Quasi-steady state chemical exchange saturation transfer (QUASS CEST) analysis—correction of the finite relaxation delay and saturation time for robust CEST measurement

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Abstract

Purpose: CEST provides a MR contrast mechanism sensitizing to the exchange between dilute labile and bulk water protons. However, the CEST effect depends on the RF saturation duration and relaxation delay, which need to be long to reach its steady state. Our study aims to estimate the QUAsi-Steady State (QUASS) CEST signal from experiments with shorter saturation and relaxation delay times.

Methods: The evolution of the CEST signal was modeled as a function of the bulk water longitudinal relaxation rate during the relaxation delay ($T_d$) and spin-lock relaxation rate during the RF saturation ($T_s$), from which the QUASS CEST effect is solved. Numeric simulations were programmed to compare the apparent CEST and QUASS CEST effects as a function of $T_s$ and $T_d$ times. We also performed CEST MRI experiments from a creatine–gel pH phantom under serially varied $T_s$ and $T_d$ times.

Results: The numeric simulation showed that although the apparent CEST effect depends on $T_d$ and $T_s$, the QUASS CEST solution has little dependence. Phantom results showed that the routine CEST pH contrast could be described by a nonlinear regression model (ie, $\Delta CEST = \Delta CEST_R^{\text{app}} \left( 1 - e^{-R_1^{\text{app}} \cdot t} \right)$). We had $\Delta CEST_R^{\text{app}} = 3.90 \pm 0.03\%$ ($P < 5e^{-8}$) and $R_1^{\text{app}} = 0.62 \pm 0.02 \text{ s}^{-1}$ ($P < 5e^{-6}$). For the QUASS CEST analysis, we modeled the pH contrast as $\Delta CEST = \Delta CEST_R^{\text{QUASS}} + s \cdot t$, using a linear regression model. We had $\Delta CEST_R^{\text{QUASS}} = 3.63 \pm 0.01\%$ ($P < 5e^{-9}$) and $s = -0.02 \pm 0.00\% / \text{s}$ ($P < 0.01$), the slope of which is minimal.

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Conclusions: The QUASS CEST algorithm provides a post-processing solution that facilitates robust CEST measurement.

Keywords
chemical exchange saturation transfer; CEST; QUAsi-Steady State CEST; QUASS CEST

1 | INTRODUCTION

Chemical exchange saturation transfer (CEST) contrast mechanism is sensitive to the exchange process between dilute labile groups and bulk water protons.\(^1\) It has been increasingly adopted for examining disorders such as acute stroke,\(^2\)–\(^7\) tumors,\(^8\)–\(^11\) and epilepsy.\(^12\),\(^13\) For example, pH-sensitive endogenous amide proton transfer (APT) MRI refines the routine diffusion/perfusion mismatch paradigm in acute stroke.\(^14\)–\(^17\) Exogenous CEST agents have been explored for tumors\(^18\)–\(^23\) and kidney imaging.\(^24\)–\(^29\) However, it is worth noting that the CEST effect depends not only on labile proton ratio and exchange rate but also on experimental conditions,\(^30\) including the amplitude\(^31\)–\(^33\) and duration of RF saturation\(^34\)–\(^36\) as well as the relaxation delay between RF saturation.\(^37\) On the other hand, CEST scans were not performed under long RF irradiation duration and relaxation delay because of scan time constraints.\(^38\),\(^39\) The maximal RF saturation duration and duty cycle may be limited, making it somewhat challenging to compare results across different platforms and sites. This is because unless identical repetition and saturation times are used, CEST findings across multiple centers, even under the perfect field homogeneity and an agreed-upon B\(_1\) amplitude, could vary substantially. As such, it is necessary to develop a post-processing strategy to derive the QUAsi-Steady State (QUASS) CEST effect from experimental measurements, which will improve the robustness of CEST experiments.

