ORIGINAL ARTICLE



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Gamma Knife radiosurgery for glomus tumors: Long-term results in a series of 30 patients

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Abstract

Background: Glomus tumors are rare and benign hypervascular tumors. Surgery represented the mainstay of their treatment, even if it has been associated with high morbidity and mortality rates. Recently, the treatment shifted to a multimodal approach and Gamma Knife radiosurgery represents one of the treatment options. **Methods:** Authors retrospectively analyzed the clinical and radiological outcome of a series of patients who underwent Gamma Knife radiosurgery for glomus tumors. **Results:** Thirty patients underwent Gamma Knife radiosurgery. Mean tumor volume was 7.69 cc (range 0.36-24.6). Mean tumor margin dose was 16 Gy (range 13-18). Median follow-up was of 91 months (mean 90; range 11-172). Overall clinical control rate was 100%; overall volumetric tumor control rate was 96.6%. Patients' and tumors' characteristics, treatment data, and outcome have been analyzed.

Conclusion: Gamma Knife radiosurgery represents a safe and effective treatment for glomus tumors. Longer follow-up and larger cohort studies are needed to definitively outline the role of Gamma Knife radiosurgery for glomus tumors.

KEYWORDS

chemodectoma, Gamma Knife, glomus tumor, radiosurgery, skull base

1 | INTRODUCTION

Glomus tumors are rare, generally benign, slow growing, and hypervascular tumors arising from the paraganglia of the chemoreceptor bodies at the carotid body, the jugular bulb, and the vagal ganglia.^{1,2}

They can also be located with the tympanic branch of the glossopharyngeal nerve or the auricular branch of the vagus nerve.³ According to their origin, they are classified as glomus jugulare, glomus tympanicum, glomus caroticum, and glomus vagale.^{4,5}

The incidence of glomus tumors is about 1 per 1.3 million people usually occurring between 50 and 60 years of age and affecting more frequently women.^{1,3,6} Glomus tumors account for 0.6% of all cranial tumors and they are generally sporadic, however familiar cases have been reported in approximately 20%.^{7–10} Dopamine secretion is detected in about 1%-3% of tumors.^{7,11–14} Glomus tumors are benign but locally aggressive tumors with growth of about 0.79 mm/year.^{7,12,15}

Malignant changes can occur in about 3% of cases; in 1%-4% of cases they can be metastatic at the diagnosis. 12,16,17

Patients usually experience hearing loss, pulsatile tinnitus, vertigo, lower cranial nerves deficits, dizziness, and labile blood pressure or tachycardia in case of secreting tumors.^{1,7,11,15}

The treatment of glomus tumors is still a matter of debate. Surgery has been considered the first choice treatment for decades, however it is still related to high morbidity and mortality.^{12,13} The surgical mortality rate ranges from 2.6% to 13% in the pertinent literature, while the rate of cranial nerve (CN) injury ranges from 18.7% to 44% depending on the series.^{12,13,18}

Endovascular embolization of feeding vessels from the ascending pharyngeal artery has been adopted to reduce intraoperative bleeding during tumor resection.^{7,8,19}

Radiation therapy (RT), and more recently fractionated-RT, has been also considered in the treatment algorithm of glomus tumors with acceptable tumor control, nevertheless

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the patients may be exposed to the risk of radiation-related long-term complications. $^{6,12-14}$

Gamma Knife radiosurgery for glomus tumors has been introduced in the 1990s, and to date, a total of 770 patients undergoing Gamma Knife radiosurgery have been reported.²⁰

The purpose of this study was to retrospectively analyze the outcome of a series of 30 patients underwent Gamma Knife radiosurgery for skull base glomus tumors in our institution.

2 | MATERIALS AND METHODS

2.1 | Patients' selection

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The medical records, treatment protocols, and the most recent clinical and radiological follow-up data of patients treated with Gamma Knife radiosurgery for skull base glomus tumors in our institution until 2015 were prospectively collected and retrospectively analyzed. Clinical, radiological, and follow-up data of patients treated before 2002 were not fully available, making it necessary to exclude them from the analysis process.

All patients signed the informed consent for personal data treatment and all the procedures were performed according to the ethical standards.

2.2 | Radiosurgical procedure

The Leksell Gamma Unit Model C (Elekta Instruments, Inc., Stockholm, Sweden) was used until August 2007, whereas after 2007 to date, the Perfexion Model (Elekta Instruments, Inc., Stockholm, Sweden) was adopted. The Leksell stereotactic head frame (model G) was positioned and magnetic resonance images (MRI; 1.5-tesla; Magnetom Vision, Siemens, Munich, Germany) were performed. The MR imaging sequences used are as follows: T1-weighted and T2-weighted without contrast and T1-weighted with contrast. Slices were obtained every 2 mm in axial and coronal planes. For those patients operated before, a CT scan was performed and fused with the MRI study. The GammaPlan system (Elekta Instruments, Inc., Stockholm, Sweden) was used for treatment planning, volume, and dose calculation. All Gamma Knife radiosurgery treatments were delivered in a single dose. A team including a neurosurgeon, neuroradiologist, and a medical physicist performed the Gamma Knife radiosurgery dose planning. All patients were discharged the day after the treatment.

