High-resolution diffusion-weighted imaging at 7 Tesla: Single-shot readout trajectories and their impact on signal-to-noise ratio, spatial resolution and accuracy

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\textbf{A R T I C L E  I N F O}

\textbf{Keywords:}
Diffusion MRI
Ultra-high field
Field monitoring
T2\textsuperscript{*} blurring
Effective resolution
Signal-to-noise ratio

\textbf{A B S T R A C T}

Diffusion MRI (dMRI) is a valuable imaging technique to study the connectivity and microstructure of the brain in vivo. However, the resolution of dMRI is limited by the low signal-to-noise ratio (SNR) of this technique. Various multi-shot acquisition strategies have been developed to achieve sub-millimeter resolution, but they require long scan times which can be restricting for patient scans. Alternatively, the SNR of single-shot acquisitions can be increased by using a spiral readout trajectory to minimize the sequence echo time. Imaging at ultra-high fields (UHF) could further increase the SNR of single-shot dMRI; however, the shorter T2\textsuperscript{*} of brain tissue and the greater field non-uniformities at UHFs will degrade image quality, causing image blurring, distortions, and signal loss.

In this study, we investigated the trade-off between the SNR and resolution of different k-space trajectories, including echo planar imaging (EPI), partial Fourier EPI, and spiral trajectories, over a range of dMRI resolutions at 7T. The effective resolution, spatial specificity and sharpening effect were measured from the point spread function (PSF) of the simulated diffusion sequences for a nominal resolution range of 0.6–1.8 mm. In-vivo partial brain scans at a nominal resolution of 1.5 mm isotropic were acquired using the three readout trajectories to validate the simulation results. Field probes were used to measure dynamic magnetic fields offline up to the 3rd order of spherical harmonics. Image reconstruction was performed using static $\Delta B_0$ field maps and the measured trajectories to correct image distortions and artifacts, leaving T2\textsuperscript{*} effects as the primary source of blurring. The effective resolution was examined in fractional anisotropy (FA) maps calculated from a multi-shell dataset with b-values of 300, 1000, and 2000 s/mm\textsuperscript{2} in 5, 16, and 48 directions, respectively. In-vivo scans at nominal resolutions of 1, 1.2, and 1.5 mm were acquired and the SNR of the different trajectories calculated using the multiple replica method to investigate the SNR. Finally, in-vivo whole brain scans with an effective resolution of 1.5 mm isotropic were acquired to explore the SNR and efficiency of different trajectories at a matching effective resolution. FA and intra-cellular volume fraction (ICVF) maps calculated using neurite orientation dispersion and density imaging (NODDI) were used for the comparison. The simulations and in vivo imaging results showed that for matching nominal resolutions, EPI trajectories had the highest specificity and effective resolution with maximum image sharpening effect. However, spirals have a significantly higher SNR, in particular at higher resolutions and even when the effective image resolutions are matched. Overall, this work shows that the higher SNR of single-shot spiral trajectories at 7T allows us to achieve higher effective resolutions compared to EPI and PF-EPI to map the microstructure and connectivity of small brain structures.

1. Introduction

Diffusion MRI (dMRI) is sensitive to the motion of water molecules in tissue and thus provides insight into its microstructure (Afzali et al., 2021; Basser et al., 1994; Jones, 2010). As gradient pulses are employed to encode diffusion in a specific direction, the loss of phase coherence due to motion along that direction results in attenuation of the MR signal (Jones, 2010; Tanner, 1979). This signal attenuation together with long diffusion-encoding times significantly reduces the signal-to-noise ratio (SNR) of dMRI and thus limits the spatial resolution that can be achieved (Polders et al., 2011; Polzehl and Tabelow, 2016). 2-D fast imaging approaches typically used for diffusion imaging further

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https://doi.org/10.1016/j.neuroimage.2023.120159.
Received 3 February 2023; Received in revised form 31 March 2023; Accepted 4 May 2023
Available online 5 May 2023.
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reduce the SNR compared to 3D acquisitions normally performed for anatomical scans. Several imaging techniques have been implemented in dMRI to reduce the echo time (TE) in order to minimize the signal loss due to T2 decay without sacrificing scan time, including accelerated parallel imaging (Griswold et al., 2002; Pruessmann et al., 2001, 1999), partial Fourier echo-planar imaging (PF-EPI) (e.g., Noll et al., 1991; Blaimer et al., 2009), non-Cartesian trajectories such as spirals (Block and Frahm, 2005; Assländer et al., 2013), and high performance gradients (Foo et al., 2020; Setsompop et al., 2013; Wang et al., 2021).

Complementary techniques have also been developed to increase image resolution that are based on acquiring k-space in multiple shots. These techniques include acquiring multiple interleaves in the phase encode direction (e.g., Butts et al., 1996), multiple segments in the readout direction (e.g., Robson et al., 1997; Porter and Heidemann, 2009; Heidemann et al., 2010), using multi-shot non-Cartesian trajectories (e.g., Liu et al., 2004; Wang et al., 2005; Pipe and Zwart, 2006; Truong and Guidon, 2014), and 3-D multi-slab acquisitions (Dai et al., 2021; Engström and Skare, 2013; Moeller et al., 2020; Wu et al., 2016). These multi-shot techniques are sensitive to phase differences between shots due to motion and artifacts caused by physiological motion such as breathing, which must be corrected (e.g., Chen et al., 2013; Guhaniyogi et al., 2016; Mani et al., 2017). The above techniques can be combined with g-slider, a multi-shot technique to increase resolution along the slice direction. g-Slider uses a tailored RF pulse profile to excite a slab that modulates single slice information. The acquisition is repeated the same number of times as the slice number each with different RF pulses, and then individual slices are unaliased using the acquired scans (Setsompop et al., 2018; Ramos-Llordén et al., 2020; Wang et al., 2021; Ramos-Llordén et al., 2022). Using this method, resolutions as high as 500 μm have recently been achieved (Liao et al., 2022). In addition to these techniques, reduced field-of-view (rFOV) imaging has been also proposed in which reduction in the FOV results in an increased distance between two adjacent k-space lines allowing shorter readout duration to minimize T2* signal decay (e.g., Feinberg et al., 1985; Karimpinios et al., 2009; Saritas et al., 2014). Although this method covers a small region, it can be used repetitively for a whole-brain acquisition which increases the scan time similar to other techniques. Using these techniques, a typical diffusion-weighted sequence with 64 directions can take ~45–60 min, which limits the application of high-resolution dMRI in clinical research. This has motivated the development and optimization of single-shot readout approaches to improve dMRI SNR and resolution.

