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## Bevacizumab-induced tumor calcifications as a surrogate marker of outcome in patients with glioblastoma.

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### Abstract

Therapy-induced calcifications in glioblastoma are rarely recognized. They may represent regressive changes in the tumor tissue, but their occurrence and possible predictive or prognostic value have not been systematically assessed. The observation of hyperintense lesions on precontrast T1-weighted magnetic resonance images (MRIs) in 2 index patients with glioblastoma after therapy with bevacizumab, subsequently identified as calcifications on computed tomographs (CTs), prompted us to prospectively screen for these radiographic changes. Therefore, 36 patients with recurrent glioblastoma prospectively treated with bevacizumab in an observational trial were examined every 8 weeks by MRI and, if clinically necessary, by CT. In 22 patients (61.1%), T1 hyperintense lesions became apparent after bevacizumab treatment. The median time to detection of these lesions was 55 days. In 14 (63.6%) of 22 patients, CTs were available and confirmed the existence of tumor calcifications. No substantial changes in T1 hyperintense lesions or calcifications were recognized on additional MRI or CT scans. Interestingly, the patients with therapy-induced T1 hyperintense lesions had better durations of progression-free survival than patients without these changes (median, 5.8 vs 3.5 months;  $P < .001$ ), and the duration of overall survival was also superior (median, 9.7 vs 5.0 months;  $P = .006$ ). There was a striking correlation between the appearance of therapy-induced T1 hyperintense lesions and overall response to bevacizumab. Therefore, this phenomenon is a rather early and time-limited event during the first weeks of treatment and appears to be response related. In summary, T1 hyperintense lesions are common in patients with glioblastoma who have been exposed to bevacizumab, may represent a novel biomarker of response and outcome, and seem to correspond to tumor calcifications.

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