SWIFT Imaging of Myelin Loss in Traumatic Brain Injury in Rats

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INTRODUCTION Multiple diseases involve myelin loss in the white matter, including traumatic brain injury (TBI) [1] and multiple sclerosis. Myelin loss has been studied using e.g. magnetization transfer (MT) [2] and diffusion MRI [3]. Myelin and myelin loss have been ascribed to short T2 (sT2) components for which conventional pulse sequences offer limited sensitivity due to their relatively long echo time. SWIFT (sweep imaging with Fourier transformation) is a sequence with close to zero acquisition delay, because excitation and acquisition are interleaved using gapped frequency-modulated pulses [4]. In this study, we applied SWIFT to a TBI animal model using normal, long T2, and sT2 SWIFT contrasts. Interestingly, even though SWIFT has no TE, SWIFT has recently been shown to detect calcifications through its phase component [5]. Hence, also the phase contrasts of the white matter structures were investigated.

MATERIALS AND METHODS Sprague-Dawley rats (n=10) were subjected to lateral fluid percussion brain injury and control animals (n=5) were sham operated. The animals were sacrificed five months TBI and imaged *ex vivo* using SWIFT. Imaging was conducted at 9.4 T vertical magnet with Agilent DirectDrive console using a 19 mm quadrature volume coil. The SWIFT parameters were TR = 8.2 ms, sw = 31.125 kHz, α = 6°, FOV = 3.7^3 cm^3, a matrix size of 256^3, 128000 spokes and four averages. SWIFT images were taken with a sT2 suppression magnetization preparation using two consecutive 20 ms hyperbolic secant (n = 4, R = 20) pulses every 16 acquisitions at ±1.5 kHz off-resonance. To preserve equal effective TR, the preparation was replaced with a 40 ms delay in the normal SWIFT scans. After imaging, the brains were sectioned coronally and stained for myelin.

A region of interest (ROI) analysis was conducted for white matter structures in normal magnitude, sT2 suppressed magnitude (long T2) and subtraction of the aforementioned (sT2) images and the corresponding phase images. The phase of the sT2 component was calculated as the angle of the complex subtraction of normal and sT2 suppressed images. The white matter changes were quantified as the contrast of the contralateral structure to the ipsilateral structure in magnitude $\Delta mag = [mag(C)-mag(I)]/mag(I)*100\%$ and as a phase difference between contra- and ipsilateral structures $\Delta\varphi = \varphi(C)-\varphi(I)$. Statistical difference between control and TBI groups was tested with Mann-Whitney U-test ($p<0.05$).

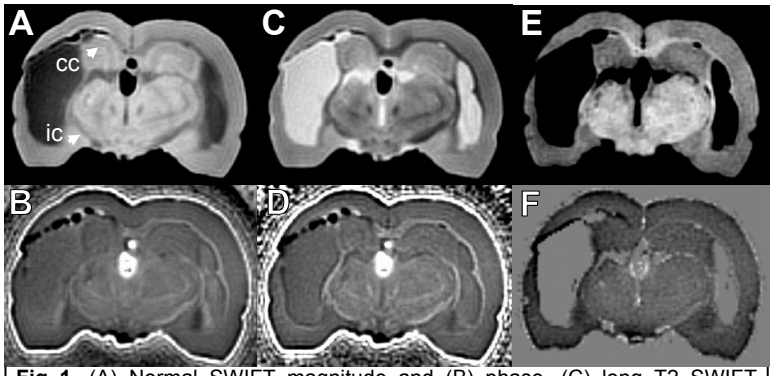

Fig 1. (A) Normal SWIFT magnitude and (B) phase, (C) long T2 SWIFT magnitude and (D) phase, (E) short T2 (subtraction of (A) and (C)) magnitude and (F) phase. Phase images are in scale. Arrows indicate the corpus callosum (cc) and internal capsule (ic) in (A).

