**Irradiation of glomus jugulare tumors: a historical perspective**

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Glomus jugulare tumors are rare, slow-growing vascular lesions that arise from the chief cells of the paraganglia within the jugular bulb. They can be associated with the tympanic branch of the glossopharyngeal nerve (Jacobson nerve) or the auricular branch of the vagus nerve (Arnold nerve) and are also referred to as chemodectomas or nonchromaffin paragangliomas. Optimal treatment of these histologically benign tumors remains controversial. Surgery remains the treatment of choice, but can carry high morbidity rates. External-beam radiation was originally used for subtotal resections and in patients who were poor surgical candidates; however, radiosurgery has recently been introduced as an effective and safe treatment option for patients with these tumors. In this article the authors discuss the history of radiation therapy for glomus jugulare tumors, focusing on recent radiosurgical results. (DOI: 10.3171/FOC-07/12/E13)

**KEY WORDS** • CyberKnife • glomus jugulare • historical perspective • radiosurgery

**Glomus jugulare tumors**, which are also termed nonchromaffin paragangliomas or chemodectomas, are indolent hypervascular tumors that originate from the chief cells of the paraganglia within the jugular bulb. They can be associated with the tympanic branch of the glossopharyngeal nerve (Jacobson nerve) or the auricular branch of the vagus nerve (Arnold nerve) and are also referred to as chemodectomas or nonchromaffin paragangliomas. Optimal treatment of these histologically benign tumors remains controversial. Surgery remains the treatment of choice, but can carry high morbidity rates. External-beam radiation was originally used for subtotal resections and in patients who were poor surgical candidates; however, radiosurgery has recently been introduced as an effective and safe treatment option for patients with these tumors. In this article the authors discuss the history of radiation therapy for glomus jugulare tumors, focusing on recent radiosurgical results. (DOI: 10.3171/FOC-07/12/E13)

**Overview**

According to Bickerstaff and Howell,2 glomus jugulare tumors were first described in 1840 by Valentin, who originally characterized the lesion as a ganglion. As Ruben23 recounts, however, it was not until 1941 that the term was coined by Guild at the American Association of Anatomists meeting in Chicago. Four years later, Rosenwasser published the first case report of a glomus jugulare tumor, in a 36-year-old man who presented with left facial paralysis, a mass in the left external auditory canal, and left-sided hearing loss. These tumors account for 0.6% of all cranial neoplasms and are generally sporadic, although they can sometimes be familial, with autosomal dominance and incomplete penetrance. Clinically, patients often present with large tumors. The most common symptoms include conductive hearing loss and pulsatile tinnitus. Patients can also present with cranial nerve deficits of the 9th, 10th, and 11th cranial nerves secondary to the mass effect on neighboring structures such as cranial nerves and vasculature.10 Others present with thrombus of the nearby venous structures, whereas a small percentage of patients initially present with labile blood pressures and tachycardia secondary to catecholamine release by the tumor.5,19

**Surgical Treatment**

One of the first reported surgically treated cases of glomus jugulare tumor was published by Rosenwasser. According to Ruben,21 Rosenwasser performed surgery on a 36-year-old patient on April 18, 1942, and described a large purple mass in the middle ear that was attached to the hypotympanum. He was only able to achieve a subtotal resection due to the constraints of the opening and complex anatomy. Since then, significant advances in the surgical treatment of this tumor have been made due to developments in microsurgery.21 Despite this progress, surgical treatment of glomus jugulare tumors continues to carry a high rate of morbidity. Complications from resection include stroke (8–20%) and cranial nerve injury (33–44%). In addition, the overall mortality rate from this surgery

**Abbreviations used in this paper:** GKS = Gamma Knife surgery; LINAC = linear accelerator.
remains at 5–13%.5 The complex anatomy of critical cranial nerves and vessels within the jugular bulb and through the tumor often prevents a complete resection.

