Original Research

Halving Imaging Time of Whole Brain Diffusion Spectrum Imaging and Diffusion Tractography Using Simultaneous Image Refocusing in EPI

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Purpose: To increase the efficiency of densely encoded diffusion imaging of the brain, such as diffusion spectrum imaging (DSI), we time-multiplex multiple slices within the same readout using simultaneous image refocusing echo-planar imaging (SIR-EPI).

Materials and Methods: Inefficiency in total scan time results from the long time of diffusion encoding gradient pulses which must be repeated for each and every image. We present a highly efficient multiplexing method, simultaneous image refocusing (SIR), for reducing the total scan time of diffusion imaging by nearly one-half. SIR DSI is performed in 10 minutes rather than 21 minutes, acceptable for routine clinical application.

Results: Two identical studies were completed, comparing conventional single-slice EPI DSI and SIR-EPI DSI, showing equal signal-to-noise ratio (SNR) and contrast and small differences in registration, likely due to typical subject motion. Comparison of DSI and DTI tractographs showed matching quality and detection of white matter tracts.

Conclusion: The net reduction to nearly half the number of diffusion encoding gradient pulses in SIR-EPI significantly reduces acquisition times of DSI and DTI.

Key Words: MRI; diffusion imaging; fast imaging; tractography; pulse sequences.
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MR DIFFUSION TENSOR IMAGING (DTI) (1–3) and MR densely encoded diffusion imaging, such as diffusion spectrum imaging (DSI) (4), high-angular resolution diffusion imaging (HARDI) (5,6), or Q-ball imaging (7) measure the 3D intravoxel spin displacement for each voxel in a 3D multislice MR scan. This results in a dataset with true six-dimensional (6D) information. Diffusion encoding requires the application of strong magnetic field gradients during the MR signal evolution time (8). Signal attenuation results from dispersion of spin phase along the applied gradient axis and this provides image contrast. In DSI, many (typically hundreds) of sets of images with different encoding intensities and gradient directions must be acquired. The range and distribution of gradient intensities and orientations is determined so as to resolve the needed angular separation and to span the expected spread of intravoxel spin displacements. From the resulting diffusion anisotropy spectra, the directional components of diffusion in each voxel can be linked graphically to visualize fibrous tissue structure (9). DSI of the brain promises the visualization of neural connectivity previously unattainable by noninvasive means.

The usual acquisition technique for diffusion encoding in vivo by MRI is echo-planar imaging (EPI) (10). In diffusion imaging, global motion such as involuntary changes in position of the subject in the presence of the requisite lengthy and intense gradients cause large and unpredictable changes in the phase of the MR signal. These phase changes prevent complex summation of the unreconstructed signal from multiple excitations, and imaging techniques where each image is assembled from signals acquired over time (ie, spin warp) become problematic. Since EPI collects an entire image plane instantaneously, the effects of any movement on the reconstruction of a single image are negligible. Diffusion only affects the image magnitude, so the ensemble of magnitude images needed for any diffusion encoding scheme can be acquired and assembled without regard to their image-to-image phase coherence.

For DSI, our interest is in the 6D character of the entire imaged volume, viewed from any angle, and not in the 2D display of individual slices. We require that the voxel dimensions be close to isotropic, with full coverage of the brain or other anatomy of interest. This requires dividing the imaged volume into many more slices than typically used in MRI for anatomic display. The large number of slices means that the minimum TR

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of the EPI acquisition is long compared to the T1 relaxation time. T2 effects are minimized by choosing the shortest possible acquisition time, given the time required for diffusion encoding. Since relaxation contrast affects DSI contrast only secondarily, as much of the experiment time as possible is spent either encoding diffusion with strong gradients or sampling the MR signal.

This diffusion encoding requires the application of longer duration and higher amplitude gradient pulses than used in any other MR imaging technique. These long gradients create technical problems unique to diffusion acquisitions. DSI in particular requires diffusion encoding gradients on the order of 100 msec in total length compared to EPI spatial encoding on the order of 25 msec, for b-values of about 8500 s/mm^2. These large diffusion gradients therefore comprise the largest fraction of the total acquisition time. Scanning efficiency depends most strongly on the fraction of the total acquisition time spent sampling the MR signal. EPI, and other fast MRI techniques, are usually efficient because they spend most of the acquisition time sampling the MR signal. The long diffusion encoding times and resulting long TEs make DSI much less efficient than the usual EPI acquisition.

