ZAPI analysis of Z-spectral components in acute cerebral ischemia

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Introduction Z-spectroscopy provides a tool to investigate both magnetization transfer (MT) and exchange *in vivo* [1]. The exchanging species, mainly amides around +3.5 ppm from free water, result in a dip in the Z-spectrum. A similar dip in the Z-spectrum is produced by MT of aliphatic protons a few ppm upfield from water. MT produces a broad, flat signal drop stretching over tens of ppm. On top of that, direct saturation of water (DS) overlaps with the other components. Separation of these is complicated but often necessary, and a method ZAPI [2], based on T_2-selective saturation of the MT component, is applied here in experimental focal cerebral ischemia of rat.

Theory The phase of the low amplitude saturating irradiation is manipulated to discriminate between short and long T_2 species. If the irradiation uses constant phase (Cφ), a normal Z-spectrum is obtained. If the phase of the irradiation is alternated (Aφ) 0°, 180°, 0°, 180* ..., the saturation of macromolecules ($T_2 << \tau$) remains, whereas long T_2 signals on resonance will not be saturated. Low power Aφ ZAPI at 0 Hz offset detects pure MT; a similar effect can be achieved with more complex saturation patterns [3].

Methods Male Wistar rats (N = 13) were anesthetized with isoflurane for 60 min middle cerebral artery occlusion. MRI was carried out during the reperfusion phase using a Magnex 4.7 T magnet interfaced to a Varian Inova console. Timepoints for ZAPI were 2, 3 and 24 hours from the onset of stroke. Saturation time was 5 s, relaxation delay 7 s and CW (Cφ, $\gamma B_1/2\pi$ = 50 Hz) or sinusoidally modulated (Aφ, 10 kHz modulation, peak $\gamma B_1/2\pi = \sqrt{2} \times 50$ Hz) saturation was applied at 250 ppm (reference) and ±3.75, ±3.5, ±3.25, ±3 ±0.9, ±0.5, ±0.25 and 0 ppm for Cφ, and ±3.5, ±3.25 and 0 ppm for Aφ (all offsets are from free water).

The images were acquired with a fast spin echo (128x64 pixels, 25.6 x 25.6 x 1 mm^3 FOV, 16 echoes, τ 6 ms). The centers of the Z-spectra were shifted to 0 Hz and ROIs covering the ischemic and the contralateral striatum were studied. The data were normalized to the reference images. The amount of pure MT was measured at 0 Hz (label A in Fig.1). Both the amide (B in Fig.1) and aliphatic features (C in Fig.1) were analyzed. Also the asymmetries of MT (A1-A2 in Fig.1) and of the Z-spectrum at 3.5 ppm (D in Fig.1) were computed.

Results In agreement with [4], MT decreased in ischemic tissue, as evident in Aφ ZAPI at 0 Hz offset, parameter A in Fig 2. In the non-ischemic hemisphere, MT asymmetry is slightly negative, in line with a recent paper [5], and the asymmetry seems to disappear in ischemic brain (not statistically significant). As shown in Fig 3, there was no change in the aliphatic feature at -3.5 ppm (par. C) in acute ischemia while the amide exchange slowed down (par. B; +3.5 ppm dip decreased), as expected [1]. At 24 h, increase in T_2 exceeds the increase in T_1, leading to reduction of DS near water. This over-compensates the decrease in MT (Fig 4), resulting in a drop in pars. B and C at 24 h.

Discussion and Conclusions

ZAPI can be used to differentiate Z-spectral features: to estimate MT at water resonance and MT asymmetry, or to quantify the MT component of Cφ data (leaving exchange and DS contributions). The analysis of amide and other long T_2 components is less sensitive to inaccurate water offset in ZAPI than in methods based on asymmetry, and studies of the semisolid pool via MT asymmetry [5] may be easier.

The present results show a long-lasting decrease in amide exchange in ischemia that behaves differently to the MT during evolution of ischemic stroke. It also shows that aliphatic Z-spectral features are not influenced by acute ischemia.

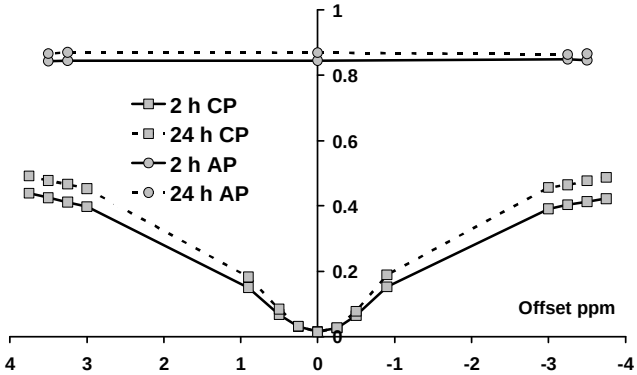

Fig. 4 Evolution of Z-spectra from 2 h (solid) to 24 h (dotted line) during ischemia

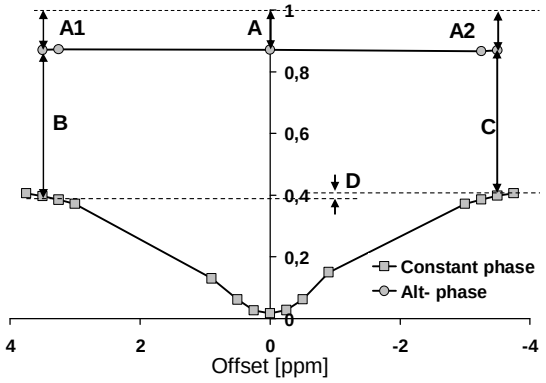

Fig. 1 *in vivo* Z-spectra, circles = Aφ, squares = Cφ: Calculation of parameters A, B, C and D is shown.

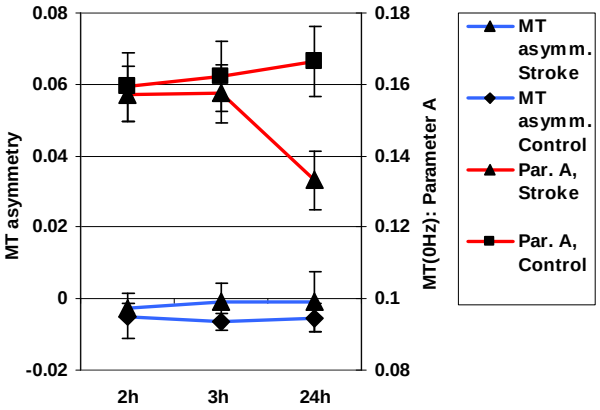

Fig. 2 MT asymmetry (blue) and pure MT (red) in Aφ.

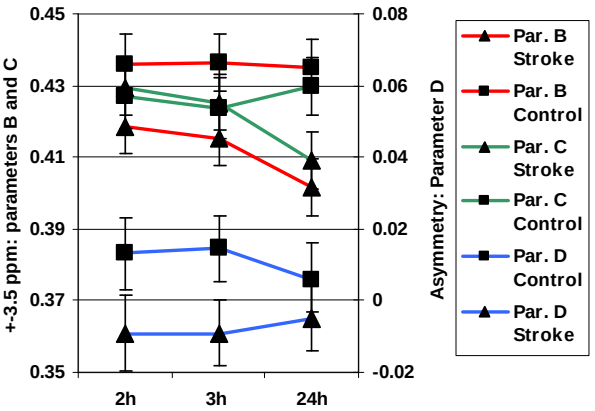

Fig. 3 Analysis of amides (B, red), Aliphatics(C, green) and Cφ asymmetry at 3.5 ppm (D, blue).

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