We postulated that the QUASS CEST effect could be solved by modeling magnetization evolution throughout the pulse sequence. Briefly, in the absence of RF saturation, the magnetization recovers toward its fully relaxed equilibrium state following the longitudinal relaxation rate. During the RF saturation, the magnetization signal approaches the CEST steady state following the spinlock relaxation rate.\(^40\)–\(^42\) As such, the ground truth spinlock relaxation rate can be derived from the experimental (apparent) measurements, from which the QUASS CEST effect can be calculated. The solution’s accuracy was evaluated with numeric simulation by comparing the apparent CEST and QUASS CEST effects under different RF saturation times (Ts) and relaxation delays (Td). We tested the QUASS algorithm experimentally using a 2-compartment creatine–gel pH phantom, under serially varied Td and Ts times. The results showed that although the apparent CEST effect strongly depends on Td and Ts, the QUASS CEST showed little dependence. To summarize, our study demonstrated that the proposed QUASS CEST solution provided a straightforward post-processing approach to enhance CEST measurement’s accuracy.

2 | THEORY

The CEST effect has often been calculated by normalizing the saturated scans \(I_{\text{sat}}^{\text{app}}\) with the unsaturated control scan \(I_0^{\text{app}}\), in which the superscript \(\text{app}\) denotes the apparent signals
obtained under a given set of $T_d$ and $T_s$. For fast image readout such as EPI, the image readout time is negligible compared to saturation duration and relaxation delay. The control scan without RF saturation can be shown to be

$$ I_{0}^{\text{app}} = I_0 \cdot \left(1 - e^{-R_1w \cdot (T_s + T_d)}\right) \approx I_0 \cdot \left(1 - e^{-R_1w \cdot T_R}\right), \quad (1) $$

in which $R_1w$ is the bulk water longitudinal relaxation rate in the absence of RF saturation, and $I_0$ is the equilibrium bulk water magnetization. For the saturated scans, we have

$$ I_{\text{sat}}^{\text{app}} = I_0 \cdot \left(1 - e^{-R_1w \cdot T_d} e^{-R_1\rho \cdot T_s} + \frac{R_1w}{R_1\rho} \cos^2 \theta \left(1 - e^{-R_1\rho \cdot T_s}\right)\right), \quad (2) $$

where $R_1\rho$ is the spinlock relaxation rate under a given RF saturation scheme and $\theta = \tan^{-1}(\omega_1/\Delta_1)$, where $\omega_1$ and $\Delta_1$ are the RF irradiation level and offset, respectively. The apparent Z-spectrum can be shown to be

$$ I_{\text{sat}}^{\text{app}} = \frac{I_0}{I_0} \cdot \left(1 - e^{-R_1w \cdot (T_s + T_d)} e^{-R_1\rho \cdot T_s} + \frac{R_1w}{R_1\rho} \cos^2 \theta \left(1 - e^{-R_1\rho \cdot T_s}\right)\right) \quad (3) $$

We can reorder the terms to simplify Equation (3), equating the relaxation-corrected apparent Z signal (ie, $I_{\text{sat}}^{\text{app}}$, $I_0^{\text{app}} \cdot \left(1 - e^{-R_1w \cdot (T_s + T_d)}\right)$ and a CEST effect that approaches its modified steady state (ie, $\frac{R_1w \cdot \cos^2 \theta}{R_1\rho \cdot \left(1 - e^{-R_1w \cdot T_d}\right)}$). Specifically, we have

$$ \frac{I_{\text{sat}}^{\text{app}}}{I_0^{\text{app}}} \cdot \left(1 - e^{-R_1w \cdot (T_s + T_d)}\right) = e^{-R_1\rho \cdot T_s} + \frac{R_1w \cdot \cos^2 \theta}{R_1\rho \cdot \left(1 - e^{-R_1w \cdot T_d}\right)} \cdot \left(1 - e^{-R_1\rho \cdot T_s}\right) \quad (4) $$

From the ratios of the measured signals, it is possible to estimate $R_1\rho$, and the QUASS CEST effect is defined as

$$ \left(\frac{I_{\text{sat}}}{I_0}\right)^{\text{QUASS}} = \frac{R_1w}{R_1\rho} \cos^2 \theta, \quad (5) $$

that approximates the steady-state CEST effect obtainable under the condition of long $T_s$ and $T_d$ times.