As a result of its requisite long TEs, isotropic spatial coverage, and large number of encoding axes, the acquisition time for DSI is quite long. Using the usual multislice single-excitation EPI technique, DSI has been limited to use with cooperative and motivated volunteers due to the long study times required, typically 20–30 minutes or more.

Our objective was to increase the scanning efficiency of diffusion MRI and to shorten the total acquisition time for DSI in particular. We used the simultaneous image refocusing (SIR)-EPI method (11) to increase the fraction of acquisition time used for sampling data without sacrificing the motion-freezing properties of EPI that enable clinical diffusion scanning. In the following work we present a method for reducing the total scan time for a DSI scan by nearly one-half to make it acceptable for routine in vivo brain imaging and demonstrate the general application of SIR-EPI to DTI, with similar reductions in total scan time.

MATERIALS AND METHODS

SIR-EPI resembles the usual EPI acquisition, with the modification of the excitation pulse. Instead of the usual windowed *sinc(t)* radiofrequency (RF) excitation pulse, two windowed *sinc(t)* excitation RF pulses with different frequency offsets are used, separated by an additional readout dephasing gradient. Each RF pulse selects a different and adjacent slice. The signal is rephased by the readout gradient as two echoes centered in each half of the raw spatial frequency (k-space) data. These echoes are then divided into separate raw data matrices and reconstructed and displayed individually. In this way SIR-EPI multiplexes the signal from two slices into a single EPI readout train.

The SIR-EPI diffusion pulse sequence is shown in Fig. 1. The two slice selective RF pulses are placed as close in time to each other as possible given the constraint of

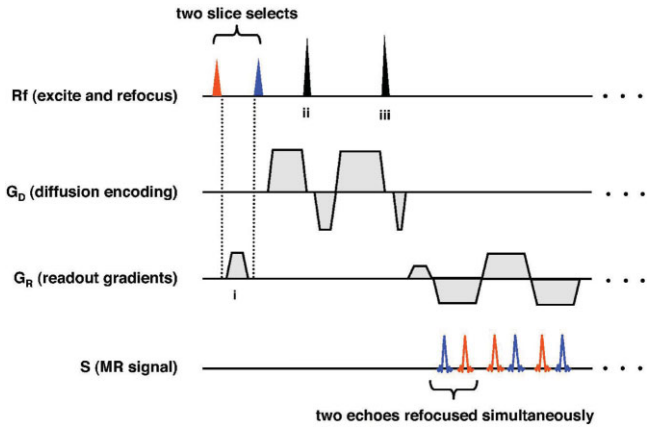

Figure 1. The SIR-EPI echo planar DSI sequence acquires two adjacent slices in each echo planar readout. Two slice selective RF excitations (solid color) are separated by a readout dephasing gradient (i) that with standard time reversal places the echo for each slice in its respective half of the resulting k-space. Use of two RF refocusing pulses (ii and iii) allows the durations of the diffusion encoding gradient lobes to be adjusted to minimize eddy currents. Each EPI readout gradient lobe contains two echoes, one for each slice. When reconstructed, the data are divided in half to form two arrays, then 2D FT transformed into two images, one for each slice. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

the time needed for the initial readout dephasing and slice refocusing, typically about 2.5 msec. Time separation between the echo pairs in the readout equals half the total sampling time per line, about 350 μs. The initial dephasing pulse on the read gradient axis only effects the signals from the preceding first excitation RF pulse to displace these echoes in the readout period with respect to the echoes from the second RF pulse. The second readout dephasing pulse centers the echo pair in the readout periods. This in effect separates the two slices into the two halves of k-space.

Following the time-reversal of alternate lines and phase correction required for EPI reconstruction, we divide the complex raw data in half along the middle of the read axis and reconstruct each half. A pair of N × M images requires 2N × M raw data points in each acquisition, obtained by doubling the readout axis k-space distance needed for a single image. Doubling the distance does not double the minimum readout time per line because the time-consuming gradient switching in the EPI readout does not need to be repeated.

