Radiosurgery for glomus jugulare: history and recent progress

ZACHARY D. GUSS, A.B.,¹ SACHIN BATRA, M.B.B.S., M.P.H.,¹ GORDON LI, M.D.,²
STEVEN D. CHANG, M.D.,² ANDREW T. PARSIA, M.D.,³ DANIELE RIGAMONTI, M.D.,¹
LAWRENCE KLEINBERG, M.D.,⁴ AND MICHAEL LIM, M.D.¹

*Departments of ¹Neurosurgery and ⁴Radiation Oncology, The Johns Hopkins Hospital, Baltimore, Maryland;
²Department of Neurosurgery, Stanford University Medical Center, Stanford;
and ³Department of Neurological Surgery, University of California, San Francisco, California*

In this article the authors review the literature for recent studies of radiosurgical treatment for glomus jugulare. These studies demonstrate that radiosurgery results in similar glomus jugulare tumor control and a superior morbidity profile compared with surgical treatment. In addition, patients treated with radiosurgery usually remain stable clinically or improve. Given the indolent nature of these tumors, however, more follow-up is required to ensure that the immediate benefits are lasting. These preliminary reports demonstrate that the use of radiosurgery as a primary treatment for glomus jugulare should be extended to encompass more of the patients who are currently assigned to microsurgical treatment. (DOI: 10.3171/2009.9.FOCUS09195)

KEY WORDS • radiosurgery • glomus jugulare • CyberKnife •
Gamma Knife • linear accelerator

GLOMUS jugulare tumor treatment is at a crossroads. Decades of progress in surgery, external-beam radiation, and radiosurgery have led to the development of novel approaches that are well suited to control tumor growth and provide symptom relief for patients with glomus jugulare. The particularly indolent nature of glomus jugulare tumors, however, frustrates attempts to determine which treatment is optimal for these patients. To further this discussion, we provide a brief historical and contemporary context for the interventions used for glomus jugulare as well as a review of recent studies on glomus jugulare radiosurgery.

Overview of Glomus Jugulare

Despite being highly vascularized, glomus jugulare tumors are indolent; a study by Jansen et al.¹⁶ estimated the doubling time of jugulotympanic tumors to be 13.8 years and the annual growth rate to be 0.79 mm/year. Furthermore, that group found that jugulotympanic tumors were on average smaller in volume and growth rate than other head and neck paragangliomas such as carotid body or vagal body tumors.

Glomus jugulare tumors are rare: in all, glomus tu-

mors affect 1 in 30,000 people,²⁶ and the incidence of glomus jugulare specifically is ~ 1 in 1.3 million people.³¹ Azzarelli et al.² reported on a series of patients who presented with glomus jugulare tumors that had dopamine in the cells; such secretory tumors account for 1–3% of glomus jugulare cases.^{33,34} Although the commanding majority of glomus jugulare tumors are benign, a small fraction are metastatic. Brewis et al.⁴ estimated that between 1 and 4% of all glomus jugulare tumors are metastatic, although they note that this may be an overestimate due to preferential reporting of metastatic cases and to clinicians misidentifying benign multicentric glomus jugulare tumors as metastatic.

Overall, glomus jugulare tumors occur more frequently in women than in men.¹ Van der Mey et al.⁴⁶ reported, however, that this overrepresentation among women only applies to patients without a family history of glomus jugulare. Furthermore, within the group of nonfamilial glomus jugulare tumors, only 23% of cases were multicentric. Patients with familial glomus jugulare tumors displayed very different traits. For patients with a family history of glomus jugulare, the median age at diagnosis was younger, 48% of these patients had multicentric tumors, a higher proportion had bilateral tumors,⁴⁵ and neither sex was overrepresented compared with the nonfamilial cases. Later generations of familial cases also appeared to be diagnosed at earlier ages.

Abbreviations used in this paper: GKS = Gamma Knife surgery; LINAC = linear accelerator.

