pulse could be used within a conventional SE sequence with slice select and phase encode gradients applied. For isotropically weighted DWIs the same principle holds. The isotropically weighted spectroscopic SE sequence can be applied as a filter to an MRI block or incorporated within an MRI block.

In general, there is a large and growing family of DWI methods that do not use the ADC or DTI models to obtain useful information about tissue microstructure and architecture. High Angular Resolution Diffusion Imaging (HARDI)[10] acquisitions arise in many higher order diffusion MRI applications. Examples include Q-ball MRI[35], PAS MRI[36], DOT[37], Generalized DTI[38, 39], etc. Other methods of analyzing DWI data that are not model specific, such as k - and q -space MRIs[40], Diffusion Spectrum MRI (DSI)[41], SHORE 3D[42] etc., which attempt to measure the average propagator directly from the DWI data, also can employ these new DWIs to improve data fidelity. Such applications should become more feasible particularly as gradient hardware improves, i.e., gradient strength and slew-rate increases.

A possible extension of this method for obtaining DWIs is to use the bipolar gradient acquisition scheme above in multiple wavevector or multiple pulsed gradient field (mPFG) NMR and MRI measurements[. Research indicates the measurements may be very useful in identifying features of microstructure within tissues and other media without requiring strong diffusion gradients[43]. In these mPFG applications at least two Stejskal and Tanner single PFG blocks are concatenated to produce a multiple PFG MR sequence. The single

sided bipolar PFG sequence can replace the two Stejskal-Tanner gradient pulses to obtain this novel type of diffusion weighting.

7. Conclusion

This new DW sequence is designed to fill a critical need for measuring diffusion parameters over short time periods in presence of tissue motion, both accurately and robustly. Our intent is to continue to develop and apply this snapshot DWI sequence in a variety of *in vivo* applications where motion makes conventional DWI acquisitions problematic.

Acknowledgments

RZF thanks Kenneth Kempner and Dr. Benes Trus for their support and encouragement. The authors would like to thank Drs. Alexandru Avram, Martin Lizak, and Joelle Sarlls for helpful discussions and Liz Salak for editing this paper. We would also like to thank the those who were involved in providing this research with the pig spinal cord tissue: Mr. R. R. Clevenger, Mr. T. J. Hunt, Ms. G. J. Zywickie, Mr. A. D. Zetts, Mrs. K. Keeran, Mr. S. M. Kozlov, and Mr. K. R. Jeffries, from LAMS, NHLBI. This research was sponsored by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Center for Information Technology, National Institutes of Health, Bethesda, Maryland.

