Strategies for MTR acquisition time reduction in the spinal cord

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INTRODUCTION: The spinal cord (SC) has been shown to be affected in neurological disorders such as multiple sclerosis (MS), with both focal and diffuse abnormalities detected in cord white (WM) and grey matter (GM) (1). Techniques based on Magnetisation Transfer (MT) imaging provide markers for both brain and spinal cord pathology and the MT ratio (MTR) has previously been shown to be decreased in the SC in MS (2,3), and spinal cord injury (SCI) (4).

However, there are some technical challenges associated with making quantitative measurements in the SC *in vivo* due to its small cross-sectional size and the potential for SC motion (both physiological and bulk motion) during scans.

Many previous SC MTR studies have used a spoiled gradient echo sequence for acquisition (2, 3, 4), however this can be time consuming and is more likely to suffer from motion-related artefacts. One of the most common fast imaging techniques, echo-planar imaging (EPI), suffers from geometrical distortions in the presence of susceptibility gradients such as those found near the vertebrae surrounding the SC (bone and tissue/CSF interface). Two possible strategies for controlling such distortions are (i) to use multi-shot gradient echo EPI, at the cost of increasing the sensitivity to bulk motion or (ii) to use single shot EPI but implementing ZOOM-EPI (zonally magnified oblique multi-slice EPI) (5, 6, 7), which is based on an inner volume (IV) imaging technique and makes use of a decreased field-of-view (FOV) and thus shorter echo train length (ETL), thereby reducing artefacts caused by susceptibility changes between soft tissue and the adjacent vertebrae.

We have evaluated the two types of EPI-based acquisitions with regards to image quality and reproducibility of cord MTR measurements compared to the reference spoiled gradient echo MTR sequence in 6 healthy volunteers.

METHODS: Using a 3T Philips Achieva MRI system with RF multi-transmit technology (Philips Healthcare, Best, the Netherlands) and a 16-channel neurovascular coil the following sequences were acquired in 6 healthy volunteers (4F, 2M, aged 36.7 ± 6.7 years) for comparison. MT off (without MT weighting) and MT on (with MT weighting) scans were acquired for each sequence within the same protocol. All sequences were repeated 3 times on separate occasions in one volunteer to allow assessment of intra-subject MTR variation. For all 3 sequences MT weighting was achieved using Sinc-Gaussian shaped MT saturating pulses of nominal α=450º, offset frequency 1kHz, duration 15ms applied prior to the excitation pulse (although the amount of MT weighting achievable for each sequence will be different due to differing sequence acquisition parameters). For the ZOOM-EPI sequence a train of 10 MT pulses was applied prior to excitation to enable steady state to be reached, and a dummy scan was also performed prior to the start of the acquisition. All protocols acquired 21 5mm axial slices, with an in-plane resolution of 0.75x0.75mm^2, reconstructed to 0.5x0.5mm^2. The field of view (FOV) was centred at the level of the C2-3 intervertebral disc, and spanned levels C1-C5 in all volunteers. Other parameters specific to each protocol were:

Spoiled gradient echo – 7:35mins: 3D slab selective spoiled gradient echo sequence with two echoes (TR=36ms, TE1/TE2=3.5/5.9ms, flip angle α= 9°, FOV=180x180 mm^2, acquisition matrix 240 x 240, SENSE factor = 2 in the foot/head (F/H) direction).

Multi-shot spoiled gradient echo EPI – 3:33mins: 3D spoiled gradient echo sequence with multi-shot EPI readout (EPI factor=3, TR=110ms, TE=13ms, α=9°, FOV=180x180 mm^2, acquisition matrix 240 x 240, SENSE factor=2 in the F/H direction).

ZOOM-EPI: 2D single-shot EPI sequence with reduced FOV (TR=6650ms, TE=48ms, FOV=54x48mm, acquisition matrix 72x62, SENSE factor=1.5 in the F/H direction, halfscan factor 0.74). The slice thickness of the IV refocusing pulse was 26 mm. This sequence was acquired 3 times for each subject with number of signal averages (NSA)=2 (2:19mins), 3 (3:19mins) or 4 (4:19mins).

Image analysis: Registration of MT on to MT off images was performed using the linear registration tool within the FSL software package (www.fmrib.ox.ac.uk/fsl) before MTR calculation. Cord masks were manually drawn on the central 7 slices of the MT off image, encompassing levels C2-C3 for each subject, and then applied to the calculated MTR maps.