Familial glomus jugulare, which is transmitted from the father to his offspring, can be explained by genetic imprinting. Advances in epigenetics research will result in further understanding of the epidemiological features of glomus jugulare tumors.

The clinical presentation of glomus jugulare tumors is varied, with patients often presenting with multiple and varied symptoms. Several of the most common symptoms, however, are tinnitus and aural pulsations, decreased hearing, ear fullness, ear pain, and vertigo.¹⁹ Radiographic analysis can be obtained by MR imaging or high-resolution CT.^{7,19,41} Using these technologies allows the clinician to assign the glomus jugulare tumor a grade according to the Glasscock-Jackson (see Jackson et al.¹⁴) or Fisch⁸ classification scheme.

Surgical Treatment

Surgery in the jugular bulb began to be used in the 1930s,²⁴ and it has been the dominant treatment for glomus jugulare for decades. Progress came in the form of incremental improvements, as surgeons honed microsurgical techniques for better preservation of cranial nerve function and introduced preoperative embolization to reduce blood loss while resecting the tumor.²⁸

Although these improvements have lowered the rate of morbidity, complications of microsurgery remain more frequent and severe than those of radiosurgery. Green et al.¹² reported in 1994 on a group of 52 previously untreated patients who received microsurgery; 2–6% of those patients developed complications such as pneumonia, pulmonary embolus, wound infection, aspiration, and meningitis. Furthermore, 19% of patients were treated for paralyzed vocal cord, 8% required thyroplasty, and 8% required prolonged nasogastric tube feedings. Also, 29% of patients reported persistent hoarseness and 29% reported dysphagia. In 2001, Jackson et al.¹⁵ reported the results in 176 patients who received surgical treatment for glomus jugulare tumors; 5.5% of patients experienced tumor recurrence, with a median time to recurrence of 70 months. Postsurgery, new cranial nerve deficits were as follows: 57% in the 9th cranial nerve; 40% in the 10th; 62% in the 11th; and 54% in the 12th. Postoperative complications included meningitis, aspiration, and pneumonia. Recently, attempts have been made to combine surgery with other treatments for glomus jugulare, such as radiosurgery.²⁹

External-Beam Radiation

Fractionated conventional radiation therapy emerged as an attractive alternative to invasive surgery, because it avoided many of the causes of morbidity and death associated with the latter. The results for conventional radiation treatment of glomus jugulare tumors have demonstrated that this treatment controls tumor growth, although follow-up durations have been brief.^{18,41} Unlike surgery, in which treatment results in immediate and significant reduction in tumor volume, radiation therapy results in stable or reduced tumor size.³² Given the slow growth behavior of these tumors, it remains unproven that glomus jugulare tumors that receive radiation therapy will not

require additional treatment in the ensuing decades. Furthermore, although radiation therapy avoids some of the undesirable risks associated with surgery, it carries other serious hazards. In addition to short-term side effects such as alopecia, radiation therapy has been implicated in impairing cognitive function.⁴⁹ In 1991, Springate et al.⁴⁴ performed a literature review to investigate whether external-beam radiation or surgery is superior for treating glomus jugulare tumors. These investigators found that radiation alone was as effective as surgical or combined treatments, and carried a much lower risk of serious complications.

Radiosurgical Treatment

Radiosurgery has emerged as a treatment option that incorporates the benefits of radiation therapy while minimizing the adverse side effects. The sharp drop-off in radiation outside the targeted area allows clinicians to deliver a high dose of radiation precisely to the glomus jugulare while sparing healthy tissue. Additionally, studies have posited that glomus jugulare tumors themselves are radiation resistant, and that the benefits of radiation therapy for glomus jugulare tumors are due to the additional effects of radiation on the vasculature supporting the tumor.³ Radiosurgery has been used successfully to treat other vascular malformations, and therefore it may be distinctly advantageous against highly vascularized tumors such as glomus jugulare, compared with conventional radiation therapy.⁴⁸

