Generating MRI Contrasts in Rotating Frames of Rank 1 ≤ n ≤ 5 in the Human Brain at 4 T and Mouse Brain at 7 T

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Introduction Limited effort had been devoted to the investigation of molecular motion in the high rank rotating frames (of rank n > 2), although 3rd frame relaxation measurements in solids allow to assess ultra-slow motion and to reduce the magic angle from 54.5 to 39 degrees [1]. Recently, we have shown that the fictitious field which is generated in the 2nd rotating frame by sweeping of the effective field under non-adiabatic conditions allows generating relaxation dispersion in living tissue [2-4]. The method, entitled RAFF (Relaxation Along a Fictitious Field), provided correlation between relaxation time constant T_{RAFF} and histologically derived cell density in rat glioma gene therapy model [3]. Here, we demonstrate the advantage of high rotating frame relaxation contrasts of rank n > 2, and introduce the method RAFFn. By utilizing fictitious fields, novel MRI contrasts in the human and mouse brains had been generated. The method allows for low specific absorption rates and less sensitive to B_0 inhomogeneities (broader bandwidth) as compared to RAFF. RAFFn can probe slow motion and generate novel rotating frame relaxation contrast at high magnetic fields.

Materials and Methods The amplitude and frequency modulations ($\omega_1(t)$ and $\Delta\omega(t)$, respectively) to generate constant magnetic field in the 1st rotating frame are $\omega_1(t)=\Delta\omega(t)=\omega_1^{max}$. The recursions defined as $\omega_1^n(t)=\Delta\omega^{n-1}(t)\sin\left(\int\omega_1^{n-1}(t)dt\right)$ and $\Delta\omega_1^n(t)=\Delta\omega^{n-1}(t)\cos\left(\int\omega_1^{n-1}(t)dt\right)$ for n = 2, 4, 6,… and $\omega_1^n(t)=\omega_1^{n-1}(t)\sin\left(\int\Delta\omega^{n-1}dt\right)$, and $\Delta\omega_1^n(t)=\omega_1^{n-1}(t)\cos\left(\int\Delta\omega^{n-1}dt\right)$ for n = 3, 5, 7, … were used to generate RAFFn pulse wave forms for experiments which lead to the rotating frames of ranks from 2 to 5. With these definitions, the amplitude of effective field is $\sqrt{2}\omega_1^{max}$ for all pulses. In all measurements $\omega_1^{max}/(2\pi)$ = 625 Hz and pulse duration $T_p=4/(\sqrt{2}\omega_1^{max})$ were used [1]. The locking property of the pulses was confirmed by Bloch simulations of magnetization under RAFF irradiation without relaxation. The signal intensity decay was measured by increasing the number of $PP^{-1}P_\pi P_\pi^{-1}$ packets as described in [1]. Five human subjects were scanned at 4 T using an Agilent DirectDrive Image console using fast spin echo readout (TR=5, effective TE=74 ms s, ETL=16, Field-of-View 256 x 256 mm^2 and slice thickness 4 mm) with RAFF weighting between 0 and 144 ms. Male c57bl mice (weight 24.4±3.4 g, n=4) were imaged at 7 T Bruker Pharmascan using volume transmitter and mouse quadrature surface receiver. FISP readout after RAFF preparation was used with TR/TE = 6/1.6 ms and 2.5 s between RAFF pulses. RAFF relaxation time constants maps were calculated on pixel-by-pixel basis taking into account formation of the steady state [1]. ROIs were hand drawn based on T_1 weighted in mouse and T_2 weighted in human measurements.

Results and Discussion

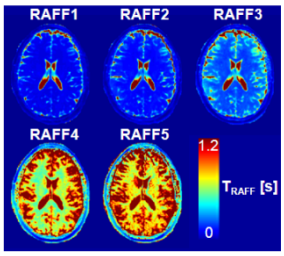

Fig. 1 Representative example of relaxation time constant maps from one volunteer measured in the rotating frames 1-5.

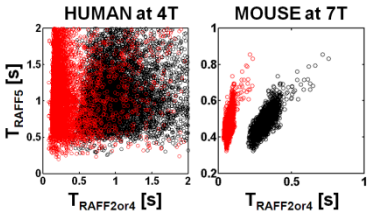

Fig. 2 Correlation plots between RAFF2 vs. RAFF5 (black) and RAFF4 vs. RAFF5 (red) in the human and mouse brains at 4 T and 7 T, respectively.

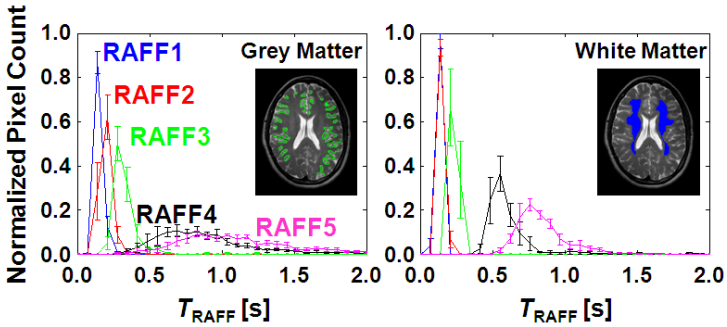

Fig. 3 Average (mean±std.) T_{RAFFn} histograms in human grey and white matter at 4 T. Note, RAFF1 line under RAFF2 line in white matter panel.

Tab. 1 Contrast between grey and white matter in human brain at 4 T (5 subjects). Contrast=(T_{RAFFn}(GM)-T_{RAFFn}(WM))/ T_{RAFFn}(GM)

RAFFn	Contrast (mean ± SEM)
RAFF1	18 ± 5 %
RAFF2	23 ± 7 %
RAFF3	29 ± 4 %
RAFF4	32 ± 3 %
RAFF5	25 ± 6 %

Bloch simulations demonstrate that magnetization tips with smaller tip angle in the laboratory frame when the rank of frame n increases. This leads to the lengthening of T_{RAFF}. SAR decreases from RAFF1 to RAFF5 by over 96 %. The relaxation maps obtained in the human brain with RAFFn (Fig. 1) demonstrate change of the MRI contrast when n increases from 1 to 5, as it is also suggested by the correlation analysis (Fig. 2). Indeed, the correlation between T_{RAFF2} and T_{RAFF5} is different from the correlation between T_{RAFF4} and T_{RAFF5} both in the human and mouse brains (Fig. 2). Also tissue specificity of RAFFn varies with the increase of n, i.e. the distribution of relaxation time constants were different in the grey matter only with RAFF1-3, however they were different with RAFF2-5 in the white matter (Fig. 3). The grey/white matter contrast increases at high rotating frames (Tab. 1), reaching the maximum with RAFF4. It is possible that magnetization transfer contributes to the RAFFn contrast in tissue, although its contribution requires further evaluation. Using simulations based on product operators we found that the sensitivity of RAFFn to anisochronous exchange ($\delta\omega\neq0$) is shifted to slower motional regime as compared to $T_{1\rho}$ and Carr-Purcell-Meiboom-Gill relaxation techniques (simulations not shown). The methods developed provide unique possibility for performing relatively artifact free rotating frame experiments with minimal SAR at high magnetic fields.

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