The SIR-EPI DSI pulse sequence uses twice-refocused alternating polarity diffusion gradients (12) to minimize the eddy currents generated by the long diffusion gradients (13). The reconstruction program was modified to divide and reconstruct the raw image data in real time with the image acquisition. The present technique was implemented to provide acceleration with GRAPPA (14) by allowing the GRAPPA reconstruction to operate on the entire k-space matrix, including both slices. The images were then split into their component slices as the last step. This is functionally equivalent to GRAPPA operating on a single k-array. Image-based acceleration methods, such as SENSE (15),

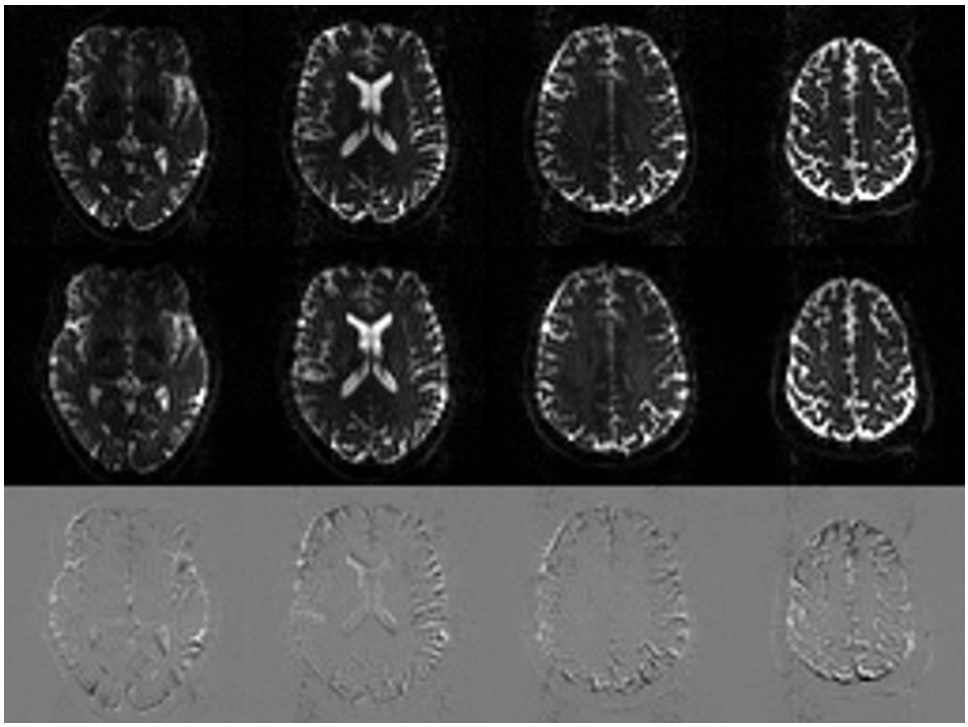

Figure 2: Unattenuated (T2-weighted) source images acquired using conventional (row 1) and SIR-EPI (row 2) echo planar DSI from the same subject and session. Subtraction of the two sets of images after realignment is shown in row 3. Both original and realigned images were compared, with equal results. Differences in the two sets of images appear as either differences in CSF contrast (due to the different TRs) or misregistration differences that are typical for two sets of diffusion slices acquired at different times in the same imaging session. Both acquisitions used a b-value of 8500 s/mm^2 and an isotropic 3.2-mm resolution. The conventional EPI required 19 minutes to complete (TE = 145 msec, TR = 4370 msec), while the SIR-EPI required almost half as long, at 10 minutes (TE = 150 msec, TR = 2340 msec).

would require additional and extensive reconstruction coding, and were not tested here. The data appears in the usual fashion in the database on the scanner, separated into individual images with the proper aspect ratio and slice order.

Processing of the magnitude image dataset into fiber tracts was completed offline. The magnitude images in DICOM format are converted to ANALYZE format (Mayo Foundation for Medical Imaging and Research, Rochester, MN) and then converted to fiber track sets using an algorithm developed by Wedeen et al (4,9). Following reconstruction of the orientational dependence of the spin displacement density by integral transform at each voxel (3D-FT followed by radial projection), data at each voxel were reduced to the set of vectors *{V}* that are the orientations of maximum diffusion. Fiber tracts were reconstructed with a streamline algorithm: tracts are initiated at the center of every voxel for every orientation vector of maximum diffusion V_i and extended into a new voxel along the vector of maximum diffusion closest to its incoming orientation. Fibers terminate when no maximum vector exists within a fixed angular tolerance, typically set to 0.5 radian, or when the boundary of the image mask is reached. An RGB (red, green, blue) code determines the color of each fiber based on the orientation of the vector between the fiber endpoints. Calculation of the tract files required less than 2 minutes for the entire study on a 2.5 GHz generic PC. The tracts are viewed in 3D using a program developed by the authors with the Visualization Toolkit (VTK; Kitware, Clifton, NY).