A review by Gottfried et al.¹¹ in 2004 compared radiosurgery and conventional surgical approaches for glomus jugulare tumors and determined that radiosurgery was equally effective as surgery for tumor control and possessed lower morbidity and mortality rates. However, these authors also expressed several reservations about radiosurgery. Although the early results for radiosurgery are promising, they noted that it is unknown whether recurrences will occur in subsequent decades after treatment. Additionally, the mechanism by which radiosurgery is effective against glomus jugulare tumors remains unresolved. These tumors are radioresistant, and a leading theory about radiation's effectiveness against glomus jugulare is that radiation therapy attacks the highly developed vasculature of the tumors. However, angiographic studies obtained postradiation have not supported this hypothesis.

What follows is a discussion of the outcomes of the studies in which various radiosurgery modalities have been applied to treat glomus jugulare tumors. Table 1 summarizes the outcomes of 9 recent radiosurgical studies conducted from 2005 onward.

Gamma Knife Surgery. The GKS modality is a form of radiosurgery that uses 201 small ⁶⁰Co sources for accurate direction of a large dose of therapeutic radiation to a precise target, with radiation dropping off sharply outside of the target area. The GKS modality has been the most widely represented type of stereotactic radiosurgery reported in the literature for the treatment of glomus jugulare, and the results have consistently demonstrated this technology's potency and effectiveness. Early series

Radiosurgery of glomus jugulare

TABLE 1: Literature review of the use of radiosurgery for glomus jugulare: history and recent progress

Authors & Year	Modality	No. of Patients	Mean Mos of Follow-Up	Tumor Control (%)*	Symptom Control (%)*	Mean Margin Dose (Gy)
Miller et al., 2009	GKS†	5	34.0	80	100	15.0
Ganz & Abdelkarim, 2009	GKS	14	28.0	100	100	13.6
Sharma et al., 2008	GKS	24	26.1	100	100	16.5
Lim et al., 2007	LINAC‡	18	60.0	100	100	20.3
Henzel et al., 2007	LINAC	17	40.0	100	100	15–16§
Gerosa et al., 2006	GKS	20	50.9	100	90	17.3
Varma et al., 2006	GKS	17	48.0	71	88	15.3
Poznanovic et al., 2006	LINAC	8	15.6	100	100	15.0
Sheehan et al., 2005	GKS	8	28.0	100	100	14.7

* Control is defined as unchanged or improved status following radiosurgical treatment of glomus jugulare tumor.

† Patients received staged treatment of microsurgery followed by GKS.

‡ Thirteen patients were treated with CyberKnife radiosurgery.

§ Total dose of multiple fractions delivered was equivalent to single-fraction treatment of 15–16 Gy.

reports demonstrated the potential for this technique. A large multicenter study conducted by Liscak et al.,²³ in which the median follow-up time was 24 months, included 66 patients with glomus jugulare treated with GKS. Of these patients, 95% either had clinical improvement or remained stable; 47 were then followed with CT or MR imaging studies, and 60% of glomus jugulare tumors remained unchanged in size, whereas 40% of these decreased in size.

More recent studies have reported similarly encouraging outcomes for GKS for glomus jugulare. Saringer et al.³⁷ followed a group of 13 patients for an average of 50.4 months, in which all tumors were controlled and 3 (23%) regressed in size. All 12 patients who were followed (1 was lost to follow-up) were at least clinically stable, and half of the patients improved. Sheehan et al.⁴² reported results in a group of 8 patients in which all participants experienced tumor control and clinical stability or improvement over a median clinical follow-up period of 28 months and 32 months of radiographic follow-up. Sharma et al.⁴⁰ and Ganz and Abdelkarim⁹ similarly reported that all of their patients experienced control of tumor growth and clinical stability or improvement.

