CEST Peak Extraction method for multi peak fitting

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Target Audience: Radiologists, scientists and engineers who have an interest in CEST imaging

Purpose: MTR asymmetry (MTR_{asym}) is often used as a CEST parameter. However, high B_1 preparation RF saturates Z-spectrum because of binding water MT effect and MTR_{asym} becomes relatively small. In this study, stable multi peak Lorentzian Fitting was tried by transforming Z-spectrum.

Methods: *<u>CEST Peak Extraction</u>:* Phase Cycle type preparation pulse[1] was used in this study. Approximation solution of Z-spectrum in two pool model (A: free water pool, B: CEST pool) is given in Eq.1.1[1,2,3] and Eq.1.2,

$$\frac{1}{Z} \approx \frac{R_{1\rho}}{{R_1}^a \cos\theta} \approx \cos\theta + \frac{\sin^2\theta}{\cos\theta}\frac{{R_2}^a}{{R_1}^a} + \frac{\sin^2\theta}{{\omega_1}^2}\frac{a_1}{a_2+c_1(1-\cos(\Delta\varphi-\Delta\varphi_c))}, \text{ Eq.1.1}$$

$$\begin{pmatrix} T_{iter} = 0.560[ms] = 1/(4\gamma B_0 \times 3.5[ppm]), \\ c_1 = 2/{T_{iter}}^2, \omega_1[radian/sec] = 2\pi\gamma B_1, \\ \Delta\varphi[rad] = T_{iter} \times 2\pi\gamma B_0 \times \text{offset freq}[ppm] \\ \quad = \pi \times \text{offset freq}[ppm]/7[ppm], \\ \Delta\varphi_c[rad] = T_{iter} \times \Delta\omega_c[rad/sec], \\ \Delta\omega_c = 2\pi\gamma B_0 \times \text{CEST offset freq}, \\ a_1 = \frac{{M_0}^b\, k\, {\Delta\omega_c}^2 {\omega_1}^2}{{M_0}^a {R_1}^a}, a_2 = k^2 + {\omega_1}^2, \\ \cos^2\theta = \frac{c_1(1-\cos\Delta\varphi)}{c_1(1-\cos\Delta\varphi)+{\omega_1}^2}, \sin^2\theta = \frac{{\omega_1}^2}{c_1(1-\cos\Delta\varphi)+{\omega_1}^2}, \\ \text{Eq.1.2} \end{pmatrix}$$

where ${R_1}^a/{R_2}^a$ is T_1/T_2 relaxation rate of pool A, k is chemical exchange rate from pool B to A, ω_1 is mean B1of RF pulse, $\Delta\varphi$ is RF phase, ${M_0}^{a/b}$ is M_0 of pool A/B, respectively. By the approximation in Eq.1.3 and the function in Eq.1.4, Eq.1.1 can be transformed to Eq.1.5 as follows,

$$\cos\theta \approx 1, {\omega_1}^2/\sin^2\theta \approx c_1(1-\cos\Delta\varphi) = F(\Delta\varphi), (c_1(1-\cos\Delta\varphi) \gg \omega_1), \text{ Eq.1.3}$$

$$F_{CPE}(\Delta\varphi) = \left(\frac{1}{z}-1\right)F(\Delta\varphi), \text{ Eq.1.4} \quad F_{CPE}(\Delta\varphi) \approx \frac{{R_2}^a{\omega_1}^2}{{R_1}^a} + \frac{a_1}{a_2+F(\Delta\varphi-\Delta\varphi_c)}. \text{ Eq.1.5}$$

In Eq.1.5, the first term is a relaxation of pool A. The second term extracts the CEST effect as a peak, which is equivalent to a Lorentzian function. F_{CPE} is named CEST Peak Extraction (CPE) spectrum in this study.

