Enhanced tissue classification of acute ischemic diffusion kurtosis lesion with intrinsic kurtosis heterogeneity correction

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Purpose Kurtosis, a measure of non-Gaussian diffusion, has been introduced as a metric for imaging a host of neurological disorders[1-4]. Recent animal studies of transient ischemic stroke have demonstrated that mean kurtosis (MK) lesion captures the irreversibly damaged ischemic core, and hence, delineates the standard DWI lesion for improved stratification of graded ischemic tissue injury [5]. However, unlike the relatively homogeneous trace diffusion image, the complexity of cerebral structure and composition leads to a heterogeneous MK map, in which the specificity of kurtosis abnormality to ischemia is somewhat compromised [6]. A means to minimize the intrinsic cerebral tissue MK variation would thus enhance the conspicuity of the ischemic kurtosis lesion, to in turn facilitate the practical use of kurtosis MRI in the setting of acute stroke.

Methods Animal model: Seven normal rats (n=7) and fifteen stroke rats (n=15), following a standard intraluminal middle cerebral artery occlusion (MCAO) procedure were imaged. 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 (IR, TI from 250 to 3000 ms, NSA=4) and T_2 (SE, TR/TE1/TE2=3250/30/100 ms, NSA=16) MRI. Data Analysis: We used Matlab. P-values less than 0.05 were considered statistically significant.

Results and Discussion We evaluated the relationship between MK and multivariate MRI indexes using Pearson's correlation with a Student's t distribution, excluding ventricle regions using a diffusion threshold-based mask (Fig. 1). As Fig. 1 a shows, there was little correlation between MK and MD (R^2<0.01, P>0.18), suggesting that MK is different from the standard MD index. The per-pixel analysis showed significant correlation between MK and FA (R^2=0.29, P<0.001, Fig. 1 b), MK and R_1 (R^2=0.67, P<0.001, Fig. 1 c), and MK and R_2 (R^2=0.13, P<0.001, Fig. 1 d). Notably, the correlation between MK and R_1 was significantly higher than that of MD, FA and R_2 (P<0.001). Because MD and FA may change substantially during acute stroke, we compared the univariate regression of MK and R_1 versus multiple regression of MK with R_1 and R_2. We found the coefficient of determination was 0.60 ± 0.09 (MK and R_1, P<0.001) and 0.61 ± 0.09 (MK, R_1 and R_2, P<0.01); there was no significant difference between R^2 obtained by univariate regression of MK and R_1 and that determined by multiple regression of MK, R_1 and R_2 (Two-sample t-test, P>0.80).

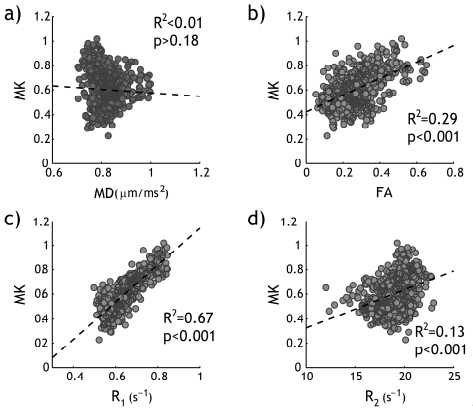

Fig. 1, Univariate regression between MK and multi-parametric MRI indexes. a) MK with MD. b) MK with FA. c) MK with R1 and d) MK with R_2.

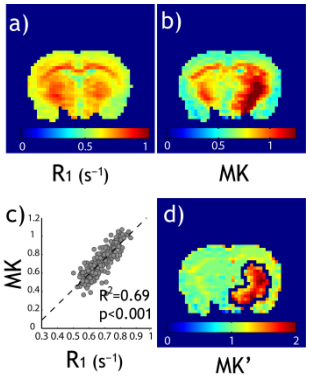

Fig. 2, a) R_1 map. b) MK map. c) Univariate regression analysis of R_1 and MK (contralateral normal brain. d) modified MK' map.

Fig. 2 compares the conventional MK map and the proposed relaxation-scaled MK (MK') map in a representative normal rat. R_1 map shows relatively small change (Fig. 2a). The conventional MK map (Fig. 2b) shows hyperintensity in regions of the striatum and corpus callosum, indicating complex local microstructure. Fig. 2c shows the estimated MK map (MK_{est}) using the univariate linear regression coefficients determined from MK and R_1, per pixel (MK_{est}= 1.51*R_1-0.37). Fig. 2d shows the proposed relaxation-normalized MK map (i.e. MK'=MK/MK_{est}), which was significantly more homogeneous than the raw MK map (Fig. 2b). The coefficient of variation (COV, i.e., S.D./mean) was 22.4% and 14.0% for the conventional MK and proposed MK' maps, respectively. This represented a relative COV decrease of 37.5%, confirming that the proposed MK' map can reasonably account for a substantial portion of the MK heterogeneity in the intact brain. Using a one-tailed paired t-test (P<0.01) we found that the kurtosis lesion volume (172±78 mm^3) was significantly less than that of diffusion (206±93 mm^3). Moreover, MD was 0.64±0.05 and 0.64±0.04 in the MD and MK' lesions, respectively, and there was no statistically significant difference (P=0.61). Importantly, MK' was significantly different between MD and MK' lesions (1.58±0.10 vs. 1.70±0.11, P<0.001). In summary, our results demonstrate that relaxation-normalized kurtosis MRI effectively reduced the intrinsic kurtosis heterogeneity, enabling automated tissue segmentation of the kurtosis lesion during acute ischemic stroke.

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