References

1. Nevo U, Ozarslan E, Komlos ME, Koay CG, Sarlls JE, Basser PJ. A system and mathematical framework to model shear flow effects in biomedical DW-imaging and spectroscopy. *NMR Biomed.* 2010; 23(7):734–744. URL <http://dx.doi.org/10.1002/nbm.1591>. 10.1002/nbm.1591 [PubMed: 20886564]
2. Reese TG, Weisskoff RM, Smith RN, Rosen BR, Dinsmore RE, Wedeen VJ. Imaging myocardial fiber architecture in vivo with magnetic resonance. *Magn Reson Med.* 1995; 34(6):786–791. [PubMed: 8598805]
3. Hsu EW, Muzikant AL, Matulevicius SA, Penland RC, Henriquez CS. Magnetic resonance myocardial fiber-orientation mapping with direct histological correlation. *Am J Physiol.* 1998; 274(5 Pt 2):H1627–H1634. [PubMed: 9612373]
4. Tseng WY, Reese TG, Weisskoff RM, Wedeen VJ. Cardiac diffusion tensor MRI in vivo without strain correction. *Magn Reson Med.* 1999; 42(2):393–403. [PubMed: 10440965]
5. Dou J, Reese TG, Tseng WYI, Wedeen VJ. Cardiac diffusion MRI without motion effects. *Magn Reson Med.* 2002; 48(1):105–114. URL <http://dx.doi.org/10.1002/mrm.10188>. 10.1002/mrm.10188 [PubMed: 12111937]
6. Helm P, Beg MF, Miller MI, Winslow RL. Measuring and mapping cardiac fiber and laminar architecture using diffusion tensor MR imaging. *Ann N Y Acad Sci.* 2005; 1047:296–307. URL <http://dx.doi.org/10.1196/annals.1341.026>. 10.1196/annals.1341.026 [PubMed: 16093505]
7. Gamper U, Boesiger P, Kozerke S. Diffusion imaging of the in vivo heart using spin echoes—considerations on bulk motion sensitivity. *Magn Reson Med.* 2007; 57(2):331–337. URL <http://dx.doi.org/10.1002/mrm.21127>. 10.1002/mrm.21127 [PubMed: 17260376]
8. Toussaint N, Sermesant M, Stoeck CT, Kozerke S, Batchelor PG. In vivo human 3D cardiac fibre architecture: reconstruction using curvilinear interpolation of diffusion tensor images. *Med Image Comput Comput Assist Interv.* 2010; 13(Pt 1):418–425. [PubMed: 20879258]
9. Padhani AR, Liu G, Koh DM, Chenevert TL, Thoeny HC, Takahara T, Dzik-Jurasz A, Ross BD, Cauteren MV, Collins D, Hammoud DA, Rustin GJS, Taouli B, Choyke PL. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia.* 2009; 11(2):102–125. [PubMed: 19186405]
10. Tuch, DS.; Weisskoff, RM.; Belliveau, JW.; Wedeen, VJ. High angular resolution diffusion imaging of the human brain. *Proceedings of the 7th Annual Meeting of ISMRM; Philadelphia.* 1999. p. 321

11. Stejskal EO, Tanner JE. Spin diffusion measurements: Spin echoes in the presence of a time-dependent field gradient. *J Chem Phys.* 1966; 42(1):288–292.
12. Taylor DG, Bushell MC. The spatial mapping of translational diffusion coefficients by the NMR imaging technique. *Phys Med Biol.* 1985; 30(4):345–349. [PubMed: 4001161]
13. Merboldt K, Frahm HWJ. Self-Diffusion NMR Imaging Using Stimulated Echoes. *Journal of Magnetic Resonance.* 1985; 64(3):479–486.
14. Bihan DL, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology.* 1986; 161(2):401–407. [PubMed: 3763909]
15. Wesbey GE, Moseley ME, Ehman RL. Translational molecular self-diffusion in magnetic resonance imaging. i. effects on observed spin-spin relaxation. *Invest Radiol.* 1984; 19(6):484–490. [PubMed: 6511255]
16. Hahn EL. Detection of sea-water motion by nuclear precession. *Journal Of Geophysical Research.* 1960; 65(2):776–777.
17. Alexander AL, Tsuruda JS, Parker DL. Elimination of eddy current artifacts in diffusion-weighted echo-planar images: the use of bipolar gradients. *Magn Reson Med.* 1997; 38(6):1016–1021. [PubMed: 9402204]
18. Hong X, Dixon WT. Measuring diffusion in inhomogeneous systems in imaging mode using antisymmetric sensitizing gradients. *Journal of Magnetic Resonance.* 1992; 99(3):561–570. 10.1016/0022-2364(92)90210-X
19. Gross B, Kosfeld R. Application of Spin-Echo method in measurement of auto-diffusion. *MESSTECHNIK.* 1969; 77(7–8):171.
20. Chien D, Buxton RB, Kwong KK, Brady TJ, Rosen BR. MR diffusion imaging of the human brain. *J Comput Assist Tomogr.* 1990; 14(4):514–520. [PubMed: 2370348]
21. Thomsen C, Henriksen O, Ring P. In vivo measurements of relaxation process in the human liver by MRI. the role of respiratory gating/triggering. *Magn Reson Imaging.* 1988; 6(4):431–436. [PubMed: 3185137]
22. Ordidge RJ, Helpen JA, Qing ZX, Knight RA, Nagesh V. Correction of motional artifacts in diffusion-weighted MR images using navigator echoes. *Magn Reson Imaging.* 1994; 12(3):455–460. [PubMed: 8007775]
23. Anderson AW, Gore JC. Analysis and correction of motion artifacts in diffusion weighted imaging. *Magn Reson Med.* 1994; 32(3):379–387. [PubMed: 7984070]
24. Basser PJ, Mattiello J, LeBihan D. MR diffusion tensor spectroscopy and imaging. *Biophys J.* 1994; 66(1):259–267. [PubMed: 8130344]
25. Mattiello J, Basser PJ, LeBihan D. Analytical expressions for the b-matrix in NMR diffusion imaging and spectroscopy. *Journal of magnetic resonance Series A.* 1994; 108(2):131–141.
26. Renoux J, Facon D, Fillard P, Huynh I, Lasjaunias P, Ducreux D. MR diffusion tensor imaging and fiber tracking in inflammatory diseases of the spinal cord. *AJNR Am J Neuroradiol.* 2006; 27(9):1947–1951. [PubMed: 17032873]
27. Callaghan P. Rheo-NMR: nuclear magnetic resonance and the rheology of complex fluids. *Reports on Progress in Physics.* 1999; 62(4):599–670.
28. Basser PJ, Mattiello J, LeBihan D. Estimation of the effective self-diffusion tensor from the NMR spin echo. *J Magn Reson B.* 1994; 103(3):247–254. [PubMed: 8019776]
29. Freidlin RZ, Ozarslan E, Komlos ME, Chang LC, Koay CG, Jones DK, Basser PJ. Parsimonious model selection for tissue segmentation and classification applications: a study using simulated and experimental DTI data. *IEEE Trans Med Imaging.* 2007; 26(11):1576–1584. URL <http://dx.doi.org/10.1109/TMI.2007.907294>. 10.1109/TMI.2007.907294 [PubMed: 18041272]
30. Freidlin RZ, Ozarslan E, Assaf Y, Komlos ME, Basser PJ. A multivariate hypothesis testing framework for tissue clustering and classification of DTI data. *NMR Biomed.* 2009; 22(7):716–729. URL <http://dx.doi.org/10.1002/nbm.1383>. 10.1002/nbm.1383 [PubMed: 19593779]
31. Pajevic S, Pierpaoli C. Color schemes to represent the orientation of anisotropic tissues from diffusion tensor data: application to white matter fiber tract mapping in the human brain. *Magn Reson Med.* 1999; 42(3):526–540. [PubMed: 10467297]