Other studies have demonstrated the potential for GKS and have highlighted occasional treatment failures. Jordan et al.¹⁷ included 8 patients; 1 worsened clinically, although all tumors were controlled and all of the other patients were stable clinically or improved. In Pollock's study,³⁵ nearly all of the 37 tumors analyzed were controlled, including 12 lesions that regressed. One tumor, however, increased in size. In a study by Gerosa et al.,¹⁰ all 20 patients displayed unchanged or decreased tumor size, but only 90% improved or remained stable clinically. Varma et al.⁴⁸ displayed the lowest rate of control in their group of 17 patients, with 15 (88%) stable clinically and 12 (71%) experiencing tumor control. Miller et al.²⁹ recently published a study that implemented a novel approach in which 5 patients received partial microsurgical resection followed by GKS. Similar approaches have re-

cently been successful for treating brain metastases.⁶ All patients in the study reported by Miller et al. improved clinically, although 1 tumor was not controlled.

Several observations can be drawn from these recent studies. Most importantly, as seen in Table 1, the follow-up times are brief. Given that neuropathies due to radiosurgery can occur > 1 year after treatment,³⁰ and considering that glomus tumors are indolent, the conclusions drawn from these recent studies are preliminary. The median time to recurrence in the surgical study of Jackson et al.¹⁵ was 70 months, which is longer than the follow-up for most of the recent radiosurgical studies. However, the available results do suggest that GKS has a low rate of morbidity and no deaths associated with its use for treatment of glomus jugulare. Of the 88 patients in Table 1 treated by GKS, only 3.4% displayed transient morbidity, and 2.3% displayed permanent toxicity associated with treatment. Transient symptoms included facial nerve palsy, tinnitus, hearing loss, and otalgia. Permanent symptoms were hearing loss and trigeminal neuralgia.

Several studies reported that there was no association between radiation dose and clinical outcome,⁴⁸ tumor control,^{13,48} or toxicity.^{22,37} The latter stands in contrast to the study published by Miller et al.,³⁰ which concluded that the most significant risk factor for developing trigeminal neuropathy after radiosurgery for vestibular schwannomas is the radiation dose. This group recommends doses < 16 Gy and notes that doses > 18 Gy were the strongest predictors of development of trigeminal neuropathy. This relationship may become apparent in radiosurgery for glomus jugulare as study populations increase, because the current low number of patients who have undergone glomus jugulare radiosurgery and who have experienced morbidity frustrates attempts to draw statistical inferences.

The LINAC and CyberKnife Modalities. The LINACs use a single radiation source rotated through one or more arcs. In this way, radiation is focused on the target for the entire duration of the operation, yet only passes through healthy tissues briefly.³⁸

Although the literature regarding LINAC treatment for glomus jugulare is sparse compared with that of GKS, the available results appear convincing as well. Poznanski et al.³⁶ published a series report in which 8 patients received LINAC treatment for glomus jugulare, and all patients exhibited tumor control and clinical stability over an average follow-up time of 15.6 months. Maarouf et al.²⁵ followed 12 patients who received LINAC treatment for glomus jugulare for a median duration of 48 months. Although no tumors increased in size (80% regressed and 20% remained unchanged), 8 improved clinically and 4 worsened.

Another option for radiosurgery treatment of glomus jugulare is the CyberKnife, a frameless system developed in the 1990s. By mounting a LINAC unit onto a robotic manipulator, the CyberKnife obviates the need for skeletal fixation. This feature is particularly useful for treating glomus jugulare tumors that extend beyond the limits of conventional frame-based radiosurgery devices such as the Gamma Knife.²¹ A report by Lim et al.²² in 2007 provides the most comprehensive data available for CyberKnife treatment for glomus jugulare. This study followed 18 patients with 21 glomus jugulare tumors, of whom 13 were treated with CyberKnife and the remainder were treated with conventional LINAC. After radiosurgery, all patients were clinically stable and all tumors either regressed (33%) or remained stable (67%), and little morbidity was reported. In addition, the investigators had a subset of patients that had > 10 years of follow-up. This cohort showed 100% control with no side effects. Given that the average time for tumor growth for glomus jugulare tumors is ~ 4.5 years, those authors concluded that they were able to observe tumor control for more than twice the tumor growth period. They suggested that radiosurgery was a durable treatment modality and recommended considering it as first-line therapy.

