## ABSTRACT

Radiology. 2022 Feb;302(2):410-418. doi: 10.1148/radiol.2021210826. Epub 2021 Nov 9.

Myo-Inositol Levels Measured with MR Spectroscopy Can Help Predict Failure of Antiangiogenic Treatment in Recurrent Glioblastoma.

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Background Patients with recurrent glioblastoma (GBM) are often treated with antiangiogenic agents, such as bevacizumab (BEV). Despite therapeutic promise, conventional MRI methods fail to help determine which patients may not benefit from this treatment. Purpose To use MR spectroscopic imaging (MRSI) with intermediate and short echo time to measure corrected myo-inositol (ml)normalized by contralateral creatine (hereafter, ml/c-Cr) in participants with recurrent GBM treated with BEV and to investigate whether such measurements can help predict survivorship before BEV initiation (baseline) and at 1 day, 4 weeks, and 8 weeks thereafter. Materials and Methods In this prospective longitudinal study (2016-2020), spectroscopic data on ml-a glial marker and osmoregulator within the brain-normalized by contralateral creatine in the intratumoral, contralateral, and peritumoral volumes of patients with recurrent GBM were evaluated. Area under the receiver operating characteristic curve (AUC) was calculated for all volumes at baseline and 1 day, 4 weeks, and 8 weeks after treatment to determine the ability of ml/c-Cr to help predict survivorship. Results Twenty-one participants (median age  $\pm$  standard deviation, 62 years  $\pm$  12; 15 men) were evaluated. Lower ml/c-Cr in the tumor before and during BEV treatment was predictive of poor survivorship, with receiver operating characteristic analyses showing an AUC of 0.75 at baseline, 0.87 at 1 day after treatment, and 1 at 8 weeks after. A similar result was observed in contralateral normal-appearing tissue and the peritumoral volume, with shorter-term survivors having lower levels of ml/c-Cr. In the contralateral volume, a lower ratio of mI to creatine (hereafter, mI/Cr) predicted shorter-term survival at baseline and all other time points. Within the peritumoral volume, lower ml/c-Cr levels were predictive of shorter-term survival at baseline (AUC, 0.80), at 1 day after treatment (AUC, 0.93), and at 4 weeks after treatment (AUC, 0.68). Conclusion Lower levels of myo-inositol normalized by contralateral creatine within intratumoral, contralateral, and peritumoral volumes were predictive of poor survivorship and antiangiogenic treatment failure as early as before bevacizumab treatment. Adapting MR spectroscopic imaging alongside conventional MRI modalities conveys critical information regarding the biologic characteristics of tumors to help better treat individuals with recurrent glioblastoma. Clinical trial registration no. NCT02843230 © RSNA, 2021 Online supplemental material is available for this article.

DOI: 10.1148/radiol.2021210826 PMCID: PMC8805659 PMID: 34751617 [Indexed for MEDLINE]

Conflict of interest statement: Disclosures of Conflicts of Interest: M.E.E. No relevant relationships. M.R.W. No relevant relationships. P.T. No relevant relationships. M.F. No relevant relationships. D.K. No relevant relationships. A.W. No relevant relationships. J.H. No relevant relationships. A.V. No relevant relationships. M.V. No relevant relationships. O.R. Support from GE Healthcare for travel expenses as a presenter. O.A. No relevant relationships. I.A.R. Clinical trial funding support from Astex Pharmaceuticals; payment for lectures from Merck; participation on a data safety monitoring board or advisory board for Forma Therapeutics, Boehringer Ingelheim, and Agios; educational co-chair for the Society for Neuro-Oncology; receipt of equipment or materials from Astex Pharmaceuticals. D.A.F. Research support from Conquer Cancer, the ASCO Foundation; shareholder in Eli Lilly. Y.F.Y. No relevant relationships. B.R. Stock or stock options in QMENTA, BlinkAl Technologies, and Subtle Medical (no payments received to date). T.T.B. National Institutes of Health (NIH) grant to institution; royalties from Wolters Kluwer as an author for UpToDate; consulting fees from Champions Biotechnology; NIH committee co-chair; honoraria from Oakstone; former member of the GenomiCare scientific advisory board; leadership roles with the American Academy of Neurology, Society for Neuro-Oncology, American Association for Cancer Research, and American Society of Hematology. R.G.G. No relevant relationships. J.D. Royalties from Wolters Kluwer as an author for UpToDate; consulting fees from Blue Earth Diagnostics and Unum Therapeutics. E.R.G. No relevant relationships. E.M.R. Grants from NIH and the National Science Foundation; advisory board member for BrainSpec.