The QUASS CEST effect is calculated as

$$ CESTR_{\text{QUASS}}^{\text{ }} = \left(\frac{I_{\text{ref}}}{I_0}\right)^{\text{QUASS}} - \left(\frac{I_{\text{label}}}{I_0}\right)^{\text{QUASS}}. $$
3 | METHODS

3.1 | Simulation

We simulated the CEST effect using a classical 2-pool Bloch McConnell (BM) equations in MATLAB 2019a (The MathWorks, Natick, MA), assuming representative bulk water $T_{1w}$ and $T_{2w}$ of 2.5 s and 125 ms, and labile proton $T_{1s}$ and $T_{2s}$ of 1 s and 20 ms, respectively. A typical CEST pulse sequence is shown in the supporting information (Supporting Information Figure S1), which includes a relaxation delay (i.e., $T_d$), followed by RF saturation, defined by its amplitude ($B_1$), offset ($\Delta \omega$), and duration ($T_s$), and then a fast image readout. When using EPI acquisition, the readout time is negligible compared to $T_d$ and $T_s$, and we have $TR \approx T_d + T_s$. The control signal ($I_0^{app}$) monotonically increases toward its equilibrium state. In comparison, the label ($I_{sat}^{app}$ (sat)) and reference ($I_{sat}^{app}$ (ref)) signals deviate from the control signal when the saturation RF pulse is switched on to approach their respective steady states. The apparent CEST effect is calculated as

$$]\text{CESTR}^{app} = \frac{I_{sat}^{app(ref)} - I_{sat}^{app(sat)}}{I_0^{app}},$$

which depends on both $T_d$ and $T_s$. For the simulation, we assumed a typical labile proton ratio and an exchange rate of 1:1000 and 100 s$^{-1}$, respectively, with a labile proton chemical shift at 1.9 ppm for a magnetic field strength of 7T. We varied the $T_s$ and $T_d$ independently from 1 to 7.5 s, in increments of 0.5 s for a representative saturation amplitude of 2 $\mu$T. Z-spectra were simulated from −3 to 3 ppm, with intervals of 0.1 ppm. We compared the simulated apparent CEST and the calculated QUASS CEST Z-spectra, asymmetry Z-spectra, and MTR asymmetry at 1.9 ppm, under different $T_d$ and $T_s$ times.

3.2 | Phantom

We prepared a 2-compartment creatine–gel pH phantom. Briefly, 1% agarose (Sigma Aldrich, St. Louis, MO) solution was heated to its boiling point, positioned in a water bath preset to 50°C to settle its temperature slightly above the agarose gelling point. Creatine was added to the agarose solution to reach a 50 mM concentration, with pH titrated to 6.5 and 6.0. The creatine–gel mixture was separately transferred to 2 compartments of the phantom holder, sealed, and solidified overnight before experiments.

3.3 | MRI

MRI experiments were performed using a 7T small-bore MRI scanner (Bruker Biospec, Ettlingen, Germany), with single-shot spin-echo EPI readout (slice thickness = 10 mm, FOV = 52 × 52 mm, image matrix = 96 × 96, bandwidth = 225 kHz with its TE being 50 ms). The field inhomogeneity was determined with the water saturation shift referencing (WASSR) MRI between ±0.2 ppm with intervals of 0.025 ppm ($B_1 = 0.5 \mu$T, $T_d/T_s = 1/0.5$ s, scan time = 27 s). For CEST MRI, we acquired 6 Z-spectra ($B_1 = 2 \mu$T), with both $T_d$ and $T_s$ varied from 1.5, 2, 3, 4, and 5 to 7.5 s. The RF offsets were varied from −3 to 3 ppm, with increments of 0.1 ppm (2 averages). The Z-spectrum scan time varies from 6 min 12 s ($T_s/T_d = 1.5s/1.5s$) to 31 min ($T_s/T_d = 7.5s/7.5s$). $T_{1w}$-weighted images were acquired with
3.4 | Data analysis