Similar to what was observed for GKS, single-fraction LINAC-based treatment for glomus jugulare reported in recent studies resulted in very low morbidity and no deaths. Of the 26 patients treated with single-fraction LINAC radiosurgery for glomus jugulare, 11.5% displayed transient morbidity, 3.8% exhibited permanent morbidity, and no deaths were reported. Ipsilateral tongue weakness that quickly resolved was noted in 2 patients, and 1 patient developed vertigo, which led to balance problems that did not fully resolve. One patient developed nausea and lower cranial nerve symptoms that required a brief hospitalization. Afterward, the cranial nerve symptoms resolved. As observed with the GKS studies, Lim et al.²² reported that there was no association between radiation dose and toxicity in patients treated with LINAC-based devices.

Fractionated Radiosurgery. Side effects from radiosurgical treatment of glomus jugulare tumors by GKS or LINAC are infrequent and generally transient. This is in part due to the radioresistant nature of cranial nerves.⁵ However, among affected patients, reported side effects include transient lower cranial nerve neuropathy,^{17,37} transient nerve palsy,⁹ and trigeminal neuralgia.⁴⁰

Although stereotactic radiosurgery has lower rates

of morbidity than surgery or conventional whole-brain radiation therapy, some investigators have proposed that fractionated stereotactic radiosurgery would further reduce the risk of cranial nerve toxicity when treating brain tumors with radiosurgery.⁴³ Groups have reported very low rates of cranial nerve deficits in treating vestibular schwannomas with fractionated radiosurgery.^{20,27,47} In similar fashion, Henzel et al.¹³ treated 17 patients who had glomus jugulare with fractionated LINAC radiosurgery, delivering small doses of radiation over ~ 30 fractions, equivalent to a single-fraction 15- to 16-Gy margin dose. All patients either improved clinically (56%) or remained stable (44%), and all tumors either decreased in size (31%) or remained unchanged (69%). The toxicity profile and clinical outcomes of this study, however, were not qualitatively different from those of single-fraction LINAC radiosurgery. In this study, 6 patients experienced low-grade nausea, and 2 each developed vertigo, headache, and mucositis. Toxicity was not associated with radiation dose. More studies are necessary to determine whether fractionated radiosurgery will yield a tangible benefit compared with single-fraction radiosurgery for patients with glomus jugulare.

Discussion

We have reported a brief history of glomus jugulare treatment, with a focus on recent radiosurgical progress. Although surgical approaches yield the benefits of immediate reduction in tumor size and pathohistological confirmation of their growth, the morbidity, mortality, and invasiveness associated with such procedures are significant. Furthermore, as demonstrated in Table 1, the tumor control and clinical outcomes for radiosurgery are excellent and harbor less risk for complications, given the non-invasive nature of radiosurgery and the radioresistance of cranial nerves. Although there is concern that radiosurgically treated glomus jugulare tumors may recur over the decades that follow treatment, the reduced risk associated with the procedure is considerable.

At present, the issue of what is the best treatment for glomus jugulare remains unresolved. Some recent guidelines for treating these lesions have either been indecisive or suggested radiosurgery only for the elderly and those unfit for surgery.^{7,13,39} Others have recommended the expansion of radiosurgery. Sheehan et al.⁴² conditionally recommend radiosurgical treatment for small tumors < 3 cm in average dimension, residual or recurrent tumor after surgery, and fractionated radiosurgery for unresectable large tumors.