One way to boost the SNR is to scan at ultra-high magnetic field (UHF), which offers an increase in the intrinsic sensitivity and thus the opportunity to acquire high-resolution scans. The SNR has a supralinear (∼B₀^0.95) relationship with the main magnetic field (B₀) over a range of about 3 to 7 T (Pohmann et al., 2016). However, due to shorter T2 and T2* relaxation times at UHFs leading to a faster signal decay, the benefit of UHF imaging for dMRI depends on the echo time (Gallichan, 2018; Uğurbil et al., 2013). Efficient readout trajectories that reduce TE can maximize the SNR increase provided by UHF imaging. Single-shot spiral acquisitions are among the most efficient trajectories (Assländer et al., 2013; Engel et al., 2018; Lee et al., 2021a; Wilm et al., 2017). Center-out spiral trajectories minimize the echo time by starting acquisition from the k-space center, resulting in a significant SNR advantage (Lee et al., 2021a). Furthermore, acquiring with a spiral pattern avoids sharp changes in the trajectory direction that decrease speed due to limitations in gradient slew rates and peripheral nerve stimulation (PNS). Additionally, spiral trajectories inherently have zero gradient moments at the k-space center which make them robust to flow artifacts (Nishimura et al., 1995). The disadvantage of this type of k-space sampling is increased sensitivity to gradient imperfections and B₀ field non-uniformities that cause image blurring and ring-shaped artifacts (Block and Frahm, 2005).

The development of field monitoring probes allows us to measure dynamic field imperfections and use this information during image reconstruction to minimize image artifacts. Application of these field probes has significantly improved dMRI image quality for EPI and spiral trajectories at 3T at a nominal in-plane resolution of 1.3 mm (Lee et al., 2021a; Wilm et al., 2015, 2017), and at 0.69 mm using high-performance gradients (Wilm et al., 2020). Ma et al. (2020) used field monitoring probes to correct artifacts caused by gradient imperfections in the Human Connectome Project with an isotropic resolution of 1.05 mm diffusion EPI protocol at 7T. To the best of our knowledge, the advantages of single-shot spirals for dMRI at 7T has not been investigated.

Although the SNR is an important factor in limiting image resolution, it is not the only contributing factor. The T2* signal decay during the readout will cause a blurring artifact that depends on the k-space sampling pattern, such that the effective resolution is lower than the nominal resolution of the scan. This blurring effect is enhanced at UHFs due to the shorter T2* relaxation times of brain tissue: T2 and T2* is nearly halved at 7T compared to 3T (Cox and Gowland, 2010; Peters et al., 2007). This lower effective resolution reduces the benefit of moving to UHF for high-resolution dMRI. Reischauer et al. (2012) showed that a lower effective resolution is achieved for dMRI at 7T in comparison to 3T using an EPI readout with the same acceleration factor. Engel et al. (2018) showed that effective resolution of a single-shot T2*-weighted gradient echo (GRE) spiral acquisition at 7T is approximately 1.4 times higher than the nominal resolution. The impact of EPI and spiral readout trajectories with different acquisition parameters on image quality has not been thoroughly investigated at 7T.

The aim of this study is to determine the optimal single-shot readout trajectory for high-resolution dMRI at 7T by investigating the trade-off between SNR and effective resolution of various k-space trajectories. We use simulations to characterize the sole impact of T2* decay on spatial resolution and accuracy of dMRI using a PSF analysis for EPI, PF-EPI and spiral readout trajectories. In-vivo scans corrected for eddy currents and static field nonuniformities are used to validate the simulation results, and compare the SNR of the different trajectories at matching nominal resolutions. Finally, scans with matching effective resolution were acquired to investigate the SNR and efficiency of the different trajectories.

2. Methods

2.1. Artifact and blurring correction due to imperfections in spatial encoding

There are spatio-temporal deviations from prescribed magnetic field gradients during the readout, mainly due to eddy currents and concomitant fields. Furthermore, there are subject-specific static field non-uniformities (∆B₀), and dynamic field perturbations related to subject motion and physiology such as breathing. These field deviations result in the accumulation of additional phase terms during the readout as a function of spin location in space, which causes inaccuracies in spatial encoding. These inaccuracies result in ghosting artifacts, blurring, and the appearance of unwanted signal patterns that depend on the readout trajectory used (Bernstein, 2004). In order to investigate the sole effect of T2* signal decay during the readout on the PSF, image artifacts caused by these sources must first be corrected. We measured the spatio-temporal dynamics of the magnetic field using 16 field monitoring probes (Skope MRT, Zurich, Switzerland) and acquired a static ∆B₀ field map. This information was included in the image reconstruction pipeline using the expanded signal encoding model described below to minimize image artifacts. The differences in image quality between the reconstructed images acquired using different k-space trajectories are therefore primarily due to T2* signal decay during the readout.

