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Gamma Knife Radiosurgery for Benign Cavernous Sinus Tumors: Treatment Concept and Outcomes in 120 Cases

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Abstract

Availability of modern computer-aided robotized devices, such as the Automatic Positioning System (APSTM; Elekta Instruments AB, Stockholm, Sweden) and PerfexionTM (Elekta Instruments AB), allowed us to develop the original concept of robotic gamma knife microradiosurgery, which is based on the very precise irradiation of the lesion with regard to conformity and selectivity; intentional avoidance of the excessive irradiation of functionally-important anatomical structures, particularly cranial nerves, located both within and in the vicinity of the target; and delivery of sufficient irradiation energy to the tumor with the intention to attain lesion shrinkage, while keeping the marginal dose sufficiently low for prevention of possible complications. The results of such treatment strategy were evaluated retrospectively in 120 patients with benign cavernous sinus neoplasms (pituitary adenomas, meningiomas, schwannomas, and hemangiomas), who were followed up from 24 to 78 months (mean 47 months) after radiosurgery. Tumor growth control and shrinkage rates were 98% and 68%, respectively. More than 50% volume reduction was noted in 25% of lesions. The most prominent volumetric tumor response was observed in hemangiomas, followed by schwannomas, pituitary adenomas, and meningiomas. Treatment-related complications were marked in 7% of cases, and were mainly related to transient isolated cranial neuropathy appearing within several months after radiosurgery. Major morbidity was limited to one patient (0.8%). Application of microradiosurgical treatment principles provides effective and safe management of benign cavernous sinus tumors and is associated with high probability of lesion shrinkage and minimal risk of complications.

Key words: gamma knife radiosurgery, microradiosurgery, automatic positioning system, cavernous sinus tumor, outcome

Introduction

Gamma knife radiosurgery (GKS) has been widely applied for the management of benign cavernous sinus tumors, such as pituitary adenomas, meningiomas, and schwannomas, and its use as an alternative to surgery or as an adjunctive option after incomplete lesion resection has led to sig-

nificant improvement of clinical outcome in such cases.^{3,10,12,21,24,25,30,33,39,41,43,45,47-49,51,56} Nevertheless, the risk of treatment-associated complications was not negligible and the reported rate of the new cranial neuropathies reached 19%.⁵¹ Moreover, up to 15% of neoplasms showed progression despite irradiation,^{12,47,49,56} which has encouraged critics of the effectiveness of GKS. However, radiosurgery is an evolving discipline similar to any other specialty. Progress is related to the development of advanced

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technologies, creation of new devices for stereotactic irradiation, improvement of the neuroimaging modalities used for targeting, and upgrading of the software applied for treatment planning and dosimetry. In this way, dramatic changes in the practice of GKS were initiated at the beginning of millennium with the introduction of the computer-aided robotized Automatic Positioning System (APSTM; Elekta Instruments AB, Stockholm, Sweden), which significantly facilitated multi-isocenter radiosurgery with application of small collimators. Availability of this device permitted us to create an original concept of robotic gamma knife microradiosurgery, which application in clinical practice during the last decade has provided effective and safe radiosurgical management of various brain tumors.^{13–16,18,22)}

The present study evaluated the results of our microradiosurgical treatment strategy in a large series of patients with benign cavernous sinus neoplasms, with particular emphasis on the tumor shrinkage rate and risk of treatment-associated complications.

Materials and Methods

The outcomes of radiosurgery for benign cavernous sinus tumors were evaluated retrospectively in 120 patients (82 women and 38 men, mean age 50 years), who underwent treatment in Tokyo Women's Medical University using a Leksell Gamma Knife[®] model 4C with APSTM (Elekta Instruments AB) and were followed up for at least 2 years thereafter. All clinical, radiological, and radiosurgical data were extracted from prospectively maintained computer databases. The majority of cases of the present series were included in previously published reports on the outcome after robotic gamma knife microradiosurgery in various types of skull base lesions.^{14–16,22)}

The tumors included 89 pituitary adenomas invading the cavernous sinus (46 hormone-secreting and 43 non-functional), 19 meningiomas, 6 schwannomas (4 originating from the abducens nerve and 2 from the oculomotor nerve), and 6 hemangiomas. Extension of the tumor on or its location within the cavernous sinus was identified on magnetic resonance (MR) imaging at the time of diagnosis and confirmed during microsurgical removal of the neoplasm if performed.

