Graphical Abstract

Accelerated Diffusion Weighted Magnetic Resonance Imaging at 7 T: Joint Reconstruction for Shift-Encoded Navigator-based Interleaved Echo Planar Imaging (JETS-NAViEPI)

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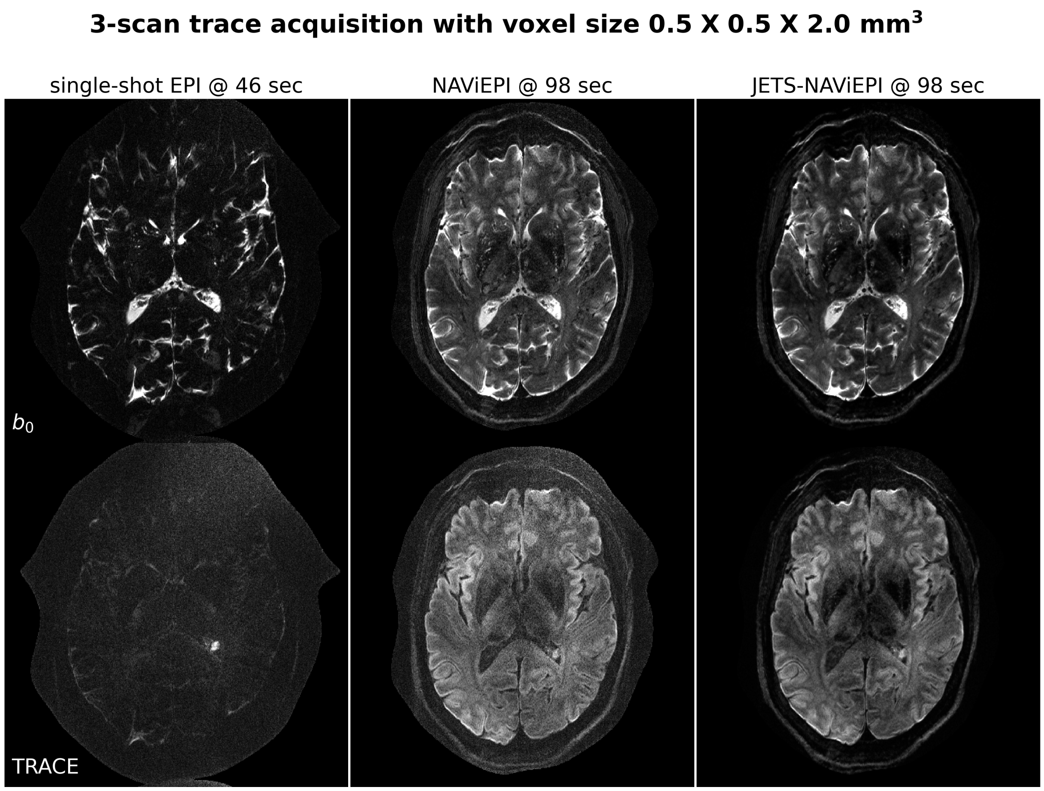

Highlights

Accelerated Diffusion Weighted Magnetic Resonance Imaging at 7 T: Joint Reconstruction for Shift-Encoded Navigator-based Interleaved Echo Planar Imaging (JETS-NAViEPI)

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- Navigator-based interleaved EPI acquisition with minimal distortion mismatch between echoes
- Novel accelerated diffusion acquisition with shifted phase encoding among diffusion directions for complementary k-q-space sampling at 7 T
- Generalized joint k-q-slice diffusion-weighted image reconstruction with overlapping locally low-rank regularization
- Efficient simultaneous multi-slice (SMS) image reconstruction
- 3-scan trace acquisition with the voxel size $0.5 \times 0.5 \times 2.0$ mm^3 and 60 slices at 1.5 min

Accelerated Diffusion Weighted Magnetic Resonance Imaging at 7 T: Joint Reconstruction for Shift-Encoded Navigator-based Interleaved Echo Planar Imaging (JETS-NAViEPI)

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Abstract

The pursuit of high spatial-angular-temporal resolution for in vivo diffusion-weighted magnetic resonance imaging (DW-MRI) at ultra-high field strength (7 T and above) is important in understanding brain microstructure and function. Such pursuit, however, faces several technical challenges. First, increased off-resonance and shorter T_2 relaxation require faster echo train readouts. Second, existing high-resolution DW-MRI techniques usually employ in-plane fully-sampled multi-shot EPI, which not only prolongs the scan time but also induces a high specific absorption rate (SAR) at 7 T. To address these challenges, we develop in this work navigator-based interleaved EPI (NAViEPI) which enforces the same effective echo spacing (ESP) between the imaging and the navigator echo. First, NAViEPI renders no distortion mismatch between the two echoes, and thus simplifies shot-to-shot phase variation correction. Second, NAViEPI allows for a large number of shots

(e.g. > 4) with undersampled iEPI acquisition, thereby rendering clinically-feasible high-resolution sub-milliemeter protocols. To retain signal-to-noise ratio (SNR) and to reduce undersampling artifacts, we developed a k_y-shift encoding among diffusion encodings to explore complementary k-q-space R248.Major.6
sampling. Moreover, we developed a novel joint reconstruction with overlapping locally low-rank regularization generalized to the multi-band multi-shot acquisition at 7 T (dubbed JETS-NAViEPI). Our method was demonstrated with experimental results covering 1 mm isotropic resolution multi b-value DWI and sub-millimeter in-plane resolution fast TRACE acquisition.

Keywords: Diffusion-weighted magnetic resonance imaging, Echo planar imaging, Navigator, Ultra-high field, Joint reconstruction, Low rank, Simultaneous multi slice

1. Introduction

Diffusion-weighted magnetic resonance imaging (DW-MRI) (Le Bihan et al., 1986; Merboldt et al., 1985) is a non-invasive modality that is sensitive to the intravoxel Brownian motion of water molecules. DW-MRI forms the basis for diffusion tensor imaging (DTI) (Basser et al., 1994; Mori et al., 1999) and high angular resolution diffusion imaging (HARDI) (Tuch et al., 2002), and has been widely used in acute brain ischemia diagnosis, in tumor detection and staging, and in neuroscience (Jones, 2010).

For DW-MRI acquisition, the commonly used pulse sequence is single-shot echo-planar imaging (SS-EPI) (Mansfield, 1977). SS-EPI is capable of rapidly acquiring one DW image per radio-frequency excitation at the order of 100 ms, and is thus motion robust. However, conventional SS-EPI, even with three-fold accelerated acquisition (Bammer et al., 2001) using parallel imaging (Roemer et al., 1990; Ra and Rim, 1993; Pruessmann et al., 1999; Griswold et al., 2002), still suffers from low spatial resolution and geometric distortions.

In the quest for high spatial-angular-temporal-resolution and minimal-geometry-distortion DW-MRI, tremendous efforts have been made. Techniques for the correction of image distortions induced by off-resonances and R249.Minor.5
eddy currents have been developed (Andersson et al., 2003). Furthermore, gSlider (Setsompop et al., 2018) with blipped-CAIPI (Setsompop et al., 2012) for simultaneous multi-slice (SMS) (Maudsley, 1980; Breuer et al., 2005) was proposed to achieve high-resolution DW-MRI. Advanced pulse sequences based on multi-shot EPI have also been developed, including but not limited to interleaved EPI (iEPI) (Butts et al., 1993), PROPELLER (Pipe et al.,

2002), and readout-segmented EPI (rsEPI) (Porter and Heidemann, 2009; Heidemann et al., 2010).

Based on four-shot iEPI, multiplexed sensitivity encoding (MUSE) image reconstruction achieved DW-MRI with a sub-millimeter in-plane resolution and maximal b-value $800\,\mathrm{s/mm^2}$ at $3\,\mathrm{T}$ (Chen et al., 2013). The four-shot iEPI employed in MUSE acquired an in-plane fully-sampled k-space, except partial Fourier. Every shot (segment), corresponding to four-fold undersampling, was then reconstructed via parallel imaging to obtain shot-to-shot phase variation. This indicates that increasing the number of shots in MUSE will result in higher undersampling per shot, and consequently, degrade shot phase estimation (Wu and Miller, 2017). On the other hand, the use of in-plane fully-sampled four-shot iEPI is challenging at ultra-high field (e.g. $7\,\mathrm{T}$), because the SAR is linearly proportional to the square of the field strength.