2.1.1. Image reconstruction using the expanded signal model

The expanded signal model is a generalized form of the Fourier transform which is typically used for image reconstruction. Unlike the Fourier transform, the power of this method is that it can model the image acquisition using any basis function for spatial encoding, and thus can include
terms to describe deviations from the prescribed linear field (Wilm et al., 2011). This approach can minimize image artifacts for cartesian and non-cartesian imaging; however, its application has been limited by its significant computational requirements leading to long image reconstruction times. With recent advancements in computing hardware, it is gradually finding its way into image reconstruction pipelines.

A discretized form of the expanded signal model in time and space that accounts for gradient imperfections and \( B_0 \) spatial non-uniformity was implemented to reconstruct images using (1),

\[
s = E m
\]

where \( s \) is a matrix of samples of the measured MR signal over time, \( m \) is a matrix of the magnetization in space, and \( E \) is the encoding matrix of which elements are calculated as in (2).

\[
E_{E,F} = c_f(\gamma, r, t) e^{-\gamma \mu_B(t)}
\]

where \( c_f(r) \) is the sensitivity of coil \( f \) at position \( r \), and \( \phi(r, t) \) is the accumulated phase of a spin at position \( r \) and time \( t \) according to (3).

\[
\phi(r, t) = \sum_{k=1}^{L} k_b(t) h_b(r) + \Delta B_0(r) t
\]

where \( k_b(t) \) is the measured zero-th order spherical harmonic term or dynamic \( \Delta B_0 \) over time, \( h_b(r) \) is the coefficient of the spherical harmonic basis function \( b \) that is calculated from the dynamic field probe measurements during the readout, and \( \Delta B_0(r) \) is the inhomogeneity of the main magnetic field (\( B_0 \)) at position \( r \). Images are reconstructed by solving for \( m \) in (1) using the Conjugate-Gradient (CG) method.

CG is an iterative reconstruction method that requires a termination criterion that is typically determined empirically. In every iteration, CG adds a small amount of noise to the solution; therefore, finding the optimal stopping point to achieve a high-quality reconstruction while avoiding excessive addition of noise is important. We used the same approach to stop the reconstruction as used by Lee and colleagues (2021b). Iteration was stopped when the difference images of two consecutive iterations had no visible structures. A minimum of 6 iterations was used. In general, higher resolutions and under-sampling factors required more iterations (up to 16). Spirals usually converged faster than EPI and PF-EPI for a given resolution.

In-house MATLAB code optimized for GPU processing was developed for image reconstruction on a workstation with Intel 11700F CPU, 64 GB of RAM, and an NVIDIA GeForce RTX 3090 graphics card with a reconstruction time of 1.8–0.3 s per slice, depending on the matrix size and trajectory duration.

2.2. Simulations

2.2.1. Sequence simulations

Diffusion-weighted spin-echo sequences with EPI, PF-EPI, and spiral readout trajectories were simulated in MATLAB. The excitation and re-focusing pulse durations used in the simulations and in-vivo scans were set to 2.56 and 64 ms respectively to suppress the fat signal using the method by Ivanov et al. (2010) as used in the Human Connectome Project (Vu et al., 2015). The diffusion-encoding duration was calculated based on trajectory specifications for a b-value of 2000 s/mm² with a maximum gradient amplitude and slew rate of 73 mT/m and 200 T/m/s respectively, as used on the Siemens Terra 7T scanner.

Readout trajectories were simulated for resolutions of 0.6 to 1.8 mm isotropic with 0.1-mm increments. Fixed parameters for all trajectories include: field-of-view (FOV) = 256 × 256 mm², repetition time (TR) = 5000 ms, and sampling rate of 1 MHz. EPI trajectories were generated with the same gradient limitations used for the diffusion-encoding, and the following parameters: acceleration factors (R) along phase encode (PE) direction = 2, 3, and 4, bandwidth-per-pixel = 1384 Hz, PF factor = 0.75, and spatial encoding in the anterior-posterior direction. Spiral trajectories were generated using the method in (Hargreaves, 2001) with a maximum gradient amplitude of 27 mT/m and slew rate of 160 T/m/s to avoid PNS and critical acoustic resonance frequencies of the gradient system. Three spiral trajectories were generated corresponding to acceleration factors R of 4, 5, and 6 respectively.

2.2.2. Point spread function characterization

For the PSF analysis, a single point in the center of the image domain was simulated with T1, T2, and T2* relaxation times of the GM/WM set to 1300/800, 72/79, 66/46 ms at 3T, and 2000/1200, 47/47, 33/26 ms at 7T respectively (Cox and Golland, 2010; Peters et al., 2007; Rooney et al., 2007; Wansapura et al., 1999). The simulated signal decay was sampled at the time points along the different trajectories to fill k-space. For PF-EPI, the missing part of k-space was filled based on the conjugate symmetry feature of k-space.

In EPI-based trajectories, considerable signal decay occurs in the PE spatial encoding direction compared to the frequency-encode (FE) direction due to the longer time difference between adjacent k-space points along the PE direction in comparison to the FE direction. Consequently, T2* blurring will be more significant along the PE direction. For spiral trajectories, the signal decays uniformly in all radial directions. The effective resolution of each protocol was determined in PE direction using the full width at half maximum (FWHM) of the PSFs for the GM and WM.