In total, 97 patients (81%) underwent microsurgical removal of the tumor before GKS, performed as initial management of all pituitary adenomas, 5 meningiomas, and 3 hemangiomas. In the vast majority of cases, there was no attempt to resect the intracavernous part of the lesion. Hypophyseal

transposition for facilitation of subsequent radiosurgery⁵⁰⁾ was not performed. The indications for GKS after open surgery were either presence of residual tumor (82 cases) or regrowth of the neoplasm (15 cases).

GKS was used as the primary treatment modality for all schwannomas, 14 meningiomas, and 3 hemangiomas. Microsurgical tumor resection was proposed for all these patients, but they preferred to undergo radiosurgery as the minimally invasive and lowest risk option. In these cases, the diagnosis of the tumor type was based on the identification of the typical symptoms and radiological findings both before and after irradiation, as well as on the evaluation of the adjacent microanatomy using Leksell GammaPlan[®] (Elekta Instruments AB) at the time of treatment. Benign nature of the tumor was strongly suspected due to slow growth rate.

On the day of treatment, a Leksell G stereotactic frame[®] (Elekta Instruments AB) was fixed on the patient's head under local anesthesia. Axial thin-slice computed tomography (CT), with bone window and contrast medium, and high-resolution MR imaging were obtained under stereotactic conditions. Our current neuroimaging protocol for microradiosurgery includes thin-slice constructive interference in steady state (CISS), CISS with gadolinium, and modified time-of-flight with gadolinium images acquired with a 1.5-T clinical MR scanner.^{17,19,20)} All radiological data were transferred to Leksell GammaPlan[®] version 5.34 or, later, 8.3 software. Fusion of bone window CT scans and MR images was done for simultaneous visualization of the soft tissue and bone structures, and three-dimensional evaluation of MR imaging distortion artifacts.²⁷⁾

Radiosurgical treatment planning was done with reference to simultaneous onscreen display of all obtained images within the three-dimensional workspace of the Leksell GammaPlan[®]. Multiple small isocenters were carefully positioned within the border of the mass to attain both conformal and selective coverage with the prescription isodose. Initially, 4-mm isocenters were used on the part of the lesion adjacent to the critical structures, such as visual pathways and cranial nerves within the lateral wall of the cavernous sinus.²⁸⁾ If possible the latter was not covered with the prescription isodose. Thereafter, 4-mm and 8-mm isocenters with various weights were placed on the bulk of the tumor, compactly located within its border. Special emphasis was put on avoidance of the projection of any isocenter onto functionally-important anatomical structures, particularly the cranial nerves. Even if such structures were located within the target, the

Fig. 1 Radiosurgical treatment planning for left cavernous sinus meningioma (upper) and three-dimensional view of the 50% isodose area distribution related to the adjacent cranial nerves (lower). Note exclusion of the oculomotor nerve from high-dose irradiation within the target area. Marked: 50% (yellow) and 80% (green) isodose areas, oculomotor (pink), abducens (blue), and trigeminal (red) nerves, and optic pathways (brown).

treatment plan was preferably created in such a way that cranial nerves were not covered by high-dose irradiation areas within a mass (Fig. 1). In cases of benign cavernous sinus tumors, we usually tried to attain conformity index above 0.95 and selectivity index above 0.90.⁵⁹⁾

Wide 80% prescription isodose area was created within the neoplasm to attain not just control of growth, but shrinkage, which might depend on the amount of the delivered radiation energy, reflected by an original parameter, designated as unit energy (mJ/cm^3).^{14,18)} For evaluation of the high-dose area within the target, the so-called homogeneity index (HI) was calculated as:

$$\text{HI} = \text{TV}_{\text{piv80\%}} / \text{TV}_{\text{piv50\%}}$$

where $\text{TV}_{\text{piv80\%}}$ and $\text{TV}_{\text{piv50\%}}$ correspond to target

volumes covered by the 80% and 50% prescription isodoses, respectively. The HI is usually maintained at the level of 0.5 or greater for GKS of benign skull base tumors. If volume or distribution of the high-dose irradiation area within the target was considered insufficient, optimization was attained with the addition of the small low-weighted isocenter(s). In cases of meningiomas, the suspected area of tumor origin on the dura mater was included into the high-dose irradiation area for possible obliteration of the feeding vessels.¹⁴⁾

For meningiomas, schwannomas, and hemangiomas, the marginal dose, corresponding to the 50% prescription isodose line, varied from 10 to 14 Gy (mean 12 Gy). In cases of pituitary adenomas the marginal dose varied widely: if the lesion volume was less than 4 cm^3 the marginal dose generally exceeded 20 Gy, especially in hormone-secreting neoplasms, but if the tumor volume was more than 4 cm^3 the marginal dose was typically kept below 15 Gy, and even lower in cases of non-functional tumors.¹⁵⁾ The irradiation dose to the visual pathways was constantly kept below 10 Gy and to the brain stem below 14 Gy.