Alternatively, navigator-based iEPI acquisition has been proposed (Jeong et al., 2013; Dai et al., 2017, 2018). These proposals may allow for a larger number of shots, and hence higher spatial resolution. However, due to the use of different ESP between the imaging echo and the navigator echo, these proposals suffered from geometric distortion mismatch between the two echoes and thus required specific compensation methods. In contrast, rsEPI (Porter and Heidemann, 2009; Heidemann et al., 2010) used the same readout segment for both echoes, and thus required no correction of the navigator echo.

Beyond the MUSE-type parallel imaging reconstruction, compressed sensing (Lustig et al., 2007; Block et al., 2007) has been explored. For instance, multi-shot reconstruction techniques based on structured low-rank matrix completion (MUSSELS) (Mani et al., 2017; Bilgic et al., 2019) achieved 5-

shot DW-MRI with 9-fold undersampling per shot. Recently, JULEP (Dai et al., 2023) incorporated explicit phase mapping into MUSSELS. These reconstruction techniques, i.e., MUSE, MUSSELS and JULEP, targeted the reconstruction of one DW image from interleaved EPI acquisition, and did not explore joint-k-q-space undersampling or reconstruction.

Joint-k-q-space undersampling can be achieved via proper regularization along the diffusion encoding direction. Relevant examples are diffusion undersampling with Gaussian process estimated reconstruction (DAGER) (Wu et al., 2019) and magnitude-based spatial-angular locally low-rank regularization (SPA-LLR) (Hu et al., 2020). However, DAGER addressed the reconstruction problem of single-shot EPI acquisition and SPA-LLR focused on the reconstruction of single-band and fully-sampled iEPI acquisition. R248.Major.2

In this work, we propose a Joint k-q-slice rEconsTruction framework for Shift-encoded NAVigator-based interleaved EPI at 7 T (dubbed JETS-NAViEPI). Our pulse sequence, NAViEPI, differs from most existing techniques. First, NAViEPI builds upon interleaved EPI, thereby allowing for fast and efficient k-space coverage. Second, inspired by rsEPI, NAViEPI ensures the same effective ESP between the imaging and the navigator echo, thereby minimizing geometric distortion and allowing for the use of a larger number of shots. NAViEPI essentially integrates the advantages of both iEPI and rsEPI. Third, NAViEPI utilizes undersampled multi-shot iEPI, thereby alleviating the SAR problem at 7 T. Fourth, NAViEPI shifts the k-space in-plane sampling pattern along the phase encoding (k_y) direction. This shifting creates complementary k-q-space sampling, which leads to the possibility of our joint k-q-slice reconstruction. Specifically, we employ spatial-diffusion overlapping LLR regularization to jointly reconstruct all diffusion encodings and multi-band slices. In vivo experiments at 7 T and comparisons with other techniques demonstrate the efficiency of our proposed method in achieving high spatial resolution DW-MRI at ultra-high field.

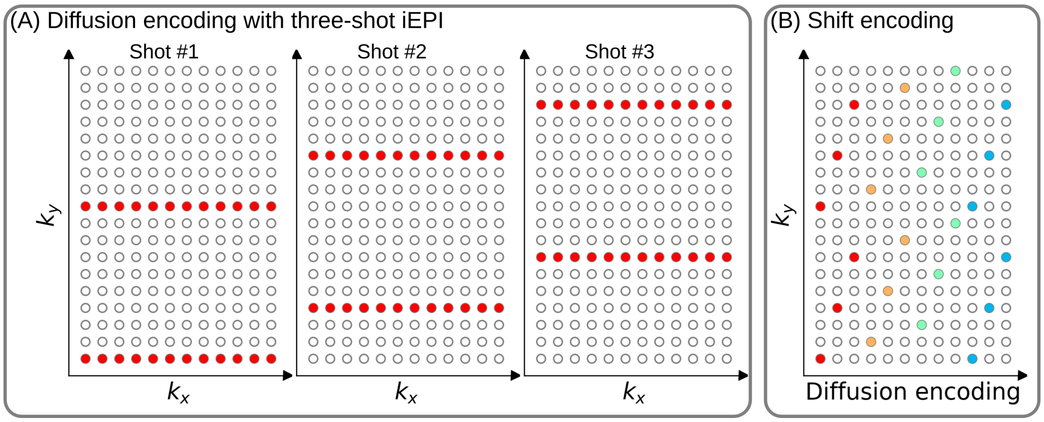

Figure 1: (A) An example DW-MRI acquisition with three-shot interleaved EPI acquisition. (B) The proposed k_y shifted diffusion encoding scheme. This example employs three shots per DW image. Therefore, every three columns have the same color.

2. Materials and methods

2.1. Multi-band shift-encoded iEPI acquisition

Fig. 1 (A) displays the diffusion-weighted image acquisition based on three-shot interleaved EPI with three-fold in-plane undersampling. Conventionally, such a sampling pattern is repeated for all diffusion directions. In contrast, we propose the k_y-shifted diffusion encoding, as shown in Fig. 1 (B). The interleaved EPI sampling pattern is shifted by one k_y line per diffusion direction, with the cycling period being the in-plane undersampling factor.

It is worth noting that, as shown in Fig. 1 (A), the undersampling factor of one segment is $R_{\text{in-plane}} \times N_{\text{shot}}$ (ignore multi-band undersampling here), yielding nine-fold in-plane undersampling in this example. In other words, the undersampling factor per segment linearly scales up with the number of shots. Consequently, conventional self-gating reconstruction techniques, e.g. MUSE, suffer from degraded shot-to-shot phase estimation, which in

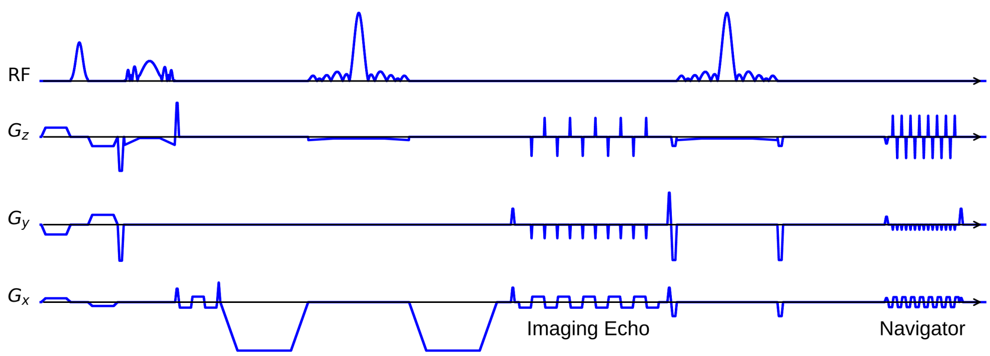

Figure 2: The NAViEPI sequence diagram. SMS is utilized for the acquisition of both imaging and navigator echoes. While the acceleration factor per navigator is the same as listed in Table 1, the acceleration factor per imaging echo is in addition linearly scaled by the number of shots.

turn limits the number of shots and spatial resolution.

2.2. NAViEPI: Navigator-based iEPI with consistent effective ESP between the imaging and the navigator echo - where iEPI meets rsEPI

Instead of the self-gated MUSE with in-plane fully-sampled iEPI and a limited number of shots, We propose NAVigator-based interleaved EPI (NAViEPI), as illustrated in Fig. 2. Moreover, inspired by rsEPI (Porter and Heidemann, 2009), NAViEPI enforces a consistent effective ESP between the imaging and the navigator echo, thereby minimizing distortion mismatch between the two echoes.