Images were processed in MATLAB R2019a. The bulk water $T_{1w}$ map was obtained using least-squares mono-exponential fitting of the signal intensities as functions of the TIs ($I = I_0(1 - \beta \cdot e^{-\frac{T1}{T_{1w}}})$). Note that the 3-parameter $T_{1w}$ fitting (ie, $I_0$, $\beta$ and $T_{1w}$) accounts for inversion efficiency and incomplete relaxation recovery. $\text{Z-spectra}$ were corrected for $B_0$ inhomogeneity following the WASSR approach. The apparent CEST asymmetry effect was calculated as $\text{CESTR}_{\text{app}}(T_d, T_s) = \frac{I_{\text{ref}}(T_d, T_s) - I_{\text{label}}(T_d, T_s)}{I_0(T_d, T_s)}$. For the proposed QUASS CEST effect, $R_{1\rho}$ was numerically solved using Equation (4), from which the QUASS Z-spectrum was calculated from Equation (5). The contrast-to-noise ratio (CNR) was calculated using $\text{CNR}_{\text{app}} = \frac{\text{CESTR}_{\text{app}}(pH1) - \text{CESTR}_{\text{app}}(pH2)}{\sqrt{\frac{1}{2} \left( \text{CESTR}_{\text{app}}^2(\text{pH1}) + \sigma_{\text{CESTR}_{\text{app}}(\text{pH2})}^2 \right)}}$, and CNR efficiency ($\text{CNR}_{\text{eff}}$) was calculated as $\text{CNR}_{\text{eff}} = \frac{\text{CNR}_{\text{app}}}{\sqrt{\text{NAE}} \cdot (T_d + T_s)}$, for the apparent and QUASS CEST effects, respectively, in which NAE is the number of averages and a factor 3 was used for 3-point CEST effect calculation (eg, control, reference, and label scans).

4 | RESULTS

Figure 1 simulates the effect of $T_d$ and $T_s$ on the CEST measurement. Briefly, Figure 1A shows 3 representative Z-spectra under short $T_d$ and $T_s$ of 1s (blue), intermediate $T_d$ and $T_s$ of 2 s (green), and long $T_d$ and $T_s$ of 7.5 s (red). The Z-spectral intensity decreases at long saturation duration and relaxation delay times because of prolonged saturation transfer. Figure 1B plots the corresponding asymmetry Z-spectra under the same 3 representative sets of $T_d$ and $T_s$ times, which increase with the saturation duration and relaxation delay, as expected. Figure 1C shows the CEST effect as a function of $T_d$ and $T_s$ times overlaid with contour lines for each 0.5% level, indicating strong time dependence. The minimal and maximal CEST effect was 5.20% and 9.88%, respectively, with its mean and standard deviation being 9.04 ± 1.15% and a coefficient of variance (COV) of 12.76%.

Figure 2 shows the QUASS signal estimated from the simulated data shown in Figure 1. Figure 2A plots the numerically solved apparent $R_{1\rho}$ (ie, $\frac{I_0^{\text{app}}}{I_{\text{sat}}^{\text{app}}} \cdot R_{1\rho} \cos^2(\theta)$) under 3 representative sets of $T_d$ and $T_s$ times, being 1s/1s (black cross markers), 2s/2s (black diamond markers), and 7.5s/7.5s (black plus markers). The corresponding QUASS $R_{1\rho}$ solutions were shown under the same 3 sets of $T_d$ and $T_s$ times, being 1s/1s (blue cross markers), 2s/2s (green diamond markers), and 7.5s/7.5s (red plus markers). Note that QUASS $R_{1\rho}$ overlapped very well with that simulated under the condition of long $T_d$ and $T_s$ times. Figure 2B,C show the calculated QUASS Z-spectra and asymmetry spectra (ie, 1s/1s inversion recovery EPI with TI ranging from 0.1 s to 5 s (relaxation delay/TE = 5s/50 ms and 2 averages, scan time = 1 min 24 s).
[blue cross markers], 2s/2s [green diamond markers], and 7.5s/7.5s [red plus markers]) and the apparent Z-spectrum and asymmetry spectrum obtained under long $T_d$ and $T_s$ of 7.5s / 7.5s (black plus markers). Both Z-spectra and asymmetry spectra overlapped very well. Figure 2D shows the derived QUASS CEST effect as a function of $T_d$ and $T_s$ times overlaid with contour lines for each 0.5% level. The minimal and maximal QUASS CEST effect was 9.08% and 9.65%, respectively (9.53 ± 0.14% [mean ± SD] and COV = 1.48%). The QUASS CEST effect is in excellent agreement with the CEST effect simulated assuming long $T_d$ and $T_s$ times of 7.5 s (ie, 9.77%). Indeed, the COV of the QUASS CEST solution (Figure 2D) is only 11.60% of that from the apparent CEST effect (Figure 1C).

