# Cerebral Gliomas: Correlation of diffusion kurtosis imaging with tumour grade and Ki-67

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## Introduction
Accurately grading and predicting the proliferation preoperatively are both important for treatment and prognosis of gliomas. Conventional DWI and DTI are not accurate enough in the grading and determining the proliferation of gliomas. DKI, a relatively recent technique, can provide a more accurate model of diffusion to detect the microstructural changes. Previous studies (1, 2) have showed great value of DKI in grading gliomas, however, they did not research the correlation between DKI and proliferative activity of gliomas. So in this study we researched the correlation of DKI with tumour grade and Ki-67.

## Methods
Seventy-four patients with histopathologically confirmed cerebral glioma, 67 primary gliomas and 7 recurrence after surgery, underwent routine MRI and DKI. Mean kurtosis (MK), axial kurtosis (Ka), radial kurtosis (Kr), mean diffusivity (MD) and fractional anisotropy (FA) were semi-automatically obtained in the solid part of tumor and the contralateral normal-appearing white matter (NAWM). The values in NAWM were used as reference to normalize. Histology was applied to determine the grade of the tumor and the expression of Ki-67. Statistical analysis included the Mann-Whitney test, receiver operating characteristic (ROC) curve and Spearman correlation analysis.

## Results
Nomaliezed MK, Ka, Kr and MD in the solid part of tumor were significantly different between high-grade gliomas(HGG) and low-grade gliomas(LGG), between grade II and grade III gliomas, between grade III and grade IV gliomas and between grade II and grade IV gliomas ($P<0.05$ for all). FA did not significantly differ between glioma grades ($P>0.05$ for all). MK had the highest sensitivity and specificity in distinguishing HGG from LGG (90% and 88.2%), grade II from grade III gliomas (84.2% and 86.7%) and grade III from grade IV gliomas (85.7% and 84.2%), so had Kr in distinguishing grade II from grade IV gliomas (95.2% and 90.0%). Significant correlations were found between Ki-67 and MK, Ka, Kr or MD ($P<0.001$ for all), but not between Ki-67 and FA ($P>0.05$).

## Discussion and Conclusion
Normalized MK, Ka, Kr and MD in solid tumor can distinguish HGG from LGG, distinguish grade II, III and IV gliomas, and non-invasively predict proliferative activity of glioma cells. DK parameters are superior than MD, whereas FA is of low value.Because LGG have the lower cellularity, bigger cellular sizes, and more infiltrative growth; they contain fewer diffusion barriers; HGG are characterized by higher cellularity, more nuclear atypia, higher pleomorphism, and more vascular hyperplasia and necrosis. Structural complexity and heterogeneity are therefore higher in HGG than in LGG, therefore, kurtosis is higher and diffusion is lower in HGG than in LGG. Increased Ki-67 means higher proliferation, higher cellularity, and more synthesized DNA, RNA, and proteins. These factors all increase barriers of water molecule movement both inside and outside the tumor cells, as a result, kurtosis increased, and diffusion decreased. Therefore, Diffusion kurtosis imaging is of important value in grading and predicting the proliferative activity of glioma cells, and DK parameters are more potential biomarkers.

## References
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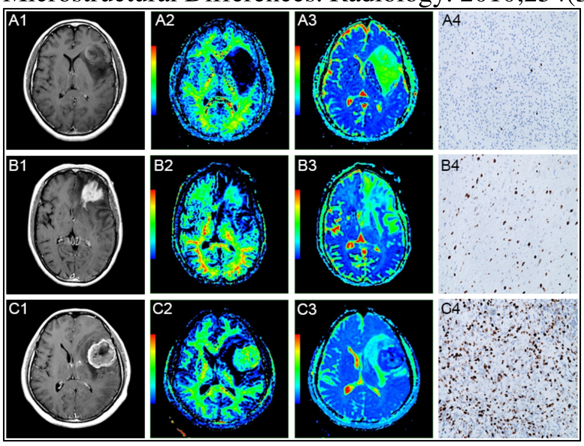


Fig.1

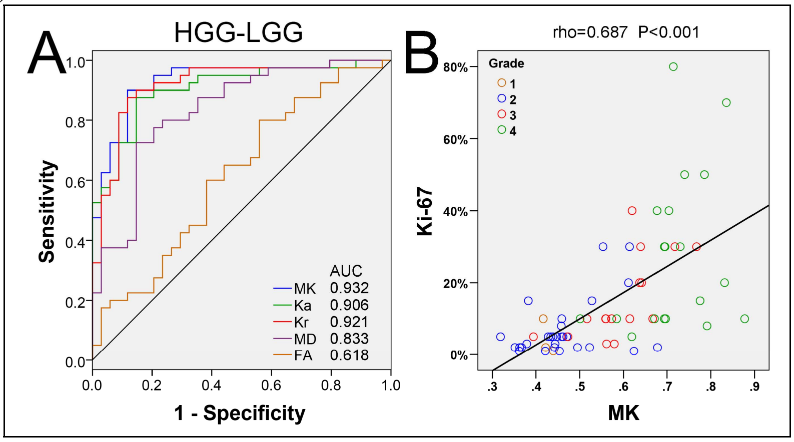


Fig.2

Fig.1: Row A-C were three patients with oligodendroglioma(WHO grade II) in the left frontal lobe and insula, anaplastic astrocytoma (WHO grade III) in the left frontal lobe and glioblastoma (WHO grade Ⅳ) in the left insula respectively. Column 1-4 were contrast-enhanced T1WI, MK, MD and Ki-67 images respectively. MK and Ki-67 increased and MD decreased as the grade increased.

Fig.2: ROC curves and AUC for parameters in the solid part of tumor to differ HGG and LGG(A); scatter diagrams demonstrating the correlations between Ki-67 and MK (B).