Since one imaging echo presents one segment in multi-shot EPI acquisition, its effective ESP is defined as

$$\text{ESP}_{\text{eff}} = \frac{\text{ESP}}{R_{\text{in-plane}} \times N_{\text{shot}}} \tag{1}$$

Here, a larger number of shots (segments) increases the undersampling factor per segment (see Fig. 1), but decreases the effective ESP. Since the navigator echo is acquired for each segment, its in-plane undersampling factor equals $R_{\text{in-plane}}$. Therefore, the effective ESP of the navigator echo must match that of the imaging echo, as given in Eq. (1). With a matching effective ESP, the base resolution of the navigator echo can then be determined.

2.3. In vivo acquisition protocols

We implemented multiple in-vivo acquisition protocols at a clinical 7 T MR system (MAGNETOM Terra, Siemens Healthineers, Erlangen, Germany) equipped with a 32-channel head coil (Nova Medical, Wilmington, MA, USA) and the XR-gradient system (maximum gradient strength 80 mT/m with a peak slew rate of 200 T/m/s). To calibrate coil sensitivity maps, reference scans employed a gradient-echo (GRE) sequence. Spectral fat saturation and mono-polar diffusion-encoding gradients were used. The phase-encoding direction was selected as anterior-to-posterior.

Table 1: NAViEPI acquisition protocols

Protocol	**1.0 mm isotropic**		**sub-millimeter**	
	#1	#2	#3	#4
Diffusion mode	MDDW [1]		3-scan trace	
Diffusion scheme	monopolar			
Diffusion direction	20	114	3	
b-value (s/mm^2)	1000	3-shell [2]	1000	
b_0	0	12	1	
FOV (mm^2)	200	220		
In-plane resolution (mm^2)	1.0		0.5	
Slice thickness (mm)	1.0		2.0	
Slices	141	114	60	
Navigator	No	No	Yes	No
Shots	4	2	5	1
TR (ms)	7700	5200	4400	8000
TEs (ms)	67	66	58/95.1	143
ESP (ms)	1.02	0.81	1.52	1.48
Bandwidth (Hz/Pixel)	1086	1460	758	
Partial Fourier	6/8			
Acceleration [3]	1×3	3×3	3×2	
TA (min) [4]	10 : 42	22 : 25	1 : 38	0 : 46

[1] MDDW: Multi-direction diffusion weighting;

[2] 3-shell: 20, 30, and 64 directions with b-values of 1000, 2000,and 3000 s/mm^2, respectively;

[3] Acceleration: Both in-plane and slice undersampling can be employed, denoted as ($R_{\text{in-plane}} \times R_{\text{slice}}$);

[4] TA: Total acquisition time.

This study was approved by the local ethics committee. Three volunteers with informed consent obtained before scanning participated in this study. Detailed acquisition protocols are listed in Table 1.

2.3.1. 20-diffusion-direction acquisition at 1 mm *isotropic resolution*

As listed in Table 1, Protocol #1 with four-shot iEPI and without in-plane undersampling was implemented. This protocol represents the acquisition scheme employed in many existing multi-shot reconstruction techniques, (e.g., MUSE, SPA-LLR, and JULEP). The acquired data from this protocol served as ground truth. Different reconstruction methods, specifically JETS, MUSE, and JULEP were compared. We compared with JULEP instead of MUSSELS, because JULEP uses not only structured low-rank constraints but also explicit phase mapping.

R248.Major.1a
R249.Minor.6
R248.Major.3a

We then retrospectively reduced the four-shot data to only one shot per diffusion encoding without and with the proposed k_y shifting to simulate four-fold in-plane undersampling. JETS reconstruction was performed on the fully-sampled data and the retrospectively undersampled data to validate the proposed k_y-shifted acquisition.

R248.Major.1b
R248.Major.1c

2.3.2. Three-shell direction acquisition at 1 mm *isotropic resolution*

Protocol #2 in Table 1 was implemented for multi-shell diffusion tensor imaging (DTI) (Basser et al., 1994). We acquired a total of 114 diffusion directions, whereas b_0 measurements were interspersed every ten diffusion directions. This protocol was used to demonstrate the capability of of JETS in achieving high spatial-angular-temporal resolution.

R248.Major.3c

2.3.3. 3-scan trace acquisition at $0.5 \times 0.5 \times 2.0$ mm^3 voxel size

As listed in Table 1, Protocol #3 was implemented based on NAViEPI with five shots per diffusion encoding. This protocol was compared against single-shot EPI (Protocol #4) with the same spatial resolution and acceleration, such as to demonstrate the sampling efficiency of NAViEPI.

2.4. Forward modeling

Our proposed acquisition method yields multi-dimensional multi-band k-space data $\mathbf{y}_{c,q,s}$, where c, q, s denotes the index of the coil sensitivity map, the diffusion encoding, and the shot, respectively. Acquisition modeling needs to consider several aspects.

First, the acquired k-space data $\mathbf{y}$ is mapped from individual shot images $\mathbf{x}_{q,s,z}$ via the forward model,

$$\begin{aligned} \mathbf{y}_{c,q,s} &= \mathbf{P}_{q,s}\mathbf{\Sigma}\mathbf{\Theta}_z\mathbf{F}\mathbf{S}_c\mathbf{x}_{q,s,z} \\ \mathbf{y} &\coloneqq \mathbf{E}_1\mathbf{x} \end{aligned} \tag{2}$$

Here, the encoding matrix $\mathbf{E}_1$ comprises a chain of linear operators. Every shot image $\mathbf{x}$ is point-wise multiplied by a set of coil sensitivity maps ($\mathbf{S}$) and Fourier transformed ($\mathbf{F}$). The output is then point-wise multiplied by the multi-slice phase map ($\mathbf{\Theta}$) with z the slice index in simultaneously excited slices. This operator shifts individual slice along the phase-encoding direction via varying phase modulation (Breuer et al., 2005). The SMS k-space data is then summed (collapsed, $\mathbf{\Sigma}$) along the slice dimension and masked (point-wise multiplied, $\mathbf{P}$) by the sampling pattern of each diffusion encoding and shot.

Second, for diffusion MRI based on multi-shot EPI, multiple shots acquired for a given diffusion encoding need to be combined as one DW image ($\tilde{\mathbf{x}}$). One possibility is to perform magnitude average (Chen et al., 2013) or root-sum-squares (RSS) (Mani et al., 2017) of shot images. This method R249.Minor.7
is robust to in-plane motion, but sub-optimal concerning SNR (Guhaniyogi et al., 2016). Alternatively, shot combination can be done via shot-to-shot phase variation correction (Liu et al., 2005; Chen et al., 2013). This can be incorporated into our formulation as point-wise multiplication between the R249.Minor.8
shot-to-shot phase variation ($\mathbf{\Phi}$) and the DW image ($\tilde{\mathbf{x}}$),

$$\mathbf{x}_{q,s,z} = \mathbf{\Phi}_{q,s,z}\tilde{\mathbf{x}}_{q,z} \tag{3}$$

Note that $\tilde{\mathbf{x}}$ can be obtained by applying the adjoint of $\mathbf{\Phi}$ to $\mathbf{x}$. In MUSE, $\mathbf{\Phi}$ is obtained by parallel imaging reconstruction of all shots with subsequent phase smoothing of every shot image. Based on this phase correction, the complete forward model follows

$$\mathbf{y} := \mathbf{E}_2\tilde{\mathbf{x}} = \mathbf{E}_1\mathbf{\Phi}\tilde{\mathbf{x}} \tag{4}$$

where the encoding matrix $\mathbf{E}_2$ comprises the chain of the shot-to-shot phase variation $\mathbf{\Phi}$ and the encoding matrix $\mathbf{E}_1$. We implemented these two encoding matrices in SigPy (Ong and Lustig, 2019).

2.5. Joint k-q-slice reconstruction

Based on the generalized forward models in Eqs. (2) and (4), our proposed joint k-q-slice reconstruction can be formulated as a three-step approach.