After completion of the treatment plan, the position of all isocenters was adjusted according to the presence of distortion artifacts evaluated three-dimensionally using the fused bone window CT scans and MR images. For this purpose, several anatomical landmarks in the vicinity of the target were defined and correspondence of their position on the MR images was compared to the CT scans in the axial, sagittal, and coronal planes. If any difference was identified, this was considered to result from MR imaging distortion artifacts. Therefore, coordinates of all isocenters were shifted in a measured corresponding distance along the X, Y, and Z axes to compensate for the mislocalization error.

All patients were followed up by the attending neurosurgeon with clinical examinations and serial neuroimaging, which were performed once every 6 months for 2 years after treatment and yearly thereafter. In cases of pituitary adenomas, regular endocrinological testing was done as well. Tumor volume during follow-up was calculated using T_1 -weighted MR imaging with gadolinium according to the following formula: greatest length (cm) $\times$ greatest height (cm) $\times$ greatest width (cm) $\times$ 0.5. Shrinkage or enlargement of the neoplasm was defined as at least 10% change in volume, compared to the baseline data determined at the time of radiosurgery. The length of follow-up varied from 24 to 78 months (mean 47 months).

Table 1 Outcomes of gamma knife radiosurgery for benign cavernous sinus tumors

Tumor type	Number of cases	Mean marginal dose, Gy	Mean (range) length of follow up, mos	Tumor growth control rate	Tumor shrinkage rate		Morbidity rate	Type of complications (number of cases)
					More than 10% volume reduction	More than 50% volume reduction		
Pituitary adenoma	89	hormone-secreting tumors: 25.2, non-functional tumors: 18.2	36 (24–76)	97%	64%	24%	2%	transient III nerve palsy (1), transient VI nerve palsy (1)
Meningioma	19	12	55 (36–78)	100%	68%	11%	5%	transient VI nerve palsy(1)
Schwannoma	6	12	45 (24–62)	100%	100%	33%	83%	transient III nerve palsy (2), transient VI nerve palsy (2), permanent VI nerve palsy (1), unilateral deterioration of vision with transient blindness (1), formation of the intratumoral cyst (1)
Hemangioma	6	12	52 (30–78)	100%	100%	83%	0%	—
Whole cohort	120	15.9	47 (24–78)	98%	68%	25%	7%	—

Results

No early complications or adverse effects after GKS were noted in any case of the present series. Table 1 summarizes the outcomes of treatment. Tumor growth control was attained in 117 patients (98%). During follow-up after radiosurgery, 82 lesions (68%) demonstrated shrinkage. In 30 cases (25%) more than 50% volume reduction was noted. The most prominent volumetric tumor response was observed in cavernous sinus hemangiomas, followed by schwannomas, pituitary adenomas, and meningiomas. Three tumors demonstrated growth during follow-up, which were all adrenocorticotrophic hormone (ACTH)-secreting pituitary adenomas. GKS was repeated in all recurrent cases.

Eight patients (7%), including 5 with schwannomas, 2 with ACTH-secreting pituitary adenomas, and 1 with meningioma, experienced treatment-related complications. Only transient isolated oculomotor or abducens nerve palsy was noted in 7 cases at mean 3 months (range 1–6 months) after irradiation, but completely resolved during several subsequent weeks with or without administration of steroid therapy. Retrospective analysis of the radiosurgical treatment plans in these cases revealed inclusion of the affected cranial nerve into the high-dose irradiation area within the target in 2 patients (one with ACTH-secreting pituitary adenoma and another one with meningioma), but not in another patient with ACTH-secreting pituitary adenoma, who underwent GKS twice.¹⁵⁾ On the other hand, cranial neuropathy in patients with schwannomas was seemingly caused by transient enlargement of the lesion, which is rather common after radiosur-

gery for this type of tumors and probably relates to inflammatory changes after irradiation.^{6,11,18,34)} Meanwhile, transient abducens nerve palsy in one patient with cisternocavernous abducens nerve schwannoma fully resolved but re-appeared 2 years after radiosurgery due to formation of the intratumoral cyst, which showed spontaneous regression during the longer follow-up period.