RESULTS Statistically significant contrast changes after TBI were observed using all the magnitude and phase contrasts. Figure 1 shows a representative case of a brain after TBI using the (A,C,E) magnitude and (B,D,F) phase contrasts. The sT2 phase image (f) is shown as an average of three slices and has been masked. Internal capsule (ic) has a visible signal change in all the images. Effect of brain microbleeds can be seen in the ipsilateral corpus callosum (cc) and external capsule. Largest statistically significant changes are shown in Table 1. Also other areas exhibited statistically significant differences. Ipsilateral myelin loss due to TBI was confirmed by histology (Figure 2)

Table 1. Contra-ipsi contrast results. ROI mean over animals ± sd (*p<0.05)

	TBI	Control	TBI	Control	TBI	Control
Structure	**Normal, Δmag (%)**		**Long T2, Δmag (%)**		**sT2, Δmag (%)**	
cc	-1.1 ± 1.4*	-0.4 ± 1.1*	-4.3 ± 3.0*	-0.8 ± 1.5*	-3.4 ± 2.0*	0.0 ± 1.0*
ic	-3.8 ± 2.1*	-0.7 ± 1.4*	-9.4 ± 3.5*	-1.3 ± 1.6*	-3.8 ± 4.0	0.0 ± 1.4
Structure	**Normal, Δφ (10^{-2} rad)**		**Long T2, Δφ (10^{-2} rad)**		**sT2, Δφ (10^{-2} rad)**	
cc	1.5 ± 0.8*	0.6 ± 0.2*	1.1 ± 1.0*	0.1 ± 0.4*	2.0 ± 0.7*	1.0 ± 0.3*
str	1.7 ± 0.5*	0.9 ± 0.2*	1.5 ± 1.0	0.5 ± 0.2	1.9 ± 0.7*	0.8 ± 0.1*

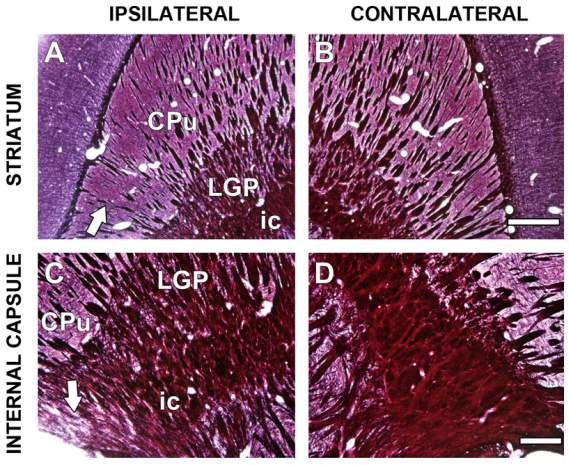

Fig 2. Myelin stained sections of ipsi- and contralateral (A,B) striatum and (C,D) internal capsule. Arrows point to dysmyelinated axonal fibres. Scale bar 1 mm for (A,B), 250 µm for (C,D). CPu = caudate putamen, LGP = lateral globus pallidus, ic = internal capsule.

DISCUSSION AND CONCLUSION Myelin loss was detected by SWIFT in multiple white matter structures including the sT2 phase contrast. TBI group had a relatively larger variation in contrast, indicating variability in the trauma. Internal capsule showed a large change in magnitude but not in phase, whereas striatum showed a difference only in phase. This may be related to the smaller fraction of myelin in striatum and the fact that phase contrast of SWIFT is likely to be stronger for smaller structures [6]: myelin loss has a smaller effect on overall striatum signal, but on the other hand individual white matter structures are smaller than in the internal capsule. The sT2 signal may be related to myelin water [7] in close interaction with myelin macromolecules and possibly to lipid methylene groups in myelin itself [8].

Results in corpus callosum may be affected by the microbleeds, although they were avoided while drawing the ROIs. Although the used sT2 suppression scheme is likely to be imperfect and produce MT, SWIFT will also have additional information from sT2 components. Hence, SWIFT may prove to be valuable tool in assessing myelin loss both through magnitude and phase.

REFERENCES [1] Bramlet et al. Acta Neuropathol 2002. [2] Henkelman et al NMR Biomed 2001. [3] Horsefield et al. NMR Biomed 2002. [4] Idiyatullin et al. JMR 2006. [5] Lehto et al. Submitted & ISMRM11. [6] Carl et al. MRM 2011. [7] Bjarnson et al. MRM 2005. [8] Horch et al. MRM 2011.

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