At our institution, patients with incidentally discovered asymptomatic glomus tumors are initially observed. We then recommend radiation or surgical intervention once the tumors grow or if a patient becomes symptomatic. In the past, surgery was the favored modality of treatment. However, we currently favor radiosurgery as a frontline treatment. We also found that surgery can carry significant morbidity, whereas our patients who received radiation had good tumor control with minimal side effects. In general, we agree with Sheehan et al. and recommend radiosurgery for patients who have tumors that

Radiosurgery of glomus jugulare

are < 3 cm in diameter. For patients with larger lesions, fractionated stereotactic radiosurgery is recommended. There will always be some patients, however, for whom surgery is appropriate, such as patients who present with large symptomatic tumors with mass effect on the brainstem.

The growing body of research demonstrates the effectiveness and safety of radiosurgery for treatment of glomus jugulare, and the data in many studies support the extension of the use of radiosurgery as the primary treatment for a wider population base.

Conclusions

Radiosurgery is a safe and effective treatment for glomus jugulare. Its application should be extended beyond patients who are elderly or ill suited for surgery to become the standard of care for primary treatment of glomus jugulare lesions < 3 cm in diameter.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

1. Alford BR, Guilford FR: A comprehensive study of tumors of the glomus jugulare. **Laryngoscope** 72:765–805, 1962
2. Azzarelli B, Felten S, Muller J, Miyamoto R, Purvin V: Dopamine in paragangliomas of the glomus jugulare. **Laryngoscope** 98:573–578, 1988
3. Brackmann DE, House WF, Terry R, Scanlan RL: Glomus jugulare tumors: effect of irradiation. **Trans Am Acad Ophthalmol Otolaryngol** 76:1423–1431, 1972
4. Brewis C, Bottrill ID, Wharton SB, Moffat DA: Metastases from glomus jugulare tumours. **J Laryngol Otol** 114:17–23, 2000
5. Chong V: Imaging the cranial nerves in cancer. **Cancer Imaging 4 Spec No A**:S1–S5, 2004
6. Do L, Pezner R, Radany E, Liu A, Staud C, Badie B: Resection followed by stereotactic radiosurgery to resection cavity for intracranial metastases. **Int J Radiat Oncol Biol Phys** 73:486–491, 2009
7. Fayad JN, Schwartz MS, Brackmann DE: Treatment of recurrent and residual glomus jugulare tumors. **Skull Base** 19:92–98, 2009
8. Fisch U: Infratemporal fossa approach for glomus tumors of the temporal bone. **Ann Otol Rhinol Laryngol** 91:474–479, 1982
9. Ganz JC, Abdelkarim K: Glomus jugulare tumours: certain clinical and radiological aspects observed following Gamma Knife radiosurgery. **Acta Neurochir (Wien)** 151:423–426, 2009
10. Gerosa M, Visca A, Rizzo P, Foroni R, Nicolato A, Bricolo A: Glomus jugulare tumors: the option of gamma knife radiosurgery. **Neurosurgery** 59:561–569, 2006
11. Gottfried ON, Liu JK, Couldwell WT: Comparison of radiosurgery and conventional surgery for the treatment of glomus jugulare tumors. **Neurosurg Focus** 17(2):E4, 2004
12. Green JD Jr, Brackmann DE, Nguyen CD, Arriaga MA, Telischi FF, De la Cruz A: Surgical management of previously untreated glomus jugulare tumors. **Laryngoscope** 104:917–921, 1994
13. Henzel M, Hamm K, Gross MW, Surber G, Kleinert G, Failing T, et al: Fractionated stereotactic radiosurgery of glomus jugulare tumors. Local control, toxicity, symptoms, and quality of life. **Strahlenther Onkol** 183:557–562, 2007
