Radiolabeled temozolomide can measure bevacizumab induced vascular modulation in patients with recurrent GBM.

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BACKGROUND: Anti-angiogenic agents have been hypothesized to work via vascular pruning as well as by vessel normalization. However, these mechanisms are not mutually exclusive and may occur in the same patient but at different time points during treatment.

METHODS: After labeling temozolomide with the positron emitter [11C], we performed MR-PET scans in patients receiving bevacizumab 10mg/kg Q2weeks and temozolomide 50mg/m2 daily. Patients were initially scanned pre-bevacizumab and 1 day post first bevacizumab infusion. The first MR-PET was performed after steady state for oral temozolomide had been achieved to minimize nonspecific binding. MRI included routine sequences and perfusion/permeability imaging. Tumor regions of interest were outlined on the post-contrast images and registered to the PET and MRI images to generate tumor values for SUV, cerebral blood volume, cerebral blood flow, and k\text{trans}.

RESULTS: At this time, MRI and PET data is available for 2/7 patients who underwent scanning. In patient 1 the volume of tumor enhancement increased 34% from baseline to 1 day post bevacizumab, median k\text{trans} increased 10%; median CBV decreased 14%; median CBF increased 1.6%, and mean SUV increased 54%. The volume of tumor enhancement in patient 2 decreased 59%, median k\text{trans} decreased 38%; median CBV decreased 43%; median CBF decreased 39%; and mean SUV decreased 38%.

CONCLUSIONS: These 2 patients demonstrated different early vascular responses to bevacizumab. Labeling drugs so that they are visible with PET is an intriguing and noninvasive way to measure tumor biology and response to treatment in individual patients. When coupled with dynamic MRI sequences, this technique can be used safely, longitudinally, and may allow for patient-specific adjustment of therapy.