Radiosurgery for recurrent Grade 2 meningioma

TO THE EDITOR: We read with interest the recent article by Aboukais and colleagues (Aboukais R, Zairi F, Lejeune JP, et al: Grade 2 meningioma and radiosurgery. *J Neurosurg* 122:1157–1162, May 2015). In this article, the authors report on 27 patients with recurrent Grade 2 meningioma treated with radiosurgery alone. Patients were treated with a mean of 15.2 Gy. The actuarial local control rates were 75%, 52%, and 40% at 12, 24, and 36 months, respectively.

The results of this study do not significantly differ from those of other series (recently reviewed in Rogers et al., 2015), with the exception that increased treatment doses appear to yield somewhat higher control rates than those seen in this study, as noted by the authors. The authors conclude that radiosurgery is safe and effective for local control of recurrent atypical meningiomas. While we do not dispute the lessened short-term morbidity of radiosurgery compared with surgery, particularly at the doses used in this study, we would suggest that a 40% local control rate (i.e., a 60% failure rate) at 3 years does not indicate efficacy, as suggested by the authors. For reference, we have overlaid the authors’ progression-free survival Kaplan-Meier plot on the recurrence-free survival plot of Grade 2 meningiomas, which shows the course of these tumors with no treatment (Fig. 1). We acknowledge that there are limitations in this comparison, but to us, it calls into question the effect of radiosurgery on the tumor in that it does not seem to alter the natural history of the disease.

Based on this study and others, we would argue that radiosurgery alone is not sufficient therapy for Grade 2 meningiomas and should be reserved for the treatment of recurrence in patients who cannot undergo a second resection.

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DISCLOSURES
The authors report no conflict of interest.

References

Response
We would like to thank Mr. Bonney and Dr. Sughrue for taking the time to provide their insightful comments regarding our recent publication. Indeed, it is well known that surgery is the main treatment at initial management. As Grade 2 meningiomas represent severe disease and are characterized by a high rate of local recurrence, currently many authors recommend early postoperative radiotherapy to improve local control. Although the treatment of local recurrence remains controversial, we also strongly believe that surgery must be considered first when feasible. Nevertheless, poor general condition and tumor location near to critical structures are likely to dramatically increase surgical morbidity, making some patients not suitable for such strategy. As described in our article, the vast majority of patients included in our series harbored tumor recurrences located in a critical zone, such

FIG. 1. Kaplan-Meier plot demonstrating recurrence-free survival (solid line) of patients with Grade 2 meningiomas (modified with permission from Fig. 34.4, from Perry A, Meningiomas, in McLendon RE, Rosenblum MK, Bigner DD (eds): *Russell & Rubenstein’s Pathology of Tumors of the Nervous System*, ed 7. London: Hodder Arnold, 2006, pp 427–468) with overlaid local progression-free survival (dashed line) presented by Aboukais et al., 2015. The similarity of these plots may suggest that the natural growth of these tumors is altered little by radiosurgery.
Meckel’s cave, the sagittal sinus, or the cavernous sinus. Only 4 patients had recurrences located on the convexity; 3 of these patients had previously undergone multiple surgical procedures and radiation therapy, and 1 patient was 79 years old and had limited autonomy. The treatment of tumor recurrence in such situations is challenging and requires consideration of other therapeutic options, such as radiosurgery. In our study, we aimed to evaluate the efficiency of radiosurgery in patients not suitable for surgery who had clear evidence of tumor recurrence. Indeed, the 12-, 24-, and 36-month actuarial local control rates were 75%, 52%, and 40%, and we stated that radiosurgery was a “safe and effective treatment for local control of delayed progression after resection of a Grade 2 meningioma.” These results are modest but involve patients for whom therapeutic options were very limited. Our conclusion was based on our results, and also on the literature review, which reported improved local tumor control likely due to increased treatment doses. In the study by Choi and colleagues,1 the 12-, 24-, and 36-month actuarial local control rates were 100%, 100%, and 73%, with a mean dose of 22 Gy. Therefore, the major lesson of our study was to increase the prescribed dose to almost 20 Gy.

Like the authors, we believe that “radiosurgery alone is not sufficient therapy for Grade 2 meningiomas” and we place major hopes on the emergent medical therapies.2

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INNOVATIONS IN NEUROSURGERY

TO THE EDITOR: We would like to comment on the article by Marcus et al.1 (Marcus HJ, Hughes-Hallett A, Kwasnicki RM, et al: Technological innovation in neurosurgery: a quantitative study. J Neurosurg 123:174–181, July 2015) that was recently published in the Journal of Neurosurgery. In this study the authors searched a patent database to identify the top-performing patent codes, which were subsequently grouped into “technology clusters.” Concurrently, they queried PubMed to identify peer-reviewed publications. Patents and publications were used as metrics of technological development and clinical translation. The top-performing technology clusters identified using this methodology were image-guidance devices, clinical neurophysiology devices, neuromodulation devices, operating microscopes, and endoscopes. This article represents one of the first attempts to quantitatively evaluate technological innovation in the field of neurosurgery.

There are several aspects of this article’s methodology that we feel should be critiqued. First, the authors declare they searched for “granted patents,” but the description in the Methods section is insufficient to confirm that the search strategy included the patent codes for granted patents. Furthermore, the authors later describe compiling the “codes . . . for which the greatest number of patent applications had been submitted,” implying applications not granted patents. The authors compiled the “top 50 performing patent codes.” This is confusing, as “code” implies the type of patent document. Patent “classifications” are the US or International class codes that specify a subject area. Patent classifications would be meaningful to this analysis; patent codes less so.

The number of filed patents is used in this analysis as a proxy for technological advancement. This number can be highly influenced by factors relating to changes in patent law—for example, the change in patent terms in 1995, or with the more recent change from “first to invent” to “first to file.” These changes in patent law should be factored out. Moreover, filing patent applications costs a fair amount of money. Thus, the availability of funds can influence the number of patent applications rather than solely their “innovation impact.” Medtronic may have had an outsized influence on the results set, as a large commercial enterprise with plenty of funds would inherently be expected to file many patents.

Next, medical procedures themselves are not patentable. Therefore, using patents to track innovation may create an inherent bias against other contributions to changes in clinical practice. If the authors’ definition of innovation in clinical practice was limited to new technology, this definition would neglect any non-technological advancement.

The database utilized in this study is problematic as well. The database (DOCDB) does not contain the full text of patents nor the claims, only bibliographic data and abstracts. The appearance of key words in granted patent claims would be of more value than the appearance of key words in an abstract. Additionally, DOCDB is also a worldwide database. The data would be highly redundant, and the innovation sought by the authors is more likely to be centered in the US and Europe.

Lastly, the lead time from patent filing to clinical application is likely to be on the order of several years, and perhaps as long as a decade. Thus, today’s clinical advancements would be related to a cluster of patents filed sometime around 2005. Further examination of this phenomenon would be interesting. Marcus et al. quantitatively evaluated technological innovation in the field of neurosurgery,