Demonstration of fast diffusion kurtosis MRI for imaging acute ischemic stroke diffusion/kurtosis lesion mismatch

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Purpose DWI captures acute ischemic tissue that is likely to infarct and has become one of the most widely used techniques for acute stroke imaging [1]. However, the graded ischemic tissue injury could not be reliably segmented using the severity of apparent diffusion coefficient (ADC) drop, while there is no well-established imaging method for stratification of DWI lesions[2]. To this end, diffusion kurtosis, an index that measures non-Gaussian diffusion of water molecules, has been investigated for stroke imaging. Recent studies have shown that DWI lesions with no change in mean kurtosis (MK) are likely to respond favorably to early reperfusion while lesions with abnormalities in both mean diffusion (MD) and mean kurtosis show poor recovery, suggesting that diffusion kurtosis imaging (DKI) is capable of stratifying the heterogeneously injured DWI lesion [3-5]. Because the standard DKI protocol requires collecting DWI images with multiple b values along varied diffusion directions, it results in relatively long acquisition times. Hansen et al. recently proposed a fast DKI acquisition and processing approach and demonstrated its ability to map both apparent mean diffusion (MD') and apparent mean kurtosis (MK') in fixed brains and control subjects [6]. Our study evaluated the fast DKI scheme in an animal model of acute ischemic stroke prior to clinical translation.

Methods Animal model: Twenty-two rats were imaged, including 10 normal rats (n=10) and 12 stroke rats (n=12), following a standard intraluminal middle cerebral artery occlusion (MCAO) procedure. Two MCAO rats showed minimal ischemic lesions in striatum and were excluded from the analysis. MRI: All experiments were conducted at a 4.7T small-bore MRI scanner after acute MCAO. We acquired perfusion (TR/TS/TE=6500/3250/14.8ms, NSA=32), diffusion (TR/TE=3250/54ms, b=250, 500, 750, 1000, 1500, 2000, 2500, and 3000 s/mm^2, NSA=4), T_1 (inversion recovery, TI from 250 to 3000 ms, NSA=4) and T_2 (SE MRI, TR/TE1/TE2=3250/30/100 ms, NSA=16) MRI. Fast DKI MRI was obtained following the protocol of Hansen et al. In addition, cerebral blood flow (CBF) was acquired with arterial spin labeling (AM-ASL) EPI (TR/TE = 6500/14.8 ms, NSA = 32, time of saturation = 3250 ms). P-values less than 0.05 were considered statistically significant.

Results and Discussion Fig. 1 shows multi-slice CBF, MD', and MK' maps from a representative acute stroke rat. The contralateral normal CBF, MD' and MK' were determined to be 1.36 ± 0.19 ml/g. min, 0.86 ± 0.02 μm2/ms, 0.52 ± 0.03, respectively. Diffusion (Fig. 1a) and kurtosis (Fig. 1b) lesions in the ipsilateral ischemic brain were determined if MD' and MK' were two standard deviations beyond the mean. Because the coefficient of variation for CBF (14.0%) was substantially higher than that of MD' (2.3%) and MK' (5.8%), CBF threshold was set to be one standard deviation below its mean. Fig. 3 shows that the threshold-based tissue segmentation algorithm can provide reasonable delineation of heterogeneous ischemic tissue. CBF, MD' and MK' lesion volumes were found to be 218 ± 61 mm^3, 139 ± 82 mm^3 and 97 ± 55 mm^3, respectively. CBF lesion was significantly larger than MD' lesion (P=0.03, Paired t-test), consistent with the observation that there is substantial perfusion and diffusion mismatch immediately following ischemia. In addition, MK' lesion was significantly smaller than MD' lesion (P<0.01), supporting the prior finding that kurtosis lesion defines the most severely injured DWI lesion. We compared diffusion and kurtosis lesion size determined using the fast DKI method and the conventional DKI protocol (Fig. 2). We found significant correlation between MD and MD' lesions (R^2=0.93, P<0.01, Pearson Correlation) and between MK and MK' lesions (R^2=0.91, P<0.01, Pearson Correlation). This demonstrated that the fast DKI protocol provided good measurement of diffusion and kurtosis in imaging acute ischemic stroke, in excellent agreement with the conventional DKI protocol. In summary, our study showed that the size and severity of diffusion and kurtosis lesions obtained using the fast DKI approach significantly correlated with those obtained using the standard DKI protocol. Therefore, the fast stroke DKI method holds great promise for investigating the spatiotemporal evolution and therapeutic relevance of diffusion and kurtosis lesions, and ultimately facilitating translational kurtosis imaging in the acute stroke setting.

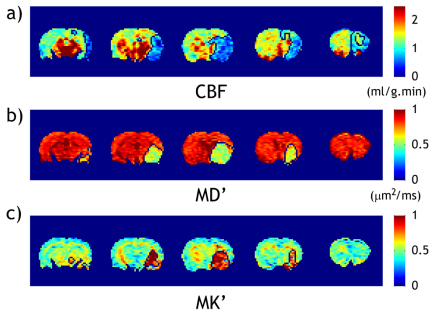

***Fig. 1**, CBF (a), MD' (b) and MK' (c) MRI from a representative acute stroke Wistar rat. Lesions were determined using a threshold based tissue segmentation algorithm.*

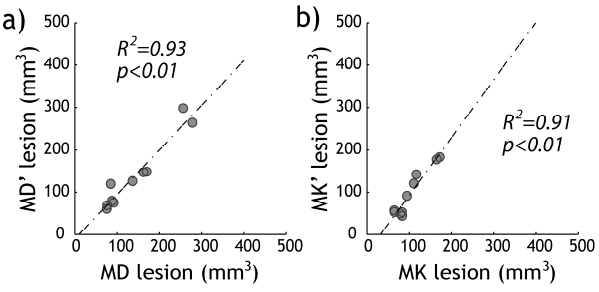

Fig. 2, Comparison of diffusion and kurtosis lesion determined from the standard DKI protocol and the fast DKI approach. a) MD lesion size vs. that of MD' (R2=0.93, P<0.01). b) MK lesion size vs. that of MK' (R2=0.91, P<0.01).

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