In treatment planning, we try to treat the tumor volume with at least a marginal dose of 14 Gy at 50% isodose, when possible, because lower doses are associated with poor tumor control.^{9,21,22}

2.3 | Clinical and radiological assessment

All patients underwent a complete neurological evaluation before performing Gamma Knife radiosurgery and after treatment, every 6 months for the first 3 years and every year thereafter. Patients were classified as clinically unchanged, improved or worsened, and every symptom of new onset was followed during follow-up.

All patients underwent a contrast-enhanced MRI study at follow-up. Tumor volume at treatment and at follow-up was measured on GammaPlan system (Elekta Instruments, Inc., Stockholm, Sweden). Reduction was defined as a volume decrease of $\geq 20\%$; while progression was considered for a volume increase of $\geq 20\%$; all the remaining cases were considered unchanged.²³

2.4 | Statistical analysis

Data recorded were statistically analyzed by using Prism software (version 5.0a, GraphPad Software Inc., La Jolla, California). The data were reported by using mean and median values. The paired t test was applied to dependent samples. A P value of less than 0.05 was considered to indicate statistical significance.

3 | RESULTS

3.1 | Patients' and tumor' characteristics and treatment data

A total of 30 patients underwent Gamma Knife radiosurgery for skull base glomus tumors in our institution between 2002 and 2015.

The mean age was 65.6 years (median 68; range 40-89 years); 25 patients were female (83.3%) and 5 were male (16.6%). Twenty-one patients (70%) underwent Gamma Knife radiosurgery as a primary treatment; whereas in the remaining nine cases (30%), Gamma Knife radiosurgery was delivered on residual or recurrent tumor after previous surgery. Among these cases, one residual tumor (case #10) was initially treated with fractionated radiation therapy in another institution, and the patient underwent Gamma Knife radiosurgery after further tumor progression (Table 1).

According to tumor location and extension, the cases were classified as tympanic in 6 cases (20%); jugular in 8 cases (26.6%); jugulo-tympanic in 10 cases (33.3%); jugulo-carotid in 4 cases (13.3%), and carotid-tympanic in the remaining 2 cases (6.6%).

Tumors were located on the left side in 17 cases (56.6%) and on the right side in 11 (36.6%) cases; two (6.6%) patients harbored bilateral lesions. One of them underwent bilateral surgery elsewhere and Gamma Knife radiosurgery was performed for a left residual tumor; the other one underwent surgery for the left tumor and was treated with Gamma Knife radiosurgery for the right lesion. None of our patients were bearer of secreting tumor.

Prior to the treatment, one patient (3.3%) experienced V CN deficit; seven experienced VII CN deficit (23.3%); VIII

