pH-weighted imaging in diabetes mellitus suffering acute cerebral ischemic stroke

Zhuozhi Dai[1,2], Yanlong Jia[2], Gen Yan[2], Fei Duan[2], Gang Xiao[3], Zhiwei Shen[4], Hongfu Sun[1], Alan H. Wilman[1], and Renhua Wu[2,4]

[1]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada, [2]Medical Imaging, 2nd Affiliated Hospital, Shantou University Medical College, Shantou, Guangdong, China, [3]Math and Information Technology, Hanshan Normal University, Guangdong, China, [4]Provincial Key Laboratory of Medical Molecular Imaging, Guangdong, China

Purpose: The presence of diabetes increases the risk and severity of stroke. Diabetic stroke has poorer functional outcomes and higher mortality rates than non-diabetic stroke, but conventional MRI examinations cannot distinguish between diabetic and non-diabetic stroke. The purpose of our study was to determine the specificity to diabetic stroke of amide proton transfer[1,2], a novel pH-weighted imaging method.

Materials and Methods:

Animal models: Diabetes models were produced in four adult male Sprague-Dawley (SD) rats by intraperitoneal injection of streptozotocin. Animals were fed with a normal diet for three months, while blood sugar was monitored every five days to ensure levels of ~ 30 mM. After 3 months, permanent middle cerebral artery occlusion (MCAO) was produced using thread embolism on the diabetic group and on an age and sex matched healthy control group.

MRI: Data were collected in the first 3 hours after occlusion at 7.0 T on an animal MRI system using a standard body coil for RF pulse transmitting and receiving. Image sequences included pH-weighted imaging, Z-spectra, diffusion-weighted imaging, T1-weighted imaging and T2-weighted imaging. We used a continuous wave as the presaturated component, saturation time 5 s, saturation power 0.75 μT, amino proton frequency offset 3.5ppm, reference offset -3.5 ppm. For Z-spectra, we serially altered the frequency offset from -4.7 ppm to 4.7 ppm, in steps of 0.2 ppm. We used single-shot echo planar imaging (EPI) as a readout component to obtain images and Point Resolved Spectroscopy sequence to obtain the Z-spectra. Others parameters for EPI were set as follows: TR 6000 ms, TE 6ms, Number of average 32, bandwidth 50 kHz, imaging matrix 64 × 64.

Analysis: All the data were post-processed using in-house programs in Matlab. MTR asymmetric analysis methods were used to calculate pH-weighted images. Regions of interest (ROIs) were drawn on the ischemic lesions and contralateral normal regions both in diabetes and non-diabetes. Assessment of the contrast between the diabetes and non-diabetes was performed via paired t-test. Values were presented as mean ± SD, and $p < 0.05$ was considered as statistically significant.

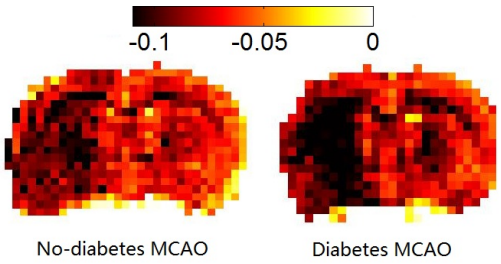

Fig. 1 pH-weighted imaging in diabetic and non-diabetic MCAO. The signal intensity in diabetic ischemic lesion was significantly decreased.

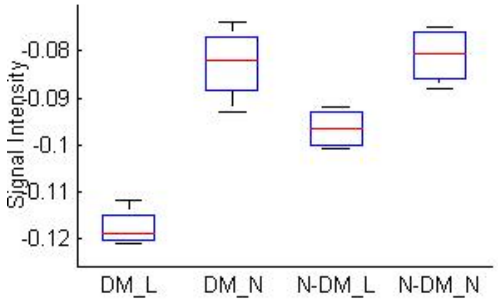

Fig. 2 MTR asymmetry signal intensity of different regions using ROI analysis. There was significant distinction in the ischemic lesions between diabetic and non-diabetic MCAO, but no distinction in contralateral normal regions.

Results and discussion: As expected, there was no visible difference between the diabetic (DM) and non-diabetic (N-DM) MCAO models in routine MRI. In pH-weighted imaging (Figs. 1, 2), the signal in the ischemic lesion in DM was significantly lower than that in N-DM ($p < 0.05$), which indicated a more substantial decrease in pH in DM after occlusion. However, the signals in the contralateral normal regions in DM and N-DM were essentially identical, meaning the pH values were not correlative with the level of blood sugar under normal supply of blood and oxygen. In the Z spectra (Fig. 3), there is clear distinction at about 3.5 ppm between the DM lesion, N-DM lesion and normal region, which further verifies our pH-weighted imaging results, because the amide proton concentration was constant in the first three hours after occlusion.

Conclusion: To our knowledge this is the first report on pH-weighted imaging in diabetic stroke models. We obtained a significant pH decrease in the ischemic lesion in diabetes compared with non-diabetes in vivo, which may provide a marker of specificity of diabetic stroke.

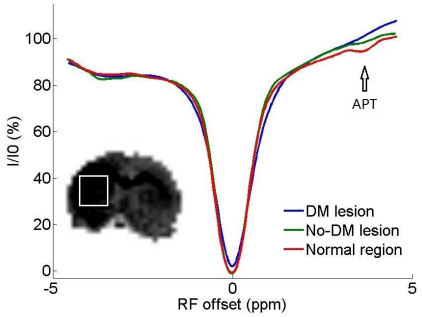

Fig. 3 Z-spectra of diabetic ischemic lesion, Non-diabetic ischemic lesion and controlateral normal region. there was clear distinction at about 3.5 ppm.

References: [1] Nature Medicine. 2003;9: 1085-1090. [2] Nature Medicine. 2011;17: 130-134.