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# ADC histograms predict response to anti-angiogenic therapy in patients with recurrent high-grade glioma.

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### Abstract

**INTRODUCTION:** The purpose of this study is to evaluate apparent diffusion coefficient (ADC) maps to distinguish anti-vascular and anti-tumor effects in the course of anti-angiogenic treatment of recurrent high-grade gliomas (rHGG) as compared to standard magnetic resonance imaging (MRI).

**METHODS:** This retrospective study analyzed ADC maps from diffusion-weighted MRI in 14 rHGG patients during bevacizumab/irinotecan (B/I) therapy. Applying image segmentation, volumes of contrast-enhanced lesions in T1 sequences and of hyperintense T2 lesions (hT2) were calculated. hT2 were defined as regions of interest (ROI) and registered to corresponding ADC maps (hT2-ADC). Histograms were calculated from hT2-ADC ROIs. Thereafter, histogram asymmetry termed "skewness" was calculated and compared to progression-free survival (PFS) as defined by the Response Assessment Neuro-Oncology (RANO) Working Group criteria.

**RESULTS:** At 8-12 weeks follow-up, seven (50%) patients showed a partial response, three (21.4%) patients were stable, and four (28.6%) patients progressed according to RANO criteria. hT2-ADC histograms demonstrated statistically significant changes in skewness in relation to PFS at 6 months. Patients with increasing skewness ( $n = 11$ ) following B/I therapy had significantly shorter PFS than did patients with decreasing or stable skewness values ( $n = 3$ , median percentage change in skewness 54% versus -3%,  $p = 0.04$ ).

**CONCLUSION:** In rHGG patients, the change in ADC histogram skewness may be predictive for treatment response early in the course of anti-angiogenic therapy and more sensitive than treatment assessment based solely on RANO criteria.

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