TABLE 1	Summary of p	atients' characte	ristics									
Patient	Age/sex	Lesion [treated]	LOC	Symptoms	Previous treatment	Marginal dose (Gy)	Isocenters	Pretreatment tumor volume (cc)	FU	Tumor volume	Symptoms	New symptoms
1	52/F	2 [L]	Ŧ	T VIII	BIL SUR	18	14	1.9	76	U	I	None
2	59/M	1L	ſ	L IX, X, XI	None	18	18	7.3	103	U	I	None
ю	73/F	1L	J-T	L V, VII, IX, X, XI	SUR	16	7	15.3	113	U	U	None
4	81/M	1 L	J-T	L VII, VIII, IX	None	14	25	16.9	123	D	I	Vertigo ^a
5	49/F	2 [R]	C-J	L IX, X, XI	L SUR	18	6	2.7	62	U	U	None
9	76/F	1 L	ſ	L XI	SUR	15	7	0.397	162	U	I	None
٢	74/F	1 L	ſ	L XI	SUR	18	6	3.3	103 ^b	U°	I ^c	None
8	72/F	1L	F	L VII, VIII	None	18	23	10.2	129	U	I	None
6	60/F	1L	J-T	L IX, X	Surgery	15	3	0.384	85	U	U	None
10	87/F	1 R	F	R VII, VIII	SUR + RT	13	19	9.6	156	U	U	None
11	70/F	1 L	J-T	L VIII, IX	None	15	18	71	168	D	I	TN^{a}
12	81/F	1 L	F	L VIII	None	16	11	11.6	128	U	U	None
13	52/F	1 L	C-J	L VIII	None	14	25	14.6	69	U	U	None
14	68/F	1 R	C-J	R VIII	None	18	11	7.9	96	U	Ι	None
15	58/F	1 R	J	R IX, X, XI	None	16	21	7.9	68	U	U	None
16	56/F	1 R	J-T	R VII, VIII	SUR	16	23	10.6	108	U	U	None
17	89/F	1 R	J	R IX	None	16	14	0.918	67	U	U	None
18	60/M	1L	J	L IX, X, XI	None	14	26	8.1	172	U	I	None
19	77/F	1 R	Ŧ	R VIII	None	14	24	24.6	149	U	I	None
20	77/F	1 R	J-T	R VIII, IX, XI	None	15	18	11.2	138	D	U	None
21	63/F	1 R	C-T	R VIII	None	15	18	9.6	49	U	U	None
22	77/F	1 R	C-T	R VIII	None	18	10	4.1	49	D	I	None
23	69/F	1 R	C-J	R IX, X, XI	None	16	6	3.4	58	U	I	None
24	42/M	1L	ſ	L IX, X, XI	SUR	18	4	0.36	59	U	U	None
25	58/F	1L	Ŧ	L VII, VIII	None	16	24	11.3	58	U	U	None
26	68/F	1L	J-T	L VIII, XII	None	15	25	13.7	51	D	I	None
27	47/M	1L	J-T	L VIII	None	18	11	4.03	19	U	U	None
28	78/F	1L	J-T	L VIII, XII	None	16	6	3.44	11	U	U	None
29	40/F	1 L	J-T	L VII, VIII	None	15	15	6.22	17	U	U	None
30	55/F	1 R	ſ	R IX, XII	None	16	8	2.3	22	U	U	None
Abbreviatio	ons: BIL, bilateraj	l; C-J, carotid-ju	gular; C-T, c	sarotid-timpanicum; D, decri	eased; F, female; F	U, follow-up; I, impr	oved; J, jugulare;	J-T, jugular-timpanicum; L, l	left; LOC, t	umor' localiza	tion; M, male; R,	right; RT, radiation

therapy; SURG, surgery; T, timpanicum; TN, trigeminal neuralgia; U, unchanged. ^a Transient. ^b Overall follow-up after 2 Gamma Knife Radiosurgery treatments. ^c After second treatment for tumor relapse.

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FIGURE 1 Axial contrast-enhancement MRI study of Gamma Knife radiosurgery treatment-planning, showing glomus tumors and isodose line (upper); axial contrast-enhancement MRI study after 138 months of follow-up period (case #20), showing tumor control (lower) [Color figure can be viewed at wileyonlinelibrary.com]

CN in 18 cases (60%); IX CN in 13 cases (43.3%); X CN in 9 cases (30%); XI CN in 10 cases (33.3%); and XII CN in 3 cases (10%).

Mean tumor volume was 7.69 cc (range 0.36-24.6; median 7.6). Median follow-up was 91 months (range 11-172; mean 90).

The mean tumor margin dose was 16 Gy (range 13-18; median 16); the isodose line for the tumor margin varied from 46% to 50%; 29 tumors (96.6%) were treated with a 50% isodose line. The mean volume of brainstem receiving 10 Gy (V10) was 12.13 cc (range 0.836-37.7). The mean volume receiving 12 Gy (V12) was 9.01 cc (range 1.3-27.2).

3.2 | Tumor control

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Considering those cases with stable or decreased tumor volume, the overall tumor control was 96.6%. At the last radiological evaluation (Figure 1), tumor volume was unchanged in 25 cases (83.3%); a volumetric decrease was recorded in five cases (16.4%). One patient experienced tumor progression at follow-up. The residual tumor after surgery (case #7) was treated with a marginal dose of 18 Gy, with 100% cover index to the target. After initial radiological regression and clinical improvement, 41 months after first Gamma Knife radiosurgery treatment an extra-field tumor relapse at the treatment margin, without clinical changes, was detected. The patient underwent a second Gamma Knife radiosurgery treatment with 18 Gy at the margin of the growing part of the tumor (volume: 0.8 cc). At the last follow-up after 62 months, the tumor volume and the patient's clinical status were unchanged.

In those tumors showing volumetric regression, the mean volumetric decrease was of 4.06 cc.

By excluding the case of *extra-field* retreatment, the mean tumor volume variation of -0.95 cc was statistically significant (P < 0.0001).

3.3 | Clinical outcome

At the last follow-up evaluation, 17 patients were unchanged (56.6%) and 13 patients (43.4%) experienced improvement of their clinical status. Among these, three patients (10%) experienced vertigo improvement; one of seven cases (3.3%) experienced VII CN improvement (from House and Brackmann scale grade III to grade II); while in the remaining six cases, the impairment was stable at follow-up.

