Mean Kurtosis: a new potential biomarker for brain tumor grading?

S. Van Cauter[1], J. Veraart[2], J. Sijbers[2], U. Himmelreich[3], R. Peeters[1], S. Van Gool[4], W. Van Hecke[1,2], and S. Sunaert[1]
[1]Department of Radiology, University Hospitals of Leuven, Leuven, Belgium, [2]Vision Lab, Department of Physics, University of Antwerp, [3]Biomedical NMR Unit/Molecular Small Animal Imaging Center, Department of Medical Diagnostic Sciences, Catholic University Leuven, [4]Pediatric neuro-oncology, University Hospitals of Leuven

Background and objective: Current routinely used magnetic resonance (MR) techniques are often insufficient in accurate grading of gliomas. Hence, in most cases a biopsy is warranted in order to obtain a definitive diagnosis. Diffusion kurtosis imaging (DKI) is a recently developed imaging technique in which the deviation from Gaussian diffusional behavior is quantified, thereby providing additional information on the mobility of protons as derived from diffusion-weighted imaging and diffusion tensor imaging [1]. In this study, we evaluate the potential role of DKI in the grading of gliomas.

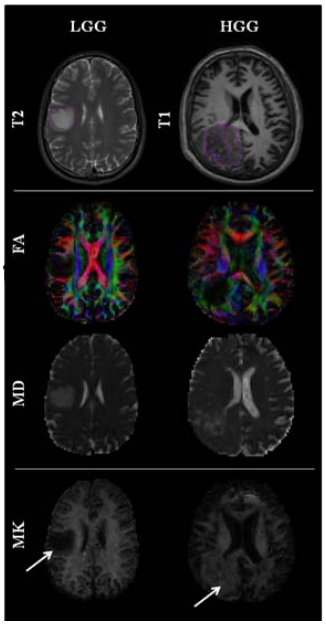

Fig.1 Manual segmentation of the solid tumoural tissue (outlined in purple) was based on transverse T2- or T1- weighted MR images. Single slices of some DTI maps (FA and MD) and a DKI map (MK) were shown for LGG and HGG.

Material and Methods: 16 patients with cerebral gliomas prior to any treatment participated in this study (3F/13M; age range: 20-76, median age: 64). The patient group consisted of 9 patients with grade IV glioma (high grade gliomas, HGG) and 7 patients with grade II glioma (low grade gliomas, LGG). All DKI data were acquired at a 3T MR scanner using a spin-echo (SE) diffusion- weighted imaging (DWI) sequence. The DKI protocol [2] consisted of 4 separate scans, which were merged during post-processing. Implemented b-values were 700, 1000 and 2800 s/mm², applied in 25, 40 and 75 uniformly distributed directions respectively. Additionally, 7 images without diffusion sensitization were obtained. Other imaging parameters were kept constant throughout the DKI data acquisition sequences: TR/TE: 3200/90 ms, δ/ Δ: 20 /48,3 ms; FOV: 240 x 240 mm², matrix: 96 x 96, NEX: 1, slice thickness/gap: 2,5/0 mm, slices: 44, parallel imaging factor: SENSE with factor 2 anterior-posterior. Anatomical reference images were obtained (T2 and T1 after contrast administration). Regions of interest (ROI) were manually drawn around the solid part of the tumor, central necrosis if present, perilesional edema if present, contralateral normal appearing white matter (NAWM) and contralateral normal thalamic grey matter (GM). For each ROI, diffusional parameters - mean diffusivity (MD), fractional anisotropy (FA) and mean kurtosis (MK) - were derived from the diffusion tensor and diffusion kurtosis tensor respectively which were voxelwise estimated using a constrained maximum likelihood estimator assuming a Rician noise model (Figure 1). Preceding to the tensor estimation, diffusion weighted data was corrected, involving signal modulation and b-matrix rotation (3), for head motion and eddy currents by a global affine transformation. MD, FA and MK in solid tumoural tissue were normalized to the MD, FA and MK of NAWM respectively (normMD, norm FA, and normMK). MD, FA and MK in NAWM, GM, solid tumoral tissue and edema as well as normMK, normMD and normFA from tumoral tissue were compared among the HGG and LGG , using the Mann-Whitney test. Statistical threshold for significance was set at $p<0.05$.

Results: MK of solid tumoural tissue was significantly higher in HGG (0.61 +/- 0.12) than in LGG (0.40 +/- 0.11) (p: 0.007), whereas no statistical difference between HGG (MD: 1.16 +/- 0.26 x 10^{-3} mm^2/s, FA: 0.17 +/- 0.07) and LGG (MD: 1.54 +/- 0.41 x 10^{-3} mm^2/s, FA: 0.14 +/- 0.05) could be demonstrated with respect to MD and FA. NormMK, normMD and normFA in tumoural tissue differed significantly between HGG en LGG (p: 0.005, 0.008 and 0.021 respectively) (Figure 2). NormMK and normFA were higher in solid tumoural tissue from HGG (normMK: 0.61 +/- 0.12, normFA: 0.5 +/- 0.22) compared to LGG (normMK: 0.38 +/- 0.14 , normFA: 0.31 +/- 0.12), whereas normMD decreased in HGG (1.38 +/- 0.27), compared to LGG (2.0 +/- 0.55). FA from NAWM was significantly lower in HGG (0.38 +/- 0.05) than in LGG (0.47 +/- 0.08) (p: 0.018) . Areas of necrosis were only present in HGG. MK, MD or FA from edema did not significantly differ between HGG and LGG (p: 0.794, p: 0.602, p: 1.0 respectively). There was no statistical difference between the two tumour grades with respect to MK, MD or FA in grey matter, nor to MD and MK in NAWM.

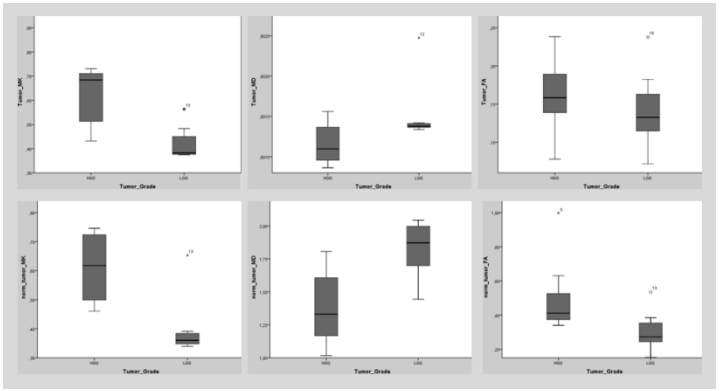

Fig. 2. Boxplots of MK, MD and FA values resp. in solid tumor in HGG (left plot) and LGG (right plot) (top row) and the corresponding normalized values (the bottom row).

Conclusion: This study demonstrates significant differences in MK between high and low grade gliomas, thereby showing a better separation in comparison to parameters from conventional diffusion imaging. MK is a potential a new biomarker in grading of gliomas.

References: [1] Jensen JH et al. (2005) MRM 53(6):1432-1440, [2] Poot et al. (2010) IEEE TMI 29(3): 819-829, [3] Jones and Cercignani (2010) MRM 23(7):803-802, [4] Kinoshita M et al. (2008), Neuroimage 43(1): 788-93