EDITORIAL

Laser ablation for recurrent intracranial ependymoma**Mark M. Souweidane, MD**

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RECURRENT intracranial ependymoma in children remains a vexing clinical problem and a frequently frustrating surgical endeavor. Owing to the strong correlation between extent of tumor removal and disease-free interval, the surgical demands are heavy, especially in light of the often-involved brainstem and lower cranial nerves. The relative resistance to chemotherapy and radiotherapy demonstrated by these tumors also compounds this clinical challenge. Dr. Patel and colleagues in their current paper offer an additional adjuvant approach for consideration.¹ They highlight the use of MRI-guided laser-induced thermal therapy (MRgLITT) in patients with recurrent intracranial anaplastic ependymoma. The integration of predictive modeling through a software advancement, the thermal damage estimate (TDE) is hypothesized to offer the surgeon the ability to prescribe a time-energy “dose” that might positively impact the time to tumor recurrence. This principle of pretreatment dose planning is logical and mirrors what is commonplace for conformal radiation therapy.

On the surface, the use of MRgLITT has some real appeal in recurrent intracranial ependymoma, especially in young children with the compounded risks associated with multiple radiation therapy courses. The authors present 4 patients in whom 9 tumors were treated in an attempt to correlate the TDE with the degree of tumor ablation (percentage volume ablated [PVA]) and disease-free interval. The patients were varied with respect to age (2 children), anatomical site, previous treatment course, and tumor burden (tumor volume and metastatic staging). In addition to the baseline variance, the few numbers of treatments and the wide-ranging results make any meaningful conclusions regarding efficacy, safety, or correlation problematic. The two treatments with the best PVA (both 97%) did result in prolonged disease-free intervals compared with the others (as short as 2 months). This supports the authors' hypothesis but is far from confirmatory.

Commentary is warranted in assessing the potential efficiency of this treatment. Of concern is that the mean PVA for the 9 tumors was only 64.4%. This degree of undertreating, an operational prescript to limit juxtaposed injury, does raise questions as to how that mismatch might be overcome. Of the 2 patients with the best outcomes, 1 patient (Case 2) underwent a posttreatment craniotomy and radiation therapy for tumor control. One can legitimately question if the same result may have been achieved without MRgLITT. Furthermore, 1 patient treated for a recurrent third ventricular lesion did suffer irreversible dysfunction, presumably from hypothalamic insult. Of interest, the percentage area ablated (PAA) was 87% and the PVA was only 49% for that particular tumor. These disconnections between the TDE, actual treated tumor volume, and bystander injury are most likely a result of conformational issues related to the thermal distribution. In any event, this 1 case does raise some skepticism about the reliability of the TDE as a measure of efficacy and safety.

It is impossible not to take note of the conflict of interest (COI) that exists for one of the coauthors (A.S.). The authors prudently disclose this COI, but might consider independent outside validation of results or a future multicenter evaluation to erase any such concerns.

It is clear that the authors do have misgivings about this initial experience and do not present this limited clinical experience as a call to arms. They dutifully and comprehensively report on the limitations of this information and will hopefully use this experience as a springboard for future evaluations.

In summary, based on this pilot data, it is not clear that the balance between tumor control and morbidity is any better than the typically relied upon strategies of surgery or focused radiation therapy for recurrent intracranial ependymoma. MRgLITT definitely has appealing features in this disease. Clearly a more robust data set

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with independent validation is required, however, to sort out important issues pertaining to treatment planning for MRgLITT. Additionally, comparative evaluations with surgery and radiation therapy are going to be necessary for making determinations about the potential role of this innovative treatment approach for recurrent intracranial ependymoma.

