Ultra-fast one-shot Z spectrum acquisition
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Target Audience: Those interested in chemical exchange saturation transfer (CEST) and magnetization transfer (MT).

Purpose: The conventional way to explore CEST and MT phenomena is plotting the normalized z-polarization of water protons after applying off-resonance pre-saturation at different offset frequencies. A Z spectrum1,2 is then composed out of many individual experiments. Moreover, to fully characterize the CEST and/or MT phenomena, several of these need to be performed for different irradiation times and power, or for different agent concentrations. In this study, we propose one fast method exploiting a gradient field to acquire the z-polarization of water protons simultaneously at many frequency offsets, thereby achieving a great speed-up to obtain a full Z spectrum.

Method: The pulse sequence used in this study is shown in Fig. 1. The gradient field during the pre-saturation period shifts the frequency offset of the saturating RF irradiation relative to the water resonance frequency along the gradient direction. At the end of the pre-saturation period, the z-polarization of water protons depends on the relative spatial position in a sample. After a readout pulse, spatial signal dependence is encoded back in the frequency domain under the action of the same or a different gradient. A reference spectrum is used for normalization.

The method has been tested on a 500 MHz NMR spectrometer with Eu-DOTAM (10 mM in H2O) and glutamic acid (10 to 150 mM in 1:1 mixture of H2O/D2O), which are respectively paraCEST1 and regular CEST (diamagnetic CEST) agents. For Eu-DOTAM, the strength and duration of the pre-saturation pulse were respectively $\gamma B_1/2 \pi = 500$ Hz and 2 s; and for glutamic acid, they were 100 Hz and 1 s, respectively. For Eu-DOTAM, the offset frequency of the pre-saturation pulse was 15 kHz relative to the reference frequency during the acquisition period.

Results: The spectra obtained with Eu-DOTAM were shown in Fig. 2a. The blue line is the reference spectrum, and the red line is the spectrum with pre-saturation. The ultrafast Z spectrum resulting from these two spectra is given in Fig. 2b. The ultrafast Z spectra for glutamic acid at difference concentrations are presented in Figs. 3a.

Discussion: As seen in Fig. 2, even a paraCEST effect can be observed together with the direct saturation of the water protons, which make it possible to measure the chemical shifts of the exchangeable site from a single experiment. For Eu-DOTAM, the chemical shift was measured as 53.6 ppm, which is the same as measured with the conventional method.

For diaCEST agents, our method easily produces the whole Z spectra, which can be used for the following analysis. From the Z spectra for glutamic acid at different concentrations (Fig. 3a), the MT asymmetry curves clearly revealed the CEST peak due to amide protons at 3.5 ppm (Fig. 3b). The intensity of the CEST peak increases as the concentration (Fig. 3c).

Conclusion: We demonstrated an ultrafast method to obtain full Z spectra. A spectrum can be obtained in under 10 s by this new method, compared to about 15 minutes by the conventional way. The new method can be useful for fast screening of imaging phantoms and paraCEST contrast agents under different experimental conditions.


Fig. 1. (a) RF, Zz, Gz, and (b) RF, G2, and Gx

Left: Fig. 2. a, b: Eu-DOTAM; Above and right: Fig. 3. a, b,c: Glutamic acid.