To demonstrate the reduced DSI scan time using SIR-EPI, comparable sets of data with similar acquisition parameters were collected with multislice SIR-EPI and conventional EPI. All data were collected using a Siemens TIM Trio 3 T scanner (Siemens Medical Systems, Erlangen, Germany) running Numaris 4 software v. VB12T. The maximum gradient amplitude for the Trio is 40 mT/M, but due to gradient duty cycle constraints the peak gradient was limited to 28 mT/M. A 32-channel matrix head coil, developed in our laboratory, was used for all acquisitions. Normal volunteers were scanned with informed consent using an Institutional Review Board (IRB)-approved protocol.

The EPI and SIR-EPI DSI acquisitions use the same diffusion encoding scheme. The b-value was set to 8500 s/mm^2, and a set of 258 encoding vectors uniformly sampling a hemisphere of Q-space was chosen. The imaged volume covered the whole brain at isotropic 3.2 mm resolution, with a 64 $\times$ 64 image matrix; 26 conventional and 13 SIR-EPI adjacent double slices were acquired in 19 minutes and 10 minutes, respectively. The images were reconstructed using GRAPPA (14) with an acceleration of 2 and 32 reference lines. The SIR-EPI images had a TE of 150 msec, a readout time of 22.1 msec, and a TR of 2340 msec, and without SIR-EPI the prescription required a TE of 145 msec, a readout time of 13.8 msec, and TR of 4370 msec. In both cases the total acquisition and readout times were minimized according to the sampling and gradient capabilities of the scanner. Aside from minor changes to accommodate a SIR-EPI prescription, the slices are prescribed, acquired, reconstructed, and displayed in the same manner as with the Siemens clinical diffusion EPI sequence.

RESULTS

A representative sample of the T2-weighted images is shown in Fig. 2. Side-by-side comparison of the images shows near identical quality of the two sets of images. A subtraction image, shown below, indicates that the main difference in the corresponding EPI and SIR-EPI

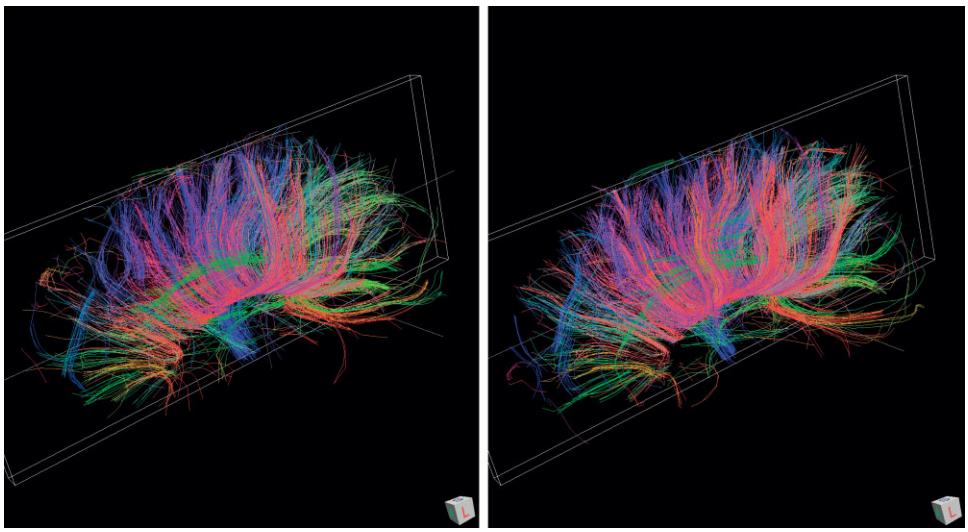

Figure 3. Tractographs constructed using conventional (left) and SIR-EPI (right) echo planar DSI from the same subject and session. Representative source images and the acquisition parameters for these tractographs are shown in Fig. 2. All fibers are incident on a 6.4 mm sagittal plane, and are greater than 19.2 mm in length. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

images comes from misregistration, likely due to subject motion, as eddy current-dependent displacements have been nulled by the diffusion encoding scheme.

Comparison of the tractographs from the two methods in Figs. 3 and 4 showed matching quality and detection of white matter tracts, differing only in the time required for acquisition. Observable differences in the source images can be attributed to differing relaxivity contrast between the scans (due to differences in TE and TR), image noise, and slight position changes by the subject. These differences can seed slightly different sets of fibers, but the depiction of fiber tracts, including their orientation, length, and intersection, did not change.