We performed phantom experiments to compare the apparent and QUASS CEST effects. Figure 3A shows the apparent CEST asymmetry images at 1.9 ppm obtained under $T_d/T_s$ times of 1.5s/1.5s, 2s/2s, 3s/3s, 4s/4s, 5s/5s, and 7.5s/7.5s. The magnitude of the apparent CEST effect increased with $T_d$ and $T_s$ times. The Z-spectral signal (Figure 3B) decreased at long $T_d$ and $T_s$ because of prolonged saturation transfer. Signals from the inner and exterior pH compartments were marked in solid and dash-dotted lines, respectively. Such a strong time dependence causes substantial variation in the apparent CEST asymmetry spectra (Figure 3C). For the exterior pH compartment, the minimal and maximal apparent CEST effects were 2.17% and 3.62%, respectively (3.11 ± 0.61% [mean ± SD] and COV = 19.55%). In comparison, the interior pH compartment has its minimal and maximal apparent CEST effects being 4.52% and 7.48%, respectively (6.39 ± 1.21% [mean ± SD] and COV = 18.93%).

Figure 4 shows the results from the proposed QUASS CEST analysis. Figure 4A shows the calculated QUASS CEST images under the $T_d/T_s$ times of 1.5 s/1.5 s, 2 s/2 s, 3 s/3 s, 4 s/4 s, 5 s/5 s, and 7.5 s/7.5 s. The magnitude of the QUASS CEST effect showed little $T_d$ and $T_s$ dependence. The QUASS Z-spectra (Figure 4B) and QUASS asymmetry spectra (Figure 4C) overlapped well for different $T_d/T_s$ times. We had the minimal and maximal QUASS CEST effects for the exterior pH compartment being 3.62% and 3.85%, respectively (3.76 ± 0.08% [mean ± SD] and COV = 2.26%). The interior pH compartment had its minimal and maximal QUASS CEST effects being 7.44% and 7.55%, respectively (7.50 ± 0.05% [mean ± SD] and COV = 0.62%).

We further evaluated the time-dependence of the routine CEST ($CESTR_{app}$) and QUASS CEST ($CESTR_{QUASS}$) effects. Figure 5 shows that $CESTR_{app}$ approaches its steady state exponentially. We modeled it using $CESTR_{app} = CESTR_{eq}^{app} \left(1 - e^{-R_1^{app} \cdot t}\right)$ with a nonlinear regression model in MATLAB (Figure 5A). For the exterior pH compartment, we had

$$CESTR_{eq}^{app} = 3.81 \pm 0.07\% \text{ (} P < 5e - 7 \text{)}$$

and $R_1^{app} = 0.59 \pm 0.03 s^{-1} (P < 5e - 5)$. For the interior pH compartment, we had

$$CESTR_{eq}^{app} = 7.71 \pm 0.10\% \text{ (} P < 5e - 7 \text{)}$$

and $R_1^{app} = 0.60 \pm 0.02 s^{-1} (P < 5e - 5)$. In comparison, the QUASS CEST analysis provided consistent CEST measurements. We modeled it using $CESTR^{QUASS} = CESTR_{eq}^{QUASS} + s \cdot t$ with a linear regression model. For the exterior pH compartment, we had

