Molecular imaging of brain with multiple sclerosis using CEST MRI at clinical 3T

Ziyan Wang[1], Yingying Lin[1], Peng Cao[1], Chia-Wei Lee[2], Pei Cai[1], Jiawen Wang[1], Chi Yan Lee[3], Kyongtae Ty Bae[1], Henry KF Mak[1], Kannie WY Chan[4-5], Koon Ho Chan[3], Jianpan Huang[1*]

*[1] Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong, China; [2] Research Group, GE Healthcare, Taipei, Taiwan; [3] Department of Medicine, The University of Hong Kong, Hong Kong, China; [4] Department of Biomedical Engineering, City University of Hong Kong, Hong Kong, China; [5] Hong Kong Centre for Cerebro-cardiovascular Health Engineering; * Corresponding Author.*

INTRODUCTION: Multiple sclerosis (MS) is a predominant autoimmune disorder characterized by demyelination and axonal damage[1]. Timely and effective diagnosis and intervention are critical in managing the condition. Chemical exchange saturation transfer (CEST) MRI is a molecular imaging technique that can selectively saturate exogenous or endogenous molecules containing exchangeable protons by applying targeted radiofrequency pulses[2]. Lipids and proteins, which are highly abundant in myelin, are detectable by CEST MRI[3-7]. Our study aims to investigate the clinical potential of using CEST MRI technique for molecular imaging of MS pathologies in the human brain at 3T.

METHODS: The research was approved by the local institutional review board and conducted according to the guidelines. 43 consecutive subjects (29 healthy controls and 21 MS patients) were included in this study. Informed consent was obtained from each subject. All MRI scans were performed on a GE Signa 3T scanner. CEST sequence was a continuous-wave (CW) saturation module followed by a 3D CUBE readout module. The saturation parameters were set as follows: saturation power (B_1)=0.8 μT, saturation length (t_{sat})=2 s. M_0 images at frequency offset of -300 ppm and 43 CEST images at frequency offsets ranging from -20 to 20 ppm were acquired. Other MRI readout parameters were as follows: repetition time (TR)=3.5 s, echo time (TE)=60 ms, field of view (FOV)=220×220×72 mm^3, reconstruction matrix size=256×256×12, slice thickness=6 mm, voxel size = 1.7 × 3.4 × 12 mm^3. The scan time for each CEST dataset was about 10 minutes. Data analysis was performed using custom-written code in MATLAB (MathWorks, USA). Amide at 3.5 ppm, relayed nuclear Overhauser effect (rNOE) at −3.5 ppm, and magnetization transfer (MT) at −2.5 ppm was extracted using multi-pool Lorentzian fitting (MPLF). Lorentzian difference analysis (LDA) and magnetization transfer ratio asymmetry (MTR_{asym}) were performed for comparison.

RESULTS & DISCUSSION: Fig. 1 shows the comparison of CEST maps between a MS patient and a HC subject, using three analysis methods. Through comparison, it was evident that MS brain displayed increased heterogeneity in brain regions as well as larger ventricle regions (indicated by blue arrow) in all CEST maps generated by three different analysis methods. These observations can be attributed to the processes of demyelination and brain atrophy. In the group comparison (Fig. 2), the CEST signals MS group were significantly lower compared to those of the HC group using three different analysis methods (MPLF: p=0.0347 for amide, p<0.0001 for rNOE and p<0.0001 for MT; LDA: p=0.0008 for amide, p<0.0001 for rNOE; MTR_{asmy}: p=0.004 for amide). Notably, MPLF method exhibited the highest performance in distinguishing MS patients from HC subjects, as evidenced by the highest area under the curve (AUC) value of 0.938 in the receiver operating characteristic (ROC) curve (Fig. 3D). This superiority can be attributed to the MPLF's ability to effectively separate and extract multiple CEST contrasts compared to the LDA and MTR_{asym} methods. These findings underscore the importance of selecting the appropriate analysis method when investigating MS using CEST MRI. Clinical assessments, such as the expanded disability status scale (EDSS), will be useful in correlation analysis between CEST MRI and disability levels in MS.

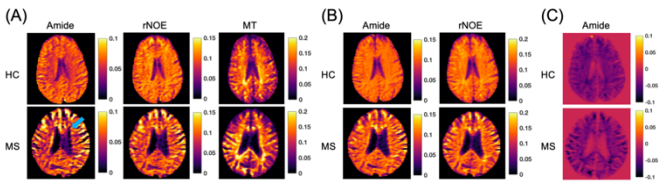

Fig.1. CEST maps of a HC and a MS patient extracted by three methods. (A) MPLF. (B) LDA. (C) MTR_{asym}.

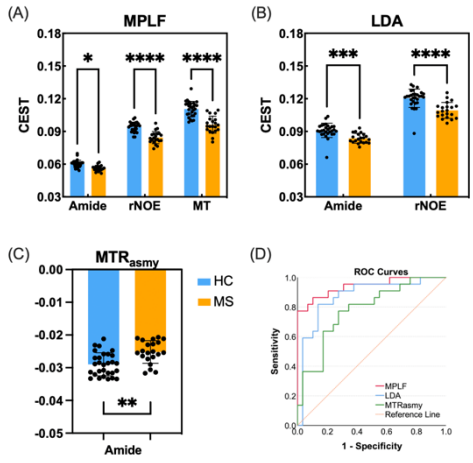

Fig.2. Group comparison of HC with MS using different CEST analysis methods. (A) MPLF. (B) LDA. (C) MTR_{asym}. (D) ROC curves of three methods in differentiating MS from NC. AUC (MPLF)=0.938, AUC (LDA)=0.867, AUC (MTR_{asmy})=0.777.

CONCLUSION: This study investigated the utility of CEST MRI in imaging the MS brains. The results revealed a significant decrease in CEST signals in MS patients compared to HC subjects. All three CEST analysis methods demonstrated the ability to differentiate between MS and HC, with MPLF exhibiting the highest performance. These findings highlight the potential of CEST MRI in detecting molecular changes in the brains of MS patients, thereby offering supplementary information for MS diagnosis.

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