Non-transferred Magnetization Ratio (NOMAR) Filtering: A New Technique to Create Tissue Selective CEST contrast maps

Guanshu Liu1,2, Kannie WY Chan2,3, Xiaolei Song2,3, Jiayang Zhang2,4, Assaf A Gilad2,3, Jeff WM Bulte2,5, Peter CM van Zijl4,5, and Michael T McMahon2,4
1F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States, 2Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States, 3Cellular Imaging Section, Institute for Cell Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States, 4F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, Maryland, United States

INTRODUCTION

Recently, Chemical Exchange Saturation Transfer (CEST) has emerged as a promising MRI contrast mechanism. In vivo, applied NOMAR filtering to produce tissue selective CEST contrast maps. For example, the separation of CSF containing pixels from brain parenchyma in MS studies and removal of background tissue from contrast-enhanced blood signal. Here, we demonstrate how this simple MT segmentation technique can be applied to improve in vivo detection of DIACEST Liposome (DL) contrast.

METHODS AND MATERIALS

Phantom and in vitro MRI: A phantom was prepared consisting of either 0 or 10 mM L-arginine (Large, Sigma) and 0%, 5%, 10%, 15%, or 20% heat cross-linked (80°C, 10 minutes) Bovine Serum albumin (BSA, Sigma) in 0.1 M PBS (pH=7.3), and imaged on a 9.4T Bruker scanner using the in vitro CEST MRI acquisition described previously. We acquired MT-weighted (MT-w) images (ω/2π=150 Hz, τm=3 sec) with the saturation frequency swept from -100 ppm (-40 kHz) to 100 ppm (40 kHz) in 5 ppm (2 kHz) steps. An unsaturated image (S0) was also acquired with the same τm but ω/2π=0.

In vivo MRI: A 10 mM CESTLys SL (mice bearing the CD45.1 alloantigen (Jackson Labs) and B78-H1 GM-CSF-expressing bystander melanoma cells) to produce an immunoresponsive enlargement of the popliteal lymph nodes 1 week prior to DL injection. Fresh L DLS (~ 100 nm) were prepared as described previously, and intradermally injected (40 μL, ~30 mM DL solutions) into the right hind footpad of mice. In vivo CEST-MRI was conducted on a horizontal 9.4T Bruker scanner 24 hours after injection using the method described previously. The MT-w images were acquired at -12.5 ppm and -50 ppm using ω/2π=150Hz, τm=3 sec.

RESULTS AND DISCUSSION

Based on the previous studies and our simulations, we proposed to use MT-w images at -12.5 ppm to separate tissue pixels where CEST agent may localize. To reduce the possible influence of B1 inhomogeneity, we normalized S(-12.5 ppm) with a reference image, S(-50 ppm), to produce a new metric, NOMAR. To prove this NOMAR value can effectively separate tissues with different semi-solid concentrations, we first tested it on a phantom containing tubes either with or without the CEST contrast agent (10 mM Larg) embedded in cross-linked BSA (0-20%). As shown in Figs. 1A&B, the NOMAR value strongly correlated with the BSA (or water) concentration, varying from 1.00 to 0.37 as BSA concentration increased from 0 to 20%. With the histogram shown in Fig. 1C, we could determine the separation threshold for the concentration of BSA. As shown in Fig 1D, compartment-selective CEST contrast maps were produced by applying NOMAR filters at 0.8 or 0.67 to remove pixels containing the lowest concentrations of BSA (i.e. 0% and 5% BSA respectively). The presence of CEST agents did not significantly alter the segmentation. By filtering with an appropriate NOMAR threshold, the CEST contrast in samples containing higher BSA content was retained without the interference from those in lower BSA samples. For samples with BSA >15%, the CEST contrast disappeared, presumably due to interactions between the compounds resulting in a reduction in exchange rate. We then applied NOMAR filtering to produce tissue-selective CEST contrast maps in vivo. Figs. 2A&2B show the T1-w and NOMAR images for a mouse injected with Large DLS, with the injected leg on the left of the image. A WASSR B0 map is shown in Fig. 2C, with the variation in B0 ~1000Hz (2.5 ppm). Figs. 2D and 2E show that, filtering by NOMAR < 0.7 produces a CEST mapping contrast only within the lymph node by effectively separating ‘hot spots’ (yellow and blue arrowheads), which are likely induced by residual fat or fluid. This separation is verified by the mean MTR_pym plots of the selected ROI. This example clearly shows that tissue selection reduces the possibility of misinterpreted CEST signal due to erroneous tissues becoming contrast-enhanced, as facilitated by our NOMAR filter. The use of NOMAR is expected to be insensitive to small to moderate B1 inhomogeneities (i.e. B0 shifts <1 ppm) and B1 inhomogeneities.

CONCLUSION

We proposed a new NOMAR segmentation technique for “cleaning up” CEST images. This can be accomplished by simply adding an acquisition of two additional saturation images to a CEST study.

REFERENCES