How safe, really, is jugular paraganglioma radiosurgery?

TO THE EDITOR: The contribution by Patel et al. showing excellent control of jugular paragangliomas with a treatment approach including Gamma Knife radiosurgery (GKRS) is welcomed (Patel NS, Carlson ML, Pollock BE, et al: Long-term tumor control following stereotactic radiosurgery for jugular paraganglioma using 3D volumetric segmentation. J Neurosurg [epub ahead of print April 13, 2018; DOI: 10.3171/2017.10.JNS17764]). Cranial nerve (CN) and other morbidities potentially associated with gross-total resection can be avoided with the use of radiosurgery. We noted the extremely low rate of new lower CN palsies (3%) after radiosurgery and could not find the baseline rates of tumor-induced or iatrogenic lower CN palsies in their patient cohort.

This information is important for two reasons: first, there may be little advantage (and increased risks both from preoperative embolizations and perioperative complications) to the use of surgery in patients who will require radiation postoperatively. The morbidity of surgery is added to the morbidity from irradiation. Second, the true risk of new cranial neuropathies may be higher in patients who are treated with definitive radiosurgery for jugular paragangliomas than was reported by Patel et al.; a nonfunctioning CN before radiosurgery cannot be further injured by the radiosurgical procedure.

In addition, recent reports highlight the possibility of confusing the pathology of an apparent jugular paraganglioma with other entities such as mesenchymal chondrosarcoma1 or metastatic renal cell carcinoma.2 In what situations would the authors recommend performing a biopsy to verify the diagnosis prior to administering radiosurgery?

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References

Disclosures
The authors report no conflict of interest.

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Response
We thank Drs. Knisely, Ramakrishna, and Schwartz for their insightful comments and questions. We agree that accurate characterization of the risks and anticipated morbidity of single or multimodality treatment is important for patient counseling. In the jugular paraganglioma literature, authors have reported CN function outcomes in a variety of ways. Also, not all cranial neuropathies from tumor or treatment are binary (e.g., partial vs complete paralysis; temporary vs permanent, etc.), further obfuscating data reporting. Additionally, a “gradual onset” cranial neuropathy that may occur due to progressive tumor growth or after radiosurgery, especially as it relates to vagal nerve function, may be well tolerated and even go unnoticed in many patients, whereas the sudden loss of the vagus nerve, as can occur during microsurgery, usually results in more prominent dysphagia and dysphonia. For the sake of simplicity, we originally reported the overall rate of new or worsened cranial neuropathy by using the total number of patients studied as the denominator. We believed that this was the most direct and intuitive method of reporting complications attributable to radiosurgery.

Among patients who underwent primary radiosurgery,
23% had pre-surgical radiosurgery (SRS) lower cranial neuropathy resulting from disease progression. Among patients who underwent SRS after prior microsurgical resection, 20% had baseline lower cranial neuropathy prior to any treatment. Iatrogenic lower CN palsy was noted in 32% of patients who underwent surgery either at our institution or elsewhere prior to radiosurgery.

As Drs. Knisely, Ramakrishna, and Schwartz point out, a CN rendered dysfunctional by prior surgery or tumor effect is no longer at risk at the time of radiosurgery. To allow the readers to draw their own conclusion from the data, we have included all available pre- and posttreatment CN function data for all patients treated since 1990 at our institution for analysis (Tables 1 and 2).

When analyzed in this manner, there were 174 CNs (with VII, X, and XII) at risk, with 2 new or worsened palsies. This might suggest a rate of new CN palsy of 1.1%. Alternatively, the rate of lower CN dysfunction would be 1.8% (2 new palsies of 110 CNs, with X and XII at risk). Regardless of how the data are evaluated, it is apparent that the rate of new or worsening CN paralysis is quite low whether SRS is used primarily or after prior microsurgical resection.

