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Partial skull base tumour resection in combination with radiosurgery: an escape procedure or a reasonable solution of treatment?

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Summary Despite advancement in microsurgical techniques for skull base tumour surgery, approaches of this kind still represent a significant challenge for neurosurgeons due to the size of the tumour and its interference and proximity to important neural and vascular structures. After incomplete resection, gamma knife radiosurgery is becoming an alternative or adjunctive treatment option. In this article, some examples of our experience in combined treatment of the skull base tumours with surgical procedure and gamma knife therapy for the remaining tumour tissue are presented.

Keywords Skull base · Radiosurgery · Tumour resection · Residual tumour · Surgery

Introduction

In the past decades, great advancement has been made in microsurgical techniques for skull base tumour surgery. However, approaches of this kind represent a significant challenge for most neurosurgeons due to interference and proximity to important neural and vascular structures and because of the size of the tumour. Although mortality rates following surgery have been reduced from more than 50 % before 1970 to less than 10 % in recent years, the rate of permanent postoperative impairment may be as high as 50 %, especially in petroclival meningiomas [1–4]. To prevent relapses and postoperative neurological damage, a total resection of the skull base tumour, and meningiomas in particular, would be an ideal solution. However, this is difficult to achieve. Therefore, the tumour recurrence rate in smaller tumours (Simpson grade I) is 9 %, whereas in larger tumours (Simpson grade IV), the recurrence rate is as high as 40 %. On average, after 6 years, the recurrence rate for skull base meningiomas following surgery is 10 % [5–8].

Along with the development of microsurgery technique, the gamma knife radiosurgery as an alternative treatment option or an adjunctive therapy after incomplete resection of skull base tumours is now becoming more and more accessible [1, 5]. Compared with radical surgical resection, radiosurgery has been proven to reduce tumour recurrence rates between 82 and 100 % in terms of short-term results. At present, there are no reliable data regarding tumour behaviour or tumour growth control and neurological changes over a period of time exceeding 7 years [5, 6].

According to the literature, radiosurgical success is based on radiologically assessed regression or 2-mm shrinkage in tumour diameter and depends on pretherapeutic tumour volume, administered dose and time of radiological follow-up after radiosurgical therapy. To treat large tumours, fractionated stereotactic radiotherapy or gamma knife therapy of multiple sessions has been developed with similar efficiency for tumour growth control (98–100 %) in a follow-up period up to 5 years [9–11].

The growth of petroclival meningiomas seems to be slow, and a good functional result after the gamma knife therapy can be guaranteed [1, 3]. Therefore, the combination of planned incomplete resection of larger symptomatic skull base tumours and gamma knife therapy for tumour remnants should be considered as

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a treatment option enabling greater control of residual tumours. In this way, patients are not exposed to radical tumour resection with its unacceptably high postoperative morbidity rates. However, radiosurgery is becoming increasingly important in the treatment of asymptomatic patients with tumours of size 3 cm or smaller [1, 4, 12].

Some examples of our experience in combined treatment of the skull base tumours treated with surgical procedure and gamma knife therapy for the remaining tumour tissue are presented in this article. In one case, this kind of treatment was planned in advance, whereas in the rest of the cases, the gamma knife therapy was applied as an adjunctive therapy following a non-radical tumour removal or a its relapse.

Case reports

Patient 1

In 2000, a 62-year-old woman underwent surgery due to para- and retrosellar petroclival meningioma in another hospital (Fig. 1a). The surgery was smooth, and no postoperative neurological malfunctions were reported. Postoperative follow-up showed a complete removal of the tumour. A control computer tomography (CT) scan in 2003 revealed a petroclival meningioma recurrence on the left side. In 2004, the patient was successfully treated with a gamma knife that covered 90 % of the irregularly shaped recurrent tumour (Fig. 1b). Secondary to radiation, the patient experienced double vision due to left abducens palsy that subsided later. A control magnetic resonance imaging (MRI) 1 year after treatment showed a significant shrinkage of the remaining tumour tissue, measuring approximately 3 cm in diameter before the gamma knife surgery (Fig. 1c).

