

# Magnetic Resonance Contrast Based on Relaxation Along a Fictitious Field (RAFF)

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**Introduction:** Relaxation in the presence of radio frequency (RF) irradiation (i.e., rotating frame longitudinal and transverse relaxations,  $T_{1p}$  and  $T_{2p}$ ) is governed mainly by spin dynamics with slow motional correlation times ( $\tau_c = 10^{-3}$ - $10^{-6}$  s) and therefore provides different information than  $T_1$  and  $T_2$ . A practical limitation of such rotating frame relaxation measurements is the relatively high RF power and specific absorption rate (SAR) required by conventional (continuous-wave) spin-lock, as well as by recent adiabatic methods [1,2]. The high RF power requirement of the latter approach is a consequence of the need to satisfy the adiabatic condition,  $|d\alpha/dt| \ll \omega_{eff}(t)$ , where  $\omega_{eff}$  is the rotating frame effective field (in units of angular velocity,  $\omega_{eff}(t) = [(\omega(t))^2 + (\Delta\alpha(t))^2]^{1/2}$ , with  $\omega = \gamma B_1$  and  $\Delta\alpha =$  offset frequency), and  $\alpha$  is the time-dependent angle between the vector  $\omega_{eff}(t)$  and the laboratory frame z-axis. In an effort to reduce RF power requirements, in this work we investigated the possibility of creating a time independent fictitious effective field ( $E$ ) for  $T_{1p}$  and  $T_{2p}$  measurement in a second rotating frame of reference [2]. This novel approach exploits frequency modulation in the sub-adiabatic condition, and therefore, is less restricted by RF power considerations. The method is expected to behave similarly to two separate RF fields in an orthogonal manner [3]. In the present case, the fictitious field is created by modulating  $\omega(t)$  and  $\Delta\alpha(t)$  by sine and cosine functions with equal amplitudes achieving  $|d\alpha/dt| = \omega_{eff} = \text{constant}$ . This new method is called relaxation along a fictitious field (RAFF).

**Materials and Methods:** The modulation functions of the RAFF pulse are  $\omega_1 = \omega_1^{max} \sin(\omega_1^{max} t)$  and  $\Delta\omega = \omega_1^{max} \cos(\omega_1^{max} t)$ , where  $\omega_1^{max}$  is the maximum amplitude of  $\omega_1(t)$ . In the second rotating frame of reference, the fictitious field is  $E = (\omega_{eff}^2 + (d\alpha/dt)^2)^{1/2} = \text{constant}$ , where  $\alpha(t) = \tan^{-1}(\omega(t)/\Delta\alpha(t))$ . To overcome problems of RF inhomogeneity, a composite version of the pulse was designed denoted as R (Fig. 1). Variation of the nutation angle about  $E$  due to resonance offsets was minimized by concatenating the pulse (R) with its time reversed counterpart ( $\bar{R}$ ) in the scheme  $R\bar{R}R\bar{R}$ . All experiments were conducted with a 4 T (human) or 4.7 T (phantoms) magnet (OMT, Inc., Oxon, UK) with Varian UnityINOVA consoles (Varian Inc., Palo Alto, CA). To investigate relaxation due to dipolar interactions, 100 mM acetate was dissolved into two glycerol/water (g/w) mixtures with weight ratios 0.9/0.1 and 0.5/0.5. The signal decay of the methyl protons resonating at 2 ppm was analyzed. The effects of exchange on water relaxation was investigated using a 0.5/0.5 water/ethanol mixture. The signal decays were measured using RAFF pulses with  $\omega_1^{max} / (2\pi) = 625$  Hz by increasing the number of  $R\bar{R}R\bar{R}$  segments (1-32) leading to pulse train lengths of 4.53-144.82 ms. Adiabatic  $T_{1p}$  and  $T_{2p}$  measurements were performed for comparison (0-32 pulses,  $T_p = 3.2$  ms,  $\omega_1^{max} / (2\pi) = 3.5$  kHz), as described in [4,5]. Localization by adiabatic selective refocusing (LASER) [3] was used for voxel selection. Brains of healthy volunteers (n=5) were scanned using a volume TEM RF coil. Signal intensity decay was measured with RAFF,  $T_{1p}$ , and  $T_{2p}$  weightings from slices in planes including striatum and substantial nigra separately using TurboFLASH imaging readout (TR/TE=10/5 ms), TR between segments= 5 s, number of segments = 4, NEX=4, NP=256, NV=256, FOV = 20 x 20 cm<sup>2</sup>, slice thickness = 3 mm). The RAFF weighting was applied similarly as in phantoms. For adiabatic  $T_{1p}$  and  $T_{2p}$  weighting, pulse length = 6 ms, number of pulses in trains = 0, 4, 8 and 16 and  $\omega_1^{max} / (2\pi) \approx 1300$  Hz) were used.