Two-dimensional PSFs of the simulated k-space data for the WM were calculated on a 4096 × 4096 grid image using the image reconstruction method described in Section 2.1. Shape and magnitude of the main lobe and side lobes affect the contribution of other voxels to the final value of the central voxel, and its contrast with respect to neighbouring voxels. To characterize these effects, we define below the specificity, sharpness, and effective resolution of the PSF adapted from previous works (Chaimow et al., 2018; Engel et al., 2022). The specificity is defined as the integral of the main lobe within the nominal voxel size in both PE and FE directions normalized by the integral of the rest of the PSF outside the nominal voxel.

\[
Specificity = \frac{\sum \text{main lobe}}{\sum \text{side lobes} + \text{residual main lobe}}
\]

While positive side lobes have an overall blurring effect, negative lobes cause sharpening of the resulting image. Sharpness is defined as in Eq. (5), of which higher values indicate a greater sharpening effect of the PSF.

\[
Sharpness = \frac{\sum \text{negative side lobes}}{\sum \text{positive side lobes} + \text{residual main lobe}}
\]

2.3. Experiments

2.3.1. In-vivo scans to validate simulation results

To validate the simulation results, a volunteer (female, 24 years old) was scanned on a 7T Terra scanner running VEI2U-SP01 (Siemens, Erlangen, Germany) using a single channel transmit and 32-channel receive coil (Nova, Wilmington, USA). All scans were approved by the Research Ethics Board of the Montreal Neurological Institute, and informed consent was obtained from all subjects.

Most scan parameters were similar to the Human Connectome Project 7T protocol (Vu et al., 2015). The subject was scanned at a nominal isotropic resolution of 1.5 mm. While only a few (40) slices were acquired to reduce the reconstruction time, the TR of the protocols was set to 5 s to avoid signal saturation. All scan parameters are listed in Table 1. Coil sensitivity and \( \Delta B_0 \) field maps were estimated using a bipolar GRE scan with 6 echos, TE1 = 3.81 ms, and \( \Delta B_0 \) was 1.07 ms, in-plane resolution = 1.5 mm covering the same field of view as the diffusion scans. A multi-shell diffusion-weighted spin echo protocol was acquired with b-values = 0, 300, 1000, and 2000 s/mm² in S, 5, 16, and 48 directions respectively. The TE of all sequences was adjusted for a b-value of 2000 s/mm². 
Table 1
In-vivo scan parameters at 7T for three experiments to validate simulation results, calculate SNR, and investigate SNR and efficiency of trajectories with a matching resolution.

| Parameter                | Nominal resolution (mm) | SNR measurement | Effective resolution |
|--------------------------|-------------------------|-----------------|----------------------|
|                         | 1.5                     | 1.2             | 1                    |
| Trajectory               | EPI         |   PF-EPI       |   Spiral      |   EPI         |   PF-EPI       |   Spiral      |   EPI         |   PF-EPI       |   Spiral      |
| TE (ms)                  | 82.73/72.63/46         | 102.82/72.63/59 | 46                  | 118.92/81.67/63 | 46              | 101.87/86.72/66 | 46              | 86/71/46       |
| TR (ms)                  | 5000                   | 6700            | 6700                 | 6700           | 11100           | 10300           | 8300           |
| FOV (mm²)                | 256×256×60             | 256×256×36      | 256×256×36          | 256×256×36     | 256×256×144     |
| Slice thickness (mm)     | 1.5                    | 1.5             | 1                    | 1.5            |
| R                        | 3.4                    | 2.3             | 4.5                  | 2.3,4          | 2.3,4           | 4.5,6           | 3.4            | 2.3,4          | 4.5,6           | 3         | 4         | 5         |
| PF factor                | -                      | 0.75            | -                    | 0.75           | -               | 0.75            | -               | 0.75           | -               |
| Bandwidth-per-pixel (Hz) | 1384                   | 1384            | 2906                 | 1384           | 2906            | 1374            | 2336           | 1396           | 1953           | 1798           | 1776           | 1953           |
| Number of slices         | 40                     | 24              | 30                   | 36             | 36              | 36              | 36             | 36             | 36             |
| Scan time (min)          | ~7                     | ~1              | ~1                   | ~1             | ~1              | ~15             | ~15            | ~10            | ~10            |

* The bandwidth for the spiral trajectory was calculated by dividing the sampling time by the matrix size.

All scans, including the GRE sequences, were monitored using field monitoring probes in a separate session and the field measurements were used for offline image reconstruction as described in Section 2.1 to correct for B₀ non-uniformity and gradient imperfections. For PF-EPI, we included only the acquired part of k-space in the image reconstruction, which results in similar quality to the k-space zero-filling approach implemented on the scanner. However, there are several techniques available to reconstruct PF-EPI scans that improves the quality and reduces the blurring, such as projection onto convex sets (POCS) (Haacke et al., 1991) and the virtual coil concept (Blaimer et al., 2009).

Motion correction was performed on all images of the partial brain scans with nominal isotropic resolution of 1.5 mm and effective resolution of 1.5 mm using the Multidimensional diffusion MRI (MD-dMRI) (Nilsson et al., 2018) toolbox in MATLAB. No further pre-processing that could impact image resolution (e.g., denoising or Gibbs ringing correction) was performed. Fractional anisotropy (FA) maps were generated from the motion corrected images including all acquired b-values using MRtrix3 (Tournier et al., 2019). We compared the calculated FA maps as opposed to the raw diffusion-weighted images, since differences in the TEs results in differences in the T2-weighted image contrast.

2.3.2. In-vivo scans to investigate SNR

Twenty-seven images without diffusion encoding (b-value = 0) were acquired in a volunteer (male, 31 years old) to calculate the SNR of the different readout trajectories at three isotropic nominal resolutions of 1, 1.2, and 1.5 mm with parameters in Table 1. The TR was all scans was matched to the longest TR of the protocols, and the TE was adjusted for a b-value of 2000 s/mm².