14. Jackson CG, Glasscock ME III, Harris PF: Glomus tumors. Diagnosis, classification, and management of large lesions. **Arch Otolaryngol** 108:401–410, 1982
15. Jackson CG, McGrew BM, Forest JA, Netterville JL, Hampf CF, Glasscock ME III: Lateral skull base surgery for glomus tumors: long-term control. **Otol Neurotol** 22:377–382, 2001
16. Jansen JC, van den Berg R, Kuiper A, van der Mey AG, Zwinderman AH, Cornelisse CJ: Estimation of growth rate in patients with head and neck paragangliomas influences the treatment proposal. **Cancer** 88:2811–2816, 2000
17. Jordan JA, Roland PS, McManus C, Weiner RL, Giller CA: Stereotactic radiosurgery for glomus jugulare tumors. **Laryngoscope** 110:35–38, 2000
18. Larner JM, Hahn SS, Spaulding CA, Constable WC: Glomus jugulare tumors. Long-term control by radiation therapy. **Cancer** 69:1813–1817, 1992
19. Larson TC III, Reese DF, Baker HL Jr, McDonald TJ: Glomus tympanicum chemodectomas: radiographic and clinical characteristics. **Radiology** 163:801–806, 1987
20. Lederman G, Lowry J, Wertheim S, Fine M, Lombardi E, Wronski M, et al: Acoustic neuroma: potential benefits of fractionated stereotactic radiosurgery. **Stereotact Funct Neurosurg** 69:175–182, 1997
21. Li G, Chang S, Adler JR Jr, Lim M: Irradiation of glomus jugulare tumors: a historical perspective. **Neurosurg Focus** 23(6):E13, 2007
22. Lim M, Bower R, Nangiana JS, Adler JR, Chang SD: Radiosurgery for glomus jugulare tumors. **Technol Cancer Res Treat** 6:419–423, 2007
23. Liscak R, Vladyka V, Wowra B, Kemeny A, Forster D, Burzaco JA, et al: Gamma Knife radiosurgery of the glomus jugulare tumour—early multicentre experience. **Acta Neurochir (Wien)** 141:1141–1146, 1999
24. Lundgren N: Tympanic body tumours of the middle ear; tumours of the carotid body type. **Acta Otolaryngol** 37:367–379, 1949
25. Maarouf M, Voges J, Landwehr P, Bramer R, Treuer H, Kocher M, et al: Stereotactic linear accelerator-based radiosurgery for the treatment of patients with glomus jugulare tumors. **Cancer** 97:1093–1098, 2003
26. Mariman EC, van Beersum SE, Cremers CW, van Baars FM, Ropers HH: Analysis of a second family with hereditary non-chromaffin paragangliomas locates the underlying gene at the proximal region of chromosome 11q. **Hum Genet** 91:357–361, 1993
27. McClelland S III, Gerbi BJ, Higgins PD, Orner JB, Hall WA: Safety and efficacy of fractionated stereotactic radiotherapy for acoustic neuromas. **J Neurooncol** 86:191–194, 2008
28. Michael LM II, Robertson JH: Glomus jugulare tumors: historical overview of the management of this disease. **Neurosurg Focus** 17(2):E1, 2004
29. Miller JP, Semaan M, Einstein D, Megerian CA, Maciunas RJ: Staged Gamma Knife radiosurgery after tailored surgical resection: a novel treatment paradigm for glomus jugulare tumors. **Stereotact Funct Neurosurg** 87:31–36, 2009
30. Miller RC, Foote RL, Coffey RJ, Sargent DJ, Gorman DA, Schomberg PJ, et al: Decrease in cranial nerve complications after radiosurgery for acoustic neuromas: a prospective study of dose and volume. **Int J Radiat Oncol Biol Phys** 43:305–311, 1999
31. Moffat DA, Hardy DG: Surgical management of large glomus jugulare tumours: infra- and trans-temporal approach. **J Laryngol Otol** 103:1167–1180, 1989
32. Mukherji SK, Kasper ME, Tart RP, Mancuso AA: Irradiated paragangliomas of the head and neck: CT and MR appearance. **AJNR Am J Neuroradiol** 15:357–363, 1994

