Diffusion tensor echo planar imaging of mouse brain after brief focal middle cerebral artery occlusion at 14T

H. Lei[1,2], Y. Van de Looij[1,3], N. Kunz[1,3], C. Berthet[4], L. Hirt[4], and R. Gruetter[1,5]

[1]LIFMET, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [2]Radiology, University of Lausanne, Lausanne, Switzerland, [3]Pediatrics, University of Geneva, Geneva, Switzerland, [4]Neurology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, [5]Radiology, University of Geneva, Geneva, Switzerland

INTRODUCTION DWI has been shown to detect acute ischemia and identify ischemic lesion at early stage when no abnormal T2WI and CBF (1,2 and references therein). Additionally, the change of ADC could help predicting ischemic damages (3). Accurate determination of ADC required the acquisition of the full diffusion tensor. Indeed, diffusion tensor imaging (DTI) has shown remarkable results in assessing tissue microstructure information but remains time consuming because of a minimum seven experiments with different gradient orientations. Recent studies suggested that quality EPI images of rat brains using a surface coil at high magnetic fields, could be acquired, such as single shot or segmented approaches (4,5). However, magnetic susceptibilities magnified with increases in both magnetic fields and surface-to-volume ratio in mouse brain. Even though, studies demonstrated that measuring ischemic mice using MRS were feasible at high magnetic fields and sustained tremendous metabolic information (6). Thus, we sought to establish the feasibility of DTI measurements on mouse brain using EPI, which allow precise measurements of ADC and could open possibilities to study ischemic mice for additional functional status at high magnetic fields, such as fMRI and CBF etc. On the other hand, localized ^{1}H MRS could be applied more precisely to extend biochemical information for better understanding reversible and irreversible ischemia evolution (7). The aim of this study was to evaluate the feasibility of DTI using segmented SE-EPI at 14.1T.

METHODS All animal experiments were approved by the local veterinary authorities. Six adult iCR-CD1 mice (male, 22-35g) were subjected to brief endoluminal middle cerebral artery occlusion (MCAO) by the filament technique at 0-hr under 2-2.2% isoflurane mixed with N_2O:O_2 in a 2:1 ratio. 10 minutes later, the filament was withdrawn and animal was prepared for MR studies. Throughout the entire procedures and measurements, animals were remained anesthetized under 1-2% isoflurane and well-maintained rectal temperature in the range of 35-37°C. All MR experiments were performed on a 14.1T/26cm horizontal magnet inserted with a 12-cm gradient coil (400mT/m, 120µs). A home-built quadrature coil with two physically decoupled 12mm-diameter loops in a half volume shape was used as RF transceiver. Immediately after stereotaxically fixing mouse brain and adjusting the field homogeneities over the region of interests (ROIs) (3,4 and references therein), approximately ~30 min after removing filaments, DT images were acquired using segmented (4 shots) semi-adiabatic double spin echo EPI (RO×PE=23×15mm^2, 128×64 data matrix) with additional diffusion gradients (G_{diff}=21G/cm, δ=3ms, Δ=20ms and giving a *b*-value of 1079s/mm^2) along 14 directions: dual gradient 7 directions as well as the 7 opposite directions to cancel *b*-value cross terms(8). 5 of 0.8-mm-thickness contiguous coronal slices were acquired with TE/TR=42.5/2000ms and 7 averages. Nyquist ghosts were minimized by adopting a previously described "negative readout gradient" strategy (8). The total scan time was 17 minutes. ADC maps were derived from the acquired DT images using Matlab. Four different ROIs were analyzed over the slices including striatum: ipsilateral striatum and cortex; contralateral striatum and cortex. Localized ^{1}H MRS was measured on one of mouse at 8h with abnormal ADC expressed using SPECIAL (6 and references therein).