Unfortunately, 2 years later, the tumour recurred again. The patient's surgeon and radiosurgeon decided to repeat the gamma knife treatment in 2007. They were able to completely remove the recurrent tumour. The patient recovered well after the second session of gamma knife surgery and did not experience any additional neurological deficits. However, 1 year later, a large recurrent malignant meningioma appeared, which was radically removed by the neurosurgeon in 2009. Unfortunately, the tumour recurred a few months later, and according to the patient's neurosurgeon, it was inoperable. On her last follow-up in 2010, the patient was significantly affected, hemiplegic and cognitively impaired. Unfortunately, after 1 year, she died.

Patient 2

In 1997 a 53-year-old man underwent surgery twice due to a dumb-bell neurinoma of the right hypoglossal nerve. During the first session, transcondylar approach was used to remove the intracranial portion of the tumour. The remaining tumour tissue protruding into the neck was non-radically removed in another session by mobilisation of the carotid artery. Preoperatively, the patient suffered a complete right hypoglossal nerve dysfunction. Postoperatively, the right vagus, glossopharyngeal and accessory nerve functions were temporarily impaired. In 2004, a relapse occurred in the infratemporal region. An incomplete resection through infratemporal approach was performed. A transient left-sided hemiparesis occurred. The remaining tumour was treated with the gamma knife surgery in 2004. After therapy, the patient's condition has improved, and the tumour growth was well controlled. During the follow-up, the tumour was reduced in size from 7.8 cm^3 before gamma knife surgery to 6.8 cm^3 after radiation. On the last follow-up in 2010, the size of the tumour did not increase. Moreover, the clinical status of the patient was steady without additional neurological dysfunctions.

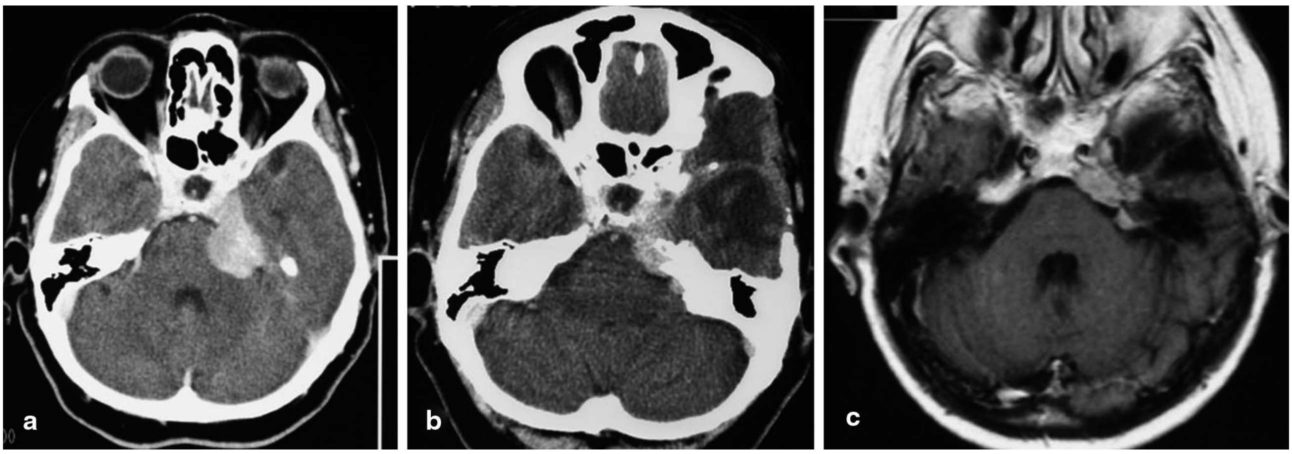

Fig. 1 A preoperative computed tomography (CT) of a 4-cm parasellar and retrosellar petroclival meningioma (**a**). The control CT image showing a relapse of the petroclival meningioma, which was operatively removed 3 years earlier (**b**). The same tumour after gamma knife irradiation. A significant reduction of the tumour mass can be seen 18 months after the radiosurgery on axial magnetic resonance imaging scan (**c**)

