Maximizing Tissue Contrast in MRI Using RAFFn Preparation with SWIFT and Spin Echo Readouts

Timo Liimatainen[1], Djaudat Idiyatullin[2], Jinjin Zhang[2], Hanne Hakkarainen[1], Silvia Mangia[2], Michael Garwood[2], and Shalom Michaeli[2]

[1]*A.I.Virtanen Institute, University of Eastern Finland, Kuopio, FI, Finland,* [2]*Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, United States*

Introduction: Relaxation experiments in high rotating frames of ranks n > 2 uniquely offer the possibility to probe the slow motional regime. This is important for *in vivo* applications since slow molecular motions are altered in pathologic tissue changes, for instance focal or gradual demyelination processes or iron accumulation. A recently developed relaxation methodology called RAFFn (Relaxation Along a Fictitious Field in n^{th} rotating frame) has high expectation to be a useful tool for MRI because it provides sensitivity to slow motions and can be performed with low specific absorption rate (SAR) [1,2]. However, slow motions are characterized by short transverse relaxation time (T_2), and thus, the sensitivity to detect changes due to slow motions depends heavily on the choice of pulse sequence used for image readout. The goal of the current work is to probe fast relaxing tissue components which are typically filtered out during the echo time (TE) used in conventional gradient and spin echo (SE) sequences. We investigate tissue contrast by comparing single pulse and SE spectral readouts for *ex vivo* white matter (WM) and grey matter (GM) samples, and secondly whole *ex vivo* brain using magnetization-prepared SWIFT (MP-SWIFT) technique [3] with RAFFn preparation pulses (RAFFn-SWIFT). We demonstrate here that the contrast between GM and WM can be increased by shortening the TE of the SE readout. We also show that magnetization transfer (MT) and RAFFn provide different contrasts in the brain tissue.

Materials and Methods: Spectra and images were acquired at 9.4T using an Agilent small animal scanner. RAFFn weightings were performed utilizing RAFFn having amplitude and frequency modulations ($\omega_1(t)$ and $\Delta\omega(t)$, respectively) , as described before [2]. The unlocalized spectra were acquired in white and grey matter samples separately with five different RAFFn pulse train durations (0-144 ms, multiples of $PP^{-1}P_\pi P_\pi^{-1}$ rotary echo packets [3]) using 6 µs 90° pulse or spin echo (TE = 8 ms) readout. The SWIFT images were acquired with weighting pulse train durations of 18 ms and 72 ms on *ex-vivo* mouse brains. The MT and RAFFn preparation pulses were inserted every 16^{th} TR period, as describe in [3] or with delays of the same duration (Delay-SWIFT) to alter the steady state generated by SWIFT. Acquisition parameters were: flip angle 6°, BW=62 kHz. The corresponding MT images with same preparation durations and SWIFT images with no preparation modules but having same delays were performed. The brains were perfused with 4% paraformaldehyde and washed out with saline prior to the imaging.

Results and Discussion:

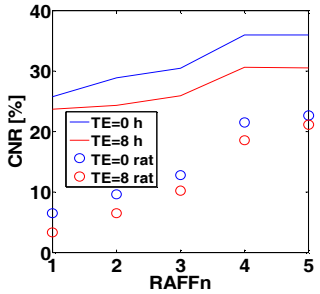

Figure 1 Relative relaxation time difference RRTD=T_{RAFFn}(GM)-T_{RAFFn}(WM))/T_{RAFFn}(GM)x100% in human (h) and rat (r) samples with 6 µs excitation pulse (TE=0ms) and spin echo (TE=8ms).

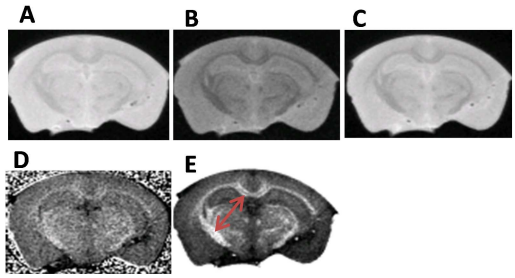

Figure 2 Delay-SWIFT image with delay of 18 ms (A); RAFF4-SWIFT weighted image, pulse train duration of 18 ms (B); MT-SWIFT magnetization transfer weighted image with 18 ms MT pulse (C); Division A/C (D); Division D/B (E).

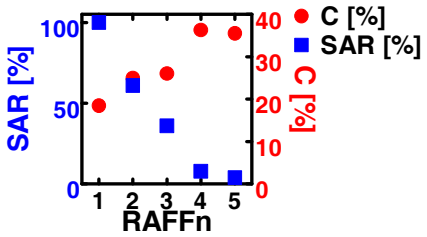

Figure 3 WM/GM contrast (C, %) obtained with RAFFn-SWIFT using 18 ms pulse train, and relative SAR of RAFFn pulses.

Significant increase of the relative relaxation time difference (RRTD) between GM and WM was observed when the TE was decreased from 8 ms to almost no echo time (the duration of the excitation pulse was 6 µs). This demonstrates strong attenuation of the contrast due to T_2 weighting of the fast SE readout (**Figure 1**). The result indicates that the spin pool which is filtered out during 8 ms contributes to the relaxation time constants measured with RAFFn. In agreement with our findings obtained with TE≈0 readout, the imaging using RAFFn-SWIFT (no echo time technique) showed increased contrast (C %) when rank (n) was increased (**Figures 2 and 3**). In all images, the tissue contrast was sufficient to delineate areas of high myelin content (arrows in **Figure 2** panel E) which were best visualized by dividing (delay-SWIFT/MT-SWIFT) by RAFF4-SWIFT images (i.e., D/B in Fig. 2). The SAR of RAFFn preparation decreases while contrast increases when rank n in RAFFn-SWIFT was increased (**Figure 3**). The contrast was also increased when the duration of RAFFn pulse trains was increased. It is also visualized, that RAFF4-SWIFT provides greater contrast between GM and WM ((C(RAFF4-SWIFT)≈35% , C(MT-SWIFT)≈16%) than the MT-SWIFT, suggesting its utility for the investigation of variety of the pathologies related to demyelination. Noticeably, the ratios of equilibrium values obtained by division of delay-SWIFT to MT-SWIFT images provide a strategy to avoid T_1 and spin density effects (Fig 2 D), while the division of (SWIFT/MT-SWIFT) to RAFF4-SWIFT images allow to attenuate the MT contribution (Fig 2, E). In WM, the anisotropy of water motion and its motional restriction are likely the main origins of the high contrast observed with RAFF4 (and 5, data not shown), which further demonstrates sensitivity of rotating frame experiments with high ranks 4 and 5 to slow/restricted molecular motion.

Conclusion: The property of high rotating frame technique RAFFn to probe slow motion provides possibility to image myelin content directly.

Acknowledgments: Academy of Finland, Sigrid Juselius Foundation, NIH Grants BTRC P41 EB015894, P30 NS057091, R01 NS061866.

References: [1] T. Liimatainen et al. MRM 2010 [2] T. Liimatainen et al. ISMRM 2012, [3] J. Zhang et al, ISMRM 2013.