Radiation Therapy: Historical Review

External-Beam Radiation

In the 1950s, external-beam radiation was introduced as an adjunct to surgical removal of tumors in subtotal resections.3,12 Williams et al.26 published the results from the Mayo Clinic in 1955 and noted definite improvement at doses of 13–20 Gy delivered to the tumor over 2 weeks. Almost 20 years later, in 1973, the M.D. Anderson experience was presented by Miller, who reported on 14 patients treated between 1944 and 1964 who received 45 Gy over 35 days. A minimal mortality level was reported, with only 1 of 14 patients dying of late brain necrosis 38 months after the treatment. Springate and Weichselbaum22 reviewed 19 articles in which treatment of glomus jugulare tumors was evaluated prior to 1981. These separate reports indicated that glomus jugulare tumors were radiosensitive, which was confirmed with metaanalysis. These investigators found local control in 349 of 384 patients, with minimal morbidity and mortality levels. Indications for external-beam radiation were later expanded to include patients who were poor surgical candidates. As a result, an increase in the number of patients with glomus jugulare tumors who were being treated with external-beam radiation was observed. By 1994, Mukherji et al.23 reported that practitioners at institutions using external-beam radiation achieved tumor control, defined as stable or decreased tumor size, in ≥ 70% of their patients.

Despite high control rates, external-beam radiation requires large field sizes that extend down to the upper neck. Complications resulting from the larger field sizes were significant and included radionecrosis of bone, possible induction of secondary malignancies, and xerostomia.14,19 The advent of intensity-modulated radiation therapy has reduced the extent of normal tissue exposed to radiation, which in the future is likely to be accompanied by a decrease in side effects.

Advent of Radiosurgery

Traditional external-beam radiation is limited by the relative imprecision of radiation techniques used to target the tumor and to exclude normal tissue, and the reliance on a prolonged treatment course often requiring several weeks. The term “radiosurgery” was coined by a Swedish neurosurgeon, Lars Leksell, who initially developed a method of precisely cross-firing radiation beams to treat psychiatric diseases.12 The field of stereotactic radiosurgery has emerged as an effective means with which to address many of the pitfalls of traditional external-beam radiation. It is defined by a high degree of accuracy, precision, and rapid falloff at the periphery of target lesions, and is given in 1–5 high-dose treatments.12,13

Glomus jugulare tumors were considered ideally suited for radiosurgery because they are well-defined, nonfiltering, radiosensitive tumors. Because of the precision and rapid drop-off of radiation, a larger dose of radiation can be administered to the tumor without exceeding the tolerance of surrounding normal tissues.

Gamma Knife Surgery

Based on concepts developed by Leksell, GKS relies on rigid skeletal fixation of a stereotactic head frame to the skull; this frame is used as a reference for the precisely directed, crossfired radiation beams. The unit consists of 201 small 60Co sources distributed evenly over a portion of a sphere. Each source produces a narrow collimated beam of radiation, all of which intersect at the target point, thus producing a steep radiation-dose gradient.24 Practitioners at a few GKS centers began to treat glomus jugulare tumors with radiosurgery in the early 1990s, and the first published series appeared in 1995.6,11,17,18 Foote and colleagues reported their experience with GKS in 9 patients with glomus tumors and demonstrated tumor control with no long-term complications. Jordan et al.10 reported no tumor progression and no delayed cranial neuropathies in their series of 8 patients treated with GKS. The longest follow-up has been reported more recently by Bari et al.,1 who treated 8 patients with glomus jugulare tumors by using GKS, with a follow-up range of 52–97 months. Five of 8 patients showed a decrease in the size of the lesion at the time of follow-up, whereas the remaining 3 had stable disease. Controversy still surrounds radiosurgical treatment of these lesions; some practitioners argue that at least a 10-year follow-up period is required to make any predictions for long-term efficacy and safety.

The largest series of patients with glomus jugulare tumors treated with GKS was published by Eustacchio et al.,6 who reported tumor control in 18 of 19 patients and no complications. Liscák et al.18 published higher complication rates in their study of 14 patients treated with GKS.
even though 100% control in tumor growth was achieved. In their study, 3 of 14 patients complained of worsening hearing.