Patient 3

In 1997, a 50-year-old patient underwent a transcranial reduction of the right sellar and suprasellar meningioma with a tumour expansion into the right parasellar region. The already impaired vision of the right eye was additionally deteriorated. The patient had light and dark shadow perception with tunnel vision on the right side, significantly narrowed visual field and vision deterioration on the left side. Due to additional vision deterioration on the left side, the left optic nerve was surgically decompressed. The remaining tumour, however, was not removed.

In the following years, the vision was stable until 2006, when it started to decline on the left side. Imaging showed gradual tumour enlargement. In 2006, the patient underwent the gamma knife surgery to treat the remaining tumour tissue in the right cavernous sinus. The patient did well after the procedure, and after therapy, no vision deterioration in the left eye occurred. MRI showed an unchanged size of the tumour. A minor tumour reduction was noticed on follow-up 3 years and 6 months after the gamma knife therapy. The patient lost vision in the right eye; the visual acuity of the left eye was 0.16.

Patient 4

In 1991, a 25-year-old female patient underwent surgery for removal of a 4-cm cystic tumour in the left pontocerebellar angle extending into the parasellar space. A retromastoid approach was used. A histologically proved neurinoma of the trigeminal nerve was found and was completely removed macroscopically. Postoperatively, hypoesthesia on the left side of the face deteriorated into anaesthesia. The function of the facial nerve remained unaffected. However, left ear deafness and double vision resulted from the affected left abducens nerve.

After 14 years, a tumour of 5 cm in diameter recurred anteriorly in the left parasellar space and cavernous sinus. In 2005, the patient underwent a subtotal tumour reduction through pterional approach. Postoperatively, a minor part of the tumour tissue remained in the posterior part of the left cavernous sinus in the interpeduncular fossa. The patient did well after surgery, and the sensitivity of the left side of the face has improved.

The remaining tumour tissue was treated with gamma knife surgery in 2006, and the patient did well afterwards. No additional neurological deterioration was observed. Six months after radiosurgery, the tumour volume remained unchanged. Six years after the gamma knife surgery, the condition remained unchanged. At present, the remaining tumour is being controlled and does not grow.

Patient 5

A 54-year-old woman was admitted in 2005 due to a 5-cm petroclival meningioma with the impairment of the nerves V and VI, partially VIII and IX on the right side. On consultation with the radiosurgeon, we deliberately decided to remove only the larger petrous part of the tumour in the posterior fossa using a retromastoid approach. The whole tumour was too large to use the gamma knife surgery. The remaining tumour in the clival and right parasellar area invading into the cavernous sinus was left intentionally to be treated with the radiosurgery (Fig. 2a). Transient deterioration of the already existing impairments of the nerves V, VI and partially VIII occurred following the surgical treatment. However, the nerve function improved in the following months. In 2006, the patient underwent radiosurgery for the remaining tumour in the right cavernous sinus (Fig. 2b). The patient did well after the treatment, and no additional neurological impairments occurred. One year after the gamma knife surgery, control MRI showed approximately the same remaining meningioma in the right parasellar area. So far, no reduction is visible. On the follow-up in 2013, the remaining tumour had not grown. During the neurological investigation and subjectively, no deterioration was evident.

Patient 6

In 2006, a 6-cm petrous meningioma in the right pontocerebellar angle was subtotally removed in a 31-year-old male patient using a retromastoid approach. Postoperative control MRI showed a remaining flat tumour up to 2 cm in size along the brain stem (Fig. 3a). Transient postoperative deficits regarding the function of the nerves VII, VIII and IX improved in the following months.