$$CESTR_{eq}^{QUASS} = 3.89 \pm 0.03\% \text{ (} P < 5e - 8 \text{)}$$

and $s = -0.03 \pm 0.01% / s (P < 0.02)$. Although
the slope was significantly different from 0, its magnitude was small. It meant a change of 0.03% for a 1-s difference in saturation time and relaxation delay. For the interior pH compartment, we had $C\text{EST} R_{eq}^{\text{QUASS}} = 7.52 \pm 0.04\% \ (P < 5\text{e} - 9)$ and $s = -0.01 \pm 0.01\% / s \ (P > 0.40)$. We also compared the CEST contrast between the 2 pH compartments. For the routine CEST effect, we modeled the contrast as $\Delta C\text{EST}R = \Delta C\text{EST} R_{eq}^{\text{app}} \left(1 - e^{-R_{1p}^{\text{app}} \cdot t}\right)$, using a nonlinear regression model. We had $\Delta C\text{EST} R_{eq}^{\text{app}} = 3.90 \pm 0.03\% \ (P < 5\text{e} - 8)$ and $R_{1p}^{\text{app}} = 0.62 \pm 0.02\text{s}^{-1} \ (P < 5\text{e} - 6)$. For the QUASS CEST effect, we modeled its contrast as $\Delta C\text{EST}R = \Delta C\text{EST} R_{eq}^{\text{QUASS}} + s \cdot t$, using a linear regression model. We had $\Delta C\text{EST} R_{eq}^{\text{QUASS}} = 3.63 \pm 0.01\% \ (P < 5\text{e} - 9)$ and $s = -0.02 \pm 0.00\% / s \ (P < 0.01)$. Again, although the slope was significantly different from 0, its magnitude was negligible. Figure 5D compares the CNR efficiency from the apparent CEST and QUASS CEST effects, which decreased with TR. This suggests that CEST experiments performed at a moderate TR are of elevated sensitivity, as expected.\(^{37,42}\) The loss in the magnitude of the CEST effect can be restored with the proposed QUASS post-processing algorithm, which helps with CEST quantification.

5 | DISCUSSION

Our study proposed a QUASS CEST post-processing algorithm and demonstrated its feasibility with numeric simulations and phantom experiments. We showed that the QUASS algorithm minimizes the impact of finite saturation duration and relaxation delay on the CEST measurement. It has been shown that the SNR efficiency peaks at a moderate TR.\(^{37,42}\) However, under such conditions, the magnitude of the CEST effect is underestimated because the saturation time is not long enough. The QUASS CEST solution makes it feasible to expedite the scan without underestimating the magnitude of the CEST effect and contrast. Therefore, although the QUASS algorithm itself does not enhance SNR, it enables experiments to be conducted under the condition of high SNR efficiencies without underestimating the magnitude of the CEST effect. Quantitative CEST analyses, such as the omega plot,\(^{46–48}\) are often developed under steady-state assumptions. Therefore, the QUASS post-processing algorithm enables accurate quantitative CEST analysis without the stringent experimental conditions. Moreover, by allowing the use of moderate saturation times for CEST imaging, the QUASS algorithm provides a potential approach to reduce the specific absorption rate (SAR). Importantly, such a post-processing approach makes it feasible to compare results across multiple sites and vendors by directly accounting for the difference in experimental choices of saturation duration and relaxation delay, a step toward standardizing CEST experiments.

The proposed QUASS CEST solution requires reasonably good field homogeneity and accurate measurement of $T_{1w}$. This is because a precise tilt angle (ie, $\theta = \arctan \left(\frac{f B_1}{\Delta \omega}\right)$) is required for QUASS calculation. Because of the relatively small voxel size used in our study, there was little intravoxel inhomogeneity, and we used WASSR to correct voxel-wise field inhomogeneity. If needed, we can deploy the CEST intravoxel inhomogeneity correction
algorithm. Our experiment used a volume transmit receiver coil with an inner diameter of 70 mm over a phantom with a diameter of ~25 mm, and such a system had little B\(_1\) inhomogeneity. If needed, the B\(_1\) profile can be mapped to correct the tilt angle. On the other hand, T\(_1w\) mapping is straightforward because there is no RF saturation pulse applied during the relaxation delay, and routine T\(_1w\) sequences can be used. Although we modeled the apparent CEST effect using \[ CEST R^{\text{app}} = CEST R^{\text{eq}} \left( 1 - e^{-R^{\text{app}} \cdot t} \right) \] with a nonlinear regression model, it is important to point out that \( R^{\text{app}} \) differs from the ground truth \( R^{\rho} \) when T\(_d\) is not infinitely long.

The bulk water signal approaches its modified CEST steady state following \( R^{\rho} \) (Equation 4), which depends not only on the tissue water relaxation properties but also on the CEST effect. For dilute labile groups undergoing slow chemical exchange, the spinlock relaxation rate is comparable to \( R^{\rho} \) under the condition of weak B\(_1\) saturation. Under such circumstances, it takes a longer saturation duration (~5 × T\(_1w\)) to approach its steady state versus CEST effects that are close to the bulk water resonance, such as glucose and glycogen (~5 × T\(_1\rho\) instead of 5 × T\(_1w\)). Because of the substantial difference in amide, amine, and hydroxyl CEST exchange properties, it will be interesting to further explore QUASS CEST analysis in the future.