DISCUSSION

Encoding diffusion in MRI requires the longest and most intense gradient pulses of any known MRI tech-

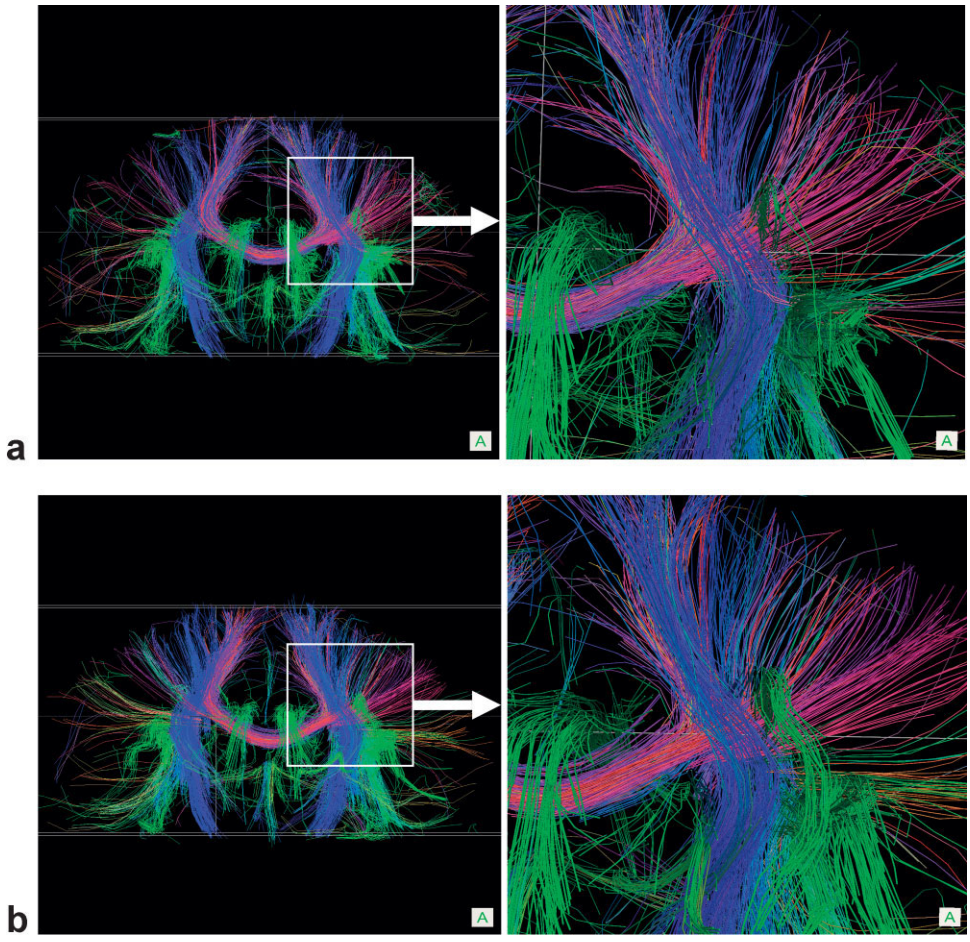

Figure 4. Tractographs constructed using (**a**) conventional EPI and (**b**) SIR-EPI DSI from the same subject and session as in Fig. 3. The acquisition parameters are as in Fig. 2. All fibers are incident on a 19.2-mm coronal plane and are greater than 6.4 mm in length. The inset enlargements demonstrate how DSI can show crossing fibers, even when the fibers cross through the same voxel. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

nique. At present, the most practical way to acquire diffusion data for clinical use is with a subsecond "motion-freezing" method such as single-shot EPI. Multi-acquisition techniques have been proposed that use navigator or calibration scans to adjust for coherent motion post facto; these techniques have not yet achieved the widespread use of diffusion EPI. Motion-freezing techniques such as EPI are particularly useful in high-B DSI due to DSI's very high velocity sensitivity. SIR-EPI retains EPI's motion-freezing characteristic while doubling the amount of information in each acquisition. One side effect of the time coherence between SIR-EPI slices is phase coherence between those slices. This property of SIR-EPI has been exploited to provide a more accurate measurement of the voxel-to-voxel phase changes due to material strain (16). However, for DSI we are only concerned with the more efficient use of the diffusion encoding time that SIR-EPI provides.