Only one patient experienced major morbidity as reported in detail elsewhere.¹⁶⁾ In brief, a 47-year-old nearly asymptomatic man underwent GKS for left orbitocavernous abducens nerve schwannoma (volume 4.9 cm³). At the time of treatment, the optic pathways were clearly kept outside the 40% isodose line corresponding to 9.6 Gy (Fig. 2). At 4 months after irradiation, the patient started to experience progressive unilateral visual impairment in the left eye, which gradually progressed despite steroid therapy. MR imaging with gadolinium disclosed increased mass volume with appearance of central lucency. At 10 months after treatment, the volume of the lesion reached its maximum of 5.9 cm³ (120% compared with pretreatment period). The proposed surgical resection of the neoplasm was rejected by the patient and his relatives. The patient became completely blind in the left eye, but later on vision returned and steadily improved up to serviceable level, with MR imaging evidence of gradual tumor shrinkage. At the time of the last follow-up examination at 62 months after radiosurgery, the volume of the lesion was 3.3 cm³ (67% compared with pretreatment period). Meanwhile, at 18 months after irradiation, the patient began to experience left abducens nerve palsy, which still persisted at the last follow-up examination.

Fig. 2 Radiosurgical treatment planning for left orbitocavernous abducens nerve schwannoma. Prescription isodose lines of 40%, 50%, and 80% are shown. Note that the left optic nerve (brown) was outside the 40% isodose line, corresponding to 9.6 Gy.

We specifically emphasize that no patient in the present series experienced diabetes insipidus, new pituitary hormone deficit, or temporal lobe abnormalities after GKS.

Discussion

Treatment of patients with cavernous sinus lesions represents a significant challenge. At present, detailed understanding of the microanatomy, advances in neuroimaging and neuroanesthesiology, availability of computer-aided devices for preoperative planning and simulation of the neurosurgical procedures, and possible use of comprehensive intraoperative neurophysiological monitoring, complex surgical approaches, and thorough microsurgical technique with adjunctive neuroendoscopy allow aggressive removal of skull base tumors in virtually any location. However, the postoperative morbidity in cases of cavernous sinus neoplasms, particularly related to dysfunction of the adjacent cranial nerves, varies from 18% to 63% even in the best hands.^{7,26,32,35,38,44} Many of these tumors are benign, so poor functional outcome, even after total removal, cannot be considered acceptable in patients with sufficiently long life expectancy.

There is considerable experience with the application of radiosurgery to the management of cavernous sinus neoplasms. In series with sufficiently long follow-up periods, such treatment provided 84–100% tumor growth control with 0–19% risk of

complications, mainly related to cranial neuropathy.^{2,3,10,12,21,24,25,28,30,33,35,39–41,43,45,47–49,51,56} The recent introduction of robotized computer-aided devices for GKS, such as APSTM and, later on, the newest model of the gamma knife named PerfexionTM (Elekta Instruments AB), have significantly increased the accuracy of radiation delivery, which now reaches 0.1 mm, thus permitting the creation of very conformal and selective treatment planning with more homogeneous high-dose distribution and avoidance of the underdosed areas within the lesion, and may result in improvement of the radiosurgical outcome.^{29,31,52,59}

Our current treatment concept, designated as robotic gamma knife microradiosurgery, is based on 3 main principles: very precise irradiation of the lesion with regard to conformity and selectivity; intentional avoidance of excessive irradiation of functionally important anatomical structures, particularly the cranial nerves, located both within and close to the target; and delivery of sufficient irradiation energy to the tumor to attain shrinkage, while retaining sufficiently low marginal dose for prevention of possible complications. Certainly, realization of such treatment principles requires detailed evaluation of the microanatomy of the target area, which is attained with advanced neuroimaging protocols.^{17,19,20} Particularly, use of CISS imaging with gadolinium may be extremely valuable in cases of cavernous sinus lesions.⁵⁷ Application of the described radiosurgical strategy in the present series of patients with benign cavernous sinus neoplasms, who were followed up for at least 2 years after treatment, resulted in 98% tumor growth control rate. The latter, in fact, was 100% in cases of meningiomas, schwannomas, and hemangiomas, since all 3 re-growing neoplasms were ACTH-producing pituitary adenomas, which probably resulted from poor identification of their borders on MR imaging during radiosurgical treatment planning.¹⁵ Re-growth of intracranial neoplasms after stereotactic irradiation may be caused by various factors, such as suboptimal targeting, insufficient doses, or resistance to irradiation, particularly caused by malignant growth potential.^{32,35,47,49} In our practice, if cavernous sinus tumor demonstrates slow re-growth despite radiosurgery, but does not exhibit evident malignant features on neuroimaging, second GKS is preferably performed before consideration of microsurgical lesion resection.

