Enhanced Contrast of Ischemic Stroke Lesions in Non-Gaussian Diffusion Imaging

Farida A. Grinberg[1], Ezequiel Farrher[1], Luisa Ciobanu[2], Françoise Geffroy[2], Denis Le Bihan[2], and N. Jon Shah[1,3]
[1]*Forschungszentrum Juelich, Juelich, Germany,* [2]*Neurospin, CEA, France,* [3]*RWTH Aachen University, Germany*

Target Audience. This abstract evaluates two non-Gaussian diffusion models as biomarkers of stroke lesions and is of interest for researchers and clinicians dealing with brain pathologies and applications of advanced diffusion MRI methods.

Purpose. Recent diffusion MRI studies of stroke in humans and animals have shown that the quantitative parameters characterising the degree of non-Gaussianity of the diffusion process are much more sensitive to ischemic changes than the *apparent diffusion coefficient* (ADC) considered thus far as the "gold standard". These studies were based on the novel non-Gaussian methods, such as diffusion kurtosis imaging[1,2] and log-normal distribution function imaging[2]. Here we analyse the applicability and sensitivity of two non-Gaussian methods, stretched-exponential function (SEM)[3] and gamma-distribution function (GDF)[4] for providing biomarkers of ischemic lesions in the animal stroke models. A special focus is placed upon enhanced contrast of fine tissue microstructure in the affected tissue.

Materials and Methods. Transient middle cerebral artery occlusion (90 min) was induced in three animals (300 g, Sprague-Dawley male rats) for the stroke experiments. The rats were imaged 24 hours after reperfusion. For immunohistochemistry and fluorescence microscopy, brains were perfused with a saline solution and with 4% paraformaldehyde, and extracted. They were kept in paraformaldehyde for 2 h, 15% sucrose solution for 12 h and 30% sucrose solution for 24 h for cryoprotection. Fluorescence microscopy was performed on an Axio Observer Z1 microscope (Carl Zeiss MicroImaging, Jena, Germany). One slice (10 µm thickness) was treated with an antibody against neuronal nuclei (NeuN, Millipore, MAB377X, alexa 488 conjugated) and with 4',6'-diamidino-2-phenylindole (DAPI) staining. Figure 1 demonstrates NeuN/DAPI labelled photomicrograph showing the cortical lamination. MRI experiments were performed on a 7T system (Bruker, PharmaScan) equipped with magnetic field gradients with maximum strength of 760 mT/m. The diffusion-weighted signal S was analysed in the range of b-values ≤ 6 µm^{-2} ms in terms of SEM (DDC, α_{SE}) and GDF (θ, κ) models. The maps were produced for the corresponding parameters.

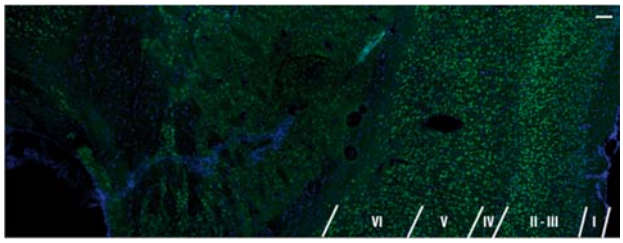


Figure 1. NeuN/DAPI labeled photomicrograph demonstrating the cortical layered structure. Scale bar 100 µm.

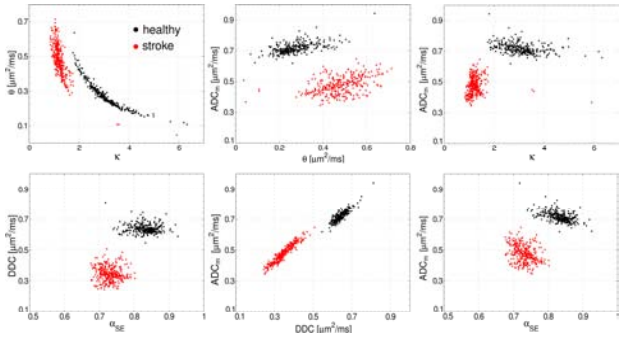
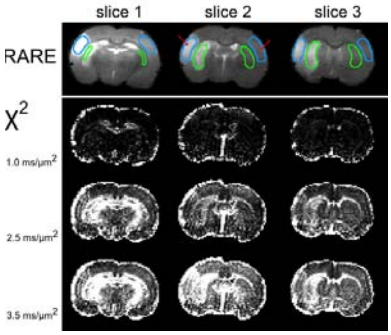


Figure 2. Scatter plots for different combinations of parameters: θ vs. κ (GDF) DDC vs. α_{SE} (SEM), and ADC_m vs. each of the GDF and SEM parameters.