32. Bihan DL, Breton E, Lallemand D, Aubin ML, Vignaud J, Laval-Jeantet M. Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. *Radiology*. 1988; 168(2): 497–505. [PubMed: 3393671]
33. Muller MF, Prasad PV, Edelman RR. Can the IVIM model be used for renal perfusion imaging? *European Journal of Radiology*. 1998; 26(3):297–303. URL <http://www.sciencedirect.com/science/article/pii/S0720048X97011613>. 10.1016/S0720-048X(97)01161-3 [PubMed: 9587760]
34. Luciani A, Vignaud A, Cavet M, Nhieu JTV, Mallat A, Ruel L, Laurent A, Deux JF, Brugieres P, Rahmouni A. Liver cirrhosis: intravoxel incoherent motion MR imaging—pilot study. *Radiology*. 2008; 249(3):891–899. URL <http://dx.doi.org/10.1148/radiol.2493080080>. 10.1148/radiol.2493080080 [PubMed: 19011186]
35. Tuch DS. Q-ball imaging. *Magn Reson Med*. 2004; 52(6):1358–1372. URL <http://dx.doi.org/10.1002/mrm.20279>. 10.1002/mrm.20279 [PubMed: 15562495]
36. Jansons KM, Alexander DC. Persistent angular structure: new insights from diffusion mri data. dummy version. *Inf Process Med Imaging*. 2003; 18:672–683. [PubMed: 15344497]
37. Özarslan E, Shepherd TM, Vemuri BC, Blackband SJ, Mareci TH. Resolution of complex tissue microarchitecture using the diffusion orientation transform (DOT). *NeuroImage*. 2006; 31:1086–1103. [PubMed: 16546404]
38. Özarslan E, Mareci TH. Generalized diffusion tensor imaging and analytical relationships between diffusion tensor imaging and high angular resolution diffusion imaging. *Magn Reson Med*. 2003; 50(5):955–965. URL <http://dx.doi.org/10.1002/mrm.10596>. 10.1002/mrm.10596
39. Liu C, Bammer R, Acar B, Moseley ME. Characterizing non-gaussian diffusion by using generalized diffusion tensors. *Magn Reson Med*. 2004; 51(5):924–937. URL <http://dx.doi.org/10.1002/mrm.20071>. 10.1002/mrm.20071 [PubMed: 15122674]
40. Callaghan PT, Eccles CD, Xia Y. NMR microscopy of dynamic displacements - k-space and q-space imaging. *Journal Of Physics E-Scientific Instruments*. 1988; 21(8):820–822.
41. Wedeen VJ, Hagmann P, Tseng WYI, Reese TG, Weisskoff RM. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. *Magn Reson Med*. 2005; 54(6): 1377–1386. [PubMed: 16247738]
42. Özarslan E, Koay CG, Shepherd TM, Blackband SJ, Basser PJ. Simple harmonic oscillator based reconstruction and estimation for three-dimensional q-space mri. *Proc Int Soc Magn Reson Med*. 2009:1396.
43. Komlosh ME, Horkay F, Freidlin RZ, Nevo U, Assaf Y, Basser PJ. Detection of microscopic anisotropy in gray matter and in a novel tissue phantom using double pulsed gradient spin echo mr. *J Magn Reson*. 2007; 189(1):38–45. URL <http://dx.doi.org/10.1016/j.jmr.2007.07.003>. 10.1016/j.jmr.2007.07.003 [PubMed: 17869147]