The conventional goal of GKS is attainment of tumor growth control, but reduction of the mass volume seems rather important for restoration of the affected neuronal functions, particularly related to direct compression of the cranial nerves. Our ex-

perience demonstrated that shrinkage of the neoplasm after radiosurgery may be directly associated with the amount of radiation energy delivered to the target.^{14,18)} This observation is in concordance with experimental results, which showed that presence of a “hot spot” within the lesion is more likely provide the desired radiobiological outcome for GKS.³⁶⁾ At the same time, the risk of complications is not increased, unless treatment is insufficiently selective and high-dose irradiation extends over the adjacent normal tissue.^{9,37)} Therefore, at present, we are trying to attain more homogeneous dose distribution with creation of the wide 80% prescription isodose area within the lesion while maintaining sufficiently low marginal dose. In the present series, application of such technique resulted in more or less prominent tumor shrinkage in two thirds of patients. Moreover, more than 50% volume reduction in a quarter of cases may be considered as clinically significant.

The most prominent volumetric response after GKS was observed in cavernous sinus hemangiomas. These benign neoplasms constitute less than 1% of all parasellar mass lesions, and are usually encountered in middle-aged women and typically characterized by marked signal hyperintensity on T₂-weighted MR imaging. However, the optimal management has been unclear. Cranial neuropathy necessitates mass reduction, but surgery in such cases is extremely difficult due to abundant vascularization of the lesion. Nevertheless, several recent studies have demonstrated that cavernous sinus hemangiomas can be well controlled with radiosurgery.^{4,22,23,55,58)} Analysis of such treatment in 59 cases with the range of lesion volume from 1.5 to 51.4 cm³ and of the marginal dose from 10 to 19 Gy found that within the mean follow-up of 49.2 months after irradiation, 67.8% of tumors demonstrated remarkable shrinkage, and 25.4% showed partial shrinkage.⁵⁵⁾ The outcome in the present series was, in fact, even better, since all neoplasms showed volumetric response (Fig. 3), whereas more than 50% shrinkage was seen in 5 of 6 cases. Neither tumor volume nor previous surgical removal are seemingly associated with the volumetric response of cavernous sinus hemangiomas after radiosurgery,⁵⁵⁾ which suggests that GKS may be considered as the method of choice for management of these neoplasms.

Earlier reports on GKS for benign skull base meningiomas mentioned 10–19% risk of cranial neuropathy^{40,51)} and 5% incidence of perilesional edema²⁾ after treatment. Despite significant improvements in neuroimaging modalities, radiosurgical equipment, and treatment planning software, even recent series from widely experienced clinical

Fig. 3 Combined management of right cavernous sinus hemangioma. **Upper row:** Magnetic resonance images before surgical intervention, including three-dimensional view of the local neuroanatomy prepared with the use of Leksell GammaPlan®. **Middle row:** Radiosurgical treatment planning after open biopsy of the highly vascular lesion with application of 12 Gy irradiation at the 50% prescription isodose line (yellow) and wide 75% isodose area within the lesion (green). **Lower row:** Neoplasm showed 30% shrinkage at 12 months after irradiation (distribution of the isodoses at the time of treatment are shown).

centers have reported complication rates of 4–10% after radiosurgery for pituitary adenomas and parasellar meningiomas.^{5,56)} Similarly, treatment-related morbidity related to cranial neuropathy was marked in 7% of our patients. Oculomotor and abducens nerves were affected most frequently, but only transiently in 7 of 8 cases. The incidence of complications was rather high in cases of schwannomas, which somewhat contradicts a previous report which did not identify any adverse effects after GKS for tumors of III, IV, and VI cranial nerves.²⁴⁾ However, 5 of 8 of those patients had trochlear nerve neoplasms, whereas 4 of 6 schwannomas in our series originated from the abducens nerve and 2 of these tumors were dumbbell-shaped.¹⁶⁾