<u>Binding water MT effect:</u> The influence of binding water MT (pool MT) is neglected in Eq.1.1. The exchange between pool A and pool MT can be described in Eq.2.1 by assuming that MT effect is independent to $\Delta\varphi$.

$$Z_{MT} = \frac{{M_0}^{MT}}{{M_0}^a} = constant - Lorentzian = b_0 - \frac{b_1}{b_2+F(\Delta\varphi-\Delta\varphi_0)}, (\Delta\varphi_0 = T_{iter} \times 2\pi\gamma\Delta B_0), \text{ Eq.2.1}$$

where ΔB_0 [Tesla] is B_0 inhomogeneity. Eq.2.1 is transformed like CPE spectrum as follows,

$$\left(\frac{1}{Z_{MT}}-1\right)F(\Delta\varphi-\Delta\varphi_0) = \frac{b_1}{{b_0}^2} + \left(\frac{1}{b_0}-1\right)F(\Delta\varphi-\Delta\varphi_0) - \left(\frac{b_1}{{b_0}^2}\right)\frac{(b_2-b_1/b_0)}{(b_2-b_1/b_0)+F(\Delta\varphi-\Delta\varphi_0)}. \text{ Eq.2.2}$$

The first term is common with Eq.1.5. However, the second term is only in Eq.2.2 and this is an MT term. The third term and $\Delta\varphi_0$ can be neglected in the condition of $\Delta\varphi \gg \Delta\varphi_0$.

<u>Multi peak Fitting:</u> In Eq.1.5, CEST term has a single Lorentzian peak. In multi peak case, each peak can be separated if the difference of $\Delta\varphi_c$ is large. By assuming a linear combination between each CEST terms and MT term, CPE spectrum can be written in Eq.3.1 and 3.2.

$$F_{CPE}(\Delta\varphi) = (1/z-1)F(\Delta\varphi) \approx c_0 + c_{MT}F(\Delta\varphi) + \textstyle\sum_n F_{L,n}(\Delta\varphi), \text{ Eq.3.1}$$

$$c_0 = \frac{b_1}{{b_0}^2} \approx \frac{{R_2}^a{\omega_1}^2}{{R_1}^a}, c_{MT} = \frac{1}{b_0} - 1, F_{L,n}(\Delta\varphi) = \frac{a_{1,n}}{a_{2,n}+F(\Delta\varphi-\Delta\varphi_{c,n})}, \text{ Eq.3.2}$$

where n is the number of CEST peaks. A CEST peak can be extracted by fitting CPE spectrum with Lorentz function F_L. However, there are at least "2+3n" unknown coefficients and non-linear least mean square fitting is unstable.

<u>Iterative fitting:</u> By removing Lorentzian peaks in Eq.3.1, CEST Peak Removed Z-spectrum (Z_{CPR}) is defined;

$$\frac{1}{Z_{CPR}} = \frac{1}{Z} - \frac{\sum_n F_{L,n}(\Delta\varphi)}{F(\Delta\varphi)+\delta(\Delta\varphi)}, \delta(\Delta\varphi) = \frac{0.25}{0.25+F(\Delta\varphi)} \text{ Eq.4.1} \qquad Z_{CPR} \approx Z_{MT} = b_0 - \frac{b_1}{b_2+F(\Delta\varphi-\Delta\varphi_0)}, \text{ Eq.4.2}$$

where $\delta(\Delta\varphi)$ is an even function to avoid division by zero. Because Z_{CPR} has pool A and MT only, Z_{CPR} is approximately equal to Z_{MT} in Eq.2.1. Eq.4.2 has only 4 unknown coefficients, which is more stable than Eq.3.1 fitting. By fitting CEST coefficients (a_1, a_2 and $\Delta\varphi_c$) with Eq.3.1 and baseline coefficients (c_0, c_{MT} and $\Delta\varphi_0$) with Eq.4.2 iteratively (see Fig.1), CEST peaks and ΔB_0 can be calculated separately and fitting becomes stable.

<u>Phantom study:</u> Raw egg white was scanned on 3T scanner (MR750w, GE Healthcare). EPI was used for data acquisition. Phase cycle[1] $\Delta\varphi$ was between $\pm\pi$ in 56 phases ($\pm$7 ppm with 0.25ppm steps). Mean B_1 of preparation RF was changed from 0.25 to 2 μT in 0.25 μT steps. Total RF irradiation time to achieve steady state was 3.5sec. Levenberg-Marquardt algorism was used for non-linear Lorentzian fitting. Iteration loop stopped if the fitting error and its difference from the former iteration was less than thresholds and the number of fitted peak was equal to that in the former iteration. Four parameters (ΔB_0 [ppm], F_L peak width (${a_2}^{0.5}$)[ppm], F_L peak area ($a_1/{a_2}^{0.5}$)[ppm^3], and MTR_{asym}) were calculated from the fitted coefficients.