Use of LINAC-Based Radiosurgery Prior to Advent of the CyberKnife

The LINAC has a single source of radiation that creates a high dose at the target point because the source is rotated through an arc or set of arcs. The radiation beam is directed at the target for the entire treatment time but passes through other parts of the brain only momentarily. Traditional LINAC-based radiosurgical systems used prior to the advent of the CyberKnife required rigid skeletal fixation to a stereotactic frame. Lim et al. reported the outcome in 4 patients with glomus jugulare tumors that were irradiated with LINAC-based radiosurgery. Although the number of cases was small, the median follow-up was 10.5 years for radiographic follow-up and 13.2 years clinically. In all 4 cases, the size of the tumors remained unchanged over this period of time and no permanent side effects were reported.

Nevertheless, not every center has reported such favorable results with LINAC radiosurgery. Feigenberg et al. reported tumor control in 3 of 5 patients when using photons from a LINAC unit, but tumors in 2 of 5 patients progressed in size at 6 and 40 months after irradiation. In another small LINAC-treated series reported by Maarouf et al., all 12 patients had stable or decreased tumor size with stable or improved clinical symptoms at a median follow-up of 4 years. It is noted that that Feigenberg et al. prescribed a higher median dose (25 Gy) than Maarouf et al., whose median dose was 15 Gy. The median dose at Stanford was 21.5 Gy.

CyberKnife Radiosurgery

The CyberKnife machine created by Stanford neurosurgeon John Adler in the 1990s represents a change from the traditional stereotactic radiosurgery machines. The CyberKnife unit is frameless and image-guided, and the radiation is delivered by a compact 6-MV LINAC unit mounted on a robotic manipulator that is able to bring in beams from 1200 directions. The CyberKnife offers the flexibility of nonisocentric beam delivery to provide optimal dose conformity without compromise of dose homogeneity. Also, by eliminating the need for fixation to skeletal structures, the CyberKnife also allows radiosurgery to be applied to targets beyond the brain. In some situations, glomus jugulare tumors may extend below the mid-C2 level, which may thereby limit frame-based treatments. Frameless systems allow extension of the treatment plan to these tumors that extend into the neck. To date, the CyberKnife has been used to treat the largest number of glomus jugulare tumors. The largest experience with CyberKnife radiosurgery for these lesions (in 15 patients with glomus jugulare tumors) was reported by Lim et al. in 2004. The results are similar to the outcomes reported after GKS and nonrobotic LINAC treatment. The mean follow-up duration was 21...
months, ranging from 4 to 114 months. Most patients received radiosurgery as their first treatment, but 3 of the 15 patients had previously undergone open surgery for their tumors. Tumor sizes were in the range of 1.5–6.2 cm (mean 3.1 cm) in terms of the maximum dimension of the tumor. Four of 15 patients treated with CyberKnife stereotactic radiosurgery alone experienced a regression of their tumor size, with the remaining patients’ tumor sizes remaining stable. Figure 1 shows a pretreatment magnetic resonance image of a patient with a right-sided glomus jugulare tumor. Figure 2 is an example of the CyberKnife treatment plan.

Two of the 15 patients experienced transient worsening of preprocedural cranial nerve deficits. These resolved within months, and there was no long-term worsening of preprocedural deficits. These results confirmed the low rate of cranial nerve injury seen with other modalities.9,10,18

Discussion and Conclusions

We have presented a brief history and overview of radiation treatment for glomus jugulare tumors, focusing on recent radiosurgical results. Due to the complex anatomy surrounding the tumors, resection often carries high rates of morbidity and mortality. External-beam radiation therapy has been used as an adjunct for subtotal resections since the 1950s, and later was used alone for patients who were poor surgical candidates. However, external-beam radiation requires large field sizes that often must include the upper neck and skull base, and complications from the larger field sizes include radionecrosis of bone, possible induction of secondary malignancies, and xerostomia. The advent of stereotactic radiosurgery has allowed the use of higher radiation doses, with increased accuracy and rapid falloff of radiation to normal tissue. Since 1995, multiple GKS-, LINAC-, and CyberKnife-based series have been reported; collectively they show excellent tumor control and relatively low complication rates. Although longer-term follow-up studies are still in progress, the results in outcome studies published to date are good enough to justify the use of radiosurgery as a first-line treatment strategy for glomus jugulare tumors.

References


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