Three causes of neurological dysfunction after radiosurgery can be identified: involvement of the cranial nerve located within the target into the high-dose irradiation area, possible accumulation of radiation injury after repeat GKS, and transient enlargement of the neoplasm after treatment with possible compression of the adjacent anatomical structures. The latter was the cause in only one case of major morbidity in our series presented with prominent

unilateral visual deterioration in a patient with dumbbell-shaped orbitocavernous abducens nerve schwannoma extending through the superior orbital fissure. Increase in the lesion volume after irradiation was strongly suspected to have resulted in severe compromise of the blood supply to the optic nerve or its direct compression within the annulus of Zinn. Transitory enlargement is a well-described phenomenon after GKS of both vestibular and non-vestibular schwannomas,^{6,11,18,34} but seems to be less prominent in pituitary adenomas,⁴² and rather infrequent in meningiomas.⁸ This self-limiting side effect usually does not create any significant clinical problems unless the neoplasm is extending into strictly confined areas, where even minimal increase of its size may result in compression of the adjacent neurovascular structures. Therefore, application of the multistage radiosurgery, stereotactic radiotherapy, or combined treatment with initial microsurgical decompression followed by irradiation might be more reasonable in some of these cases.¹⁶

Advantages of modern radiosurgical equipment allow effective management of the intracranial lesions with greater size than was conventionally considered suitable for GKS. In 116 meningiomas with volumes ranging from 10.1 to 48.6 cm³ (mean 17.5 cm³), 92% tumor growth control was achieved at 7 years after irradiation, but the complication rate was not negligible (23%).¹ In our opinion, surgical resection still represents the main treatment option for large benign cavernous sinus tumors

(with the possible exception of hemangiomas). However, the optimal functional outcome in such cases can be frequently attained after combined management with initial subtotal resection of the neoplasm and subsequent stereotactic irradiation of the remnants.^{32,35,44,46,53,54,56} Preoperative evaluation of the lesion and adjacent anatomical structures within the Leksell GammaPlan® software may allow to determine which part of the mass can be safely resected and which should be preferably left for subsequent radiosurgery.¹⁷

Due to significant variations in equipment, characteristics of patient cohorts, types of neoplastic pathology, irradiation doses and other treatment parameters, and length of follow-up, it is rather difficult to compare the results attained in our patients, treated according to the described concept of “robotic microradiosurgery,” with other reported series of GKS for benign cavernous sinus tumors (Table 2). Organization of randomized studies of different radiosurgical treatment strategies for intracranial tumors does not seem possible. Nevertheless, modern devices have significantly improved the accuracy of GKS, and currently permit effective irradiation of the lesion sparing adjacent functionally-important anatomical structures.^{13,29,31,52,59} Appropriate use of the available opportunities for advanced treatment planning and radiation dosimetry may result in optimal outcome, as demonstrated in the present study.

In conclusion, application of GKS based on microsurgical principles with creation of highly

Table 2 Results of gamma knife radiosurgery in selected series of patients with benign cavernous sinus tumors

Author (Year)	Type of pathology	Number of cases	Tumor growth control rate	Tumor shrinkage rate	Treatment-related morbidity	Tumor re-growth rate
Ikeda et al. (1998) ²¹	invasive pituitary adenomas	25	100%	100%	0%	0%
Roche et al. (2000) ⁴⁵	meningiomas	80	95%	31%	6%	5%
Chen et al. (2001) ³	mixed	69	99%	10%	3%	1%
Nicolato et al. (2002) ⁴¹	meningiomas*	122	98%	61%	4%	2%
Petrovich et al. (2003) ⁴³	invasive pituitary adenomas	78	95%	29%	4%	5%
Kuo et al. (2004) ³⁰	mixed	139	98%	38%	2%	2%
Liu et al. (2005) ³³	mixed	116	94%	54%	6%	6%
Kim et al. (2006) ²⁵	invasive pituitary adenomas	67	96%	72%	4%	4%
Mingione et al. (2006) ³⁹	invasive pituitary adenomas	61	92%	64%	0%	8%
Hasegawa et al. (2007) ¹²	meningiomas	115	88%	51%	12%	12%
Skeie et al. (2010) ⁴⁹	meningiomas*	100	84%	22%	6%	15%
Williams et al. (2011) ⁵⁶	meningiomas	138	86%	48%	10%	14%

*The series contains a small proportion of non-benign tumors.

conformal and selective treatment planning is very effective in patients with benign cavernous sinus neoplasms and may be considered as the method of choice in such cases as either the only treatment modality or as part of combined management after initial surgical resection. Delivery of a sufficiently large amount of radiation energy to the target while keeping the marginal dose relatively low will provide high probability of tumor shrinkage and minimal risk of major treatment-associated morbidity. Possible transient enlargement of the mass after irradiation should be recognized as a potential cause of complications, particularly in cases of schwannomas.

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