Extent of Resection in Glioblastoma

Nicole A. Shonka and Michele R. Aizenberg

The article by Nam and de Groot1 provides a good overview of treatment options and considerations for glioblastoma. Surgery is a critical mainstay providing diagnostic and therapeutic benefits. The importance of extent of resection for glioblastoma has been debated for decades. Not only important at diagnosis, the relevance of extent of resection at recurrence is increasing as patients with glioblastoma are surviving longer. After surgery, the neuro-oncologist or medical oncologist may be the sole provider obtaining follow-up imaging. At the time of recurrence or progression, it is crucial to identify patients who may benefit from another resection and obtain neurosurgical evaluation.

It is established that maximal safe resection should be performed if benefits outweigh risks and patient wishes are congruent with this approach. Gross total resection is the desired goal for benefit in survival times.2,3 The dogmatic all-or-nothing philosophy for resection is something to reconsider, however. Growing data support varying degrees of subtotal resection for graduated benefits in survival times.4 Another benefit of resection, either gross total resection or subtotal resection, is the acquisition of tissue for molecular testing. This is of utmost importance as we continue to elucidate factors affecting prognosis and responsiveness to therapies and develop personalized treatment plans. The definition of maximal safe resection becomes individual for each patient as variables are considered in determining the safest operative approach (biopsy, varied degrees of subtotal resection, or gross total resection) for each patient.

Whether repeat resection benefits patients is not entirely clear as a result of conflicting studies, most often performed retrospectively, based on differing surgical indications in relatively heterogeneous populations who then receive varied adjuvant therapies. In addition, the extent of resection is often not quantified, the definitions of gross total resection and subtotal resection vary, and all resections may be grouped in comparison with biopsy, further adding to our uncertainty as to the significance of resection in this setting.

The majority of both retrospective and prospective data since the turn of the century have favored repeat resection.5 Focusing on studies done within the era of temozolomide, Bloch et al6 performed a retrospective review of 107 patients undergoing resection for glioblastoma and found that gross total resection (> 95%) increased overall survival at salvage surgery for patients who initially had subtotal resection. Karnofsky performance status and extent of resection at progression independently predicted survival. The SN1 study group reported on 503 patients from 20 institutions and found that the extent of resection at recurrence, Karnofsky performance status, and adjuvant therapy after resection increased overall survival.7 Investigators matched a cohort of 71 patients receiving reresection with patients who did not undergo resection from the prospective Dose-Intensified Rechallenge With Temozolomide (DIRECTOR) trial, wherein patients were randomly assigned to one of two dose-intensified schedules of temozolomide. Overall, surgery did not improve survival, but within the resection cohort, patients with 100% resection of all enhancing tumor had a 6.4-month improvement in postrecurrence survival (P < .001).8

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Matching a cohort of 68 patients who had surgery for recurrence with patients who did not for initial extent of resection and subventricular zone involvement, Azoulay et al found a 4.3-month survival benefit ($P < .001$) from surgery, primarily limited to gross total resection. They found benefit with additional surgery after the first tumor progression as well. Similarly, an earlier review of 578 patients with recurrent glioblastoma found a correlation between number of repeat resections and increased survival, but surprisingly, this was independent of age, functional status, periventricular location, extent of resection, and adjuvant therapy. A comprehensive review of 33 articles published since 2008 on this subject reveals that 20 studies (61%) favored repeat resection. Of the 16 studies exploring extent of resection, 63% found improved survival from greater extent of resection. The majority of studies showing no benefit from repeat resection used only imaging progression to decide whether the patient should undergo surgery. One negative study had treated only 69% of patients with radiation and only 39% with chemotherapy after diagnosis, making this relatively inapplicable to current practice.

At time of diagnosis, maximal safe resection should be performed, with consideration of subtotal resection being acceptable and likely to provide benefits in survival times. Although rife with limitations inherent to retrospective reviews, the majority of studies support a benefit to repeat resection for recurrent glioblastoma, favoring those who can undergo a more extensive resection. Patients likely to derive the greatest benefit tend to share similar characteristics, including better performance status, intent to receive further adjuvant therapy, and noneloquent, nonependymal tumor location.

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Corresponding author: Nicole A. Shonka, MD, 986840 Nebraska Medical Center, Omaha, NE 68198-6840; e-mail: nshonka@unmc.edu.

**References**


AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Nicole A. Shonka  
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Michele R. Aizenberg  
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