6 | CONCLUSIONS

Our study developed a QUASS CEST algorithm and demonstrated it with both numeric simulations and phantom experiments. The post-processing solution minimizes the effect of finite RF saturation duration and relaxation delay times on the CEST measurement, improving the robustness of CEST experiments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.
Two-pool (BM) simulation of the bulk water signal dependence on the saturation time ($T_s$) and relaxation delay ($T_d$). (A) Representative $Z$-spectra simulated with $T_d/T_s = 1s/1s$ (x markers in blue), $T_d/T_s = 2s/2s$ (diamond markers in green), $T_d/T_s = 7.5s/7.5s$ (+ markers in red). (B) The corresponding asymmetry $Z$-spectra. (C) The magnitude of the simulated CEST MRI effect as a function of $T_d$ and $T_s$ times, overlaid with contour lines for each 0.5% level.
FIGURE 2.
The proposed QUASS CEST MRI solution from the simulated data shown in Figure 1. (A) Comparison of the apparent $R_{1p}$ spectra (w/o QUASS correction) obtained under $Td/ Ts = 1s/1s$ (x markers in black), $Td/ Ts = 2s/2s$ (diamond markers in black), and QUASS $R_{1p}$ (w/ QUASS correction) under $Td/ Ts = 1s/1s$ (x markers in blue), $Td/ Ts = 2s/2s$ (diamond markers in green), $Td/ Ts = 7.5s/7.5s$ (+ markers in red). (B) Calculated QUASS Z-spectra for $Td/ Ts = 1s/1s$ (x markers in blue), $Td/ Ts = 2s/2s$ (diamond markers in green), $Td/ Ts = 7.5s/7.5s$ (+ markers in red) and that simulated steady-state under both long $Td$ and $Ts$ ($Td/ Ts = 7.5s/7.5s$, + markers in black). (C) Asymmetry Z-spectra from the QUASS CEST analysis overlaid with the simulated steady-state ($Td/ Ts =
7.5s/7.5s, + markers in black). (D) 2-pool (BM) simulation showing dependence of the QUASS CEST effect on $T_s$ and $T_d$ times, overlaid with contour lines for each 0.5% level.
FIGURE 3.
The routine CEST measurement from a two-compartment pH phantom. (A) CEST images as a function of $T_d$ and $T_s$ times (1.5 s/1.5s, 2s/2s, 3s/3s, 4s/4s, 5s/5s, and 7.5s/7.5s). (B) Z-spectra from the interior (pHi, solid line) and exterior (pHe, dash-dotted line) pH compartments under different $T_d$ and $T_s$ times. (C) Asymmetry Z-spectra from both pH compartments under different $T_d$ and $T_s$ times.
FIGURE 4.
The proposed QUASS CEST MRI results from a 2-compartment pH phantom. (A) QUASS CEST images as a function of $T_d$ and $T_s$ (1.5 s/1.5 s, 2 s/2 s, 3 s/3 s, 4 s/4 s, 5 s/5 s, and 7.5 s/7.5 s). (B) QUASS Z-spectra from the interior (pHi, solid line) and exterior (pHe, dashed-dotted line) pH compartments under different $T_d$ and $T_s$ times. (C) QUASS asymmetry Z-spectra from both pH compartments under different $T_d$ and $T_s$ times.
FIGURE 5.
Comparison of the routine CEST (CESTR<sup>app</sup>) and QUASS CEST (CESTR<sup>QUASS</sup>) MRI effects. (A) CEST<sup>app</sup> effects from the interior pH compartment (circle) and exterior pH compartment (square) as a function of $T_d$ and $T_s$ times. (B) CEST<sup>QUASS</sup> effects from the interior pH compartment (circle) and exterior pH compartment (square) as a function of $T_d$ and $T_s$ times. (C) The CEST contrast between two pH compartments from the routine CEST MRI (gray diamonds) and QUASS CEST MRI (black diamonds) as a function of $T_d$ and $T_s$ times. (D) CNR efficiency for CEST<sup>app</sup> and CEST<sup>QUASS</sup> between the 2 pH compartments as a function of $T_d$ and $T_s$ times.