Multi-parametric stroke imaging protocol for mice using a 1H cryo probe at 9.4 T

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Introduction

For the investigation of focal cerebral ischemic models in the mouse brain, in particular during follow-up studies, realization of adequate spatial resolution and contrast in acceptable measurement times remains a challenge. In the present work we present a 26 min protocol for stroke imaging at 9.4 T using a 1H surface cryo coil [1]. Furthermore, the infarcted regions of mice with a permanent occlusion of the right middle cerebral artery (MCA) were compared to those of mice which underwent recombinant tissue plasminogen activator (rt-PA) therapy.

Methods

Ten male *C57 black/6J* mice (Charles River, Germany), weighing 20 to 25 g, were used throughout the study. Middle cerebral artery occlusion (MCAo) was induced as described by Orset et al [2]. Briefly, the MCA was exposed by a small craniotomy. A micropipette was introduced into the lumen of the MCA and 2 µl (1,5 U) of purified murine alpha-thrombin were injected to induce the formation of a clot. In a second group (n = 5), additionally rt-PA (10mg/ml; Actilyse) was intravenously injected into the tail vein 40 minutes after MCAo to induce thrombolysis. 10 % of rt-PA were administered as a bolus and 90 % by perfusion during 40 minutes.

The imaging experiments were performed on a 9.4 T Biospec 94/20 USR (Bruker. Germany) small animal system equipped with 740 mT/m gradients and a 1H surface cryo probe (Bruker, Germany).

24 hours after MCAo (and rt-PA administration respectively) the animals were anesthetized with 1.5-2 % isoflurane and positioned into the magnet with a laser controlled system for the animal cradles. Respiratory frequency and body temperature were monitored throughout the experiment and the latter was maintained with a water heating pad.

The protocol consisted of a T2-weighted RARE sequence, a diffusion weighted EPI sequence and a 3D flow-compensated gradient echo TOF angiography. Sequence parameters were set as follows.

RARE: TR = 2.5 s; TE = 60 ms; echo train length = 4; 4 averages; matrix size = 384 x 384; FOV = 17 x 17 mm^2; slice thickness = 0.4 mm; measurement time (12 slices) = 6 min 40 s.

EPI-Diffusion: TR = 3 s; TE = 20 ms; 4 averages; matrix size = 128 x 128; slice thickness = 0.4 mm; 3 orthogonal diffusion directions with three b-values b = 0, 100 s/mm^2, 1000 s/mm^2; measurement time (12 slices) = 5 min 36 s.

3D-TOF: TR = 22 ms; TE = 3.9 ms; flip angle = 40°; matrix size: 256 x 256 x 128; FOV = 16 x 16 x 16 mm^3; measurement time = 15 min 46 s.

Results

The measurement time for the whole protocol was 26 min. Positioning, shimming and multi-parametric imaging were performed in less than 40 minutes. Fig.1 exemplarily illustrates the results of one representative mouse 24 hours after MCAo. The T2-weighted images (Fig.1a) clearly reveal the infarcted region. The ADC maps (Fig.1b), calculated from the diffusion weighted images, present a significant signal decrease in the same region. Fig.1c shows maximum intensity projections (MIP) of the 3D-TOF measurement along the transversal (left) and coronal (right) direction. No flow signal is detectable posterior to the occlusion.

In comparison, Fig.2 illustrates the results of one representative mouse 24 hours after MCAo and subsequent rt-PA therapy. T2-weighted images (Fig.2a) show a strongly reduced infarcted region. The ADC maps in Fig.2b confirm this observation. Decreased ADC signal was measured in the infarcted areas, marked with arrows in Fig.2b. The TOF-MIP in Fig.2c demonstrates that reperfusion of the MCA was achieved by the rt-PA therapy.

Discussion and Conclusions

With the experimental setup and the described protocol it was possible to acquire T2-weighted images, ADC maps and TOF-MIPs within a measurement time of 26 minutes. All images are of high contrast in the infarcted region. The short measurement time will allow us in future temporal evolution studies to perform the whole protocol in the time between MCAo and thrombolysis. Thus, the protocol is suitable for both, detection of the MCAo success immediately after surgery and temporal evolution studies of the infarcted regions after rt-PA therapy. In a present longitudinal study the signal time curves after surgery of both animal groups are investigated. The short measurement time of the protocol allows high temporal resolution at good image quality and high stroke/tissue contrast.

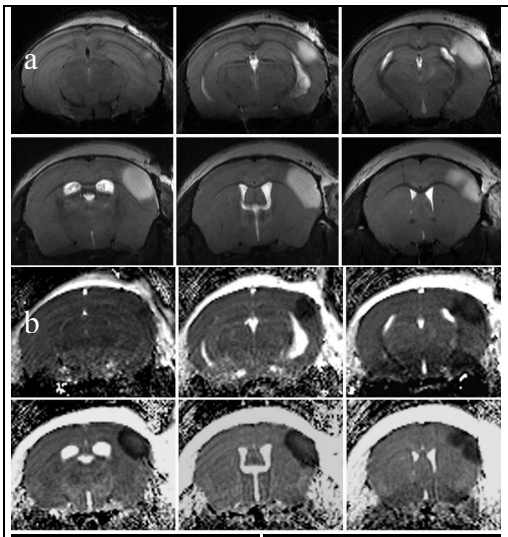


Figure 1:
a) T2-weighted RARE images of consecutive slices acquired 24 hours after MCAo (echo train length = 4, TE/TR = 60 ms/2.5 s) clearly reveal the infarcted region.

b) ADC maps, calculated from the diffusion weighted images, show a significant decrease of the ADC in the apoplexic region. Slice positioning is identical to Fig. 1

c) Transversal (left) and coronal (right) MIPs of the TOF of the mouse brain after MCAo (TE/TR=3.9/22 ms, flip angle=40°, 2 averages). No flow is detectable posterior of the MCAo (arrow).

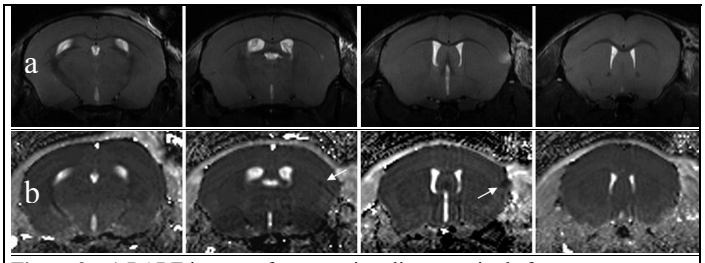
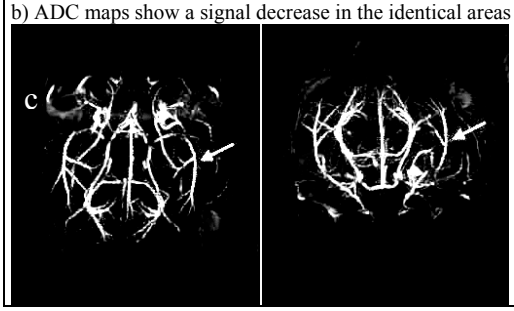


Figure 2: a) RARE images of consecutive slices acquired after MCAo and subsequent administration of rt-PA possess only a small residual infarcted region.
b) ADC maps show a signal decrease in the identical areas (arrows).



c) Transversal (left) and coronal (right) MIPs of the TOF of the mouse brain after MCAo and subsequent rt-PA administration. The MCA is reperfused posterior to the occlusion.

Acknowledgements

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References [1] Ratering D et al. Magn Reson Med 59: 1440-7 (2008); [2] Orset C et al. Stroke 38: 2771-78 (2007).