Pulsed Z-spectroscopic imaging for human MRI: theory and experimental technique

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Introduction

Z-spectroscopy is known as precise and reliable method for determination of cross-relaxation parameters in biological materials *in vitro* [1]. However this method in its classic design can not be applied in human MRI due to time and SAR restrictions inconsistent with continuous wave saturation. An idea of present work to develop quantitative Z-spectroscopic technique for human MRI which could utilize the conventional pulsed magnetization transfer (MT) imaging for data collection and relatively simple but realistic mathematical model for postprocessing. The last requirement can be fulfilled for spoiled gradient echo pulse sequence with off-resonance magnetization transfer (MT-GRE) considered under pulsed steady-state conditions.

Methods

Z-spectra of human brain (2 healthy volunteers, 3 multiple sclerosis (MS) and 2 tumor patients) were acquired with spoiled 3D MT-GRE pulse sequence (TR/TE/FA: 50 ms/9 ms/10°; MT pulse with Gaussian shape, duration 20 ms, B_1 = 4, 5 μT, offset (Δ) in range 2 - 32 kHz; matrix 128x96x8 (resolution 1.6x1.6x6 mm), NEX 4, acquisition time 2.5 min) on 0.5 T (Bruker) whole body scanner. The mean SAR produced by the sequence did not exceed 3 W/kg. The T_1-maps were obtained using variable flip angle method (same sequence without MT pulse, FA: 5, 10, 20, 30, 45°). Total experimental time was about 40-50 min. Images were processed using pixel-by-pixel nonlinear least-square fitting with theoretical model described below.

Results

Theory: Approximated equation for the magnetization transfer ratio (MTR) calculated from the images acquired with completely spoiled MT-GRE pulse sequence in pulsed steady state was derived:

$$MTR \approx \frac{sW^B}{(R_1-(1-f)\frac{\ln\cos\alpha}{TR})f^{-1}+(R_1+k-\frac{\ln\cos\alpha}{TR})k^{-1}sW^B} = \frac{sW^B}{P+QsW^B} \quad (1)$$

where $W^B = \omega_1^2 \pi g(\Delta, T_2^B)$; g is the absorption line shape of bound pool with transversal relaxation time T_2^B taken as superLorentzian [1]; R_1 is the observable longitudinal relaxation rate; k is the rate constant of cross-relaxation from free (F) to bound (B) pool; f is the relative population of bound spins, f = [B]/([F]+[B]); $\omega_1 = \gamma B_1$; s is the duty cycle; α is the flip angle. Eq. (1) was outlined under the following assumptions: (a) the direct irradiation of free pool by MT pulse and the saturation of bound pool by excitation pulse are negligible; (b) all time intervals of pulse sequence are short enough to apply 1st order approximation for the exponential matrices; (c) longitudinal relaxation rates of pools are close to each other: $R_1^F = R_1^B = R_1$; (d) $R_1^B << k/f$; and (e) $-\ln\cos\alpha << TR(k/f)$. It was shown by simulations that Eq. (1) gives a close approximation of the numerical solution of modified Bloch equations in wide range of parameters (deviation of MTR<2%). The parameters P, Q, and T_2^B can be obtained from fitting of normalized experimental Z-spectrum in MTR-form. Using the co-registered T_1 data it is possible to estimate f and k.

Experimental: Two alternative designs of experiment were applied:

A. Registration of sufficiently high number of MT images (18) at different offset and power values with subsequent computation of P, Q, and T_2^B - maps (Fig. 1).

B. Acquisition of Z-spectra at single power with minimal number of points (7-9) and co-registration of T_1 maps. The postprocessing included two-parametric fitting for parameters P and Q at fixed T_2^B = 8.5 μs followed by calculation of f and k -maps (Fig. 2).