No cases of hearing worsening were recorded and all patients experiencing hearing symptoms remained stable at follow-up (Table 2). Tinnitus was recorded in eight patients at the time of Gamma Knife radiosurgery and resolved in all

TABLE 2 Summary of clinical status before Gamma Knife radiosurgery (GKRS) and at last follow-up

	At GKRS		At last foll	ow-up
Symptoms	Cases	% (n = 30)	Cases	% (n = 30)
LCN deficit	17	56.6	9	30
Hypoacusia	16	53.3	16	53.3
VII CN impairment	7	23.3	6	20
Tinnitus	8	26.6	0	-
Vertigo	6	20	3	10
V CN impairment	1	3.3	1	3.3
Otalgia	1	3.3	0	-
Other	2	6.6	1	3.3

Abbreviations: CN, cranial nerve; LCN, lower cranial nerves.

TABLE 3	Summary of clinical response after Gamma Kn	ife
radiosurge	y (GKRS)	

	Frequency	
Symptoms	n	% (n = 30)
LCN deficit		
At GKRS	17	56.6
Improved	8	26.6
New onset	0	-
Hypoacusia		
At GKRS	16	53.3
Improved	0	-
New onset	0	-
VII CN impairment		
At GKRS	7	23.3
Improved	1	3.3
New onset	0	-
Tinnitus		
At GKRS	8	26.6
Improved	0	-
New onset	0	-
Vertigo		
At GKRS	6	20
Improved	3	10
New onset	1 ^a	3.3
V CN impairment		
At GKRS	1	3.3
Improved	0	-
New onset	1 ^a	3.3
Otalgia		
At GKRS	1	3.3
Improved	1	3.3
New onset	0	-

Abbreviations: CN, cranial nerve; LCN, lower cranial nerves. ^a Transient.

cases as well as the only case of otalgia; no improvement or new cases have been recorded.

One patient (3.3%; case #4) experienced transient vertigo 3 months after Gamma Knife radiosurgery (V10 and V12 were 7.1 and 5.8 cc, respectively); one patient (3.3%; case #11), despite clinical improvement and tumor regression on follow-up MRI studies, experienced transient trigeminal neuralgia (V10 and V12 were 4.4 and 3 cc, respectively) that disappeared after 4 months without any medical therapy. Lower cranial nerves function improved in 8 of 17 patients (47%). By considering the pattern of radiological-clinical outcome, 4 patients experienced clinical improvement on average 6 months before MRI showed a decrease of tumor' volume, 9 patients (30%) experienced clinical improvement despite a radiological evidence of tumor reduction, 16 patients did not experience tumor volume reduction and clinical changes, and in 1 patient (3.3%) tumor's volume decreased without any clinical improvements (Table 3).

4 | DISCUSSION

Surgery has represented the mainstay of glomus tumors treatment, nevertheless despite the progresses in microsurgery, the actuarial rate of gross-total resection is still low if compared to other benign skull base lesions, with a high risk of surgery-related morbidity and mortality.^{6–9,12,13,18,19,24–26} Glomus tumors treatment has gradually shifted to a multimodal approach through the use of radiation techniques, addressing surgery to symptomatic patient with intracranial hypertension or brainstem compression.^{6,13,24} RT showed good tumor control rates with lower morbidity when compared to surgical resection, however, the inaccurate target dose delivery is related to some long-term adverse effects, such as xerostomia and new CNs deficits, dermal reactions, radiation-induced malignancies, temporal bone osteonecrosis, and radionecrosis.^{1,4,6,13,14,26–33}

Gamma Knife radiosurgery was used to overcome the potential morbidity related to surgery and RT, by virtue of the focused high-dose radiation that can be delivered to the target in a single session if compared to RT.³⁴ It has been reported that tumor control rates after stereotactic radiosurgery, such as Gamma Knife radiosurgery, for glomus tumors are significantly higher than surgery (95% vs 69%-86%).⁶

In this series, we reported an overall tumor control rate of 96.6%. The overall reported tumor control rate ranges between 62.5% and 100% (Table 4). In the largest published series of about 132 patients, the reported tumor control was 93%.⁹ However, data are not directly comparable because of different patients' selection criteria, radiosurgical treatment data, and different follow-up methods. Liscak and coworkers reported the longest follow-up period in a series of 44 patients in 2014, with a 98% of tumor control (median follow-up of 118 months and 4% of transient or permanent clinical worsening).³⁵ In this series, we reported the second longest follow-up period, but with a higher mean tumor volume and a lower mean dose to the tumor. These data suggest that data even in case of large volumes Gamma Knife radiosurgery can achieve a good tumor control.

Patients may experience a clinical improvement preceding radiological tumor shrinkage on average 6 months after Gamma Knife radiosurgery.^{36–39} However, even in the absence of an MRI evident tumor volume reduction, patients may present with a clinical improvement that could be considered as a positive prognostic factor related to tumor vascularity changes.^{24,36–39}

We report a good clinical outcome in all cases and among these 56.6% showed no clinical changes at the last follow-up; in literature it has been reported between 83.3% and 100% of cases, depending upon the series. We report the highest number of cases with no permanent clinical worsening (Table 4), probably because of the lower mean marginal dose to the lesion.