SNR maps were generated using the pseudo multiple replica method (Robson et al., 2008). Briefly, the noise covariance matrix across the receive coil channels was calculated using noise scans added to the onset of the sequences, amounting to 11,000 samples in total. One hundred sets of correlated complex-valued Gaussian white noise were generated for each scan with the same dimension as the raw k-space data. To obtain 100 image replicas per scan, the synthesized noise sets were added to the raw k-space data followed by image reconstruction. Images without added noise were also reconstructed to use as original scans. A standard deviation (SD) map of the noise for each scan was generated by calculating pixel-wise SD over the stack of replicas. The real part of image replicas was used in calculating the noise SD maps. SNR maps were then estimated as the magnitude of the original images divided by the corresponding noise SD map. The final calculated SNR was the average over a WM and GM mask extracted from the "b = 0 s/mm² images.

2.3.3. In-vivo scans with matching effective resolution to investigate SNR and efficiency

In order to investigate the SNR and efficiency of different trajectories with a matching effective resolution, whole brain scans of a third volunteer (female, 26 years old) were acquired. The nominal resolution for each scan was chosen using the simulation results for a matching 1.5 mm isotropic effective resolution. TR for every protocol was chosen to minimize the scan time. The other scan parameters are listed in Table 1. In addition to FA maps, intra-cellular volume fraction (ICVF) maps were calculated using neurite orientation dispersion and density imaging (NODDI) (Zhang et al., 2012) to investigate the effect of SNR on microstructural models that require shells with high b-values. Motion corrected diffusion images were denoised using MRtrix3 (Tournier et al., 2019) then ICVF maps were generated using AMICO (Daducci et al., 2015).

2.3.4. Coil sensitivity and ΔB₂ field map estimation, and image reconstruction

Individual coil images from the GRE scan were first reconstructed by explicit multiplication of the Hermitian conjugate of the encoding matrix in (2) excluding the ΔB₂ term. Coil sensitivity maps were estimated from the first echo using ESPRIT (Uecker et al., 2014). To map
the $B_0$ non-uniformity, pixel-wise unwrapping of the phase image of each channel across all echoes was performed, followed by averaging $\Delta B_0$ maps obtained for every coil and smoothing the final map using a $7 \times 7 \times 7$-pixel spatial median filter.

Measured trajectories up to the 3rd order of spherical harmonics, coil sensitivity maps, and $\Delta B_0$ maps were used in the expanded signal model in (1) to reconstruct the diffusion-weighted images.

2.3.5. Eddy current compensation

The Siemens scanner data acquisition pipeline includes online eddy current compensation (ECC) that adjusts the system’s central frequency $f_0$ during the signal demodulation, which adds a phase term to the raw data. This correction needs to be disabled since these $f_0$ variations are also measured by the field probes, otherwise eddy current effects will be corrected twice during image reconstruction. Since this feature cannot be disabled on the 7T Terra scanner, we must invert the scanner’s ECC. The same protocols were simulated in the IDEA environment to obtain gradient waveforms, which were converted to ISMRM RD format¹ to calculate the ECC applied by the scanner to the raw data in the form of a $k_y$ phase term. The scanner ECC correction is inverted by multiplying the raw data by the conjugate values of ECC phase terms. The measured $k_y$ terms obtained by field probe measurements, which are more accurate than scanner’s simulated eddy currents, are applied instead during the image reconstruction.

3. Results

3.1. Simulation results

3.1.1. Sequence timing

Fig. 1A and B show the readout duration and echo time of the simulated trajectories as a function of nominal resolution, respectively. The readout duration of the spiral trajectory with $R = 4$ is shorter compared to EPI with the same acceleration factor for almost all resolutions, and it is shorter than PF-EPI for resolutions lower than 1 mm. The rate at which the readout duration increases at high-resolutions is greater for spirals than for PF-EPI and EPI due to the radial pattern of k-space acquisition in spiral trajectories.

Echo times in Fig. 1B were calculated for sequences with a b-value of 2000 s/mm². In spiral trajectories, the TE is independent from the resolution and remains at 44 ms over the entire range. The echo time of EPI and PF-EPI increases with resolution as expected. Results show a significant advantage of spiral trajectories over EPI-based trajectories due to the shorter TE resulting in a higher SNR, particularly at high resolutions.

3.1.2. Point spread function

The modulation transfer function (MTF) along the PE axis, reflecting the T2 and T2* signal decay along the readout trajectory, and the corresponding PSFs for EPI, PF-EPI, and spiral trajectories are shown in Fig. 2 for WM and GM. Equivalent simulation results at 3T are included in Figure S1 of supplementary material for comparison. MTF signal amplitude was normalized so that the value at $k_y = 0$ is one. The right column of Fig. 2 shows one-sided PSFs calculated from Fourier transformation of the corresponding MTFs. There are large variations in PSFs between the readout trajectories. Due to the shorter T2* time of the WM in comparison to the GM, PSFs are wider for the WM. This broadening of PSFs indicates more blurring, which results in a lower effective resolution. On the other hand, as the PSF gets sharper, the amplitude of associated side lobes becomes larger, which affects specificity and sharpness.