I. **Navigator echo reconstruction**. The acquisition of navigator echoes follows the forward model in Eq. (2), so the reconstruction of navigator echoes can be formulated as:

$$\operatorname{argmin}_{\mathbf{x}} \|\mathbf{y} - \mathbf{E}_1\mathbf{x}\|_2^2 + \lambda\mathbf{R}(\mathbf{x}) \tag{5}$$

where $\mathbf{R}(\mathbf{x})$ denotes the regularization functional with the regularization strength λ. In this work, ℓ^2 regularization was used, i.e., $\mathbf{R}(\mathbf{x}) = \|\mathbf{x}\|_2^2$. In the case of self-navigating (i.e., no navigator acquired) as Protocol #2, the central k-space region (i.e., 1/4 of the full image matrix) of each segment is used as $\mathbf{y}$ in Eq. (5).

II. **Iterative phase smoothing**. Shot-to-shot phase variation was extracted from the reconstructed navigator echo phases. Assuming that phase images are spatially smooth (Chen et al., 2013; Dai et al., 2023), we employed the iterative approach to smooth phase,

$$\mathbf{x}^{(k+1)} = \mathbf{F}^{-1}\mathcal{H}\mathbf{F}\mathbf{x}^{(k)} \tag{6}$$

where the index k denotes the phase smoothing iteration step, and $x^{(0)}$ is then the reconstructed navigator image from Step I. $\mathcal{H}$ is the Hanning window. R248.Minor.12

III. **Shot-combined reconstruction**. Joint reconstruction of all DW images using the shot-combined forward model $\mathbf{E}_2$ with shot-to-shot phase variation from Step II reads:

$$\operatorname{argmin}_{\tilde{\mathbf{x}}} \|\mathbf{y} - \mathbf{E}_2\tilde{\mathbf{x}}\|_2^2 + \lambda \|\mathbf{T}(\tilde{\mathbf{x}})\|_* \tag{7}$$

Here, LLR regularization was employed in the local spatial-diffusion matrices, based on the theory of partially separable functions (Liang, 2007; Trzasko and Manduca, 2011; Zhang et al., 2015). $\mathbf{T}$ represents a linear operator that firstly slides a local patch window through all DW images and then flattens every set of local patches to construct two-dimensional (2D) spatial-diffusion matrices. The spatial dimension equals the block R248.Minor.6 size, and the diffusion dimension is the number of diffusion encodings. $\|\mathbf{T}(\tilde{\mathbf{x}})\|_*$ is the nuclear norm, i.e. the sum of singular values of a spatial-diffusion matrix. This nuclear norm regularization was accomplished via singular value thresholding (SVT) of each spatial-diffusion matrix R249.Minor.9 (Cai et al., 2010). After SVT, the adjoint of $\mathbf{T}$, $\mathbf{T}^H$, was needed to reorder pixel values from the spatial-diffusion matrices back to DW images. To alleviate checkerboard artifacts induced by LLR regularization with non-overlapping blocks (Hu et al., 2020), we employed overlapping blocks. In this case, values from overlapping positions are summed up to the output of $\mathbf{T}^H$. To enable the correct use of $\mathbf{T}^H$, we element-wise divided the output of $\mathbf{T}^H$ by a scaling matrix. This matrix was obtained via $\mathbf{T}^H(\mathbf{T}(\mathbf{1}))$, where $\mathbf{1}$ denotes the matrix of all ones with the same shape as the input $\mathbf{x}$.

2.6. Reconstruction

The acquired raw data was read in by twixtools (`https://github.com/pehses/twixtools`). Ramp-sampling regridding and FOV/2-ghost correction were also performed in twixtools. Subsequently, coil sensitivity maps were computed from reference scans using ESPIRiT (Uecker et al., 2014) in SigPy (Ong and Lustig, 2019).

With this pre-processing as well as the implemented forward models and proximal operator, the inverse problem in Eq. (7) was solved by the alternating direction method of multipliers (ADMM) (Boyd et al., 2010).

ADMM solves the minimization problems in an alternating update scheme,

$$\begin{cases} \mathbf{x}^{(k+1)} := \underset{\mathbf{x}}{\operatorname{argmin}} \left\|\mathbf{y} - \mathbf{E}(\mathbf{x})\right\|^2 + \rho/2 \left\|\mathbf{T}\mathbf{x} - \mathbf{z}^{(k)} + \mathbf{u}^{(k)}\right\|_2^2 \\ \mathbf{z}^{(k+1)} := \mathcal{T}_{\lambda/\rho}(\mathbf{T}\mathbf{x}^{(k+1)} + \mathbf{u}^{(k)}) \\ \mathbf{u}^{(k+1)} := \mathbf{u}^{(k)} + \mathbf{T}\mathbf{x}^{(k+1)} - \mathbf{z}^{(k+1)} \end{cases} \tag{8}$$

where k denotes the ADMM iteration. $\mathbf{z}$ is the auxiliary variable ($\mathbf{z} = \mathbf{T}\mathbf{x}$), and $\mathbf{u}$ is the Lagrangian multipliers. Importantly, when solving Eq. (2), $\mathbf{x}$ denotes shot images and $\mathbf{E}$ denotes $\mathbf{E}_1$ in Eq. (8). In contrast, $\mathbf{x}$ denotes shot-combined images and $\mathbf{E}$ denotes $\mathbf{E}_2$ when solving Eq. (4). $\mathbf{x}$ can be solved using linear least square algorithms, e.g. conjugate gradients (Hestenes and Stiefel, 1952), while $\mathbf{z}$ is updated via singular value thresholding ($\mathcal{T}$) with the thresholding parameter λ/ρ. The coupling parameter ρ is effective in both the update of $\mathbf{x}$ and $\mathbf{z}$. It acts as Tikhonov regularization strength when updating $\mathbf{x}$, but also inversely scales the thresholding strength when updating $\mathbf{z}$, as shown in Supporting Information Figures S1 and S2.

In this work, 15 ADMM iterations with $\rho = 0.05$ and $\lambda = 0.04$, and a block size of 6 for LLR (refer to Supporting Information Figure S3) were used. All reconstructions were done on a single A100 SXM4/NVLink GPU with 40 GB memory (NVIDIA, Santa Clara, CA, USA).

We compared our proposed joint reconstruction with established multi-shot reconstruction techniques, specifically, MUSE (Chen et al., 2013) and JULEP (Dai et al., 2023), hosted on GitHub by Dr. Dai (Dai et al., 2023). Further, we performed the local-PCA denoising (Cordero-Grande et al., 2019) as implemented in MRtrix (Tournier et al., 2019) on the MUSE reconstructed complex DW images.

With reconstructed DW images from Protocol #2 in Table 1, color-coded fractional anisotropy (cFA) maps (Basser et al., 1994) were fitted using DiPy (Garyfallidis et al., 2014),

3. Results

3.1. Iterative smoothing of shot-to-shot phase variation

Navigators were acquired with the acceleration rate as listed in Table 1. Besides, the base resolution of navigators (e.g. 32 in Protocol #3 in Table 1) was smaller than imaging echoes. As a result, reconstructed navigator phases (refer to the first column in Fig. 3) from Step I in Section 2.5 are not spatially smooth. Such phases, when used in the shot-combined reconstruction, result in signal void artifacts in DW images. To address this problem, we utilized the iterative smoothing procedure. As shown in Fig. 3, the ripple-like phase artifact disappears after five iterations. It can also be seen that such an iterative procedure retains the shot-to-shot phase variation. R249.Minor.11 – 12

3.2. Comparison to MUSE and JULEP with four-shot iEPI acquisition

The iterative phase smoothing was also applicable to MUSE-type self-navigating reconstruction, where shot phases were reconstructed from imaging echoes. Fig. 4 compares our proposed JETS with MUSE (Chen et al., 2013), MUSE with complex-valued local-PCA denoiser (Cordero-Grande et al., 2019), and JULEP (Dai et al., 2023). The residual noise from MUSE can be largely removed by the denoiser. However, when compared to JETS, the denoiser shows residual noise patterns within the globus pallidus (indicated by the red arrow). JETS also shows better denoising than JULEP. The reason is that JETS enforces spatial-diffusion regularization, whereas JULEP formulates structured low-rank regularization of the four shots for one diffusion encoding.