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TABLE 4 Literature review of GJT Gamma Knife Radiosurgery series

Author	Year	No. of patients	Mean tumor volume	Mean dose (Gy)	Range dose (Gy)	Mean FU (months)	Tumor control (%)	Overall clinical control (%)	Complications (cases)
Foote et al ³⁶	1997	9	8.6	15	12-18	20	9/9 (100)	9/9 (100)	0
Eustachio et al ³⁴	1999	13	6.4	16.5	12-20	37.6	10/10 (100)	10/10 (100)	0
Liscak et al42	1999	66	5.7	16.5	10-30	24	52/52 (100)	49/52 (94.2)	1T 2P
Jordan et al ⁴⁰	2000	8	9.81	16.3	12-20	27	7/7 (100)	6/7 (85.7)	1T
Saringer et al44	2001	13	N/A	12	9-14	4.2	13/13 (100)	12/13 (92.3)	2T
Foote et al ³⁷	2002	25	10.4	15	12-18	35	25/25 (100)	25/25 (100)	1T
Pollock et al43	2004	42	13.2	14.9	12-18	44	38/39 (97.4)	34/39 (87.2)	2T 5P
Bari et al ³¹	2003	8	4.025	20.5	16-25	44 rad; 74 cli	5/8 (62.5)	6/8 (75)	1T 1P
Sheenan et al ⁴⁶	2005	8	10	15	12-18	32	7/7 (100)	7/7 (100)	0
Gerosa et al ²⁰	2006	20	7.03	17.3	13-24	50.85	19/20 (95)	18/20 (90)	2P
Bitaraf et al ¹	2006	16	9.8	18	14-20	18.5	14/14 (100)	16/16 (100)	1T
Varma et al ⁴⁷	2006	17	6.95	15	13-18	48	13/17 (76.4)	15/17 (88.2)	1T 2P
Feigl et al ³⁵	2006	12	14	17	12-20	33	12/12 (100)	10/12 (83.3)	2T 1P
Sharma et al45	2008	25	7.9	16.4	12-25	24	10/10 (100)	7/10 (70)	1T
Ganz et al ³⁸	2009	14	14.2	13.6	12-16	28	14/14 (100)	12/14 (85.7)	1T
Miller et al ²⁶	2009	5	N/A	15	15	34	5/5 (100)	5/5 (100)	1T
Navarro Martin et al ³	2010	10	4	14	12-16	9.7	10/10 (100)	10/10 (100)	1T
Hafez et al ³⁹	2010	13	8.4	13.5	12-15	30	13/13 (100)	12/13 (92.3)	1T
Genç et al ²	2010	18	5.54	15.6	13-20	52.7	17/18 (94.4)	17/18 (94.4)	1P
Chen et al ³²	2012	15	7.3	14.6	13-18	43.2	12/15 (80)	N/A	1P
Sheenan et al ⁹	2012	132	7.8	15	10-18	50.5	114/123 (92.6)	114/134 (85)	20P
Gandia-Gonzalez et al ¹⁹	2014	58	12	13.6	11-15	86.4	55/58 (94.8)	53/58 (91.3)	5P
Liscak et al41	2014	46	3.6 ^a	20 ^a	10-30	118 ^a	43/44 (97.7)	43/45 (95.5)	2P
Dobberpuhl et al ³³	2016	12	8.42	15.5	12-18	27.6	12/12 (100)	N/A	1P
Hafez et al ²²	2016	22	7.26	14.7	12-16	56	21/22 (95.4)	19/22 (86.3)	2P
Ibrahim et al ²¹	2016	75	7	18.3	12-25	51.5 rad; 38.5 cli	70/75 (93.3)	63/75 (84)	2P
Winford et al49	2017	38	5.8	13.6	11-15	39.1 rad	29/33 (88)	29/38 (76.3)	2T 8P
Present series	2018	30	7.69	16	13-18	90	29/30 (96.6)	30/30 (100)	2T

Abbreviations: Cli, clinical follow-up; FU, follow-up; N/A, not available; P, permanent; Rad, radiological follow-up; T, transient. ^a Median.