<http://thejns.org/doi/abs/10.3171/2014.8.PEDS14297>

Reference

1. Patel NV, Jethwa PR, Shetty A, Danish SF: Does the real-time thermal damage estimate allow for estimation of tumor control after MRI-guided laser-induced thermal therapy? Initial experience with recurrent intracranial ependymomas. **J Neurosurg Pediatr** [epub ahead of print January 16, 2015]. DOI: 10.3171/2014.10.PEDS13698]

Response

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We would like to extend our gratitude to Dr. Mark M. Souweidane for his thoughtful and valuable comments on our recent work regarding the use of MRgLITT for treatment of recurrent intracranial ependymoma. We aimed to report our initial experience with MRgLITT for recurrent cases of ependymoma along with the ability of this technology to monitor tumor destruction in real time. We hoped to analyze whether this real-time estimation of damage sheds light on the likelihood of recurrence and whether thermal ablation can be seen as analogous to resection in that regard.

One of the goals of our study was focused on determining the relationship of the PAA (derived from the TDE) and the PVA. Intuitively, it makes sense that as a larger area of tissue is ablated, the volume of ablation also increases. However, this relationship may not be true for oddly shaped tumors or those in which the reaction to thermal ablation is not uniform; this was especially pronounced in Case 3. This PAA-PVA discrepancy was believed to be due to tumor geometry. As thermal energy exits the catheter in a spherical fashion, lesions that are irregular or multilobed may have a variable distribution of thermal energy. What may appear as a near-complete ablation on a 2D scale may not correlate with the 3D volume. Examining the PAA and PVA values (Table 1 of accompanying article), PAA and PVA were in range of one another for nearly all ablations except for the final procedure in Case 3. Nonetheless, this example of a relatively large disconnection between the TDE-derived PAA and PVA (87% vs 49%, respectively) may question the reliability of the

TDE, especially in a small number of cases. For lesions that are spherical or first-order ellipsoid, the TDE largely corresponds to volume ablated. For more complex-shaped lesions, as in the third recurrence in Case 3, this relationship may vary.

Another goal of our study was to examine if the TDE correlated with likelihood of recurrence. This was particularly noted in Case 1; this patient's lesion was fairly spherical, her PAA and PVA both exceeded 95%, and she has remained recurrence-free for more than 60 months. Similarly, Case 4 also had PAA and PVA exceeding 95%. This patient died from disease progression in other locations, but the ablated tumor did not recur. Although it is not entirely clear that a high PAA corresponds to longer recurrence-free survival, our results suggest that the PAA and TDE may be correlated with local control rates.

Regarding variability in response among the 4 patients, we agree with Dr. Souweidane. Although Case 1 attained a virtual cure and Case 4 showed resolution of the treated lesion, the other two patients had an intermediate response. The patient in Case 2 eventually underwent a posttreatment craniotomy and radiation therapy, and the patient in Case 3 suffered irreversible dysfunction, presumably from hypothalamic insult. The question regarding whether Case 2 would have had the same outcome without MRgLITT is something that cannot be answered. All patients had previously undergone craniotomies. Although MRgLITT is minimally invasive, it can still result in serious morbidity. We experienced this morbidity with Case 3 in which thermal injury was the suspected cause of the hypothalamic insult.

Finally, as Dr. Souweidane states, the COI for one of our coauthors is a concern. We explicitly state that this author was part of the study simply as a consultant in regard to the mathematical and software aspects of MRgLITT. The technical details and physics of thermal energy distribution in MRgLITT is an area of expertise held by Dr. Shetty. He specifically clarified the mathematical formulas and contributed to those corresponding sections in the Methods section of the paper.

We truly appreciate the editorial comments by Dr. Souweidane. We fully agree that more detailed and robust studies are needed, with independent validation, to determine the role of MRgLITT in the treatment spectrum for intracranial ependymomas. We hope that further innovation in MRgLITT and future studies can lead to a better methodology for therapy planning, thermal distribution, and prevention of thermal injury to eloquent structures. Although our study is limited by a very small sample size, retrospective nature, and variability in overall outcomes, we hope our experience can stimulate the interest needed to develop larger studies to determine MRgLITT's utility for recurrent ependymoma.