Results: Fitted Z and F_{CPE} spectrum with B1=1.0mT is in Fig.2. Fitted results with different B1 are in Fig.3. Calculated parameters are in Fig.4

Discussion/Conclusion: F_{CPE} and Z_{CPR} spectrum could be fitted iteratively with Eq.3.1 and 4.2, respectively. The calculated ΔB_0 [ppm] was 0.17±0.03ppm (Fig.4.1). Although ΔB_0 was influenced by B_1, 0.03ppm error was small enough for F_{CPE} calculation. F_L peak width was 1.05±0.14ppm (Fig.4.2). Chemical exchange rate "k" in Eq.1.2 can be calculated from F_L peak width ${a_2}^{0.5}$ by $k=(a_2 - {\omega_1}^2)^{0.5}$. ω_1 was from 0.08 to 0.66 ppm and k was 0.97±0.09ppm. MTR_{asym} was negative at B_1=0.25 and gradually saturated near B_1=2 (Fig.3.2 and 4.4). Because the peaks at -4.0ppm in Fig 3.4 did not change with different B1, these peaks might include some fat signal and influenced MTR_{asym}. F_L peak area at +3.5ppm increased depending on B_1 (Fig.3.4 and 4.3). This is because F_L peak area ($a_1/{a_2}^{0.5}$) depends on ${\omega_1}^2$ in Eq.1.2. However, calculated F_L peak area was not simply proportional to ${\omega_1}^2$. CEST peak, k and ΔB_0 could be calculated. As a CEST parameter, F_L peak area was better than MTR_{asym}.

References: (1) Miyoshi M. et al., proceedings of ISMRM 2014, #3299
(2) Zaiss M, Bachert P. Exchange-dependent relaxation in the rotating frame for slow and intermediate exchange — modeling off-resonant spin-lock and chemical exchange saturation transfer. NMR Biomed 2013;26:507–18. (3) Trott O, Palmer AG. R1ρ relaxation outside of the fast-exchange limit. J Magn Reson 2002;154:157–60.

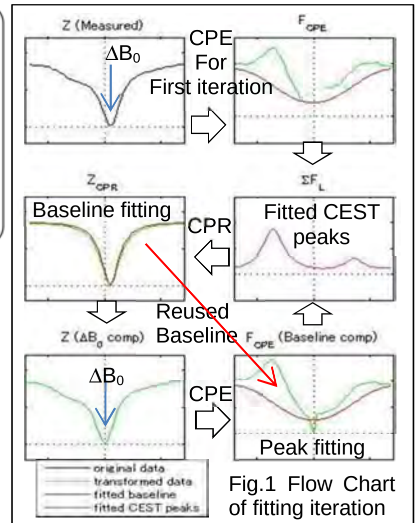

Fig.1 Flow Chart of fitting iteration

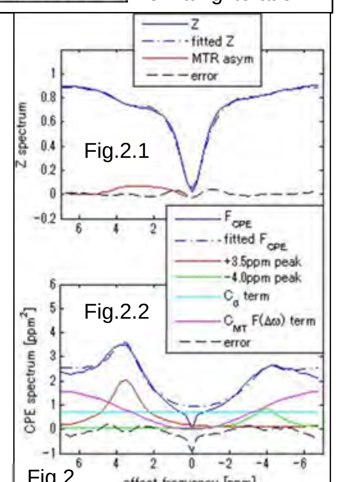

Fig.2

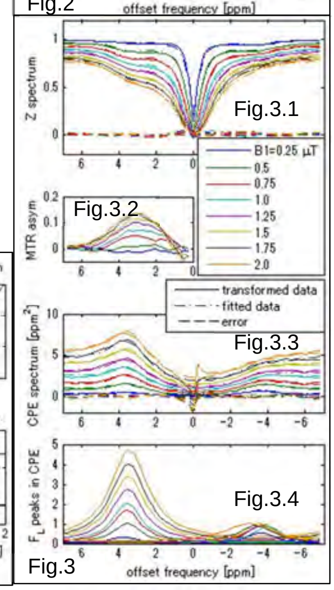

Fig.3

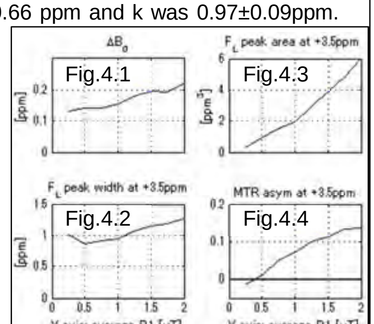

Fig.4 Calculated parameters