33. Netterville JL, Jackson CG, Miller FR, Wanamaker JR, Glasscock ME: Vagal paraganglioma: a review of 46 patients treated during a 20-year period. **Arch Otolaryngol Head Neck Surg** **124**:1133–1140, 1998
34. Pavai Z, Orosz Z, Horvath E, Seres-Sturm L, Jung J: Immunohistochemical features of paragangliomas. **J Cell Mol Med** **5**:311–316, 2001
35. Pollock BE: Stereotactic radiosurgery in patients with glomus jugulare tumors. **Neurosurg Focus** **17**(2):E10, 2004
36. Poznanovic SA, Cass SP, Kavanagh BD: Short-term tumor control and acute toxicity after stereotactic radiosurgery for glomus jugulare tumors. **Otolaryngol Head Neck Surg** **134**:437–442, 2006
37. Saringer W, Khayal H, Ertl A, Schoeggl A, Kitz K: Efficiency of gamma knife radiosurgery in the treatment of glomus jugulare tumors. **Minim Invasive Neurosurg** **44**:141–146, 2001
38. Schwartz M: Stereotactic radiosurgery: comparing different technologies. **CMAJ** **158**:625–628, 1998
39. Semaan MT, Megerian CA: Current assessment and management of glomus tumors. **Curr Opin Otolaryngol Head Neck Surg** **16**:420–426, 2008
40. Sharma MS, Gupta A, Kale SS, Agrawal D, Mahapatra AK, Sharma BS: Gamma knife radiosurgery for glomus jugulare tumors: therapeutic advantages of minimalism in the skull base. **Neurol India** **56**:57–61, 2008
41. Sharma PD, Johnson AP, Whitton AC: Radiotherapy of jugulotympanic paragangliomas (glomus jugulare tumours). **Laryngol Otol** **98**:621–629, 1984
42. Sheehan J, Kondziolka D, Flickinger J, Lunsford LD: Gamma knife surgery for glomus jugulare tumors: an intermediate report on efficacy and safety. **J Neurosurg** **102** (Suppl):241–246, 2005
43. Song DY, Williams JA: Fractionated stereotactic radiosurgery for treatment of acoustic neuromas. **Stereotact Funct Neurosurg** **73**:45–49, 1999
44. Springate SC, Haraf D, Weichselbaum RR: Temporal bone chemodectomas—comparing surgery and radiation therapy. **Oncology** **5**:131–137, 1991
45. Sugarbaker EV, Chretien PB, Jacobs JB: Bilateral familial carotid body tumors: a report of a patient with an occult contralateral tumor and postoperative hypertension. **Ann Surg** **174**:242–247, 1971
46. van der Mey AG, Maaswinkel-Mooy PD, Cornelisse CJ, Schmidt PH, van de Kamp JJ: Genomic imprinting in hereditary glomus tumours: evidence for new genetic theory. **Lancet** **2**:1291–1294, 1989
47. Varlotto JM, Shrieve DC, Alexander E, Kooy HM, Black PM, Loeffler JS: Fractionated stereotactic radiotherapy for the treatment of acoustic neuromas: preliminary results. **Int J Radiat Oncol Biol Phys** **36**:141–145, 1996
48. Varma A, Nathoo N, Neyman G, Suh JH, Ross J, Park J, et al: Gamma knife radiosurgery for glomus jugulare tumors: volumetric analysis in 17 patients. **Neurosurgery** **59**:1030–1036, 2006
49. Welzel G, Fleckenstein K, Schaefer J, Hermann B, Kraus-Tiefenbacher U, Mai SK, et al: Memory function before and after whole brain radiotherapy in patients with and without brain metastases. **Int J Radiat Oncol Biol Phys** **72**:1311–1318, 2008

Manuscript submitted August 15, 2009.

Accepted September 3, 2009.

Address correspondence to: Michael Lim, M.D., Department of Neurosurgery, The Johns Hopkins University School of Medicine, Phipps Building, Room 123, 600 North Wolfe Street, Baltimore, Maryland 21287. email: mlim3@jhmi.edu.