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# Diffusion MRI is valuable in brainstem glioma genotyping with quantitative measurements of white matter tracts

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## Abstract

**Objectives:** To investigate the value of diffusion MRI (dMRI) in H3K27M genotyping of brainstem glioma (BSG).

**Methods:** A primary cohort of BSG patients with dMRI data (b = 0, 1000 and 2000 s/mm$^2$) and H3K27M mutation information were included. A total of 13 diffusion tensor and kurtosis imaging (DTI; DKI) metrics were calculated, then 17 whole-tumor histogram features and 29 along-tract white matter (WM) microstructural measurements were extracted from each metric and assessed within genotypes. After feature selection through univariate analysis and the least absolute shrinkage and selection operator method, multivariate logistic regression was used to build dMRI-derived genotyping models based on retained tumor and WM features separately and jointly. Model performances were tested using ROC curves and compared by the DeLong approach. A nomogram incorporating the best-performing dMRI model and clinical variables was generated by multivariate logistic regression and validated in an independent cohort of 27 BSG patients.

**Results:** At total of 117 patients (80 H3K27M-mutant) were included in the primary cohort. In total, 29 tumor histogram features and 41 WM tract measurements were selected for subsequent genotyping model construction. Incorporating WM tract measurements significantly improved diagnostic performances ($p < 0.05$). The model incorporating tumor and WM features from both DKI and DTI metrics showed the best performance (AUC = 0.9311). The nomogram combining this dMRI model and clinical variables achieved AUCs of 0.9321 and 0.8951 in the primary and validation cohort respectively.

**Conclusions:** dMRI is valuable in BSG genotyping. Tumor diffusion histogram features are useful in genotyping, and WM tract measurements are more valuable in improving genotyping performance.

**Clinical relevance statement:** This study found that diffusion MRI is valuable in predicting H3K27M mutation in brainstem gliomas, which is helpful to realize the noninvasive detection of brainstem glioma genotypes and improve the diagnosis of brainstem glioma.

**Key points:** • Diffusion MRI has significant value in brainstem glioma H3K27M genotyping, and models with satisfactory performances were built. • Whole-tumor diffusion histogram features are useful in H3K27M genotyping, and quantitative measurements of white matter tracts are valuable as they have the potential to improve model performance. • The model combining the most discriminative diffusion MRI model and clinical variables can help make clinical decision.

**Keywords:** Brain stem neoplasms; Diffusion magnetic resonance imaging; Glioma; Mutation; White matter.