The speedup of the SIR technique applies to all spin-warp MR acquisitions, although in some cases SIR will be impractical because of the increased TE. A proof is simple: For N acquisitions, let E be the encoding time and R be the readout time. The conventional experiment requires $N(E+R)$ seconds, and the SIR experiment requires $\frac{N}{2}(E + 2R)$, thus $\frac{N(E+2R)/2}{N(E+R)} = \frac{E+2R}{2(E+R)} < 1 \ \forall \{E,R\}$ and the scan time reduction approaches 1/2 as $E \gg R$. We see that as the ratio of encoding time to sampling time of a scan increases, the advantage of SIR increases and the efficiency (portion of the total acquisition time spent sampling data) increases. For a range of DTI and DSI scans on our imagers, the reduction in scan time ranged from 20% (128 × 128 DTI, B = 500) to 46% (64 × 64 DSI, B = 8500). In the example in Fig. 3, SIR-EPI increases the TE from 145 to 150 msec but the TR for 26 slices went from 4.37 seconds to 2.34 seconds, approaching a halving in scan time. The increase in the number of total samples with SIR-EPI allowed our time per sample to decrease from 5.6 μs to 4.8 μs due to the more efficient shape of the readout gradient.

In addition to nearly halving the TR of the diffusion experiment, the longer readout time required by the SIR-EPI acquisition will result in more image distortion due to the magnetic susceptibility of the subject. If the readout time doubles, the distortion also doubles in the sense that the displacement of signal due to the susceptibility-induced field distortion also doubles. While the acquisition of two slices with a single SIR acquisition requires twice as many samples as a single slice, the readout time need not double. A major part of the EPI data sampling time is consumed by the need to reverse the readout gradient polarity for every line in order to sweep out the sampled region in spatial frequencies (k-space). With the SIR technique, doubling the number of samples per line does not require any additional ramping time, thus increasing the available gradient power per unit time in the readout. The degree to which this increased k-space traversal efficiency will impact the data sampling time will depend on the capability of the imaging hardware and the specifics of the EPI implementation.

For multicoil acquisitions, the highest image quality was found when using matched filtering (17) of the individual coils. Parallel imaging techniques are not necessarily required for tractographs of whole brain, but may prove useful in specific areas such as hippocampus, where susceptibility-induced effects may be limiting. The additional readout time of SIR-EPI does increase susceptibility-induced artifacts; slightly increased distortion around the frontal lobe could be detected in the SIR-EPI DSI source images when not acquired using GRAPPA, but the resulting tractographs were largely unaffected.

SIR-EPI images with readout lengths much greater than used here may show significant susceptibility-induced artifacts, although the reduction in total scan time would still approach 50% for techniques with long encoding times. Accelerated parallel imaging techniques can be used to reduce susceptibility-induced artifacts by shortening the readout period, although they do not have nearly the same impact as SIR-EPI does in reducing DSI scan time. Acceleration cannot change the one-to-one relationship of a single slice for each long diffusion encoding period. Shortening the readout time via parallel acquisition does reduce the encoding time E to readout time R (E, R described above), and this change always increases the efficiency advantage of the SIR technique. However, acceleration is not essential; unaccelerated 64 × 64 SIR images (128 × 64 raw matrix) provide excellent tractographs. Acceleration complements the SIR technique, and acceleration factors beyond 2 will allow higher spatial resolution at little cost in TE and artifacts. Encoding gradient strength and duty cycle determines the minimum TE for DSI and consequently limits the SNR; higher spatial resolution would require both faster readouts (with large acceleration factors, at a potential cost of SNR [18]) and stronger encoding gradients. Increased SIR-EPI factors with four or more slices per excitation at much lower spatial resolution have also been tested, and may be appropriate for highly accelerated scans using a very large number of receivers and densely packed RF coils, and/or low spatial resolution, high temporal resolution techniques.

While the total acquisition time has been nearly halved, the difference in clinical acceptance between a 19-minute scan and a 10-minute scan is much more consequential. At 10 minutes the DSI scan can be reasonably included in a routine clinical scan protocol without great hardship to the patient and with much lesser likelihood of patient head motion.

SIR-EPI can be applied generally to diffusion applications such as HARDI (5,6), Q-ball (7), or DTI (1–3) with a comparable degree of scan time reduction. SIR-EPI could be applied to other MRI techniques where the encoding time is long compared to the sampling time, to further shorten total scan time, extend coverage, or improve resolution according to specific diagnostic needs. Additional acquisition speed-up is forthcoming; using a new body-centered cubic table (19) in which the number of encoding steps can be reduced by 25%, reducing the present SIR-EPI DSI scan time to less than 8 minutes.

In conclusion, SIR-EPI produced DSI images of the whole brain in 10 minutes, a 46% time reduction that would likely be achievable in other diffusion encoded EPI techniques. This reduction of scan time of DSI imaging enables its routine use and incorporation into clinical protocols.

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