The remaining tumour was treated with the gamma knife surgery in 2006. The patient did well after the radiation, and so far, he is able to perform his job. Control MRI 6 months after the radiosurgery showed no remaining tumour (Fig. 3b). In 2013, a control MRI was performed to confirm that the tumour disappeared. Except the hearing loss in the right ear, the patient had no neurological impairments.

Results

Among the patients presented in this article, four were female and two male. The mean age of the patients was 45.8 years. Among the tumours, four were histologically confirmed as meningiomas (three tumours in the petroclival region with extension into the middle and posterior fossa and one sellar–parasellar cavernous tumour) and two neurinomas (one trigeminal neurinoma in the petroclival region of the middle and posterior fossa and one hypoglossal neurinoma in the foramen magnum extending extracranially into the neck region). After the first surgery and two gamma knife sessions to treat two recurrences, and a surgery to treat another recurrence, one of the meningiomas altered malignantly and the patient died.

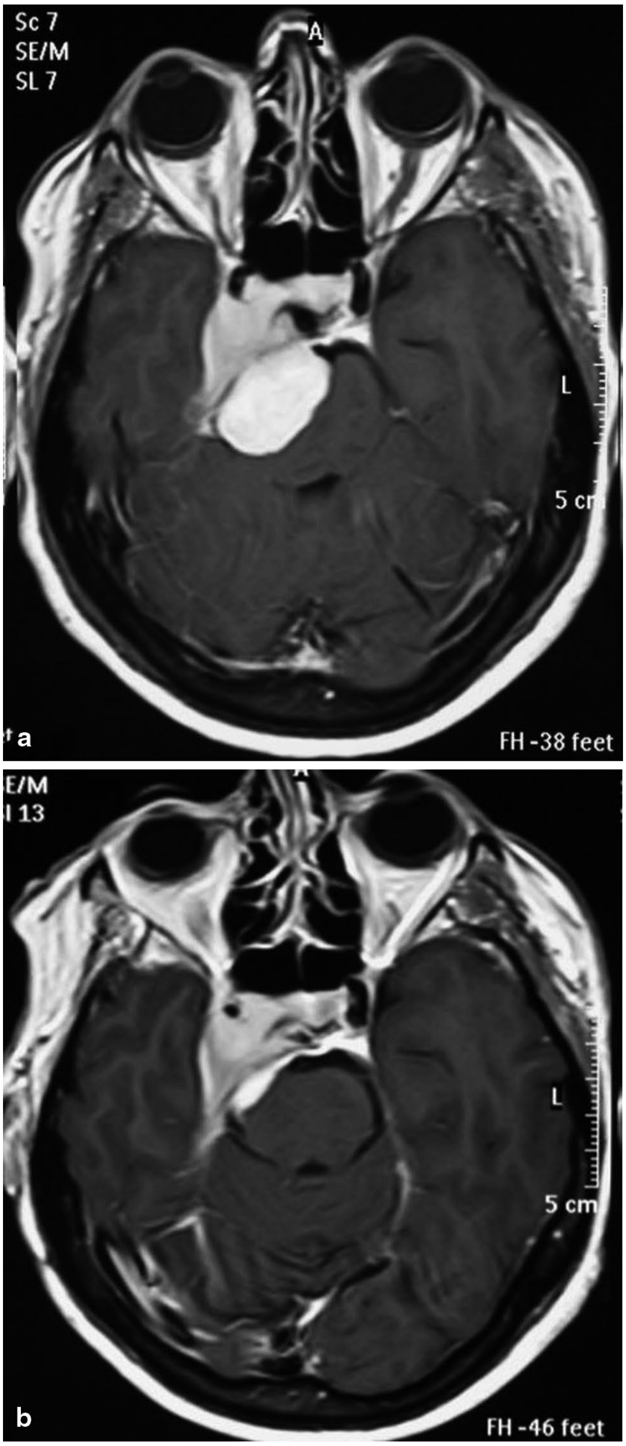

Fig. 2 A right petroclival meningioma, which was surgically reduced through retromastoid approach. The tumour in the posterior fossa was removed, and the remaining part in the parasellar space was treated by stereotactic radiosurgery (**a**). The rest of the large petroclival meningioma in the right parasellar space from the previous figure after the gamma knife irradiation. One year after the radiotherapy, the tumour volume remains unchanged (**b**)

