

Commentary: Perilesional Resection of Glioblastoma is Independently Associated With Improved Outcomes

Michael Mütther, Dr. med., MSc

Walter Stummer, Prof. Dr. med.

Department of Neurosurgery, University Hospital Münster, Albert-Schweitzer-Campus 1, Münster, Germany

Correspondence:

Michael Mütther, Dr. med. MSc, University Hospital Münster, Department of Neurosurgery, Albert-Schweitzer-Campus 1, 48149 Münster, Germany.
Email: michael.muether@ukmuenster.de

Received, December 30, 2019.

Accepted, January 11, 2020.

Copyright © 2020 by the Congress of Neurological Surgeons

With great interest we read the article “Perilesional Resection of Glioblastoma Is Independently Associated With Improved Outcomes” provided by Al-Holou et al.¹ The authors present a remarkably large cohort study on over 1200 naïve glioblastoma multiforme (GBM) treated with intralesional or perilesional resection. They conclude that circumferential perilesional resection of GBM should be preferred over intralesional resection as the former is associated with significantly higher rates of complete resection and lower rates of neurological complications. Although this work adds to the growing body of evidence on the correlation of extent of resection and survival benefit in GBM, we sincerely feel that certain aspects of the study need further discussion in the context of contemporary oncological neurosurgery.

Maximal safe resection of naïve GBM is undoubtedly the essential first part of state of the art standard treatment. Different techniques have evolved over time to achieve this goal. Technical issues of white light microsurgical resection as discussed by Al-Holou et al¹ can easily be overcome by fluorescence-guided resection. Especially finding a pseudo-plane between tumor and surrounding brain parenchyma can be challenging and puts the patient at risk for unintended neurological damage, as well appreciated by the authors. With the use of five-aminolevulinic acid (5-ALA) derived fluorescence, a plane between bright and shallow fluorescence can easily lead the surgeon around the major bulk of tumor. In addition, our group and others have shown that 5-ALA derived fluorescence-guided resection facilitates resection beyond contrast enhancement.²⁻⁵ The concept of supramarginal resection is increasingly being popularized and has been shown to be associated with increased survival times.⁶⁻⁸ We recently first demonstrated that supramarginal resections as quantified by early postoperative 18F-Fluor-Ethyl-Tyrosine positron emission tomography (FET-PET)-positron emission tomography (PET) serve

to improve survival in patients with GBM.⁹ With their study results, Al-Holou et al¹ suggest that the concept of perilesional or pseudo en bloc resection approximates the concept of supramarginal resection. Still, comparative pre- and postoperative volumetric data to prove such hypothesis are lacking. Also, in contemporary studies, contrast enhancement should no longer be the only measure of extent of resection.⁹ Also, infiltrating tumor by far exceeds contrast enhancing tumor volumes, leading to inevitable recurrence at the margin of the resection.¹⁰ Many studies have already shown a survival benefit of resections extending into surrounding diffusion tensor imaging, fluid-attenuated inversion-recovery or FET-PET volumes.^{5,8,9} Yet, the surgeon needs to keep in mind a potential drawback in survival times having caused neurological damage by aggressively increasing resection volumes.¹¹ However, this issue can mostly be addressed applying state of the art techniques of intraoperative neurophysiology and awake procedures.

Finally, the presented (pseudo) en bloc technique may facilitate less tumor spread, analogous to solid tumor surgical oncology. One may hypothesize that this affects patterns of recurrence especially concerning the likelihood of developing distant metastases. It would therefore be of enormous interest to expand on patterns of recurrence in a future study and we encourage Al-Holou et al¹ to further interrogate their database in this regard.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Stummer reports consultant and lecture activities for Medac (Wedel, Germany), Carl Zeiss Meditec (Oberkochen, Germany), and NxDe (Lexington, Kentucky).

REFERENCES

1. Al-Holou WN, Hodges TR, Everson RG, et al. Perilesional resection of glioblastoma is independently associated with improved outcomes. *Neurosurgery*. 2020;86(1):112-121.

2. Stummer W, Novotny A, Stepp H, Goetz C, Bise K, Reulen HJ. Fluorescence-guided resection of glioblastoma multiforme utilizing 5-ALA-induced porphyrins: a prospective study in 52 consecutive patients. *J Neurosurg.* 2000;93(6):1003-1013.
3. Stummer W, Reulen HJ, Meinel T, et al. Extent of resection and survival in glioblastoma multiforme: identification of and adjustment for bias. *Neurosurgery.* 2008;62(3):564-576; discussion 564-576.
4. Idoate MA, Diez Valle R, Echeveste J, Tejada S. Pathological characterization of the glioblastoma border as shown during surgery using 5-aminolevulinic acid-induced fluorescence. *Neuropathology.* 2011;31(6):575-582.
5. Roberts DW, Valdes PA, Harris BT, et al. Coregistered fluorescence-enhanced tumor resection of malignant glioma: relationships between delta-aminolevulinic acid-induced protoporphyrin IX fluorescence, magnetic resonance imaging enhancement, and neuropathological parameters. Clinical article. *J Neurosurg.* 2011;114(3):595-603.
6. Duffau H. Is supratotal resection of glioblastoma in noneloquent areas possible? *World Neurosurg.* 2014;82(1-2):e101-e103.
7. Li YM, Suki D, Hess K, Sawaya R. The influence of maximum safe resection of glioblastoma on survival in 1229 patients: can we do better than gross-total resection? *J Neurosurg.* 2016;124(4):977-988.
8. Yan JL, van der Hoorn A, Larkin TJ, Boonzaier NR, Matys T, Price SJ. Extent of resection of peritumoral diffusion tensor imaging-detected abnormality as a predictor of survival in adult glioblastoma patients. *J Neurosurg.* 2017;126(1):234-241.
9. Muther M, Koch R, Weckesser M, Sporns P, Schwindt W, Stummer W. 5-aminolevulinic acid fluorescence guided-resection of 18F-FET-PET positive tumor beyond gadolinium enhancing tumor improves survival in glioblastoma. *Neurosurgery.* 2019;85(6):E1020-E1029.
10. Watanabe M, Tanaka R, Takeda N. Magnetic resonance imaging and histopathology of cerebral gliomas. *Neuroradiology.* 1992;34(6):463-469.
11. McGirt MJ, Mukherjee D, Chaichana KL, Than KD, Weingart JD, Quinones-Hinojosa A. Association of surgically acquired motor and language deficits on overall survival after resection of glioblastoma multiforme. *Neurosurgery.* 2009;65(3):463-470; discussion 469-470.