ENHANCEMENT OF MT AND CEST CONTRAST VIA HEURISTIC FITTING OF Z-SPECTRA

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Introduction

Amide proton transfer (APT), a sub-type of chemical exchange saturation transfer (CEST), uses the chemical exchange between amide and bulk water protons in cells to create a new contrast in MR imaging [1-2]. Through off-resonant saturation at varying frequencies, parameters that depend on the transfer rate can be measured by evaluation of the z-spectra. The commonly analysis of the asymmetry around the water resonance requires B_0-correction [3] and neglects quantifiable characteristics of z-spectra. *In vivo*, methods of fitting based on physical models of MT depend strongly on starting values and require profound knowledge of the *in vivo* system which is inaccessible. Therefore, we propose an approximate model for the z-spectra which is justified by the Bloch equations. With this approach, fitting is independent of B_0 inhomogeneities and capable of distinguishing different characteristic parameters heuristically. Thus, it can be applied to gain insight into both, CEST and macromolecular magnetization transfer (MT).

Theory

The 3-pool-Bloch-McConnell equations with transfer terms permit different approximate solutions for z-spectra [4]. The solution of the Bloch equations is a Lorentzian lineshape with height $2M_0*T_2$, width $1/T_2$ and position ω_0, so we assume that the first-order transfer process can be described by a superposition of multiple Lorentzian lines $L_i(\omega)$ where a_i is the integral, Γ_i the full width at half maximum and ω_i the position of the maximum of the function. We assume that the z-spectra are depicted by

$$L_i(\omega) = \frac{a_i}{\pi}\frac{\frac{1}{2}\Gamma_i}{\left(\frac{1}{2}\Gamma_i\right)^2 + (\omega - \omega_i)^2}$$

$$S(\omega) = 1 - \sum_{i=1}^{3} L_i(\omega)$$

where the indices correspond to bulk water (1), a MT pool (2), and a CEST pool (3). These functions can be fitted to measured z-spectra and then interpreted by MT or CEST models. The integral of the CEST Lorentzian (a_3) is a measure for the magnetization transfer ratio $MTR = 1 - S_0/S_{sat}$ at a variable frequency offset from bulk water. It can be compared to the asymmetry analysis $MTR_{asym} = MTR(+\omega_3) - MTR(-\omega_3)$ which is restricted to a defined offset (3.5 ppm for APT) [2].

Materials & Methods

A study on 50 mM creatine (amide protons at 1.9 ppm) dissolved in phosphate buffered saline at different pH values was performed on a clinical tomograph (Magnetom Trio; Siemens Healthcare, Erlangen, Germany) with B_0 = 3 T using a standard 32 channel head coil. Additionally, patients with high-grade astrocytoma (> WHO III) were examined after written informed consent. Signal was acquired with a 3D RF-spoiled gradient echo (GRE) sequence with Gaussian-shaped saturation pulses (mean B_1: 1.6 µT, duration: 99 ms) before each acquisition of the 13-19 points of the z-spectra. Spoiler gradients in all 3 directions were applied after each saturation pulse. For data analysis own code in Matlab 7 (The Mathworks, Natick, MA, USA) was used and fitting was done pixel-wise with a Levenberg-Marquardt optimizer in C. The *in vivo* contrast to noise ratio CNR was estimated through comparison of signal in healthy and pathological regions.

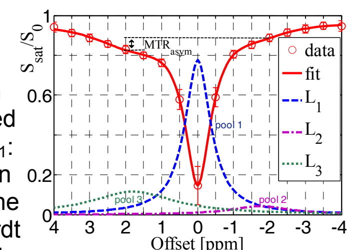

Figure 1: fitted z-spectrum of creatine phantom at pH =7.2

Results & Discussion

Spectra simulated according to Ref. [4] were fitted. The resulting R^2 (parameter of determination) of at least 0.98 indicates that analysis of z-spectra using the heuristic model is reasonable. Correlations between the fit parameters and the simulation parameters enable qualitative interpretation of the dependence of a_i, Γ_i and ω_i on B_1, T_{1i}, T_{2i}, M_{0i} and k_i. For example, $1/\Gamma_1$ gives an estimation for T_2 of water, a_3 for concentration and transfer rate of the CEST pool. Figure 1 shows a Lorentzian fit of the z-spectrum obtained by averaging over a ROI in the creatine model solutions at pH 7.2 yielding at 1.9 ppm MTR_{asym} = (0.063±0.03) and a_3 = (0.11±0.02). Figures 2 and 3 show MTR_{asym} at 3.5 ppm and a a_3 map, respectively, obtained from data of an examination of a patient with brain tumour after surgery. In both images, tumour recurrence can be observed close to the tumour centre. The CNR of the a_3 image (Fig. 3, CNR = 4.8) is more than 3 times larger than that of the MTR_{asym} image (Fig. 2, CNR = 1.4) suggesting an advantage of the fitting method compared to standard asymmetry analysis. Tumour delineation as obtained by CEST images corresponds well to Gd-enhanced T_1-weighted MR images.

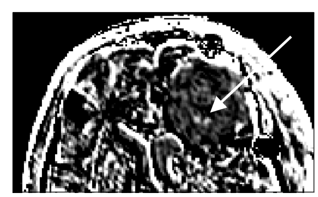

Figure 2: MTR_{asym} map

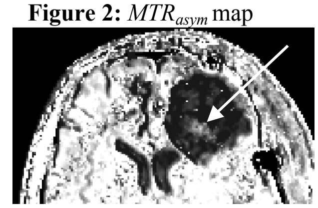

Figure 3: a_2 map

Conclusion

The parameter maps of Lorentzian line shape functions offer a more sophisticated approach to z-spectrum analysis, which is fast and less dependent on start values in comparison to a physical model fit. Although the physical meaning cannot be extracted directly, fine differences between healthy and tumor tissue can be appreciated.

References

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