The real part of the 2-D PSFs of the WM for a nominal resolution of 1 mm at 7T are shown in Fig. 3A and B for spiral and EPI trajectories, respectively. For EPI, ringing amplitudes are greater along the PE and FE axes while spiral has circular ringing that uniformly spreads in all radial directions. The effective resolution is compared to the nominal resolution at 7T in Fig. 3C and D, and at 3T in Figure S2 of the supplementary material. There are large variations in the effective resolution between the trajectories at 7T. As expected, the WM has a lower effective resolution than the GM due to its shorter T2* time. EPI and PF-EPI trajectories follow a linear trend over the range of resolutions considered, while spiral trajectories show a deviation from linearity for resolutions higher than 0.9 mm due to the extensive signal loss caused

¹ https://github.com/SkopeMagneticResonanceTechnologies/siemens_to_ismrmd
by long readout durations. This results in the suppression of high frequency components and thus a lower effective resolution. The specificity for all 2-D PSFs, defined in Section 2.2, are shown in Fig. 3E. The specificity decreases at higher resolutions for all protocols. EPI has the highest specificity, which is expected due to its sharper peak, as shown in 1-D PSFs in Fig. 2. The decrease in specificity at higher resolutions is most significant for spiral trajectories due to excessive suppression of high frequencies by the T2\* signal decay. The sharpening effects of EPI and PF-EPI remain almost constant over different resolutions, while this effect is significantly reduced at high resolutions for spirals as shown in Fig. 3F. This is due to the signal decay which causes suppression of higher frequencies leading to decreasing side lobe amplitudes, while the residual main lobe remains at a high positive value. This sharpening effect in EPI and PF-EPI causes Gibbs ringing artifacts in the image, while spirals inherently reduce them, specifically at high resolutions.

In addition to PSF simulations, a digital brain phantom was simulated to study effects of CG image reconstruction on image quality. Methods and results can be found in supplementary material. The results are similar to the PSF analysis results described above.

3.2. In-vivo scan results

3.2.1. EPI has the highest effective resolution

Fig. 4 shows FA maps derived from the 1.5-mm scans shown in Fig. 3S of supplementary material in the axial, sagittal, and coronal planes. The SNR advantage of spirals over EPI-based trajectories is clearly visible in the mean DWI images. The direction encoded color (DEC) maps of the PF-EPI scans clearly show blurring of fine structures in comparison to EPI and spirals along the anterior-posterior direction. In contrast with spiral trajectories characterized by uniform blurring in all directions in-plane, the majority of blurring due to T2\* decay in EPI-based trajectories appears along the PE direction, here the anterior-posterior direction. It is therefore expected to see a maximal blurring in the sagittal and axial planes, and minimal blurring in the coronal plane. A clear example of this in the axial and sagittal planes is the corticospinal fibers that form a striping pattern in the PE direction and are affected the most by the blurring.

EPI trajectories provide the sharpest FA maps in the sagittal and axial planes, in particular for R = 4 due to the shorter readout and thus less T2\* decay. The spiral with R = 5 shows slightly sharper FA maps compared to the spiral with R = 4 and PF-EPI with R = 3. The blurriness FA map is obtained by using PF-EPI scans with R = 2, mainly due to its longer readout duration.

To investigate the blurring effects on the calculated maps, FA values and smoothness of structures in specific regions of interest selected along the FE (Fig. 5A, B) and PE (Fig. 5C, D) axes in the 1.5-mm isotropic scans were investigated more closely using line plots. These regions were selected to include fibers oriented perpendicular to the ROI. In Fig. 5A and B, FA values obtained using EPI and PF-EPI trajectories are consistent within a range of ~0.1. Spirals show smoother FA profiles and larger differences compared to EPI and PF-EPI, as highlighted by the blue arrow in Fig. 5A. In Fig. 5C and D corresponding to the PE direction, the difference in FA values between EPI and PF-EPI trajectories is more significant than in the FE direction. These plots show sharper changes in
Fig. 3. **PSF analysis.** A, B: Spiral has similar ringing in all directions while ringing is constrained along the PE and FE axes for EPI. C, D: There is greater variability in the effective resolution of WM compared to GM due to its shorter $T_2^-$. E, F: The specificity of EPI is higher due to its narrower main lobe compared to PF-EPI and spiral. EPI and PF-EPI have a constant sharpening effect, while the sharpness of spirals reduces significantly at high resolutions due to the signal decay causing suppression of the side lobes.
Fig. 4. FA maps calculated using different trajectories at 1.5 mm isotropic nominal resolution. DEC maps in the axial plane are shown in the first row, and FA maps in axial, sagittal and coronal planes with magnified regions for better examination are shown below. EPI-based scans show a minimal blurring in the coronal direction, and maximal blurring in the sagittal plane, while blurring in the spiral trajectory occurs in all directions. The sharpest FA map is acquired using EPI with \( R = 4 \), and the map with the lowest effective resolution is generated using PF-EPI with \( R = 2 \).
3.2.2. Spirals provide the highest SNR

The SNR values calculated from the in-vivo scans using different trajectories and parameters at three isotropic resolutions of 1, 1.2, and 1.5 mm are plotted in Fig. 6. EPI with R = 2 at 1 mm was excluded due to low signal amplitude of the field monitoring probes towards the end of the readout. For a given acceleration factor R, EPI has the lowest SNR, mainly due to its longer echo time. The SNR of spiral trajectories varies the most as a function of R due to changes in the under-sampling rate in two dimensions compared to EPI and PF-EPI. Furthermore, the echo time of EPI and PF-EPI is shortened at higher acceleration factors which partially compensates for the SNR loss due to the increased undersampling. This figure clearly shows the advantage of spirals in preserving a high SNR at high resolutions.