**Results and Discussion:** With the highly viscous solution ( $\eta = 200$  cp, 0.9/0.1 g/w), the relaxations were faster as compared to the glycerol/water solution with the lower viscosity (0.5/0.5 weight ratio,  $\eta = 4$  cp). This was expected for the nearly free tumbling molecules. The increase of the relaxation rate constant of the acetate in glycerol/water 0.9/0.1 (g/w) versus glycerol/water 0.5/0.5 (g/w) measured with RAFF was smaller than with the adiabatic  $T_{1p}$  and  $T_{2p}$  (Fig. 2a). In the fast exchanging system ethanol/water (0.5/0.5), RAFF relaxation rate was found to be in the same range as the rate obtained using adiabatic  $T_{2p}$  (Fig. 2b). These phantom experiments of the dipolar and exchanging systems suggest that the RAFF method appears to slow down dipolar relaxations as compared to  $1/T_{1p}$  and  $1/T_{2p}$ , and exhibits high sensitivity to exchange processes. Similar to adiabatic  $T_{1p}$  and  $T_{2p}$  relaxation mapping, the RAFF method provided artifact free relaxation maps (Fig. 3). The relaxation time constants obtained using RAFF of the red nuclei, putamen, globulus pallidus and caudate nuclei were between and significantly different (Students t-test  $p < 0.05$ ) compared to  $T_{1p}$  and  $T_{2p}$  (Table 1). The average RF power delivered into the brain tissue during  $T_{1p}$ ,  $T_{2p}$ , and RAFF was 1.86 W/kg, 2.30 W/kg, and 1.18 W/kg, respectively. The lower power requirement of RAFF as compared to adiabatic methods may enable use of RAFF contrast also in deep body structures where external RF power delivery is challenging for high field human applications, such as endometrial and prostate imaging. Because both  $T_{1p}$  and  $T_{2p}$  contribute to RAFF, the RAFF contrast is expected to provide more complete information on the relaxation pathways in diseased versus normal states.

**References:** [1] Michaeli et al., JMR 181 (2006) 135-147, [2] Michaeli et al., MRM 53 (2005) 823-829. [3] M. Garwood, and L. DelaBarre, J. Magn. Reson. 153 (2001) 155-177. [4] M. Tabuchi, and J. Hatanaka, J Magn Reson 148 (2001) 121-125.

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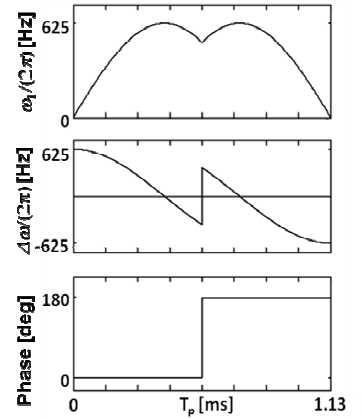


Fig. 1 Amplitude and frequency modulations of RAFF pulse (R)

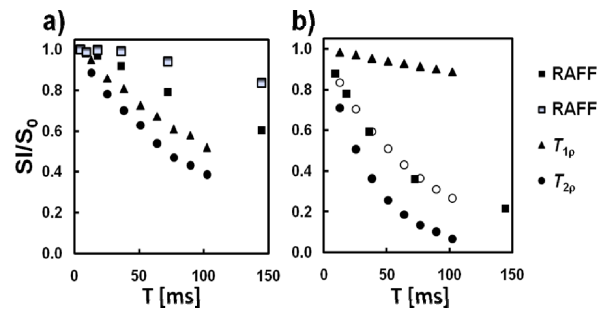


Fig. 2 a) Acetate signal decays of RAFF,  $T_{1p}$ , and  $T_{2p}$  in glycerol/water mixtures (open squares in 0.5/0.5 and all others in 0.9/0.1), b) water signal decay in water/ethanol 0.5/0.5 mixture. T refers the pulse train length in ms.

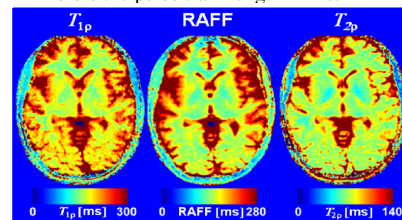


Fig. 3  $T_{1p}$ , RAFF and  $T_{2p}$  maps from one slice from the level of striatum of healthy human brain

Table 1 The average relaxation times measured using  $T_{1p}$ , RAFF and  $T_{2p}$  methods from healthy human subjects (n=5).

	$T_{1p}$	RAFF	$T_{2p}$
RD	169 ± 15	131 ± 9	71 ± 5
PU	193 ± 9	178 ± 12	70 ± 5
GP	214 ± 15	189 ± 15	81 ± 6
CN	160 ± 12	133 ± 12	60 ± 10

RN = red nuclei, PU = putamen, GP = globulus pallidus and CN = caudate nuclei.