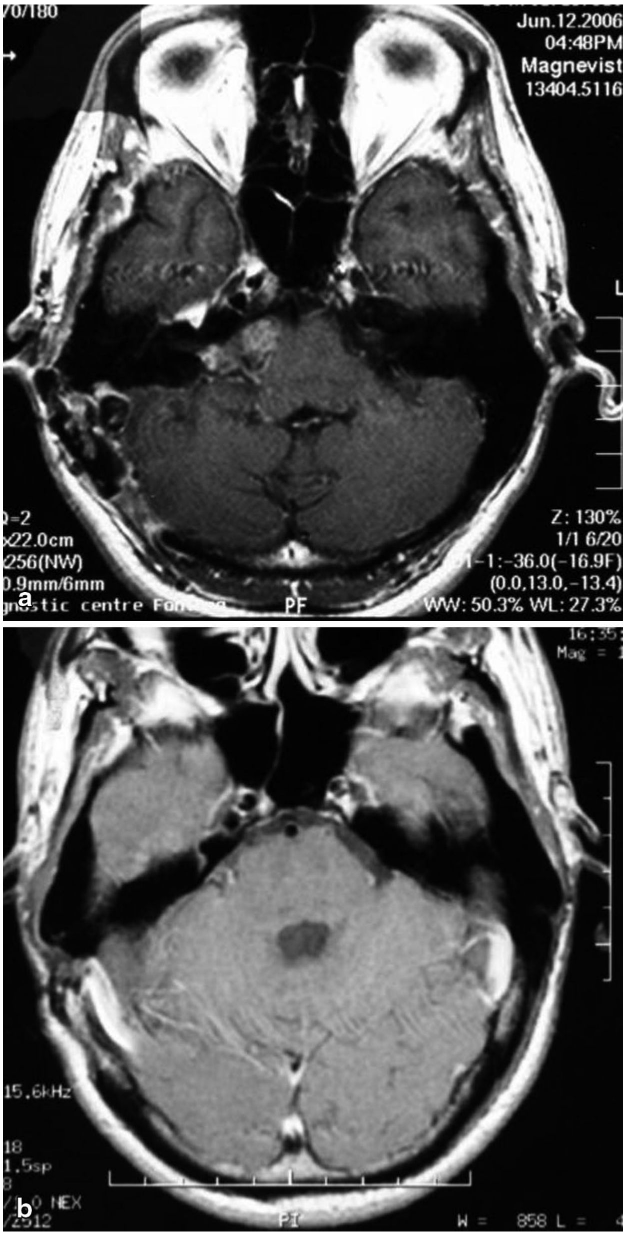

Fig. 3 A tumour residue in the right pontocerebellar angle after non-radical resection on axial magnetic resonance imaging scan (**a**). After the gamma knife treatment, the residue shrank significantly (**b**)

Only one surgery was performed radically—Simpson grade II (macroscopically complete removal with coagulation of the dural attachment in the para- and retrosellar petroclival meningioma). The other meningioma surgeries were resections of major parts of the tumour with minor or larger remaining tumour tissue in situ (Simpson grade IV). Resections of major tumour parts were successful in two neurinomas, as well. However, they were not radical.

Eleven surgical procedures were performed in six patients (five pterional approaches, three retromastoid approaches, one transcondylar approach and two infratemporal approaches on the neck) and seven gamma knife therapies (one patients received two sessions within 3 years).

