Supporting Information

Single ^{19}F probe for simultaneous detection of multiple metal ions using miCEST MRI

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Experimental Section

Sample preparation: TF-BAPTA (AG Scientific, Inc.) was dissolved in 20 mM Hepes buffer to a final concentration of either 5 mM (NMR experiments) or 10 mM (MRI experiments). The pH was adjusted to 7.4 by titration with 1 N HCl or 1 N NaOH. Stock solutions of the salts $CaCl_2$, $MgCl_2$, $ZnCl_2$, $FeSO_4$, NaCl, and KCl were prepared in 20 mM Hepes buffer and used to prepare sample solutions containing TF-BAPTA and ions, with a molar ratio of 10:1 or 50:1 TF-BAPTA:ion for the NMR and MRI experiments, respectively. For experiments performed in the presence of physiological ions, Hank's Balanced Salt Solution (HBSS) containing 1.3 mM Ca^{2+}, 0.9 mM Mg^{2+}, 5.9 mM K^+, 143 mM Na^+, and 6 mM glucose was used instead of Hepes buffer.

^{19}F NMR experiments: ^{19}F NMR spectra were acquired using an 11.7 T NMR scanner (Bruker Biospec system) equipped with a two channel (^{1}H/^{19}F, and ^{2}H for lock, broad band) rf coil. A volume of 0.5 mL of each sample was transferred into 5 mm NMR tubes with 0.5 mM added 5-FluoroCytosine (5-FC) and 50 μL D_2O. The 5-FC was assigned as an internal ^{19}F reference with a fixed frequency of -47.0 ppm. D_2O was used for signal lock.

MRI experiments: MRI experiments were performed on a vertical 17.6 T scanner (Bruker Avance system) with the temperature controlled at 37^{o}C. A 20 mm birdcage radiofrequency coil was used to acquire both ^{1}H and ^{19}F MR images by sweeping the coil frequency from the proton (750 MHz) to the fluorine (705.5 MHz) frequency. For ^{1}H MRI, a rapid acquisition with relaxation enhancement (RARE) sequence was used with

the following parameters: Repetition time (TR)/echo time (TE)=5,000/7.7 ms; RARE factor=8; 1 mm slice thickness; FOV=2.0×2.0 cm; matrix size=128×128; resolution=0.156×0.156 mm; and one average (NA=1). For ^{19}F iCEST MRI, the center frequency (O_1) was set at the frequency of the ^{19}F atom at the 6 position (0.0 ppm) of TF-BAPTA (**Figure 1a**), while signal from the ^{19}F located at the 5 position of TF-BAPTA (**Figure 1a,b**, 4.5 ppm downfield) was suppressed using a spectrally selective excitation pulse and spoiler gradient. A modified RARE sequence (TR/TE=4,000/3.4 ms, RARE factor=16, 6 mm slice, FOV=2×2 cm, matrix size=32×32, resolution=0.625×0.625 mm, NA=8 and a saturation pulse B_1=1.2, 2.4 or 3.6 μT/ 2 s) was used to acquire ^{19}F iCEST data. Mean ^{19}F iCEST spectra were obtained after B_0 correction. The CEST contrast was calculated after Lorentzian line shape fitting of the signal from each voxel in the image.

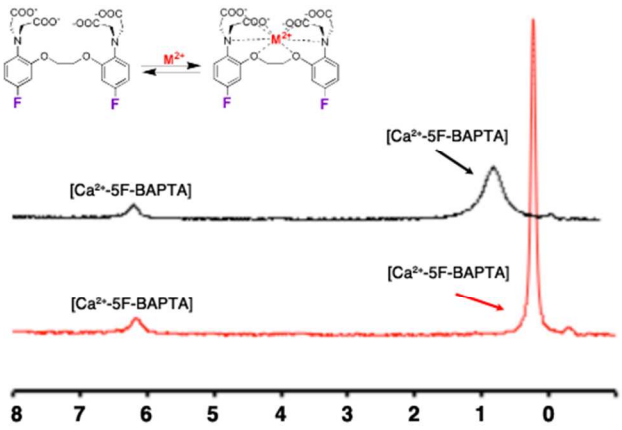

Figure S1. Chemical structure of 5F-BAPTA and ^{19}F-NMR spectra of 5 mM 5F-BAPTA in the presence of 0.5 mM Ca^{2+} with (black spectrum) and without (red spectrum) the addition of 1 mM Mg^{2+}.

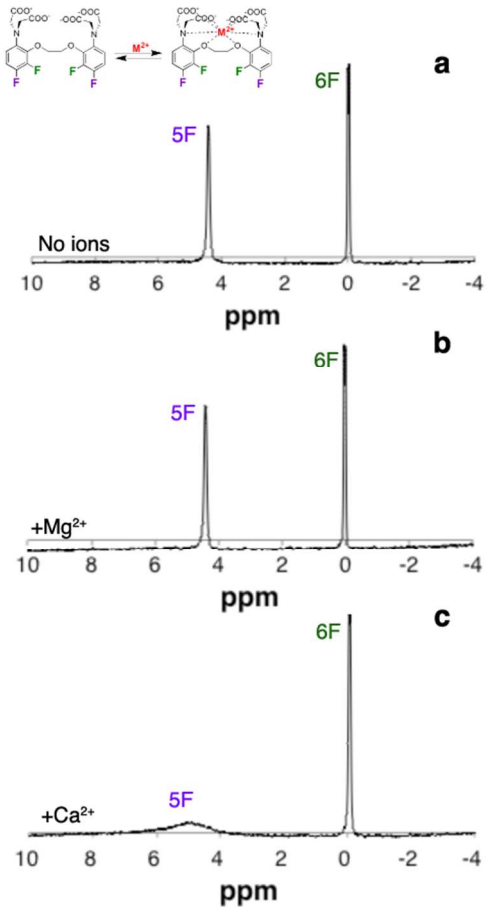

Figure S2. Chemical structure of TF-BAPTA and ^{19}F NMR spectra of 5 mM TF-BAPTA alone (**a**), in the presence of 0.5 mM Mg^{2+} (**b**), or in the presence of 0.5 mM Ca^{2+} (**c**).

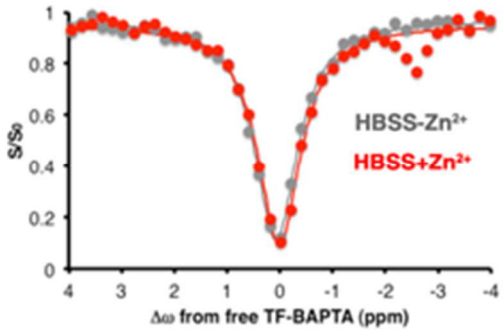

Figure S3. iCEST spectra for TF-BAPTA (10 mM) at HBSS (pH=7.2, 1.3 mM Ca^{2+}, 0.9 mM Mg^{2+}, 5.9 mM K^{+}, 143 mM Na^{+}, 5.6 mM glucose) without (gray iCEST spectrum) and with addition of 200 μM of Zn^{2+} (red iCEST spectrum).