Amide proton transfer (APT) imaging of acute cerebral infarction: a preliminary study on clinical patients

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Introduction

Amide proton transfer (APT) imaging is a type of chemical exchange saturation transfer (CEST) imaging which is based on exchange of protons between amides (-NH) and water molecules. APT signal is known to be influenced by pH: lowered pH results in reduced APT signal through reduced proton exchange rate. Previous animal experiments have shown that APT imaging can detect lowered pH due to anaerobic metabolism during acute ischemia. Moreover, it may be useful to detect ischemic penumbra. However, there is no report on a systematic study of ATP imaging in human stroke patients. Our purpose was to examine the feasibility of APT imaging in assessing clinical acute cerebral infarction.

Materials and Methods

We included 8 patients with acute cerebral infarction (M/F = 3/5; median age = 76 years) (Table). Each patient was scanned using a 3T clinical whole-body MR scanner implemented with the parallel RF transmission (Achieva TX, Philips HealthCare, Best, the Netherlands) and an 8-channel head array-coil. APT imaging was performed using a single-slice fast spin echo sequence with driven equilibrium. The strength of the saturation pulse was 2 μT. In order to evaluate the effect of saturation time on APT contrast, 3 different saturation times (Tsat = 0.5, 1, and 2 s) were used for each patient. 25 offset frequencies ranging from -6 to 6 ppm with respect to the water resonance frequency were used to obtain a z-spectrum. The offset frequency of the reference image for normalization was -160 ppm. Other imaging parameters were as follows: TR/TE = 5000 ms/6 ms; FOV = 230x230 mm^2; matrix = 128x128, slice thickness = 5 mm, NSA = 1. The imaging time was 2 min 20 s. A separate scan for B0 mapping was performed for B0 inhomogeneity correction. Diffusion-weighted imaging (DWI) (b=0 and 1000 s/mm^2) was performed as a part of our clinical routine for acute infarction. After corrections for patients' motion and B0 inhomogeneity, APT-weighted images were generated by mapping the asymmetry of magnetization transfer ratio at 3.5 ppm ($MTR_{asym[3.5ppm]}$), which corresponds to the offset frequency for amide protons. Regions-of-interest were drawn within the infarcted tissue defined by DWI as well as within the normal white matter. A mean value of APT signal ($MTR_{asym[3.5ppm]}$) was obtained for each ROI. In addition, APT contrast was calculated as the difference in APT signal between the infarction and normal tissue (normal-infarction). APT signals were compared between the infarcted and normal tissues using the least square means Student's t test. APT contrast was compared among 3 different saturation times using the Tukey HSD test.

Results

APT signal within infarcted tissue (1.08±0.51%, 0.97±0.58%, and 0.56±0.44% for Tsat=0.5, 1, and 2 s, respectively) was significantly lower than that in the normal white matter (2.05±0.59%, 1.63±0.47%, and 0.91±0.47% for Tsat=0.5, 1, and 2 s, respectively) (P<0.05). APT contrast was significantly affected by the saturation time (P<0.05). Pair-wise comparisons revealed that APT contrast with Tsat=2 s (0.46±0.65%) was significantly lower than that with Tsat=0.5 s (1.08±0.85%) (P<0.05) (Figure 1). A representative case is shown in Figure 2.

Discussion

Reduced APT signal in infarcted tissue is consistent with previous animal and human studies. Our results demonstrated the feasibility of APT imaging in clinical patients with acute cerebral infarction. Furthermore, we found that a longer saturation time (2 s) can result in reduced APT contrast between normal and infarcted tissue, suggesting the importance of optimizing imaging parameters.

References

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Table: Patient characteristics

Time after onset	<24 hrs	3 (3, 10, 19 hrs)
	24-48 hrs	3
	48-96 hrs	2
Location	MCA	5 (R2, L3)
	PCA	1 (L1)
	Multiple	2
Classification	Cardioembolic	6
	Atherothrombotic	2

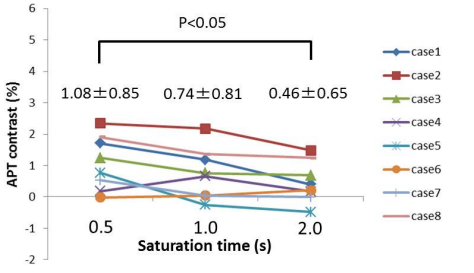

Figure 1: APT contrast ($\Delta MTR_{asym[3.5ppm]}$) compared among 3 different saturation times.

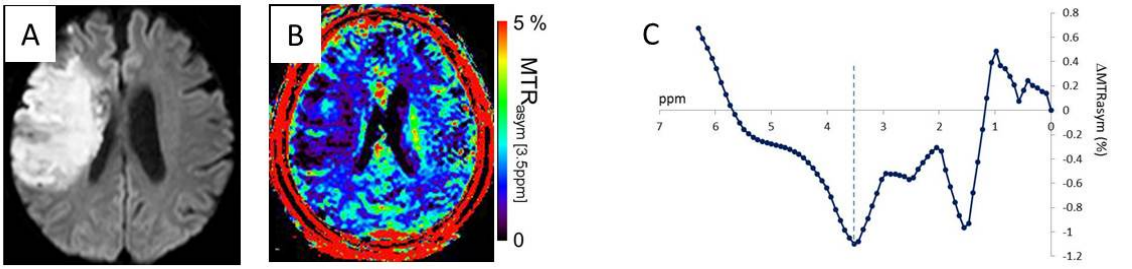

Figure 2: 76-year old man with right MCA infarction (48 hrs after onset). (A) DWI clearly shows a hyperintense lesion. (B) APT signal ($MTR_{asym\ [3.5ppm]}$) is reduced in the infarction (saturation time = 0.5 s). (C) Plot of ΔMTRasym shows a negative peak at 3.5 ppm, corresponding to the APT offset frequency.