LETTERS TO THE EDITOR

Gamma Knife surgery for trigeminal pain due to benign and malignant skull base tumors

TO THE EDITOR: We have read with great interest the recent article by Phan et al., discussing the role of Gamma Knife surgery (GKS) for trigeminal neuralgia (TN) secondary to recurrent malignant skull base tumors (Phan J, Pollard C III, Brown PD, et al: Stereotactic radiosurgery for trigeminal pain secondary to recurrent malignant skull base tumors. J Neurosurg [epub ahead of print April 27, 2018. DOI: 10.3171/2017.11.JNS172084]). The authors nicely discuss tumor control, symptom palliation, and opioid use/dependency.

The authors’ study highlights several important aspects. First, it underlines the role of single-fraction GKS as a primary treatment option for recurrent malignant skull base tumors in the context of secondary TN. Furthermore, in selected cases, the Extend system (Elekta AB) was used for hypofractionation. The potential role of the new Gamma Knife model ICON (Elekta) should also be underscored for this indication, because it allows frameless stereotactic treatment using a combination of cone-beam CT (CBCT), a thermoplastic mask system (allowing replacement in well-selected cases of the Leksell stereotactic G frame), and an infrared-based high-definition motion management camera system for patient tracking during treatment delivery. In fact, the ICON nicely combines the flexibility of the mask and CBCT with the well-known remarkable dose distribution and steep dose fall-off of the GKS treatment. Second, there is a need for tumor targeting and oncological control as a primary outcome. In cases of TNs related to benign skull base tumors, a wide variety of technical nuances have been reported, including initial targeting of the tumor only, targeting of...
the tumor and the nerve during the same session, and targeting of tumor and nerve at different time points. This makes the analysis of the outcomes, in terms of safety and efficacy, more difficult. Third, there is a radiobiological rationale that explains a more rapid decrease in lesion size compared with that of benign tumors, which would also explain, in some instances, the quick relief with regard to the nerve compression and further symptom alleviation. It is now well established that malignant tumors have higher α/β ratios, estimated to be closer to 10 and representative of early-responding tissues, whereas slow-growing benign brain tumors such as pituitary adenomas, arteriovenous malformations, and benign meningiomas have lower α/β ratios, estimated to be closer to 3 and representative of late-responding tissues.

In conclusion, the report by Phan et al. underlines the potential role of GKS in new indications, including skull base malignancies in patients with trigeminal pain, as in the context of a combined management for residual tumors after surgery and/or in cases of recurrence (Fig. 1). It also highlights the fact that GKS remains “an optimal skull base” tool due to its steep gradient, allowing optimal tumor coverage while sparing and/or improving neurological function. Furthermore, in benign, tumor-related secondary TN, the current literature is heterogeneous and does not answer to three essential questions: when (at what exact time point), what (is it the tumor? is it the nerve? both?), and how to target (retrogasserian versus root entry zone, etc.). On the other hand, in malignant skull base tumors, local control is the primary aim, and so there is limited room for technical nuances.

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References

Disclosures
The authors report no conflicts of interest.

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Response
We thank Dr. Tuleasca and coauthors for their kind comments and interest in our study. This manuscript was written shortly after FDA clearance of the Gamma Knife ICON model (Elekta AB), and therefore the patients included in this study were largely treated with frame-based, single-fraction Gamma Knife radiosurgery (GKS), with 4 cases treated with fractionated GKS using the Extend cranial immobilization system. As the authors from Lausanne have nicely summarized, the Gamma Knife ICON has a mask-based immobilization system, an infrared-based high-definition motion management system to track intrafraction motion, and cone beam CT image guidance. This system has the potential to deliver frameless single- and multi-fraction GKS and can be considered for use in the treatment of malignant skull base tumors causing trigeminal pain, as described in this article. We agree the patients in this study treated with Gamma Knife Extend (end-to-end accuracy < 2 mm) are also appropriate candidates for treatment with the ICON system. A potential advantage of the ICON system is increased tolerability and comfort with a frameless mask system. In our experience, the Extend system requires candidates to have calm demeanors, good dentition due to a vacuum-assisted bite block with custom prosthesis, and to be absolute non-gaggers.

As Tuleasca et al. appropriately alluded to, our goal and intent for each case is to treat the entire tumor to establish oncological control. There were a few exceptions when the entire tumor was not treated because the area in question was near a critical structure and not conclusively identified as tumor on imaging. However, in retrospect, these areas likely harbored tumor and subsequently progressed on MRI. This supports a major theme in this study that it is necessary to completely cover the tumor, and a frank discussion with the patient should take place regarding the potential toxicity risks associated with reirradiation. We believe one of the significant findings in this study is that among those with radiographic evidence of tumor control after GKS, there is a significant palliative impact that is
clinically measurable in terms of improved pain control and reduction in opioid requirement. We hypothesize that the facial pain is associated with the rapid growth observed with most malignant tumors and agree with our colleagues from Lausanne that the higher α/β ratios of these malignant tumors likely explain the pain relief and reduction in opioid analgesics that can be observed by 3 months posttreatment. Conversely, worsening of facial pain after a period of stability or improvement can be a harbinger of tumor progression.

A particular challenge with skull base reirradiation is the delivery of tumoral dose without exceeding the cumulative dose tolerance of nearby critical structures. This is further complicated by the likelihood that recurrent malignant tumors after prior conventionally fractionated (approximately 2 Gy per fraction) radiotherapy will harbor radioresistant clonogens. Thus, it is generally accepted that ablative doses with a high biologically effective dose (BED) are needed to achieve good tumor control. However, the optimal BED for malignant skull base tumors is yet to be determined. In our study, the median prescription dose of 17 Gy prescribed to the 50% isodose line in single-session-GKS patients corresponded to a mean dose > 27 Gy and calculated BED_{10} > 90 Gy. A similar BED is calculated for fractionated GKS when using 24 Gy in 3 fractions prescribed to the 46% isodose line. Extrapolating from the non–small cell lung cancer stereotactic body radiation therapy (SBRT) data, a BED > 100 Gy is required to achieve > 90% local control. Similarly, SBRT studies for recurrent squamous cell carcinomas of the head and neck suggest a BED > 90 Gy is associated with improved local control.

Lastly, we believe the mean dose and BED received by the entire target volume (margin tumor dose) should also be considered when evaluating a GKS plan. Even when the prescribed dose is the same, the mean and maximum doses received by the tumor volume can be very different, depending on factors such as dose distribution, shot placement, and choice of prescription isodose line. Evaluating the optimal BED as well as the BED and mean dose to the tumor in those patients with in-field recurrences are the subject of our current research.

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References

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