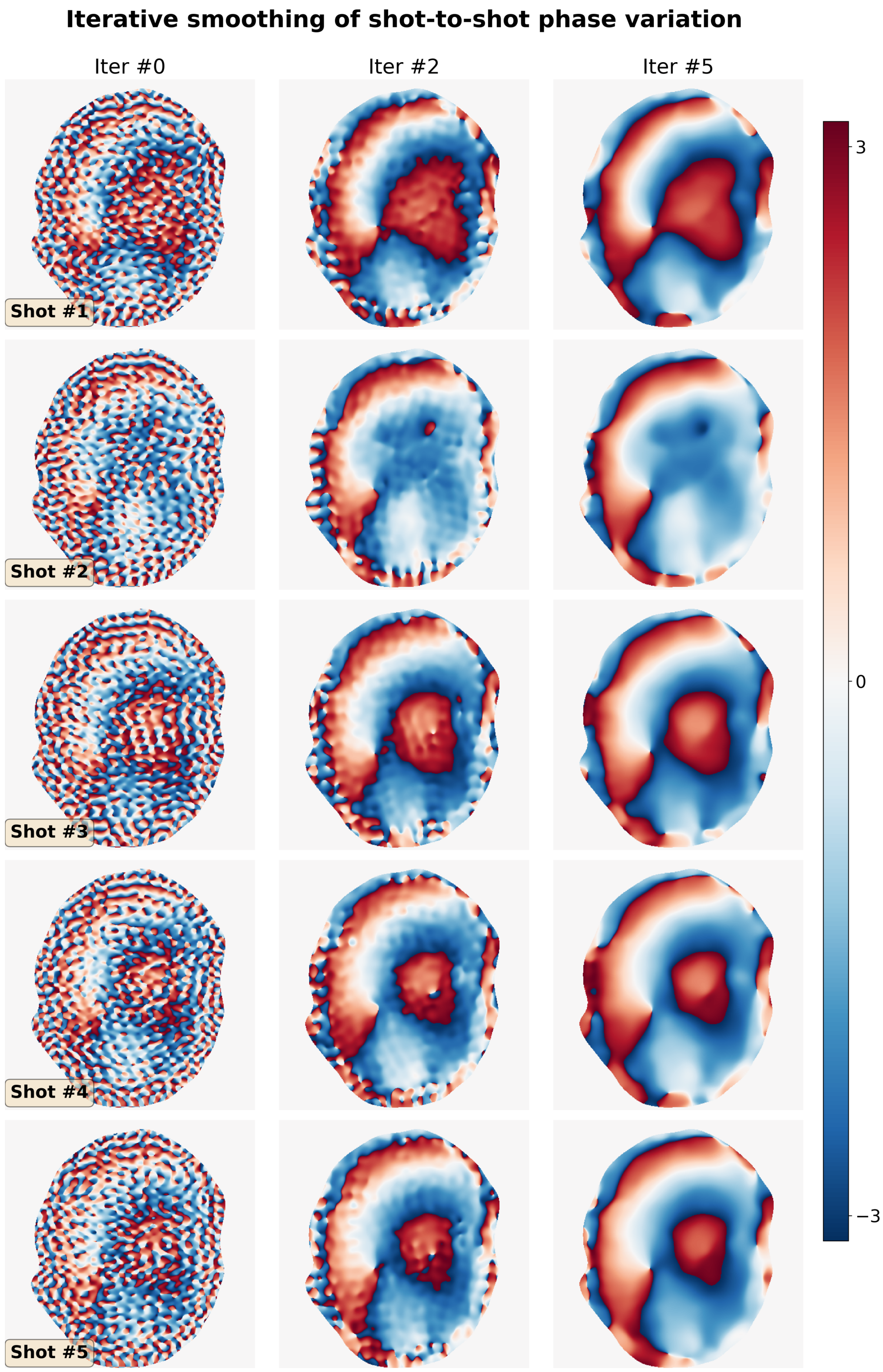

Figure 3: Iterative smoothing of shot-to-shot phase variation according to Eq. (6). Navigators from Protocol #3 were reconstructed based on Step I in Section 2.5 and then used as the input (iter #0, left column).

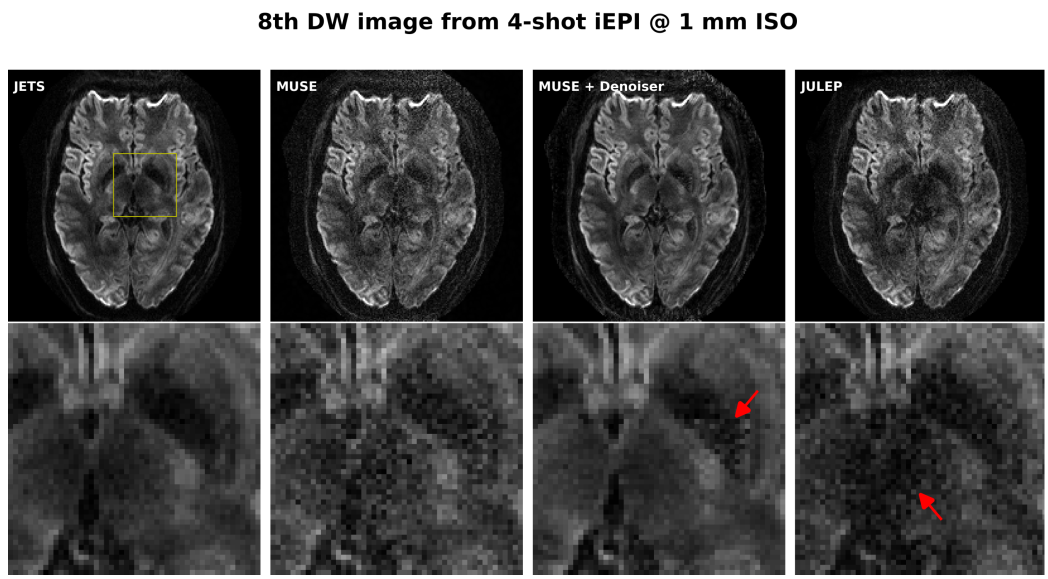

Figure 4: Reconstructed DW images (the 8th diffusion encoding) based on 4-shot iEPI acquisition with 1 mm isotropic resolution (Protocol #1 in Table 1). Four reconstruction methods are compared (from left to right): JETS, MUSE, MUSE with denoiser, and JULEP. The 2nd row displays the magnified views of the yellow square. The image from the denoiser (3rd column) shows residual noise patterns within the globus pallidus (indicated by the red arrow). The JULEP reconstruction (4th column) shows signal dropout in the central region (indicated by the red arrow).

