Reply to Letter

Evidence for rCBV as an early response marker following bevacizumab treatment

I appreciate the thoughtful letter from Schmainda et al. regarding the utility of rCBV derived from MRI as a biomarker of response to bevacizumab therapy in patients with recurrent glioblastoma (GBM). The authors cite their recent work in which they found that tumoral rCBV changes were predictive of overall survival at 2 and 16 weeks, but not 8 weeks, after the start of bevacizumab therapy in patients with GBM.\(^1\) Certainly this issue is not settled science, and I hope that further studies will be performed by the authors or others to clarify the timing at which perfusion imaging adds value to standard MRI in the assessment of patients with brain tumors. In my editorial,\(^2\) I suggest that the use of rCBV as an early response marker for bevacizumab therapy is not well supported to date. On one hand, there are the data from the authors, based on a cohort of 13 patients (point of reference: n for the Kickingereder et al\(^3\) paper showing a relationship between pretreatment rCBV and outcomes was 71) suggesting a relationship between changes in rCBV and survival at 2 and 16 weeks. Interestingly, no relationship was found at 8 weeks, when the cohort size was 17 rather than 13. (In the interests of full disclosure, I was the associate editor who recommended the paper be published.) On the other hand, because negative results are typically (and unfortunately) unreported, we do not know how many patients with perfusion data treated with bevacizumab were similarly analyzed over the last decade but whose data were never published because of the lack of association between rCBV changes and outcomes. Based on conversations with colleagues over the years, I would suggest this is not a few, so I think it is important to consider publication bias for positive results. This was part of the rationale for suggesting that Schmainda et al.'s\(^4\) recent study of 13 patients notwithstanding, the evidence in support of rCBV as an early response marker to bevacizumab therapy is not as robust today as would have been predicted 10 years ago.

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References

1. Schmainda KM, Zhang Z, Prah M, et al. Dynamic susceptibility contrast MRI measures of relative cerebral blood volume as a prognostic marker for overall survival in recurrent glioblastoma:

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