Results and Discussions. Clear deviations from the mono-exponential behaviour occurred for $b > 1000$ mm^{-2} s. Figure 1 (left) shows lesion locations in the anatomical RARE images and χ^2-maps of the mono-exponential fits for various b-value ranges. Clearly, the deviations increase with increasing b-value and reveal increasing contrast between GM and WM (consider "bright" WM tracts). Stroke lesions cannot be recognised in χ^2-error maps for $b \leq 1000$ mm^{-2} s but become strikingly enhanced for larger b, providing a clear evidence for higher degree of non-Gaussianity in lesions than in healthy tissue. GDF provided larger relative changes of both parameters (~ 75% for θ and and ~ 60% for κ) in stroke than the "gold standard" apparent diffusivity, ADC (~ -35%). SEM demonstrated a larger change of DDC (-51) than that of the ADC %, but a smaller change of α_{SE}. However, the scatter plots of SEM and GDF parameters allowed us to delineate affected tissue with a very high reliability; see Figure 2. An interesting finding of this work is the appearance of laminar cortical structures in stroke lesions; see Figure 3. The genuine differences in cortical layer microstructure are well-known from histology (Figure 1) but cannot be easily visualised by MRI. In healthy regions, no clear laminar contrast was observed but became distinguishable in the lesions represented by α_{SE}-, θ- and κ-maps. This fine structure is hardly visible in the ADC maps. Our finding allows us to propose that the cascade of ischemic processes tends to non-uniformly affect the cortical layers differentiating by their cyto- and myeloarchitecture. Selective vulnerability of cortical layers to ischemia was reported in a few works[5]. A significant difference between cortical layers in the time profile of eosinophilic neurons in the post-ischemic cortex was reported by Sun et al.[5] However, based on diffusion studies, such a phenomenon has not been observed before.



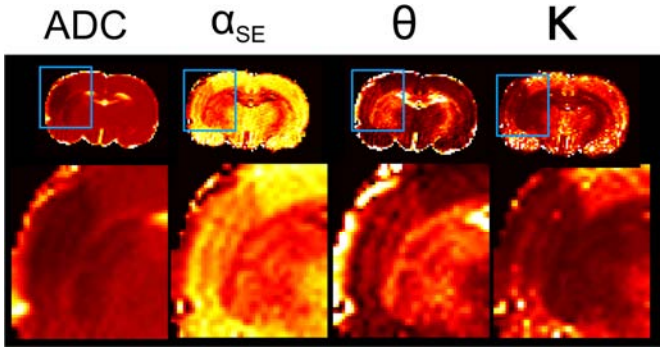


Figure 3. (left) Anatomical RARE images and χ^2- maps for various b-value ranges. The errors increase throughout the image with increasing b. In lesions and WM regions, the increase is especially strong leading to a more clear contrast at larger b; (right) Parameter maps for ADC, α_{SE} (SEM), θ and κ (GDF) representing the layered structure in the lesions. The DDC-map is not shown as the difference to the ADC-map in visualising the layers was not significant.

Conclusion. In conclusion, the non-Gaussian models, SEM and GDF, enable enhanced cortical layer visualization in stroke lesions in comparison to the ADC. The implications of this need to be further evaluated.

References. [1] Jensen JH, Falangola MF, Hu C, et al. (2011) Preliminary observations of increased diffusional kurtosis in human brain following recent cerebral infarction. NMR Biomed 24: 452-457; [2] F. Grinberg, L. Ciobanu, E. Farrher, N.J. Shah, Diffusion kurtosis imaging and log-normal distribution function imaging enhance the visualisation of lesions in animal stroke models, NMR Biomed., 25(2012) 1295-304; [3] K.M. Bennett, K.M. Schmainda, R.T. Bennett, et al., Characterization of continuously distributed cortical water diffusion rates with a stretched-exponential model, Magn. Reson. Me
d., 50 (2003) 727-734; [4] Röding M, Bernin D, Jonasson J, et al. (2012) The gamma distribution model for pulsed-field gradient NMR studies of molecular-weight distributions of polymers. J Magn Reson 222: 105-111. [5] Sun L, Kuroiwa T, Ishibashi S, et al. (2006) Time profile of eosinophilic neurons in the cortical layers and cortical atrophy. Acta Neurochir Suppl 96: 272-275.