Preoperatively, the ongoing neurological impairments were noted: hypoglossal paralysis, severe vision impairment and visual field narrowing with tunnel vision. Postoperatively, these impairments did not improve. Postoperative neurological impairments occurred in two patients as a permanent impairment (affection of the nerves VI, IX and X), and in three patients as transient impairment (affection of the nerves VI, VII and XI), that improved later. Postoperatively, one female patient experienced improvement of the fifth nerve function. Out of six patients, one female patient died of a malignant alteration of a benign meningioma, after two surgeries and two gamma knife surgeries. Some transient deterioration and abducens paresis was noticed in one patient following the first session of the gamma knife surgery without further impairments.

A decrease in tumour size after the radiosurgery was noticed in two patients (in one of these two cases, the tumour has grown once again, followed by the second session of the gamma knife surgery 3 years later). Postradiation MRI controls for four cases show a halted growth or controlled size of the tumour in a period of 1–3 years following the gamma knife surgery. The median follow-up of patients was 10 years (range from 7 to 15 years).

Discussion

A review of the most up-to-date literature on experience in treating skull base tumours showed a particularly noticeable trend of treating these tumours with radiosurgery (gamma knife or linear accelerator) being less threatening to patients compared with radical resection of this kind tumours resulting in inacceptable high postoperative morbidity [12–15]. Total resection of these tumours is often associated with postoperative damage of important structures, mostly brain nerves and vascular structures in the region of the cavernous sinus, apex of the petrous bone and jugular bulb. The neurological consequences may be expressed by bulbomotoric disorders, hearing deficits, facial paresis, dysfunctions of the glossopharyngeal and vagus nerves [1, 16]. The gamma knife surgery is becoming a primary alternative for these patients, as it significantly reduces the risk of excellent surgical techniques, preserves the functioning of brain nerves in most patients and halts the tumour growth. This applies particularly for small-sized tumours with a diameter less than 3 cm [12, 14, 17, 18]. Gamma knife surgery can be applied as additional or adjunctive therapy following initial partial resection in large-sized tumours for a long-term control of the reduced tumour volume [1, 5, 13, 19–23]. As there is no reliable data on the long-term (7 years and more) efficiency of the tumour growth control and its recurrence, it seems right to follow the recommendations of the long-term study of the combined surgical and radiosurgical treatment of petroclival meningiomas (102 months and more) on well considered, but aggressive, surgical tumour resection, followed by radiosurgery for potential remnant tumours [5, 18, 24]. This was also confirmed by our results.

Linear accelerator is another sensible option, besides the gamma knife, for radiosurgical treatment of this kind of tumours [25–27]. Both treatment modalities allow the target to receive the maximal dose, with the dose received by neighbouring tissue dropping significantly; thus, the healthy tissue receives a negligible dose of radiation. With the maximum limit of the diameter of the target being approximately 3 cm, this method is particularly appropriate for use in small brain metastases and primary intracranial lesions. The common characteristics include application of a single high dose of radiation, stereotactic localisation of the lesion with CT imaging, the use of computerised dose calculation and a steep dose-gradient [28–30]. The gamma knife is suitable for deep and surgically inaccessible intracranial lesions and for the management of lesions insensitive to conventional radiotherapy. It is also used for the treatment of functional disorders, pain syndromes, arteriovenous malformations and benign and malignant brain tumours, especially their remnants after surgery. Although it is a minimally invasive method for the treatment of a multitude of intracranial diseases, it is not without risk, and potential complications include syncopal episodes, anxiety and acute vessel complications.Linear accelerators, on the other hand, use a special device called a collimator, to shape and target rays. Circular collimators were first developed for targets smaller than 3 cm in diameter and for irregularly shaped targets. In larger targets, the volume irradiated includes an unacceptably large volume of normal tissue. This is why collimators were developed. It is now possible to treat also larger targets of 3–4 cm in diameter and geometrically more complex lesions. The benefits of the linear accelerator over the gamma knife are the ability of even more accurate shaping of the field of irradiation, a more homogenous field of irradiation for large lesions, a higher energy of irradiation, the possibility to irradiate other parts of the body, the use of modern computer programmes and lower costs. Linear accelerators are also widely used for stereotactically focused fraction radiotherapy and like the gamma knife for radiosurgical procedures [27–32].

