Quantitative CEST (qCEST) using Ω–plots in the case of trains of Gaussian–shaped saturation pulses

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Target audience: Researchers interested in quantification of pulsed CEST at clinical systems

Purpose: The contrast in Chemical Exchange Saturation Transfer (CEST) imaging experiments depends on f_B, the concentration of exchanging protons, and on their exchange rate k_{BA}. Recent studies showed that the Ω–plot method [1] is able to quantify both f_B and k_{BA} simultaneously in the case of continuous wave (cw) saturation [1–3]. Here we show that the apparent exchange–dependent relaxation rate (AREX [4]), generating the CEST contrast in a cw experiment, can be extended to the case of pulsed CEST. This extension allows to define an Ω–plot method yielding improved estimation of f_B and k_{BA} also in the case of saturation by a train of Gaussian–shaped rf pulses.

Methods: By inverting AREX [4] one obtains, in the case of cw saturation, a linear function in $1/\omega_1^2$: $\frac{1}{\mathrm{AREX}} = \frac{1}{\left(\frac{1}{Z_{lab}} - \frac{1}{Z_{ref}}\right)\cdot T_1} = \frac{1}{R_{ex}(\omega_1^2)} = \frac{1}{f_B k_{BA}} + \frac{k_{BA}+R_{2B}}{f_B}\cdot\frac{1}{\omega_1^2}$ ($\omega_1 = \gamma B_1$ is the amplitude of the saturating field, $Z_{lab} = Z(1.9\text{ ppm})$, $Z_{ref} = Z(-1.9\text{ ppm})$, $Z = M_{sat}(\Delta\omega)/M_0$). Shaped saturation pulses involve time–dependent $\omega_1(t)$. Integration of the power series of $R_{ex}(\omega_1(t))$ and comparison of the result with the original R_{ex} yields the form factor c_1 and the corresponding apparent exchange-dependent relaxation rate in the pulsed case $\mathrm{AREX}_{\text{shaped pulses}} = \mathrm{DC}\cdot f_B k_{BA} c_1 \frac{\omega_1^2}{\omega_1^2 + k_{BA}(k_{BA}+R_{2B})\cdot c_1^2\sqrt{2}}$ for Gaussian–shaped saturation pulse series. Note that ω_1 is the time–*independent* average saturation amplitude of the pulse. By fitting the linear relation ($1/\mathrm{AREX} = m\cdot 1/\omega_1^2 + n$) concentration and exchange rate can be calculated: $f_B = \left(\mathrm{DC}\cdot n\cdot c_1\cdot\left(-\frac{R_{2B}}{2} + \sqrt{\frac{R_{2B}^2}{4} + \frac{m}{n\cdot c_1^2\sqrt{2}}}\right)\right)^{-1}$ and $k_{BA} = -\frac{R_{2B}}{2} + \sqrt{\frac{R_{2B}^2}{4} + \frac{m}{n\cdot c_1^2\sqrt{2}}}$. DC is the duty cycle of the pulse train and R_{2B} an estimation of the transverse relaxation rate of pool B (we employed $R_{2B} = 66.6$ Hz [5]). The form factor c_1 can be calculated analytically for any Gaussian shape, in our case $c_1 \approx 0.5623$.

Phantom: Experiments were performed with 2 sets of seven 30–ml PBS phantoms each (14 in total). The first set contained creatine with concentrations c_{Cr} = 10, 20, 35, 50, 75, 100, and 125 m*M* (at constant pH = 7.15); in the second set pH was adjusted to 6.32, 6.54, 6.74, 6.94, 7.15, 7.40, and 7.60 (at constant c_{Cr} = 50 m*M*).

Imaging: *Z*–spectra were obtained by centric–reordered 2D–GRE–CEST MRI (FoV = 180×180 mm^2, slice thickness 5 mm, matrix: 128×128, flip angle: 10°, TR/TE: 6.9 ms/3.36 ms) implemented on a 7–T whole–body scanner (MAGNETOM; Siemens, Erlangen, Germany) using a 28–channel Tx/Rx ^{1}H knee coil. For saturation 50 Gaussian–shaped rf pulses of length t_p = 0.1 s (DC = 50 %) were applied. B_1 amplitudes were 1.17, 1.36, 1.56, 1.75, 1.94 and 2.33 µT. 43 evenly distributed frequency offsets were acquired in the spectral range from –4 to 4 ppm across the water peak. T_1–mapping was achieved by saturation recovery gradient echo with 22 different recovery times between 0.25 and 7.5 s. Image data were processed with Matlab software (The MathWorks, Nattick, Massachusetts, USA).

