## A Navigated non-CPMG Turbo Spin Echo Pulse Sequence for High Resolution Diffusion Imaging

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**Introduction:** Single-shot EPI is presently the most prevalent pulse sequence for diffusion imaging. This technique offers ultra-fast data acquisition speed and avoids image quality problems associated with bulk motion. Diffusion-weighted single-shot EPI (DW-ssEPI), however, is hampered by image distortion due to magnetic susceptibility difference, image misregistration caused by eddy currents, and low spatial resolution associated with limited matrix size. Although parallel imaging somewhat relieves these problems, complete elimination of the limitations remains challenging, especially for applications where the signal-to-noise ratio (SNR) is limited. Recent studies have shown that diffusion-weighted multi-shot Turbo Spin Echo (DW-msTSE) sequences can effectively overcome the limitations inherent to DW-ssEPI (1-3). In DW-msTSE sequences, special attention must be paid to (a) motion sensitivity and (b) the CPMG conditions. PROPELLER (1), combined with quadratic phase modulation (2), provides an elegant way to address both problems for *non-Cartesian* k-space imaging. In this study, we report a non-CPMG DW-msTSE sequence problem originating from CPMG violation by employing variable crusher gradients to eliminate stimulated echoes while preserving primary echoes. **Methods:** The non-CPMG DW-msTSE sequence (Fig.1) was developed based on a commercial TSE sequence (Siemens Medical Solutions, Erlangen, Germany). A twice refocused spin echo (TRSE) module was used for diffusion sensitization (4). Each of the four gradient lobes was designed according to the prescribed b-value,

twice refocused spin echo (TRSE) module was used for diffusion sensitization (4). Each of the four gradient lobes was designed according to the prescribed b-value, minimal echo spacing, and the most critical eddy current time constant (e.g.,  $\sim$ 30ms) for a given protocol (4,5). In order to ensure a uniform diffusion-weighting profile, the refocusing pulses ( $\theta_2$ ) in the TRSE module were designed to produce twice the slice thickness of that selected by the refocusing pulses ( $\theta_3$ ) in the echo train.

In the presence of the diffusion gradients, motion introduced substantial phase errors between k-space lines acquired with different shots (or excitations). To remove these inter-shot phase errors, a 2D navigator was acquired using an EPI sampling trajectory (16×16 points) immediately after the TRSE module (Fig.1). Phase inconsistency between shots was evaluated and subsequently removed during image reconstruction (6). Additionally, intra-shot phase errors arising mainly from residual eddy currents were also calculated from a TSE reference scan and removed using an established phase correction algorithm (7).

The TRSE module resulted in unequal echo spacing throughout the echo train, leading to violation of the CPMG conditions and inconsistent phase errors between the primary and the stimulated echoes. This problem was addressed by separating the primary echoes from the stimulated echoes using variable crushers (8) (Fig. 1). The amplitude of the crusher gradients straddling the refocusing pulses ( $\theta_3$ ) decreased linearly from 28mT/m to 9mT/m throughout the echo train.

The non-CPMG DW-msTSE sequence was implemented on a Siemens Trio Tim 3T MRI scanner, and evaluated on water phantoms and healthy volunteers using the following parameters: TE/TR = 84ms/2000ms, FOV = 22cm, matrix size =  $256\times256$ , ETL = 7, bandwidth = 130Hz/pixel, voxel size =  $0.86\times0.86\times5.0$ mm, and b=0-1300 s/mm<sup>2</sup>. In order to minimize the influence of pulsation, ECG triggering was employed during volunteer scans. To assess the performance of the non-CPMG DW-msTSE sequence, diffusion images were also acquired from the same subject using a commercial DW-ssEPI sequence with parameters similar to those described above, except for bandwidth = 1860Hz/pixel, matrix size =  $128\times128$ , and voxel size =  $1.72\times1.72\times5.0$ mm.

**Results and Discussion:** Figure 2 shows two sets of representative brain images acquired from a volunteer using the non-CPMG DW-msTSE (top row) and the DW-ssEPI (bottom row) sequences, respectively. Both images in Figs. 2a and 2b were ghost-free, indicating that (*a*) the variable crusher approach was effective in filtering out the stimulated echoes from the primary echoes, and (*b*) the combination of TRSE and the intra-shot phase correction successfully removed phase errors due to residual eddy currents. The absence of ghosts in the diffusion-weighted image (Fig. 2b) as well as the FA map (Fig. 2c) further demonstrated that the motion correction technique effectively removed motion-induced inter-shot phase errors. Comparison between the top and bottom row images revealed that image distortion (e.g., in the frontal and left temporal areas) and edge enhancement arising from eddy currents (Fig. 2f) were effectively avoided in the non-CPMG DW-msTSE images. More importantly, the increased spatial resolution afforded by the non-CPMG DW-msTSE technique was evident when comparing the FA maps (Fig. 2c and 2f).

Removal of stimulated echo from the signals will compromise the SNR. However, when  $\theta_3$  did not significantly deviate from 180° (e.g., between 150°-180°), this SNR loss was less than 10%, as observed experimentally and confirmed with simulations. Another drawback of the proposed technique is the relatively long data acquisition time (70-80s/image). This problem can be alleviated by extending the present technique to GRASE sequences and/or invoking parallel imaging. It should be noted that, with the variable crusher approach, a minimal crusher area corresponding to ~3.6 $\pi$  intra-voxel dephasing was needed in order to avoid interference from FID signals following a non-ideal refocusing pulse.

**Conclusion:** We have developed a non-CPMG DW-msTSE sequence with Cartesian k-space sampling. The technical challenges have been addressed by using variable crusher gradients, a 2D navigator, and a TRSE diffusion module. This sequence provides an alternative to ssEPI diffusion imaging in areas, such as body diffusion imaging and high-resolution brain imaging, where ssEPI may become prohibitive due to image artifacts and limited spatial resolution.



**Fig.1** A diagram of the non-CPMG DW-msTSE pulse sequence with a TRSE diffusion module, a 2D EPI navigator, and variable crushers along the slice-selection direction.



**Fig.2** Images acquired using the non-CPMG DW-msTSE (top row) and the DW-ssEPI (bottom row) sequences. (a, d): b=0 s/mm<sup>2</sup>; (b, e):  $b=1000s/mm^2$ , with diffusion gradient direction cosine (0.58, 0.58, 0.58); and (c, f): color-coded FA maps.

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