R249.Minor.13

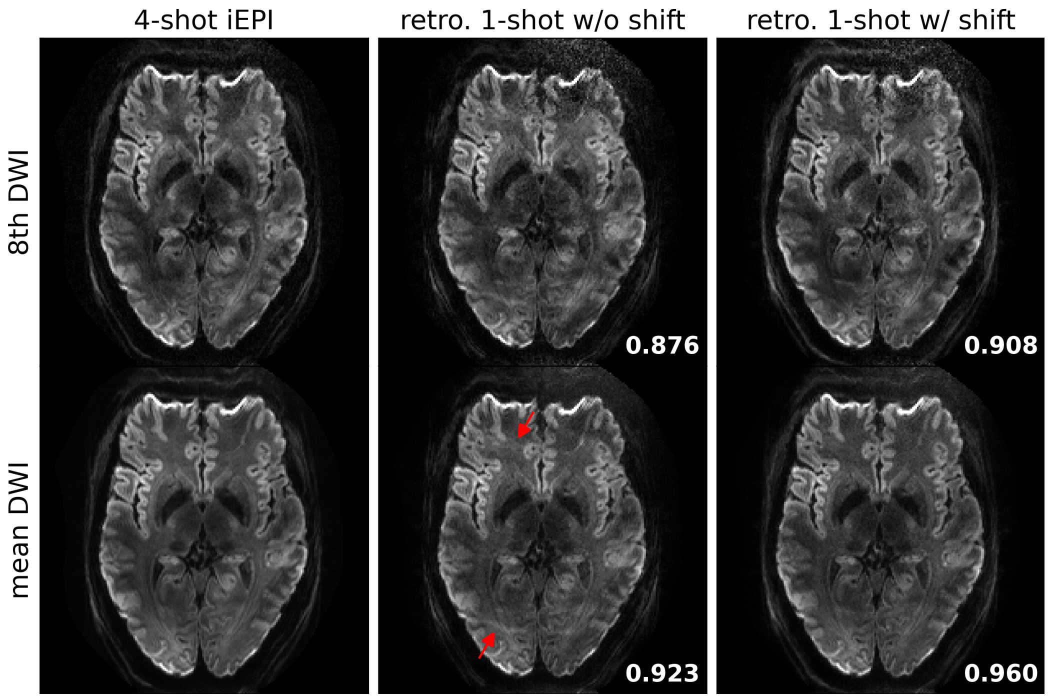

Figure 5: Quantitative validation of the proposed k_y-shift enoding sampling pattern based on 4-shot iEPI acquisition with 1 mm isotropic resolution (Protocol #1 in Table 1). (Top) the 8th diffusion encoding and (bottom) mean DWI over 20 diffusion encodings. (1st column) JETS reconstruction of 4-shot iEPI acquisition is used as the ground truth. The 2nd and the 3rd column displays JETS reconstruction of retrospectively undersampled 1-shot acquisition without and with k_y shifting, respectively. Residual aliasing artifacts are visible in the reconstruction without k_y shifting, as indicated by the red arrows. Structural similarity (SSIM) values are computed and displayed in the bottom right corners.

R249.Minor.14 – 16

3.3. Retrospectively undersampling from the four-shot iEPI acquisition

JETS reconstruction results on the four-shot prospectively fully-sampled data from Protocol #1 in Table 1, as well as on the retrospectively undersampled one-shot data without and with the proposed k_y shift are displayed in Fig. 5. Residual aliasing artifacts are visible in the reconstruction without k_y shifting, as indicated by the red arrows. In contrast, the reconstruction R249.Minor.17 with the proposed k_y shifting among diffusion encodings shows much reduced R249.Minor.18 aliasing, reduced noise, and higher SSIM.

3.4. Analysis of reconstruction parameters

Here we provide a systematic analysis of the proposed JETS reconstruction with LLR regularization applied to the spatial-diffusion dimension, as shown in Fig. 6.

First, we varied the regularization strength λ. We tested values of 0, 0.08, and 0.16. The reconstruction with $\lambda = 0$ in Eq. (7) corresponds to parallel R249.Minor.19 imaging reconstruction without LLR regularization. It is worth noting that the proposed NAViEPI sequence demonstrates high-quality sub-millimeter DW images ($0.5 \times 0.5 \times 2.0$ mm^3 in this example). The DW images can be further improved with the use of LLR regularization, i.e., reduced noise, as seen in the reconstruction with $\lambda = 0.08$. Increasing λ (e.g. 0.16) further reduces noise, but at the cost of increased blurring. Therefore, $\lambda = 0.08$ was selected in this work.

Second, besides the regularization strength, the block size (i.e., the area of 2D patches) also plays a role in denoising. We employed square blocks in this work. Here, the block width of 2 shows the best denoising as compared to 1 and 3, especially in the peripheral brain region. Among the three tested

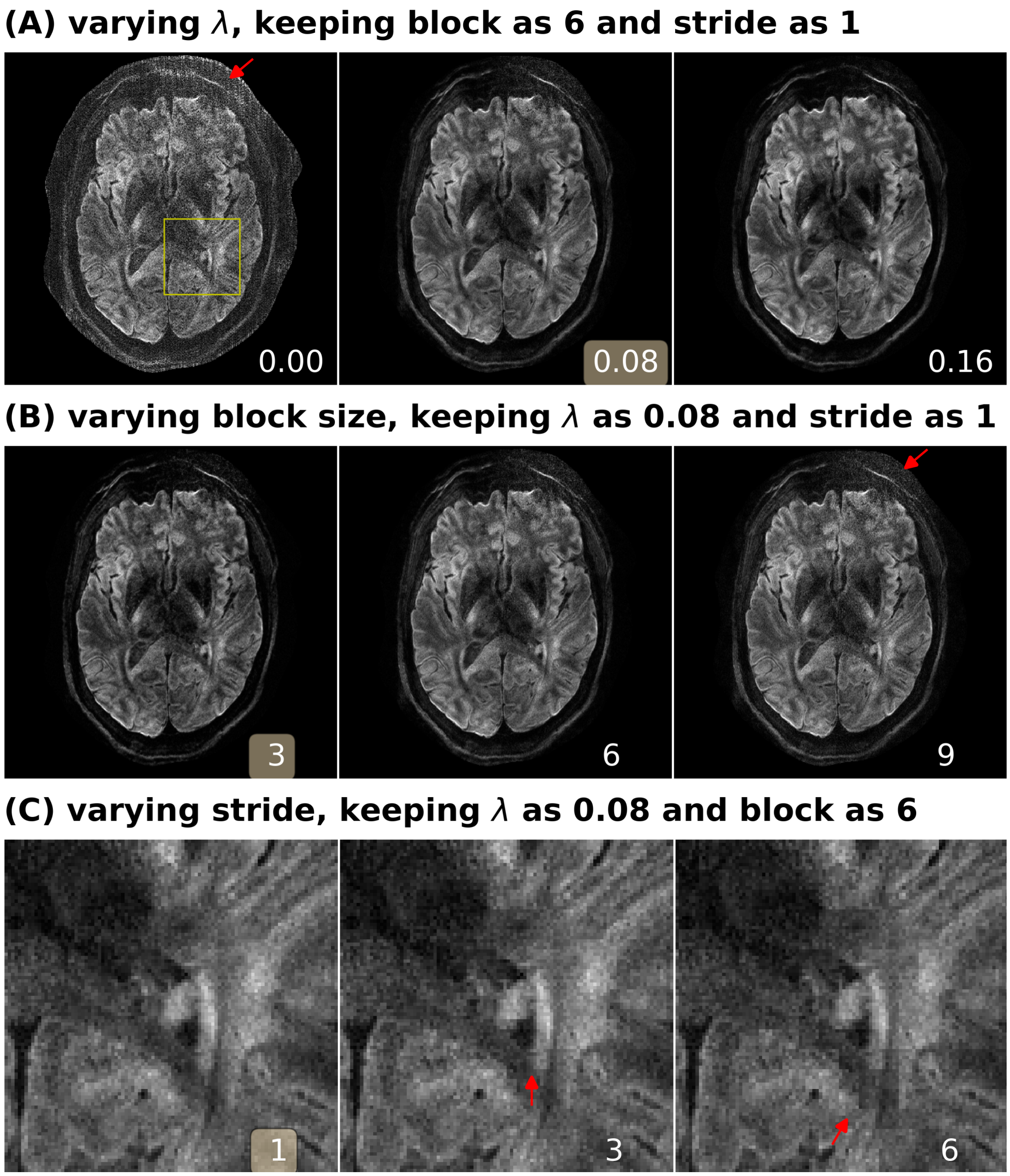

Figure 6: Analysis of reconstruction parameters based on the 3-scan trace acquisition with $0.5 \times 0.5 \times 2.0$ mm^3 (Protocol #3 in Table 1). Displayed are JETS reconstructed single-direction DW images. **(A)** Varying the regularization strength λ from 0 to 0.08 and 0.16. **(B)** Varying the block size from 3 to 6 and 9. **(C)** Varying the stride size from 1 to 3 and 6 (non-overlapping).

block widths, the block size of 4 (with the block width 2) is the smallest one which is no smaller than the diffusion directions in this 3-scan trace example (1 b_0 plus 3 orthogonal diffusion directions). This observation agrees with the suggestion that the patch size should be no smaller than and close to the diffusion directions (Cordero-Grande et al., 2019).

