

# High-resolution diffusion weighted MRI enabled by multi-shot EPI with multiplexed sensitivity-encoding

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**Target audience:** Neuroimaging researchers and clinicians who are interested in high-resolution diffusion-weighted imaging

**Purpose:** The goal of this study is to develop a novel post-processing algorithm, enabling diffusion weighted imaging (DWI) of high-quality and very high-resolution (e.g.,  $300\mu\text{m}$  in-plane resolution for human DWI at 3T) without requiring navigator echoes. DWI data have been mostly acquired with single-shot echo-planar imaging (EPI). The spatial resolution, however, is inherently limited in single-shot EPI. Multi-shot acquisition strategies could potentially achieve higher spatial resolution and fidelity, but they are generally susceptible to motion-induced phase errors among excitations, rendering the reconstructed images unusable. It has been shown that shot-to-shot phase variations may be corrected using navigator echoes, but the residual artifacts may still be pronounced when there exist nonlinear motions. To address these challenges, a novel and robust multi-shot DWI technique based on *multiplexed sensitivity-encoding* (MUSE) is developed to reliably and inherently correct nonlinear shot-to-shot phase variations and enable very high-resolution DWI.

**Methods:** The developed *multiplexed sensitivity encoding* (MUSE) method differs from the conventional SENSE algorithm in several ways. First, the conventional SENSE algorithm is designed to produce images from accelerated scans (i.e., under-sampled data), with non-ideal matrix inversion conditioning where the number of unknowns (i.e., the SENSE acceleration factor: e.g., 4) is not significantly smaller than the number of equations (i.e., the number of coils: e.g., 8). In contrast, the MUSE algorithm jointly estimates the magnitude signals of aliased voxels (due to intra-scan motion) simultaneously from all segments of segmented EPI (i.e., full k-space data), with greatly improved matrix inversion conditioning where the number of unknowns (e.g., 4) is significantly smaller than the number of equation (e.g., 8 coils  $\times$  4 segments = 32). Second, in order to account for motion induced phase inconsistencies among multiple EPI segments, the conventional SENSE method needs to be first applied to estimate the phase variations from each EPI segment. The SENSE-estimated phase information will be spatially smoothed (to minimize noises) and incorporated into the developed MUSE-based joint estimation of aliased magnitude signals.

To evaluate the performance and confirm the reliability of the new MUSE technique, high-resolution DTI images ( $300\mu\text{m} \times 300\mu\text{m}$  or  $860\mu\text{m} \times 860\mu\text{m}$ ) were obtained from 6 healthy volunteers on 3 Tesla MRI systems (GE, Waukesha, WI) equipped with an 8-channel receiver coil. DTI images (with 15 diffusion weighting directions at a b factor of either 500 or 1000sec/mm<sup>2</sup>) were acquired using a 4-shot segmented EPI pulse sequence with a twice-refocused spin-echo scheme. Scan parameters included: number of partial-Fourier over-sampling ky lines 12, in-plane acquisition matrix size  $512 \times 512$  or  $256 \times 256$ , FOV  $15.4 \times 15.4$  or  $22 \times 22$  cm<sup>2</sup>, axial-plane slice thickness 4mm, TR 5 sec, and TE 59.3 msec.

The acquired data were processed with the following steps. First, Nyquist ghost artifacts resulting from odd-even echo inconsistencies are first removed. Second, using the conventional SENSE algorithm, four full-FOV images were reconstructed from four DWI segments, and the motion-induced phase variations in each DWI segment were calculated. Third, the phase maps derived from step 2 were spatially smoothed with the total variation algorithm. Fourth, the smoothed phase maps and the coil sensitivity profiles were used to reconstruct aliasing-free DWI images from the Nyquist-corrected DWI data, based on the MUSE algorithm. To illustrate the image quality improvement uniquely enabled by the MUSE procedure, another set of aliasing-free DTI data were reconstructed by summing the magnitude maps derived from four EPI segments with the conventional SENSE, and the resultant data quality was assessed.

**Results:** Figure 1a shows the Nyquist-corrected DWI images produced by the conventional segmented EPI reconstruction (i.e., a direct k-space data combination), corresponding to 5 (out of 15) directions obtained from one representative participant. As expected, the levels of motion-induced aliasing artifacts vary significantly, depending on the degree of intrascan motion. The ghost-to-signal ratio (GSR) is 0.36 in images shown in Figure 1a. Figure 1b shows that the motion-induced aliasing artifacts can be effectively eliminated using MUSE, regardless of the levels of aliasing artifacts in the raw DWI data. The GSR is 0.08 images shown in Figure 1b. It should be noted that even though the motion-induced aliasing artifacts can also be reduced (GSR: 0.19) with a conventional SENSE procedure, the resultant images have significantly lower SNRs. Figures 1c and 1d compare the FA maps produced with the conventional SENSE reconstruction and the new MUSE technique, respectively. It is demonstrated that MUSE-enabled DWI has a significantly lower noise level due to improved conditioning for matrix inversion. Figure 2 shows a high-resolution DWI image (in-plane:  $300\mu\text{m} \times 300\mu\text{m}$ ) produced with the developed MUSE algorithm, demonstrating the feasibility of achieving high-quality and very high-resolution mapping of human white-matter architecture *in vivo* at 3 Tesla.

**Discussion:** A general and effective approach to enable high-resolution DWI through multi-shot acquisitions, termed MUSE, is presented here. The developed technique produces multi-shot DWI data with higher spatial resolution and fidelity, as compared with single-shot acquisition. In comparison to the conventional navigator-based segmented DWI, the new MUSE technique, which requires neither navigator nor reference echoes, also has several significant advantages. First, the imaging throughput of navigator-less segmented DWI is higher than that of navigator-based segmented DWI. Second, unlike navigator-based correction which could fail when the motions differ between navigation and acquisition or when there exist local and nonlinear motions (e.g., in the brainstem), the newly developed MUSE method can inherently measure and correct both linear and nonlinear phase errors.

**Conclusion:** The developed MUSE technique enables high-quality and very high-resolution DWI mapping of human white matter architectures.

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