3.2.3. Spirals provide highest SNR for matching effective resolution

FA and ICVF maps calculated from whole brain scans (Figure S4 of supplementary material) with a matching effective resolution of 1.5 mm are shown in Fig. 7. The SNR of the $b = 0$ s/mm$^2$ images for EPI, PF-EPI, and spiral were 23.7, 18.8, and 32.4, respectively. Despite the higher nominal resolution of the spiral trajectory to match the effective resolution of the other images, the SNR of spirals is still higher than for EPI. Although all scans provide FA maps of similar quality, ICVF maps clearly show the advantage of the higher SNR of the spirals for the shells with high b-values of 2000 s/mm$^2$. Furthermore, the spirals shorten the scan time by about 33% and 23% compared to EPI and PF-EPI, respectively. FA and ICVF maps of different slices are available in Figures S5 and S6 of supplementary material, respectively.

4. Discussion

4.1. Spirals are the optimal k-space readout trajectory for single-shot dMRI at 7T

The aim of this study was to characterize the effects of T2* decay on spatial resolution and quality of dMRI at 7T and to find an optimal single-shot readout trajectory that balances the trade-off between SNR and image resolution. We characterised the PSF of dMRI with EPI, PF-EPI, and spiral trajectories using sequence simulations. Three measures were proposed for comparison of the trajectory PSFs: specificity, sharpness, and effective resolution. In vivo scans were acquired at 7T to investigate consistency with simulation results, as well as to measure SNR. Field monitoring probes were used to eliminate distortions and artifacts caused by field imperfections. We showed that spirals generally have lower effective resolution and specificity compared to EPI at matching
Fig. 7. FA map of scans with a matching effective resolution of 1.5 mm. Similar structures in FA maps can be seen in all maps due to the matching effective resolution. Effect of higher SNR of the spiral scan is clear in ICVF maps.
nominal resolutions. However, the SNR advantage of spiral enables the acquisition of single-shot spiral dMRI scans at an effective resolution of ~1.5 mm for a b-value of 2000 s/mm² at a higher SNR and in a shorter scan time than EPI and PF-EPI.

4.2. Spatial specificity and sharpening factor

The PSF is typically characterised using the FWHM. Engel et al. (2022) have recently used specificity and sensitivity in addition to FWHM to characterize the PSF and determine the optimal TE for BOLD fMRI contrast using spiral and EPI trajectories. They defined specificity as the ratio between the integral over the main lobe and the L²-norm of the side lobes. Here we used a different definition for specificity: the ratio between the main lobe within the nominal voxel boundaries to the integral of the side lobes. This definition was used to better reflect the contribution of spins within the nominal voxel. This specificity measure is affected by the residual main lobe, where a sharper peak in the PSF leads to a reduction of the area under the residual main lobe. This is the main reason that PSF has the greatest specificity, even though its side lobes have higher amplitude than the other trajectories. Spirals have more variable specificity over the range of resolutions studied; higher suppression of side lobes leads to lowering side lobe amplitudes significantly. Side lobe suppression is expected to increase specificity; however, the greater area of the residual main lobe of spirals dominates and reduces the specificity.

The sharpness quantifies the effects of negative side lobes on image quality. A greater sharpening effect is not necessarily advantageous since it increases Gibbs ringing and intensifies edges. Due to suppression of high-frequency components using spirals, it has an inherent benefit of removing Gibbs ringing, especially at high resolutions.

4.3. Simulation results of the effective resolution are consistent with in-vivo scans

Simulation results in Fig. 3 clearly show differences in the effective resolution between different trajectories, which are enhanced at higher resolutions. At 1.5-mm nominal resolution, the effective resolution can be nearly divided into three different groups where EPI trajectories perform best, and PF-EPI with R = 2 have the lowest effective resolution, and other trajectories in between. In vivo FA maps in Fig. 4 and line plots of Fig. 5 confirm these considerable differences observed in the simulations, more specifically perpendicular to structures oriented along the FE direction, such as the corticospinal tract.

4.4. Trade-off between SNR and effective resolution

Several groups have investigated the gain in SNR at higher field strengths for diffusion MRI (Choi et al., 2011; Reischauser et al., 2012). In a recent study at 3T, Lee et al. (2021b) used field monitoring probes and measured the SNR benefit of spiral over EPI trajectories. They performed a PSF analysis for trajectories with an equivalent effective resolution of 1 mm. Reported SNR values are lower than what we calculated in this study by a factor of ~6 for b = 0 s/mm² at similar TE values. This SNR difference is due to imaging at 7T which is expected to provide ~5.21 (SNR∝~B^0.95) times higher SNR than 3T according to (Pohmann et al., 2016).

As mentioned above, T2 and T2* are approximately halved at 7T compared to 3T. Although we did not perform in-vivo experiments at 3T to compare them to our 7T results, simulations shown in Fig. 3 and Figure S2 of supplementary material suggest increased blurring at 7T and greater differences between the different trajectories. Effective resolution of PF-EPI and spiral are decreased ~20% compared to 3T, and differences in the effective resolution among trajectories was increased from ~13% at 3T to ~27% at 7T. Given the greater effect of T2* blurring at 7T, nominal resolutions presented in dMRI studies at 7T should be interpreted with caution, in particular for studies that investigate fine structures of the brain such as the cortical gray matter.

Future work could focus on minimizing the effect of T2* blurring by demodulating the k-space data before image reconstruction using a T2* map, at the cost of enhancing high-frequency noise. The PSF analysis can also be integrated into trajectory optimization methods to find a readout trajectory that minimizes blurring while preserving the SNR (e.g., Weiss et al., 2021).