We also agree that mimickers of jugular paraganglioma are rare but important clinical entities, and recognize the cited works by Chhabra et al. and Thomas et al. As these authors discuss, imaging techniques can be used to distinguish renal cell carcinoma and chondrosarcoma from jugular paraganglioma. In most cases, we believe that modern contrast-enhanced MRI, combined with high-resolution temporal bone CT, is sufficient to distinguish paraganglioma from other tumors originating in the lateral skull base. Furthermore, diagnostic angiography is helpful to further clarify the diagnosis in select cases. Biopsy via transmastoid or transcana! hypotympanotomy techniques is straightforward and safe, and is certainly reasonable in cases in which the history may suggest alternative pathologies (i.e., a patient with another metastatic tumor or hematological malignancy), tumor growth does not follow the typical trajectory of jugular paraganglioma, cranial neuropathy is out of proportion to tumor size, or the radiological appearance is equivocal. One patient in our series underwent biopsy at another institution because biopsy via transmastoid or transcana! hypotympanotomy was not successful. In another case, a patient with persistent otitis media with effusion presented with otalgia, otalgia, and gait instability. Biopsy via transmastoid or transcana! hypotympanotomy was performed and revealed granulomatous inflammation and blastomycosis.

We thank the writers for their critical evaluation of our work and hope that our response adds clarity to the manuscript.

### TABLE 1. Summary of functioning CNs at risk prior to GKRS for jugular paraganglioma according to treatment cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Functioning Nerves at Risk Prior to GKRS</th>
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<tbody>
<tr>
<td></td>
<td>CN VII</td>
</tr>
<tr>
<td>Primary GKRS (n = 49)</td>
<td>45</td>
</tr>
<tr>
<td>GKRS following primary surgery (n = 31)</td>
<td>17</td>
</tr>
<tr>
<td>GKRS following prior GKRS or XRT (n = 2)</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
</tr>
</tbody>
</table>

XRT = external-beam radiotherapy.

### TABLE 2. Summary of new or worsened CN dysfunction after GKRS for jugular paraganglioma according to treatment cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>New or Worsened CN Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CN VII</td>
</tr>
<tr>
<td>Primary GKRS (n = 49)</td>
<td>0</td>
</tr>
<tr>
<td>GKRS following primary surgery (n = 31)</td>
<td>0</td>
</tr>
<tr>
<td>GKRS following prior GKRS or XRT (n = 2)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
</tr>
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</table>

SRS for presumed jugular paraganglioma, it is theoretically possible that we unknowingly treated an alternate pathology. However, because no cases in which SRS failed were found to be something other than paraganglioma on final pathological investigation after salvage surgery, it is reasonable to assume that either: 1) we correctly diagnosed all lesions before SRS, or 2) we may have treated nonparaganglioma lesion(s) with a therapeutic dose of radiation that resulted in growth arrest. Notably, the second and third most common neoplasms that occur at the jugular foramen after paraganglioma are meningioma and schwannoma, which are commonly treated with marginal doses of 16 Gy and 12.5 Gy, respectively—similar to that used for jugular paraganglioma.

To the authors’ point, we have encountered two unusual pathologies of the jugular foramen: (1) a case of a large meningioma of the jugular foramen, and (2) a case of a large schwannoma of the jugular foramen. In both cases, the radiological differential diagnosis included jugular foramen meningioma and jugular foramen schwannoma. In the case of meningioma, the authors noted that modern contrast-enhanced MRI, combined with high-resolution temporal bone CT, and diagnostic angiography are helpful to further clarify the diagnosis in select cases. Biopsy via transmastoid or transcana! hypotympanotomy techniques is straightforward and safe, and is certainly reasonable in cases in which the history may suggest alternative pathologies (i.e., a patient with another metastatic tumor or hematological malignancy), tumor growth does not follow the typical trajectory of jugular paraganglioma, cranial neuropathy is out of proportion to tumor size, or the radiological appearance is equivocal. One patient in our series underwent biopsy at another institution because biopsy via transmastoid or transcana! hypotympanotomy was not successful. In another case, a patient with persistent otitis media with effusion presented with otalgia, otalgia, and gait instability. Biopsy via transmastoid or transcana! hypotympanotomy was performed and revealed granulomatous inflammation and blastomycosis.

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**References**