Revisiting Two Exchangeable Proton Environments in Human Grey and White Matter Using Free and Restricted Exchangeable Proton (FREP) Imaging

Mitsue Miyazaki[1], Cheng Ouyang[1], Xiangzhi Zhou[1], James B. Murdoch[1], Tomohisa Okada[2], Koji Fujimoto[2], Aki Kido[2], Yasutaka Fushimi[2], and Kaori Togashi[2]
[1]*Toshiba Medical Research Institute, Vernon Hills, IL, United States,* [2]*Kyoto University, Kyoto, Japan*

Introduction: Magnetization transfer (MT) contrast, a mechanism that is used to indirectly detect macromolecular properties in MRI by observing the exchange of magnetization between “free" and "restricted" water protons in macromolecules, was originally introduced over 20 years ago (1). Wide range Z-spectra have been investigated using a super-Lorentzian lineshape with acquisition of a half the frequency range (2). In this work, we revisited exchange of protons between the relatively free and restricted proton pools in macromolecule and investigated the Z-spectra acquired over a broad and symmetric range of frequency offsets by fitting it to a two Lorentzian compartment model, without the need of detailed kinetics of the exchange process. The technique we propose – free and restricted exchangeable proton (FREP) imaging – allows us to map and extract important properties and information in both the free and restricted exchangeable proton pools, including the proton fractions (F_f, F_r) and effective spin-spin relaxation times ($T_{2,f}$, $T_{2,r}$).

Materials and Methods: FREP imaging was acquired on 9 healthy volunteers (7 males and 2 females; age range, 33-71 years old, and mean age, 47 years old)). MR experiments were performed on 3 T systems (Vantage Titan 3T[TM], Toshiba Medical Systems, Japan) using a standard body coil for transmission and a thirteen-channel head-array receive coil, following a protocol approved by the Institutional Review Boards of the institution. First, MT data was acquired over a wide symmetric frequency range, and then a quartet of quantitative biomarkers, i.e., proton fractions (F_f, F_r) and spin-spin relaxation times ($T_{2,f}$, $T_{2,r}$) in both free and restricted proton pools, were mapped by fitting the measured Z-spectra to a simple two-Lorentzian compartment model on a voxel-by-voxel basis. We applied MT saturation in 53 steps over an expanded range of off-resonance frequencies from -30 KHz to +30 KHz.

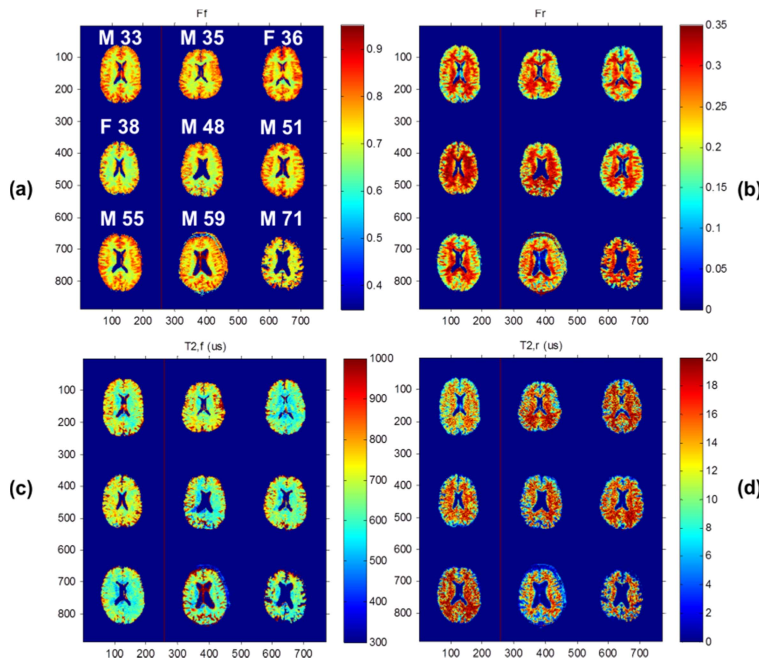

Fig. 1 Color maps of nine healthy volunteers: (a) Fraction map of the free exchangeable component, F_f, (b) Fraction of the restricted exchangeable component, F_r, (c) $T_{2,f}$ map, and (d) $T_{2,r}$ map. Note that the F_r maps are just reflections of the F_f maps since $F_r + F_f = 1$.

Table 1: Calculated fractions F_f, F_r and T_2 values $T_{2,f}$, and $T_{2,r}$ in GM and WM in 9 healthy subjects.

GM/Subject	Gender	Age	F_f	$T_{2,f}$ (μs)	F_r	$T_{2,r}$ (μs)
1	M	33	0.83	804	0.17	**11.7**
2	M	35	0.82	815	0.18	**18.4**
3	F	36	0.84	698	0.16	**23.5**
4	F	38	0.79	789	0.21	**13.5**
5	M	48	0.83	763	0.17	**14.1**
6	M	51	0.86	804	0.14	**19.1**
7	M	55	0.83	699	0.17	**21.5**
8	M	59	0.85	809	0.15	**15.0**
9	M	71	0.82	880	0.18	**22.3**
Mean		**47.3**	**0.83**	**785**	**0.17**	**17.7**

WM/Subject	Gender	Age	F_f	$T_{2,f}$ (μs)	F_r	$T_{2,r}$ (μs)
1	M	33	0.71	651	0.29	**17.6**
2	M	35	0.71	688	0.29	**22.0**
3	F	36	0.72	623	0.28	**28.3**
4	F	38	0.69	722	0.31	**19.5**
5	M	48	0.70	647	0.30	**24.4**
6	M	51	0.73	652	0.27	**26.7**
7	M	55	0.72	623	0.28	**27.2**
8	M	59	0.76	719	0.24	**20.8**
9	M	71	0.77	718	0.23	**24.5**
Mean		**47.3**	**0.72**	**671**	**0.28**	**23.4**

Results and Discussion: Figure 1 displays FREP maps from all nine volunteers of the free proton fraction F_f (Fig. 1a) and the restricted proton fraction F_r (Fig. 1b), as well as T_2 maps of the free (Fig. 1c) and restricted exchangeable components (Fig. 1d). The age and sex of the subjects are labeled on the maps. The corresponding numeric results and calculated average values are presented in Table 1. The measured mean free exchangeable proton fraction (F_f) was 0.83 in grey matter (GM) and 0.72 in white matter (WM), while the mean restricted exchangeable proton fraction (F_r) was 0.17 in GM and 0.28 in WM in healthy subjects. The estimated mean exchangeable spin-spin relaxation times were 785 μs ($T_{2,f}$) and 17.7 μs ($T_{2,r}$) in GM, 671 μs ($T_{2,f}$) and 23.4 μs ($T_{2,r}$) in WM.

Conclusion: FREP provides a simple approach estimating fractions and T_2 values of free and restricted exchangeable protons. **Reference**:
1) Wolff, S.D., Balaban, R.S. MRM. 10, 135-144, 1989. 2) Sled, J.G., Pike, G.B., 2001. MRM. 46, 923-931, 2001.