4.5. Diffusion-encoding effects

Different diffusion-encoding strengths (b-values) and schemes (linear, b-tensor (Westin et al., 2016)) affect TE and therefore potentially the effective image resolution and the SNR. We calculated the effective resolution for various echo times in the PSF analysis and obtained the same results as shown in Figure S7 of the supplementary material. T2* decay after the echo in a spin-echo sequence remains the same regardless of the echo time. However, in a gradient-echo sequence, changes in TE affect the T2* decay modulation and therefore the effective resolution of the scans (Engel et al., 2018).

As shown in Figure S7 of the supplementary material, the differences in echo time for b-values of 500 and 1000 s/mm² is very small for EPI and PF-EPI readouts compared to spirals. This is due to the added idle time in EPI-based dMRI sequences which in addition to diffusion gradient duration, affects calculation of the b-value, whereas in spirals there is no idle time between diffusion gradients and the refocusing pulse, therefore changes in the b-value depend only on the diffusion gradient duration.

The b-values selected for this study are frequently employed in dMRI studies for tractography and microstructural modeling. However, to increase the specificity to the intra-axonal compartment higher b-values (4000–7000 s/mm²) are often used (e.g., Barakovic et al., 2021; McKinnon and Jensen, 2019; Veraart et al., 2020, 2018). The enhanced SNR efficiency of spiral trajectories would benefit such protocols and can be combined with other approaches to enhance SNR, such as the stimulated echo acquisition mode (STEAM) sequence (Reischauser et al., 2012) and high-performance gradients (e.g., Foo et al., 2020).

4.6. Limitations

The objective of this study was to evaluate the image quality of dMRI at 7T using various trajectories in order to identify the ideal protocol. The PSF analysis and digital phantom simulations aim to quantify the effects of the different trajectories on the effective resolution and spatial accuracy. An aspect that is not taken into account in the simulations is the variability in tissue properties, such as proton density and relaxation times, across the brain. Despite these limitations, the simulation results at both high- and low-resolution are consistent with the in-vivo scan results.

A limited number of subjects were scanned in this study. While we expect inter-individual variations in T2 and T2* times in healthy brain tissue to have small effects on our results (i.e. within the range of variation observed across a single brain), larger variations could occur in the case of pathology. Shorter T2 and T2* times due to iron accumulation for instance will enhance the differences between the trajectories, whereas longer relaxation times due to edema would reduce these differences.

Our results show that PF-EPI has poor spatial resolution and accuracy. More advanced image reconstruction techniques such as LORAKS (Haldar, 2014) can be employed for higher PF factors to reduce the blurring significantly at the cost of increased reconstruction time.

To minimize image artifacts and blurring due to field imperfections in the in-vivo scans, we used off-line field measurements. Motion and breathing can cause changes in the zeroth order fields. These effects are negligible for single-shot imaging due to the short readout duration for each slice (~100 ms). However, subject motion could lead to changes in the static ΔB₀ map that is used for image reconstruction. To minimize
the discrepancy between the $\Delta B_0$ map used for the image reconstruction and actual $B_0$ non-uniformity, GRE scans were repeated every about 15 min.

Fig. 7 shows a bias between the ICVF maps from the three different trajectories at matching effective resolution. These differences may result from the differences in TE between the three protocols, 86, 71, and 46 ms for EPI, PF-EPI and spiral, respectively. The intra-cellular compartment has a longer T2 time than the extra-cellular compartment (Lampinen et al., 2020; McKinnon and Jensen, 2019; Verraart et al., 2018). ICVF maps calculated from data at longer TEs will thus have higher values than those at shorter TEs since the NODDI ICVF maps are actually intra-cellular T2-weighted signal fraction maps.

Lastly, the scan time of the protocols implemented in this study can be further decreased by incorporating simultaneous multi-slice (SMS) technique. Combining spiral trajectories with SMS will make high spatial and angular resolution diffusion imaging of the whole-brain more efficient and feasible in clinical populations.

5. Conclusion

The effective resolution achieved using a specific k-space trajectory should be considered as it is significantly lower than the nominal resolution entered at the scanner and typically reported in the literature, in particular at UHFs due to the shorter T2* times of brain tissue. If this is not a limiting factor, multi-shot diffusion imaging acquisitions may be preferable as they provide higher SNR, better effective resolution, and specificity. In this work, we investigated fast, single-shot protocols that can be used in clinical research. We show that diffusion imaging with spiral trajectories reconstructed using field monitoring probes to minimize distortions and blurring due to eddy currents, provide sufficient signal to achieve higher effective resolutions than EPI overall and within a shorter scan time.

Data availability

The MATLAB code used for sequence simulation are available at [https://github.com/TardifLab/dMRI_sequence_simulations]. The image reconstruction pipeline described in Section 2.1 is available at [https://github.com/TardifLab/ESM_image_reconstruction]. Raw re-constructed diffusion images and calculated maps are available at [https://doi.org/10.5683/SP3/V7TEH].

Credit author statement

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Funding

This project was funded by the Natural Sciences and Engineering Research Council of Canada, the Fonds de recherche du Québec – Santé, and Healthy Brains for Healthy Lives. The data was acquired at the McConnell Brain Imaging center, which is supported by the Canadian Foundation for Innovation, Brain Canada, and Healthy Brains for Health Lives.

Declaration of Competing Interest

The authors report no conflicts of interest or competing financial interests in relation to the work presented in this manuscript.

Acknowledgments

The authors would like to thank Ronaldo Lopez and David Costa at the McConnell Brain Imaging center for helping with the human scans, and Marcus Couch (Siemens Collaboration Scientist) for his technical support. We would like to thank Cameron Cushing and Paul Weavers (Skope MR Inc, WI, USA), and Christian Mirkes (Skope Magnetic Resonance Technologies AG, Zurich) for their technical support for the field monitoring probes.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2023.120159.

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