RESULTS AND DISCUSSION

Segmented semi-adiabatic SE-EPI images of mouse brain at14T were obtained with a maximum coverage, minimal artifacts and well-defined anatomical information (Figure 1b) when comparing to the T2WI images (Figure 1a). In consequence, the derived ADC maps from the DT images presented well-define anatomical structures (Figure 1c). In the ADC maps at 30-min after ischemia, we did observe a slight (1.3%) but not significant reduction in striatum between ipsilateral and contralateral (Figure 1c and Table 1). However, the ipsilateral cortical tissues presented a small but significant reduction in ADC values (5.7%, p=0.028). The different ADC recoveries after brief ischemia in striatial and cortical tissues observed here was close to previous rat results (1), in which no significant difference was observed. This could be explained by the increased precision in the ADC maps derived from the full diffusion tensor in this study. In summary, quality EPI images of mouse brains at 14T were feasible and thus allowed studying functional status of mouse after ischemia, such as DTI, CBF and fMRI etc. In addition, accurate measurements of the ADC maps could help us improve localizing ischemic cores when no abnormal CBF or T2WI were appeared, such as 8 h after reperfusion of brief MCAO (Figure 2a), which is nearly reflecting the ischemic lesion observed at 24h (Figure 2c).

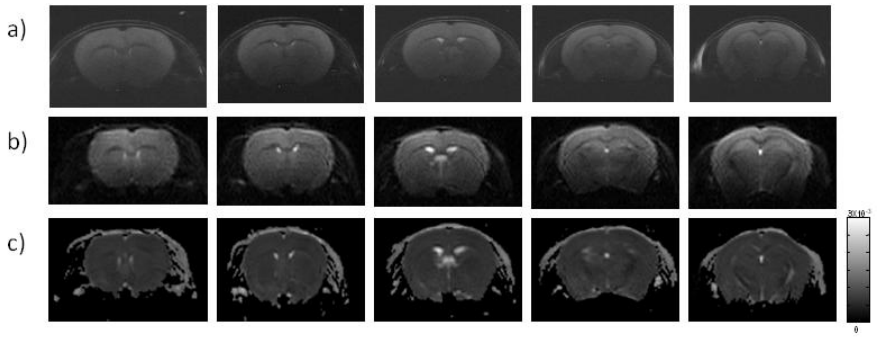

Figure 1 Fast spin echo images (a, TE/TR=50/4000ms, ETL=16, NT=2), segmented semi-adiabatic double SE-EPI images (b, TE/TR=40/2000ms, zero-filled to 256×167 data matrix) and ADC maps (c) of one mouse brain 30 minutes after 10-min transient focal ischemia. No observable ADC reductions were appeared. The scale for ADC maps were from 0 to 30×10^{-4}mm^2/s.

REFERENCES 1. Sicard KM et al. J Cereb Blood Flow Metab 2006; 26: 1451-1462; 2. Li FH et al. Stroke 2000; 31(4):946-954; 3. Hasegawa Y eta l. Neurology 1994; 44:1484; 4. Lei H et al. Magn Reson Imaging 2008 ; 26(7) :954-960; 5. Kunz N et al. Proc Intl Soc Mag Reson Med 17, 2009; 6. Lei H et al. J. Cereb Blood Flow Metab. 2009; 29(4):811-819; 7. Lei H et al. Proc Intl Soc Mag Reson Med 17, 2009; 8. Neeman M. et al. Magn Res Med 1991 21(1):138-143 9. van der Zwaag W et al.J Magn Reson Imaging 2009; 30(5):1171-1178.

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	ipsilateral	contralateral
striatum	5.88± 0.13	5.96± 0.22
cortex	5.74± 0.20*	6.09± 0.17

Table 1: ADC values measured in the ROIs 30 minutes after ischemia. ADC values are expressed in units of ×10^{-4} mm^2/s. "*" indicated significant difference with p-value = 0.028 using student paired two-tailed ttest.

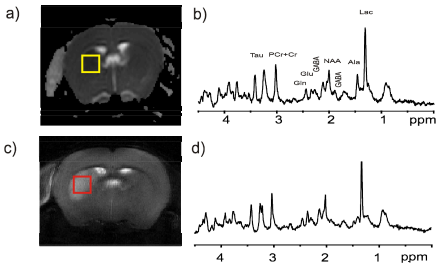

Figure 2 ADC map at 8h (a), T2WI image at 24h (c) of one mouse and MR spectra at 8 (c) and 24h (d). The spectra (SPECIAL, TE/TR=2.8/4000ms, NT=360) (5) was acquired from abnormal ADC region (yellow square, 1.4×1.2×1.6mm^3) at 8h (b) and T_2-hyper-intensive regions (red square, 1.4×1.2×1.6mm^3) at 24h (d), and displayed with Gaussian apodization (gf=0.15s).