Recurrent tumor and treatment-induced effects have different MR signatures in contrast enhancing and non-enhancing lesions of high-grade gliomas

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INTRODUCTION: It is estimated that 25 to 35% of patients experience treatment-induced effects that can mimic recurrent high-grade gliomas. This poses a significant diagnostic challenge that is complicated by the coexistence of treatment-related changes and recurrent tumor within the same lesion which limits the accuracy of classification based on summary metrics of multi-parametric MRI. This study aimed to determine whether different MR features were relevant for distinguishing pathological features of recurrent tumor from the effects of treatment in the contrast enhancing and nonenhancing lesions of recurrent high-grade gliomas.

METHODS: Leveraging our unique dataset of image-guided tissue samples that directly maps pathology to MR characteristics, we analyzed 291 tissue samples (222 recurrent tumor; 69 treatment effect) with known coordinates on imaging from 139 patients that underwent preoperative 3T MRI and surgery for a suspected high-grade recurrent tumor. 8 MR parameter values from perfusion-weighted, diffusion-weighted, and MR spectroscopic imaging at each tissue sample location were tested for association with histopathological outcome using univariate and multivariate generalized estimating equation models for enhancing and nonenhancing tissue samples. Individual cutoff values were determined and evaluated using ROC-Curve analysis with 5-fold cross-validation.

RESULTS: In tissue samples obtained from contrast-enhancing lesions, elevated relative cerebral blood volume (rCBV) was significantly associated with the presence of recurrent tumor pathology ($p<0.03$), while increases in normalized choline (nCho) and choline-to-NAA index (CNI) were significantly associated with the presence of recurrent tumor pathology in non-enhancing tissue samples ($p<0.008$). Cutoff values of 1.6(rCBV), 2.7(CNI), and 2.1(nCho) had the highest performance.

CONCLUSION: Although our results confirm the utility of rCBV in distinguishing the effects of treatment from recurrent tumor within the contrast enhancing lesion, we found that metabolic parameters can better differentiate recurrent tumor from treatment-related changes in the non-enhancing lesion of high-grade gliomas. These results will help improve future management of these patients.