The following values of f (%) and k (s^{-1}) were obtained for several normal and pathologic brain tissues: white matter - 11–15 %, 5.5–7.5 s^{-1}; gray matter - 6–8 %, 3.6–4.8 s^{-1}; MS lesions - 2.5–6.5 %, 1.8–4.5 s^{-1}; tumors (glioma and ependimoma) - 5 and 3 %, 1.5 and 2.5 s^{-1}; edema 4%, 3 s^{-1}. The values of T_2^B were found to be in range 8.0-9.5 μs and close for different tissues.

Discussion

Theoretical model (1) appeared to be in a close agreement with experimental data (Fig.1). Comparison of the methods A and B has ascertained that setting T_2^B constant causes only a little changes of parameters P and Q within error limits. Obtained values of cross-relaxation parameters are consistent with literature data based on steady-state Z-spectroscopy *in vitro* [1], however overestimation of the rate constants may be expected owing to the neglect of direct effect in theoretical model. The k and f images represent a pronounced contrast between tissues and high sensitivity to pathological changes (Fig.2). First examples of pulsed steady state Z-spectroscopic imaging in human MRI demonstrate the possibility to determine and visualize content of bound pool and cross-relaxation rate in tissues within acceptable time and SAR limits.

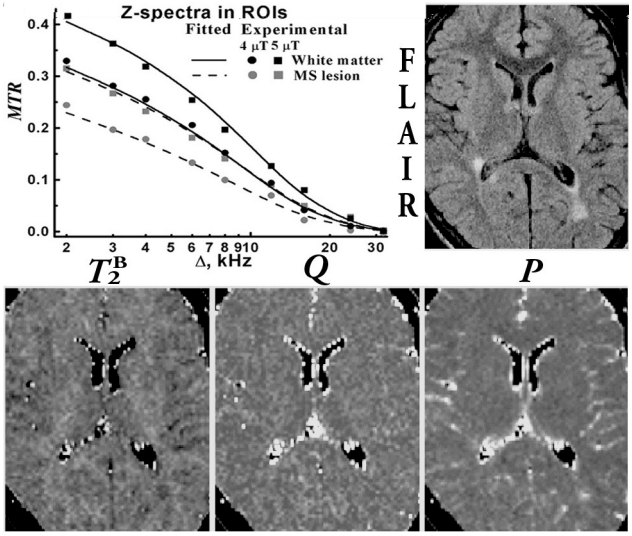

Fig.1. Z-spectra in ROIs and parametric maps for multiple sclerosis patient. FLAIR image as reference.

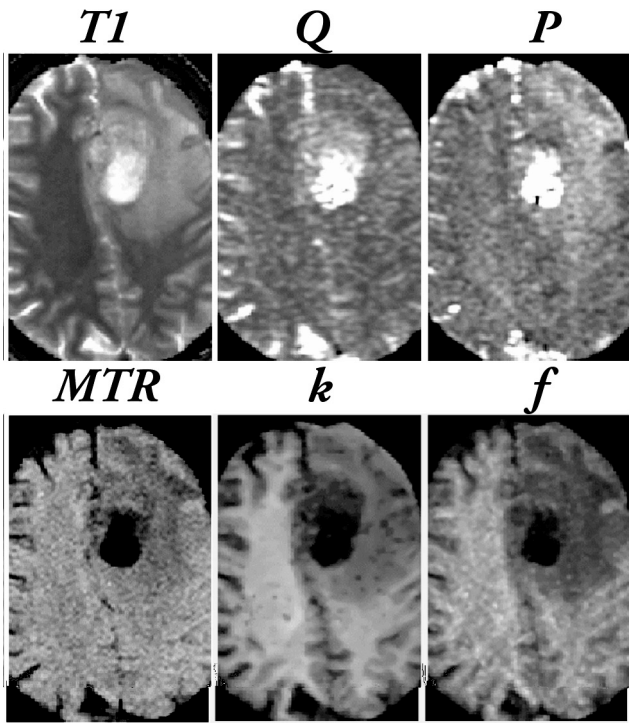

Fig.2. Z-spectroscopic parametric maps for glioma patient.

References

1. Morrison C., Henkelman R.M. Magn.Reson.Med. 1995 33:475-482.