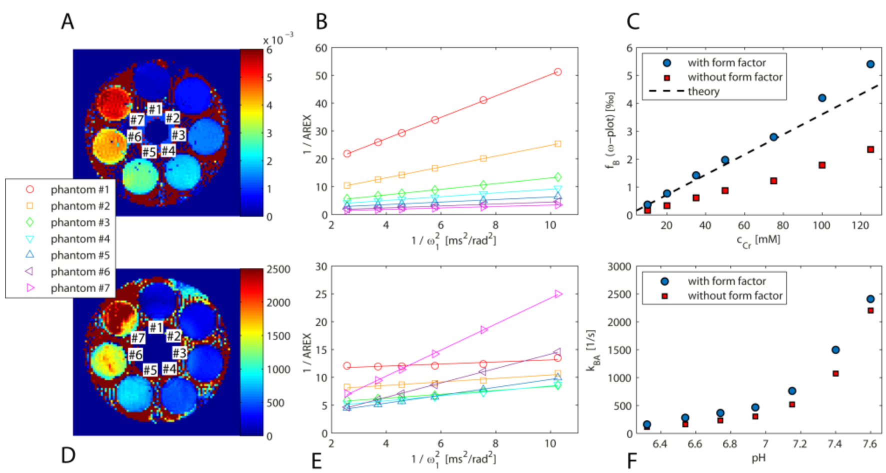

Figure 1: Parameter maps (pixel resolution) of f_B (A) and k_{BA} (D) and Ω–plot evaluation (in selected ROIs) (B, E). The linear dependence of the concentration f_B of exchanging protons on c_{Cr} (C) and the exponential dependence of the exchange rate k_{BA} on pH (F) are displayed for the based on $\mathrm{AREX}_{\text{shapedpulses}}$ solutions with and based on AREX without form factor. The expected $f_B(c_{Cr})$ is plotted for 4 exchanging protons of creatine (C). Phantoms #1– #7 of set 1 and 2, see text.

Results and Discussion: The equations for f_B and k_{BA} enable pixel–wise evaluation of phantom CEST data obtained after saturation with Gaussian–shaped rf pulses (Fig. 1A and D). The results are homogeneous across the slice except for high pH (set 2 #6, #7). In these cases one of the requirements for AREX is no longer valid [4]. Figures 1B and E show the corresponding Ω–plots for selected ROIs. The linearity between $1/\mathrm{AREX}$ and $1/\omega_1^2$ is true for the whole range of prepared creatine concentrations c_{Cr} and pH values. From these Ω–plots mean f_B (Fig. 1C) and mean k_{BA} (Fig. 1F) were calculated for each phantom based on $\mathrm{AREX}_{\text{shaped pulses}}$ (blue circles) and based on AREX with cw saturation (red squares). The concentration f_B scales linearly with the concentration of creatine (Fig. 1C), while the exchange rate k_{BA} follows an exponential function (Fig. 1F) [2,3,6]. The assumption of 4 exchanging protons for creatine [4,6] leads to a theoretical value for f_B (dashed line, Fig. 1C), which our extended Ω–plot method overestimates by only 13 %, while the cw method underestimates by 50 %. The Ω–plot method based on our derived $\mathrm{AREX}_{\text{shaped pulses}}$ yields better results for lower concentrations of creatine.

Conclusion: The proposed evaluation method via Ω–plots allowed the simultaneous determination of the concentration f_B of exchanging protons and of the exchange rate k_{BA} for the case of saturation with trains of Gaussian–shaped pulses. It extends previous approaches [1–3] and forms a first closed analytical formula for a pulsed CEST effect. The use of AREX renders spillover correction unnecessary and corrects for possible T_1–effects [4]. This approach could be the next step towards quantitative CEST studies *in vivo*.

References:

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