Third, we varied the stride, i.e., the step from one local patch to the next. The use of overlapping LLR (Fig. 6 (C) left) better suppresses blocky artifacts, compared to the partially overlapping LLR (Fig. 6 (C) middle) and the non-overlapping LLR (Fig. 6 (C) right). R248.Major.4b

3.5. Sampling efficiency of NAViEPI

As shown in Fig. 7, NAViEPI achieves sub-millimeter resolution (voxel size $0.5 \times 0.5 \times 2.0$ mm^3) with the use of a 5-shot acquisition. When compared to a single-shot acquisition with the same voxel size, the acquisition time of NAViEPI is about two times longer, but the image quality of NAViEPI is remarkably improved. R249.Minor.22

In the sub-millimeter imaging scenario, the increased base resolution requires longer TE (143 ms) in the single-shot acquisition, which results in significant signal loss due to T_2 relaxation. Therefore, sub-millimeter DWI necessitates multi-shot acquisition, which is subject to shot-to-shot phase variation and long scan time. However, NAViEPI solves both challenges. The 5-shot acquisition reduces TE to 58 ms, and thus retains SNR significantly compared to the single-shot acquisition. Moreover, the JETS reconstruction can help to reduce noise and improve structural visibility.

Fig. 8 shows the JETS reconstructed b_0 and TRACE images in different slice locations. Admittedly, the lower brain region (e.g. slice #22) exhibits in-

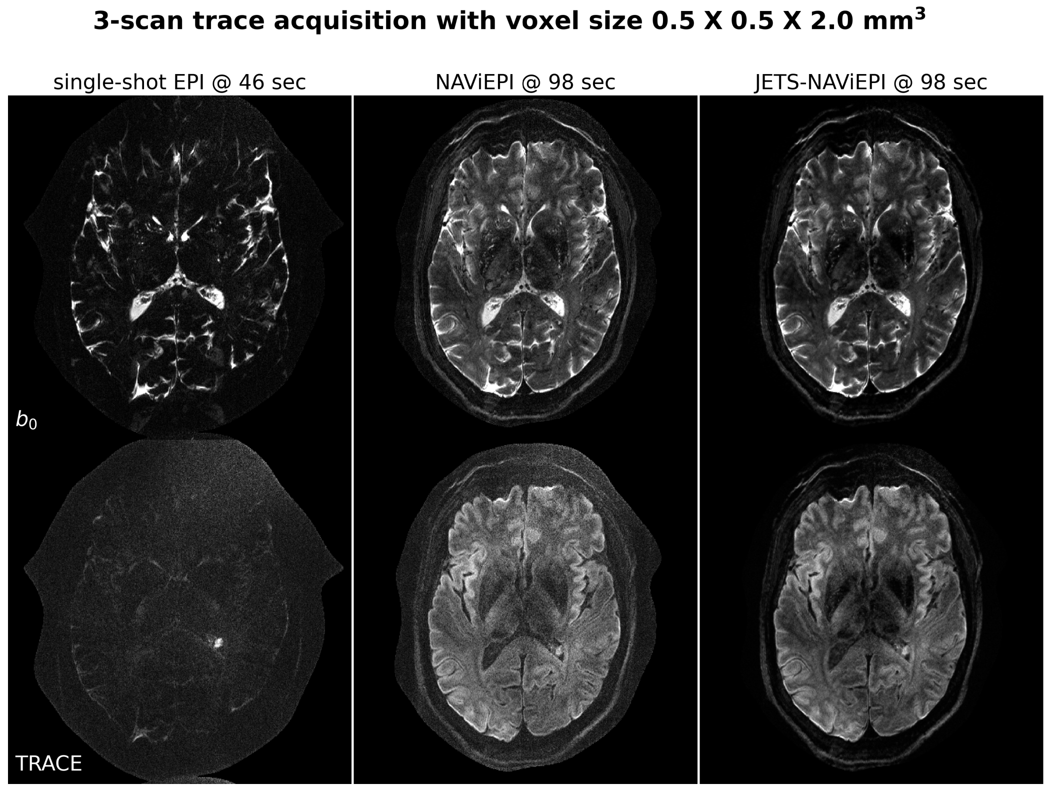

Figure 7: Sampling efficiency of the proposed NAViEPI sequence. 5-shot NAViEPI acquisition with the voxel size $0.5 \times 0.5 \times 2.0$ mm^3 (Protocol #3) was compared with single-shot EPI acquisition (Protocol #4). Both the 1st and the 2nd columns were reconstructed via parallel imaging without LLR regularization, whereas the 3rd column was reconstructed via JETS.

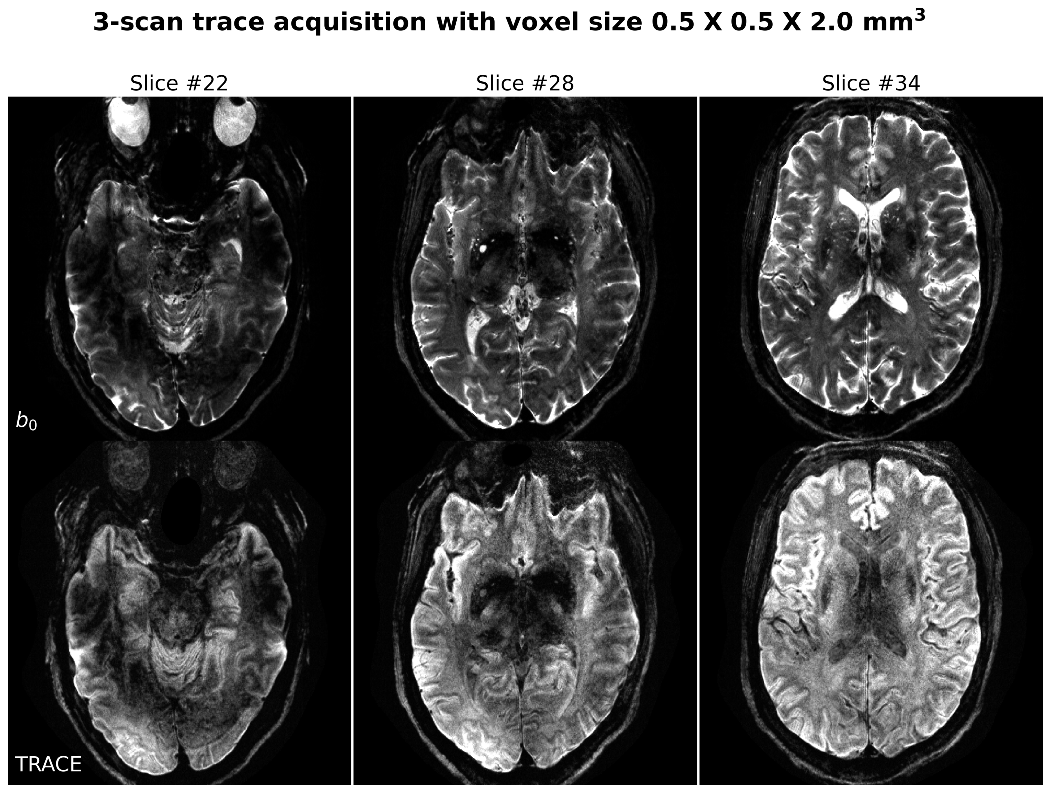

Figure 8: Reconstruction of the 3-scan trace acquisition with the voxel size $0.5 \times 0.5 \times 2.0$ mm^3 (Protocol #3) at different slices.

homogeneous and lower signal intensity than the upper slices. Such inhomogeneity can be alleviated with the use of multi-channel parallel transmission (Katscher et al., 2003; Grissom et al., 2010).

3.6. Diffusion tensor imaging

Since 30 diffusion encodings were acquired in Protocol #2, the block size in LLR regularization was lifted to 6, such that the spatial-diffusion matrix for SVT has similar width and height. The other parameter were kept the same as found in Fig. 6.

The mean DWIs in Fig. 9 illustrate high spatial resolution and high SNR. In line with Fig. 8, we can notice the signal loss in the cerebellum region, due to the use of single-channel transmission in this work. On the other hand, the reconstructed cFA maps in Fig. 9 show clear fiber orientation in all orientations. Moreover, tiny fiber structures can be visualized in the zoomed-in cFA maps. Because of the low signal sensitivity surrounding the cerebellum, residual artifacts are visible in the zoomed-in sagittal view. To enhance the DTI fitting performance, one possibility is to acquire more diffusion encodings.

