Improving Standardization and Accuracy of In vivo Omega Plot Exchange Parameter Determination using Rotating-Frame Model-Based Fitting of Quasi-Steady-State (QUASS) Z-spectra

Julius Juhyun Chung [1], Hahnsung Kim[1,3], Iris Y. Zhou[2], and Phillip Zhe Sun[1,3,4]

[1] *Primate Imaging Center, Emory National Primate Research Center, Emory University, Atlanta, GA*

[2] *Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA*

[3] *Department of Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, GA*

[4] *Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA*

INTRODUCTION:

While Ω-plot-driven quantification of in vivo amide exchange properties has been demonstrated(1), differences in scan parameters may complicate the fidelity of determination. This work systematically evaluated the use of quasi-steady-state (QUASS) Z-spectra reconstruction to standardize in vivo amide exchange quantification across acquisition conditions and further determined it in vivo.

METHODS:

Simulation and in vivo rodent brain CEST data at 4.7 T were fit with and without QUASS reconstruction using both multiple Lorentzian and rotating-frame model-based fitting approaches. pH modulation was accomplished both in simulation and in vivo by inducing global ischemia via cardiac arrest. Amide parameters were determined via Ω-plots and compared across methods.

RESULTS:

Simulation showed that Ω-plots using multi-Lorentzian fitting could substantially underestimate the exchange rate, with error being unpredictable as conditions diverged from the steady state. In comparison, model-based fitting using QUASS estimated the same exchange rate within 6% (A). Labile proton fraction also showed similar results with error increasing further from steady state (D). These results aligned with in vivo findings (B) where multi-Lorentzian fitting of native Z-spectra resulted in an exchange rate of 64 ± 13 s^{-1} (38 ± 16 s^{-1} after cardiac arrest), while model-based fitting of QUASS Z-spectra yielded an exchange rate of 126 ± 25 s^{-1} (52 ± 21 s^{-1}) which can also be seen on parameter maps (C). In vivo findings for labile proton fraction (E) with multi-Lorentzian fitting of native Z-spectra resulted in 2.7 ± 0.3 × 10^{-4} (2.1 ± 0.5 × 10^{-4} after cardiac arrest), while model-based fitting of QUASS Z-spectra results 4.0 ± 0.5 × 10^{-4} (2.6 ± 0.8 × 10^{-4}) which can also be seen on parameter maps (F).

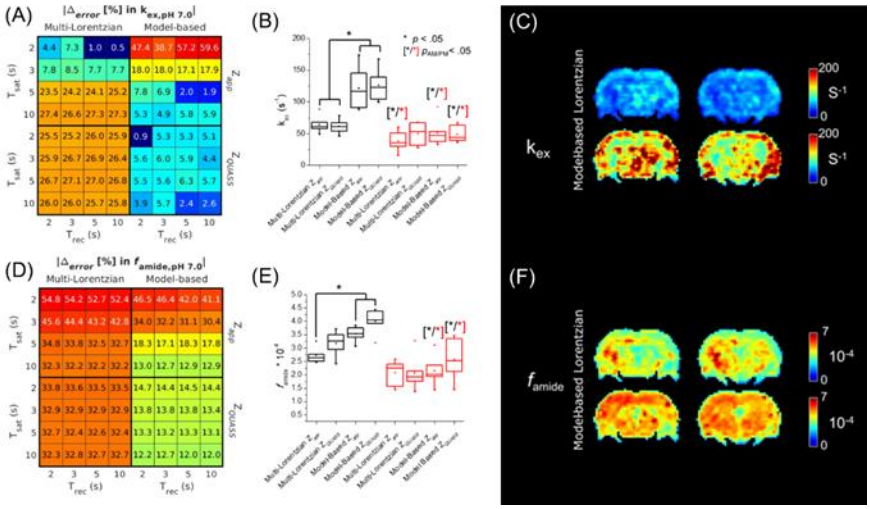

Figure Caption. Heatmaps of relative error in exchange rate (A) and proton fraction (D) calculated from simulations across various combinations of saturation time (T_{sat}) and relaxation delays (T_{rec}) with multiple Lorentzian Fitting and rotating frame model based-fitting of native and QUASS Z-spectra. Box plots of exchange rates (B) and labile proton fractions (E) calculated from Ω-plots of native and QUASS Z-spectra with multi-Lorentzian or model-based fitting before (black) and after (red) cardiac arrest. (C) k_{ex} and (F) f_{amide} maps calculated with the multi-Lorentzian or model-based fitting of QUASS Z-spectra.

DISCUSSION:

Simulation and *in vivo* results demonstrate differences in exchange rate and proton fraction determined through multiple-Lorentzian fitting versus rotating-frame model-based fitting. This may explain the broad range of amide exchange rates reported (2-4), from about 30 to 300 s^{-1}. Our calculated exchange of 126 s^{-1} was comparable with the range of reported exchange rates. Quantification benefits from using signals quantified in at least the inverse Z-domain, such as rotating-frame model-based fitting, or other 1/Z parameters: e.g. R_{ex}, $MTRR_{ex}$, or AREX.

CONCLUSION:

The rotating-frame-based model fitting of QUASS CEST Z-spectra enables consistent and accurate quantification of exchange parameters through Ω-plot construction by reducing error due to signal overlap and non-equilibrium CEST effects.

REFERENCES:

1. Ji Y, *et al.* Magn Reson Med 2023;89(1):299-307.
2. Zhou J, *et al.* Nat Med 2003;9(8):1085-1090.
3. Boyd PS, *et al.* Magn Reson Med 2022;87(5):2436-2452.
4. Liepinsh E, *et al.* Magn Reson Med 1996;35(1):30-42.