Despite a good clinical outcome, new CNs deficit have been reported even after Gamma Knife radiosurgery for glomus tumor. The most common is a hearing loss from radiation damage to the cochlea through the close relationship between the tumor and the temporal bone.^{32,40,41} Other less frequent reported cranial neuropathies after Gamma Knife radiosurgery are trigeminal neuralgia and facial weakness.^{42,43} In published series, 74 patients experienced some kind of Gamma Knife radiosurgery-related morbidity (9.6%, n = 770): 2.5% (19 cases) experienced a transient worsening of the pretreatment clinical status, while 7.1% (55 cases) experienced a permanent change. In this series, two patients experiencing transient vertigo and trigeminal neuralgia (case #5 and case #12) underwent a Gamma Knife radiosurgery treatment with a prescription marginal dose of 14 and 15 Gy, respectively. These two post-Gamma Knife radiosurgery symptoms have been already analyzed in the case of Gamma Knife radiosurgery for vestibular schwannomas and they are usually dose and volume related.⁴⁴ A prescription dose ≤ 13 Gy showed low risk of vertigo, facial impairment,

and trigeminal neuralgia after Gamma Knife radiosurgery for vestibular schwannomas, and the probability of developing trigeminal neuralgia was strictly related to the volume of brainstem exposed to a dose of 10 Gy.⁴⁴ Otherwise a dose of 12 Gy cannot effectively treat glomus tumors, while a dose ranging between 14 and 18 Gy may be effective.^{21,22} Dose increasing is related to a higher risk of radiation-induced adverse reaction, even if the lower cranial nerves are considered less radiosensitive than V, VII, and VIII CNs.^{21,24,38,45} Despite these data, the reported risk of lower cranial nerves deficit after Gamma Knife radiosurgery is lower than other CNs and it is however lower than that reported for surgery as pointed out by Ivan and coworkers in their metaanalysis.^{6,21}

Tumor's extension according to Fisch or Glasscock classifications system seems to be not related to tumor control, as observed in different Gamma Knife radiosurgery studies.^{9,24,41} The unique case of failure reported in the present series is indeed explained by an extra-field tumor progression, due to the difficulties in seeing the border of the

lesion in a postsurgery patient.^{46,47} To better outline bony and tumor borders, particularly in those patients who have undergone surgery, we recommend planning the Gamma Knife radiosurgery treatment by merging a bone-windowed CT scan on routine MRI.^{23,48} In the published series, a true tumor recurrence has been reported in up to 37.5% of cases.

Notwithstanding the similar results of Gamma Knife radiosurgery and RT, because of the potential case selection bias related to tumor volume and extension, it is not possible to compare the outcome data. Gamma Knife radiosurgery seems to offer better results in terms of tumor control and toxicity, however, the treatment of these tumors has to be tailored on the patients' age and symptoms, tumor volume, and extension.^{9,49}

Longer follow-up period and large cohorts are needed to definitively outline the role of Gamma Knife radiosurgery for glomus tumor, as glomus tumor may start regrowth even 25 years after initial RT.^{20,24,26,35,50,51} Based on these findings, Gamma Knife radiosurgery can be considered as a primary treatment in almost all cases of glomus tumor, except for those patients experiencing symptoms and signs of intracranial hypertension, or for those patients presenting with huge tumors with caudal extension, that cannot be easily approached only with a Gamma Knife radiosurgery treatment.^{3,6,9,20,24,31,35,48,52,53}

5 | CONCLUSION

Glomus tumors are rare benign tumors with a local aggressive behavior. Despite the advances in skull base surgery, their treatment is still related to high morbidity and mortality rates.

Gamma Knife radiosurgery is a safe and effective treatment modality for glomus tumor, with good tumor and clinical control in most of the cases at short-midterm follow-up and lower complication rate.

Longer follow-up periods and larger cohort studies are needed to definitively outline the role of Gamma Knife radiosurgery in the management of glomus tumors.

CONFLICTS OF INTEREST

The authors report no conflict of interest.

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REFERENCES

 Bitaraf MA, Alikhani M, Tahsili-Fahadan P, et al. Radiosurgery for glomus jugulare tumors: experience treating 16 patients in Iran. *J Neurosurg*. 2006; 105:168-174.