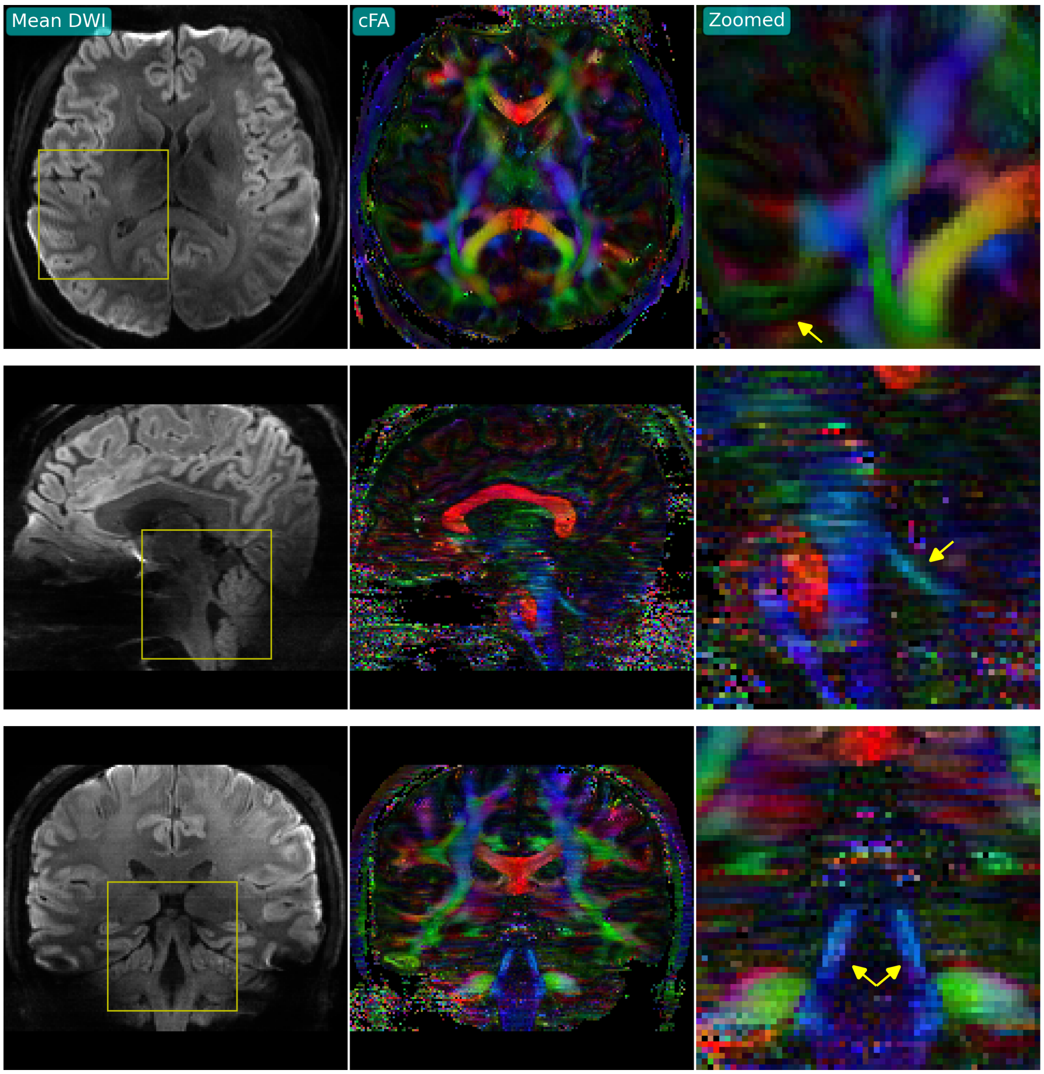

Figure 9: (Left) Mean DWI, (middle) cFA, and (right) cFA in the zoomed-in region based on JETS reconstructed DWI from Protocol #2. Three orthogonal slices (transversal, sagittal, and coronal) are displayed from top to bottom.

4. Discussion

This work reports a novel DW-MRI technique, JETS-NAViEPI. NAViEPI (1) achieves the fast and efficient acquisition of both imaging and navigator echoes, (2) enforces consistent effective ESP between the two echoes, and (3) allows for undersampled iEPI as well as a large number of shots. Moreover, compared to the single-shot acquisition, joint k-q-slice reconstruction with k_y-shift encoding on NAViEPI retains SNR and reduces aliasing artifacts in DW images. As a result, JETS-NAViEPI renders high spatiotemporal resolution diffusion MRI protocols in 7 T, e.g., a 3-scan trace acquisition with the voxel size $0.5 \times 0.5 \times 2.0$ mm^3 at 1.5 min. R249.Minor.24

One limitation of JETS-NAViEPI is the long reconstruction time due to the simultaneous reconstruction of all DW images and the use of overlapping locally low-rank regularization. The reconstruction for the Protocol #3 in Table 1 on an A100 GPU takes about 2 min per multi-band slice. To reduce the computation time, coil compression algorithms (Buehrer et al., 2007; Huang et al., 2008) can be employed to reduce the number of coils for image reconstruction. Moreover, one may deploy multi-GPU distributed computing or modern optimization algorithms (e.g. stochastic gradient descent) (Ong et al., 2020) to speed up the reconstruction.

Neither the signal modeling in Eqs. (2) and (4) nor the LLR regularization considers the subject motion. In the presence of motion, the regularized reconstruction may degrade. To overcome this problem, scout-informed motion estimation and reconstruction (Polak et al., 2022) could be integrated into the framework.

Another potential extension of this work is to incorporate distortion correction. The standard distortion correction method is known as TOPUP (Andersson et al., 2003), which acquires two scans with opposing phase-encoding directions to obtain the field inhomogeneity map and then performs conjugate phase reconstruction to correct for distortion. Alternatively, the multi-echo acquisition could be used for the coil sensitivity reference scan, R249.Minor.25 such that both coil sensitivity and B_0 field inhomogeneity maps could be reconstructed from the data.

This work employed a single regularization weight λ to enforce low rankness along the spatial-diffusion direction. However, SNR may be heterogeneous within the FOV. Therefore, one single regularization scalar may be inadequate to cover the whole FOV. Beyond this SVT-based reconstruction, one may seek to use machine learning to learn a q-space prior as the regularizer (Hammernik et al., 2018; Lam et al., 2019; Mani et al., 2021). R249.Minor.26

Although NAViEPI employs navigators for the acquisition of shot-to-shot phase variation, it is worth noting that phase behavior depends on several hard-to-control factors such as pulsatile motion, bulk motion, locations within the brain, and diffusion sensitization strength. Therefore, more comprehensive modeling or post-processing such as image registration may be considered in future work.

potential synergies between their LLR and the denoiser R248.3b

While this work reconstructs all DW images and then performs model fitting, an alternative approach is to directly estimate b_0 and diffusion tensors from measured k-q-space data using model-based reconstruction (Knoll et al., 2015; Dong et al., 2018; Shafieizargar et al., 2023). Compared to DW image reconstruction, model-based reconstruction solves for a fewer number of unknowns, but requires strict diffusion tensor modeling and the use of nonlinear least square solvers.

5. Conclusions

We demonstrated the JETS-NAViEPI technique, which integrates a k_y-shifted encoding interleaved EPI sequence and a joint reconstruction with overlapping locally low-rank regularization for high spatial-angular-temporal resolution DW-MRI at 7 T. This technique allows for high-quality DW image reconstruction with accelerated acquisitions.

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Data and code available statement

In the spirit of reproducible and open science, we publish our source code (https://github.com/ZhengguoTan/sigpy) as well as the raw k-space data (https://doi.org/10.5281/zenodo.7548595). We also provide inter- R248.8
active demonstrations of the reconstruction procedure (https://github.com/ZhengguoTan/demo_jets_diffusion_mri_7t).

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