RESULTS: Example MT off (left), MT on (centre) and MTR (right) images are shown in figure 1, and mean MTR values and standard deviations (SDs) for each sequence as well as coefficients of variation (CoVs) between subjects are given in table 1. It should be noted, however, that the absolute MTR values for each sequence cannot be directly compared since MTR measurements are known to be semi-quantitative, i.e. highly sequence dependent.

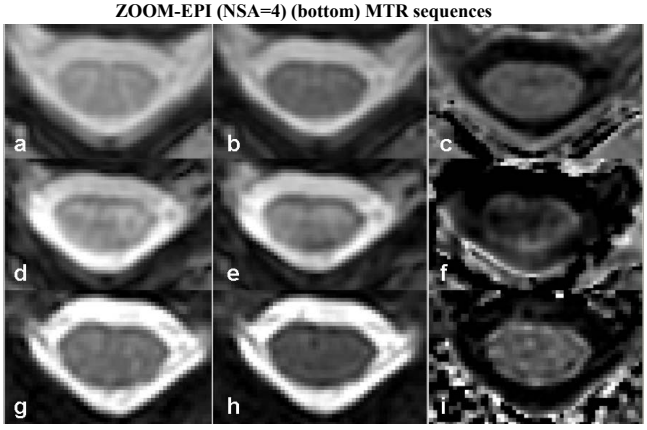
SC MTR inter-subject CoVs were found to be lower for the ZOOM sequence compared to the spoiled gradient echo or multi-shot EPI sequences (see table 1). The intra-subject CoV (from 3 repeated scans on a single subject) was 9.2% for the spoiled gradient echo sequence, 13.0% for the multi-shot gradient echo EPI sequence, and 7.9%, 3.5% or 2.7% for the ZOOM-EPI sequence with NSA=2, 3 or 4 respectively.

Table 1: Mean MTR values for each sequence

MTR sequence	MTR (± SD)	CoV (%)
Spoiled gradient echo	30.5 (± 2.0)	6.64
Multi-shot spoiled gradient echo EPI	25.6 (± 4.1)	16.2
ZOOM-EPI NSA=2	34.5 (± 0.58)	1.67
ZOOM-EPI NSA=3	34.3 (± 0.75)	2.19
ZOOM-EPI NSA=4	34.4 (± 0.81)	2.35

DISCUSSION & CONCLUSIONS: The overall image quality of the ZOOM MTR sequence is superior to multi-shot EPI. In fact, ZOOM-EPI is a single shot technique, therefore it is more robust to cord motion. It is also very rapid; with 4 signal averages it is still much shorter than the 'gold standard' spoiled gradient echo technique. However, the ZOOM-EPI sequence is 2D, whereas the other 2 sequences investigated here are 3D sequences, hence they have higher intrinsic signal-to-noise ratio (SNR). Also, there is little contrast between GM and WM in the cord using the ZOOM-EPI sequence, which is likely to depend on both the MT weighting and T_2 weighting, due to the much longer TE of ZOOM-EPI compared to the other two protocols. Whole cord ZOOM-EPI MTR values were very reproducible both within and between subjects (see table 1), making ZOOM-EPI an attractive possibility for MT imaging of the SC.

Figure 1: Example MT off (a,d, g), on (b, e, h) & MTR (c, f, i) images for the spoiled gradient echo (top), multi-shot gradient echo EPI (middle) and ZOOM-EPI (NSA=4) (bottom) MTR sequences



Future development of the ZOOM MTR sequence might include the use of cardiac gating to reduce pulsatile flow artefacts from the surrounding CSF, however this would increase the scan time. The ZOOM technique could also potentially be extended to 3D (8, 9), to increase the SNR of the acquired images, necessary for extending the protocol to quantitative MT (qMT) imaging. The use of partial Fourier imaging and SENSE parallel imaging with ZOOM-EPI could be further optimised, e.g. to achieve shorter TEs, in order to improve image SNR and contrast. The MT pulse could also be optimised (in terms of amplitude, offset frequency, duration etc), which may increase GM/WM contrast and thus enable us to make tissue specific measurements in cord WM and GM.

In summary, the ZOOM MTR technique in the SC provides contiguous-slice, reduced-FOV images that do not suffer from aliasing and have reduced magnetic susceptibility artefacts with good inter- (<3%) and intra-subject reproducibility (<8%).

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