- Genc A, Bicer A, Abacioglu U, Peker S, Pamir MN, Kilic T. Gamma knife radiosurgery for the treatment of glomus jugulare tumors. *J Neurooncol.* 2010;97(1):101-108.
- Navarro Martin A, Maitz A, Grills IS, et al. Successful treatment of glomus jugulare tumours with gamma knife radiosurgery: clinical and physical aspects of management and review of the literature. *Clin Transl Oncol.* 2010;12(1):55-62.
- 4. Hinerman RW, Mendenhall WM, Amdur RJ, Stringer SP, Antonelli PJ, Cassisi NJ. Definitive radiotherapy in the management of chemodectomas arising in the temporal bone, carotid body, and glomus vagale. *Head Neck*. 2001;23(5):363-371.
- Szyfter W, Kopec T, Kawczynski M. Glomus caroticum, jugulare and vagale--problems in diagnosis and treatment. *Otolaryngol Pol.* 2006;60(3): 305-312.
- Ivan ME, Sughrue ME, Clark AJ, et al. A meta-analysis of tumor control rates and treatment-related morbidity for patients with glomus jugulare tumors. *J Neurosurg*. 2011;114(5):1299-1305.
- Chung SM, Kim HS, Jung J, Lee HK, Lee WS. Clinical presentation and management of jugular foramen paraganglioma. *Clin Exp Otorhinolaryngol*. 2009;2(1):28-32.
- Kemeny AA. Contemporary management of jugular paragangliomas (glomus tumours): microsurgery and radiosurgery. *Acta Neurochir*. 2009;151(5): 419-421.
- Sheehan JP, Tanaka S, Link MJ, et al. Gamma Knife surgery for the management of glomus tumors: a multicenter study. *J Neurosurg*. 2012;117(2): 246-254.
- 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 (London, England)*. 1989;2(8675):1291-1294.
- Azzarelli B, Felten S, Muller J, Miyamoto R, Purvin V. Dopamine in paragangliomas of the glomus jugulare. *Laryngoscope*. 1988;98(5):573-578.
- Guss ZD, Batra S, Li G, et al. Radiosurgery for glomus jugulare: history and recent progress. *Neurosurg Focus*. 2009;27(6):E5.
- Li G, Chang S, Adler JR Jr, Lim M. Irradiation of glomus jugulare tumors: a historical perspective. *Neurosurg Focus*. 2007;23(6):E13.
- Poznanovic SA, Cass SP, Kavanagh BD. Short-term tumor control and acute toxicity after stereotactic radiosurgery for glomus jugulare tumors. *Otolaryngol Head Neck Surg.* 2006;134(3):437-442.
- 15. 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.* 2000;88(12): 2811-2816.
- Brewis C, Bottrill ID, Wharton SB, Moffat DA. Metastases from glomus jugulare tumours. J Laryngol Otol. 2000;114(1):17-23.
- Liscak R, Vladyka V, Simonova G, Vymazal J, Janouskova L. Leksell gamma knife radiosurgery of the tumor glomus jugulare and tympanicum. *Stereotact Funct Neurosurg*. 1998;70(Suppl 1):152-160.
- Makiese O, Chibbaro S, Marsella M, Tran Ba Huy P, George B. Jugular foramen paragangliomas: management, outcome and avoidance of complications in a series of 75 cases. *Neurosurg Rev.* 2012;35(2):185-194.
- 19. Valavanis A. Preoperative embolization of the head and neck: indications, patient selection, goals, and precautions. *AJNR Am J Neuroradiol*. 1986; 7(5):943-952.
- 20. Gandia-Gonzalez ML, Kusak ME, Moreno NM, Sarraga JG, Rey G, Alvarez RM. Jugulotympanic paragangliomas treated with Gamma Knife radiosurgery: a single-center review of 58 cases. *J Neurosurg*. 2014;121(5): 1158-1165.
- Lekovic GP, Smith KA, Feiz-Erfan I, Porter RW, Biggs C, Shetter AG. Radiosurgery of jugular foramen tumors. *Oper Tech Neurosurg*. 2005;8(1): 54-60.
- Pollock BE. Stereotactic radiosurgery in patients with glomus jugulare tumors. *Neurosurg Focus*. 2004;17(2):E10.
- 23. Gerosa M, Visca A, Rizzo P, Foroni R, Nicolato A, Bricolo A. Glomus jugulare tumors: the option of gamma knife radiosurgery. *Neurosurgery*. 2006;59(3):561-569.
- 24. Ibrahim R, Ammori MB, Yianni J, Grainger A, Rowe J, Radatz M. Gamma Knife radiosurgery for glomus jugulare tumors: a single-center series of 75 cases. J Neurosurg. 2017;126(5):1488-1497.