Relatively few experiences gained in combined treatment of skull base tumours being treated with the gamma knife surgery following the initial radical excision confirm the aforementioned recommendations from the most up-to-date literature [10, 17, 22]. In four out of six patients, tumour recurred (in three patients, a non-radical tumour resection was performed; in one female patient, a tumour resection was radical according to a surgeon from another institution). The gamma knife therapy was applied in three of four recurred tumours and only after the tumour growth or its recurrence was clearly visible on MRI. In one of three female patients (trigeminal neurinoma), the remnant recurrence of the tumour after a repeated subtotal resection was treated with radiosurgery immediately after the surgery, when there were no signs of a possible relapse. Similarly, the patient with an extensive petrous meningioma was referred to gamma knife surgery immediately after the incomplete tumour resection, not waiting for a possible relapse to occur, although the gamma knife surgery was not originally planned. Only in one case we planned a larger portion of the tumour to be resected in the ponto-cerebellar angle. The rest of this petroclival meningioma in the apex of the petrous bone and cavernous sinus was deliberately left to be treated using the radiosurgery as agreed with the radiosurgeon. This is the only case of this kind of deliberate and planned combined therapy for this kind of tumour.

Otherwise, benign skull base tumours recurred regardless of age, sex, histological characteristics and surgical approach (radical or non-radical). Mostly, it was established during the procedure that the planned total resection was technically impossible or was associated with an increased risk of neurovascular brain structures. Except in one case, when the therapy was planned ahead, the gamma knife was used as adjunctive therapy for the remnant tumour as an emergency procedure.

The gamma knife surgery in our patients was successful, at least in the short-term observation in the period from 1 to 3 years after radiation. In five patients, the tumour growth halted; two out of these five patients experienced evident radiological reduction of the tumour, and in one female patient, a recurrent tumour growth appeared following a transient reduction of the tumour, which again required gamma knife surgery. However, the radiosurgery in this case was not successful, and the recurrent tumour was then surgically removed. A malignant alteration of meningioma caused the tumour to relapse and the condition of the patient did not allow another surgery. This patient died shortly after that. Except for a transient abducens paresis in this patient, no further neurological impairment was noticed following the first session. This is a clear advantage of the gamma knife surgery, compared with the surgical treatment associated with numerous impairments. Long-term results on the successful halt of tumour growth and reduction in a period exceeding 10 years in our patients are missing, and this study is planned to be established in the future, as well as the review of treatment results with the linear accelerator.

Conclusions

According to the most up-to-date global literature and experience, gained in combined surgical and radiosurgical treatment of our patients, we may conclude that the combined treatment with planned partial resection of the major portion of the tumour in combination with the later-performed gamma knife surgery is becoming the method of choice for treating extensive skull base tumours in the critical locations of the skull base [6, 7, 23]. The gamma knife surgery of smaller tumours in the very same sites and of the appropriate size has gained popularity as a primary treatment [2, 4, 6, 20]. Surgical tumour removal is supposed to be radical, and at the same time, the neurovascular and brain structures should be considered. To avoid lesions of these structures, it is advised to perform a subtotal removal of the tumour in situ, which is then followed by radiosurgical treatment or to plan a reduction of non-critical parts of the tumour and to treat the tumour remnants radiosurgically (remnants smaller than 3 cm in diameter are suitable for a non-fractionated gamma knife surgery) [9, 13, 18, 19].

Conflict of interest
G. Bunc, J. Ravnik, M. Ravnik, and T. Velnar declare that there are no actual or potential conflicts of interest in relation to this article.

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