- We propose a new method for improving estimation of self-diffusion parameters in moving media.
- The proposed sequence utilizing a single bipolar diffusion sensitizing gradient within a spin echo sequence.
- This method shortens the diffusion time, while reducing the impact of inhomogeneity.
- A novel MRI phantom was designed to demonstrate the robustness of the proposed DWI sequence.
- This MRI phantom can exhibit a range of complex rotational motions.

Figure 1.

a) Stejskal-Tanner, b) Conventional bipolar Gradient Echo, c) Conventional bipolar Spin Echo, d) Oscillating gradient Spin Echo and e) Single-sided bipolar before refocusing 180° RF pulse DWI sequences

Figure 2.
Schematic drawing of the experimental setup

Figure 3.

$A(0)$ (GM - gray matter, WM - white matter), FA , and $Tr \times 10^{-3} \text{mm}^2/\text{sec}$ maps of the stationary excised pig spinal cord sample obtained with a) PGSE, b) conventional BP, and c) SS-BPSE sequences

Figure 4.

$A(0)$ (GM - gray matter, WM - white matter), FA , and $Tr \times 10^{-3} \text{mm}^2/\text{sec}$ maps of the rotating excised pig spinal cord sample obtained with a) PGSE, b) conventional BP, and c) SS-BPSE sequences (GM - gray matter, WM - white matter)

Figure 5.

Diffusion-weighted images along one direction of the stationary excised pig spinal cord sample obtained with a) PGSE, b) conventional BP, and c) SS-BPSE sequences; and of the rotating excised pig spinal cord sample obtained with d) PGSE, e) conventional BP, and f) SS-BPSE sequences

Figure 6. Direction encoded color maps

of the stationary excised pig spinal cord sample obtained with a) PGSE, b) conventional BP, and c) SS-BPSE sequences; and of the rotating excised pig spinal cord sample obtained with d) PGSE, e) conventional BP, and f) SS-BPSE sequences. *Color hue represent directions as: green is left-right, red is up-down, and blue is through the plane*

Figure 7.

Clusters, which identified homogeneity of the measured DTI field maps of the stationary excised pig spinal cord sample obtained with a) PGSE and b) SS-BPSE sequences; and the rotating excised pig spinal cord sample obtained with c) PGSE and d) SS-BPSE sequences. *The discrete colors within white matter correspond to separate clusters with a different degree of homogeneity*