⁸ ⊢WILEY-

- Jackson CG, McGrew BM, Forest JA, Netterville JL, Hampf CF, Glasscock ME 3rd. Lateral skull base surgery for glomus tumors: long-term control. *Otol Neurotol.* 2001;22(3):377-382.
- Michael LM 2nd, Robertson JH. Glomus jugulare tumors: historical overview of the management of this disease. *Neurosurg Focus*. 2004;17(2):E1.
- Gilbo P, Morris CG, Amdur RJ, et al. Radiotherapy for benign head and neck paragangliomas: a 45-year experience. *Cancer.* 2014;120(23):3738-3743.
- Gottfried ON, Liu JK, Couldwell WT. Comparison of radiosurgery and conventional surgery for the treatment of glomus jugulare tumors. *Neurosurg Focus*. 2004;17(2):E4.
- 29. Hinerman RW, Amdur RJ, Morris CG, Kirwan J, Mendenhall WM. Definitive radiotherapy in the management of paragangliomas arising in the head and neck: a 35-year experience. *Head Neck*. 2008;30(11):1431-1438.
- Krych AJ, Foote RL, Brown PD, Garces YI, Link MJ. Long-term results of irradiation for paraganglioma. *Int J Radiat Oncol Biol Phys.* 2006;65(4): 1063-1066.
- 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*. 2009;87(1):31-36.
- Miller JP, Semaan MT, Maciunas RJ, Einstein DB, Megerian CA. Radiosurgery for glomus jugulare tumors. *Otolaryngol Clin North Am.* 2009;42(4): 689-706.
- 33. Springate SC, Weichselbaum RR. Radiation or surgery for chemodectoma of the temporal bone: a review of local control and complications. *Head Neck.* 1990;12(4):303-307.
- 34. Fussey JM, Kemeny AA, Sankar S, Rejali D. Successful management of a catecholamine-secreting glomus jugulare tumor with radiosurgery alone. *J Neurol Surg B Skull Base*. 2013;74(6):399-402.
- Liscak R, Urgosik D, Chytka T, et al. Leksell Gamma Knife radiosurgery of the jugulotympanic glomus tumor: long-term results. *J Neurosurg*. 2014; 121:198-202.
- 36. Eustacchio S, Leber K, Trummer M, Unger F, Pendl G. Gamma knife radiosurgery for glomus jugulare tumours. *Acta Neurochir (Wien)*. 1999; 141(8):811-818.
- Foote RL, Coffey RJ, Gorman DA, et al. Stereotactic radiosurgery for glomus jugulare tumors: a preliminary report. *Int J Radiat Oncol Biol Phys.* 1997;38(3):491-495.
- 38. Ganz JC, Abdelkarim K. Glomus jugulare tumours: certain clinical and radiological aspects observed following Gamma Knife radiosurgery. *Acta Neurochir* (*Wien*). 2009;151(5):423-426.
- 39. Lim M, Gibbs IC, Adler JR Jr, Chang SD. Efficacy and safety of stereotactic radiosurgery for glomus jugulare tumors. *Neurosurg Focus*. 2004; 17(2):E11.
- 40. Linskey ME, Johnstone PA, O'Leary M, Goetsch S. Radiation exposure of normal temporal bone structures during stereotactically guided gamma knife surgery for vestibular schwannomas. *J Neurosurg*. 2003;98(4):800-806.

- 41. 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.* 2001;44(3):141-146.
- Bari ME, Kemeny AA, Forster DM, Radatz MW. Radiosurgery for the control of glomus jugulare tumours. J Pak Med Assoc. 2003;53(4):147-151.
- 43. 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*. 2008;56(1):57-61.
- 44. Boari N, Bailo M, Gagliardi F, et al. Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients. *J Neurosurg*. 2014;121(Suppl):123-142.
- 45. Ganz JC, Reda WA, Abdelkarim K. Adverse radiation effects after Gamma Knife Surgery in relation to dose and volume. *Acta Neurochir*. 2009;151(1): 9-19.
- 46. Chen PG, Nguyen JH, Payne SC, Sheehan JP, Hashisaki GT. Treatment of glomus jugulare tumors with gamma knife radiosurgery. *Laryngoscope*. 2010;120(9):1856-1862.
- Lee CC, Pan DH, Wu JC, et al. Gamma Knife radiosurgery for glomus jugulare and tympanicum. *Stereotact Funct Neurosurg*. 2011;89(5):291-298.
- 48. Schuster D, Sweeney AD, Stavas MJ, et al. Initial radiographic tumor control is similar following single or multi-fractionated stereotactic radiosurgery for jugular paragangliomas. *Am J Otolaryngol.* 2016;37(3):255-258.
- 49. Winford TW, Dorton LH, Browne JD, Chan MD, Tatter SB, Oliver ER. Stereotactic radiosurgical treatment of glomus jugulare tumors. *Otol Neurotol*. 2017;38(4):555-562.
- Cece JA, Lawson W, Eden AR, Biller HF, Parisier SC. Complications in the management of large glomus jugulare tumors. *Laryngoscope*. 1987;97(2): 152-157.
- Pollock BE, Foote RL, Stafford SL. Stereotactic radiosurgery: the preferred management for patients with nonvestibular schwannomas? *Int J Radiat Oncol Biol Phys.* 2002;52(4):1002-1007.
- Sager O, Dincoglan F, Beyzadeoglu M. Stereotactic radiosurgery of glomus jugulare tumors: current concepts, recent advances and future perspectives. *CNS oncology*. 2015;4(2):105-114.
- 53. Willen SN, Einstein DB, Maciunas RJ, Megerian CA. Treatment of glomus jugulare tumors in patients with advanced age: planned limited surgical resection followed by staged gamma knife radiosurgery: a preliminary report. *Otol Neurotol.* 2005;26(6):1229-1234.

How to cite this article: Spina A, Boari N, Gagliardi F, et al. Gamma Knife radiosurgery for glomus tumors: Long-term results in a series of 30 patients. *Head & Neck*. 2018;1–8. <u>https://doi.org/10.</u> 1002/hed.25517