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# Gamma Knife Radiosurgery of Skull Base Meningiomas

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## Summary

*Background.* The standart surgical treatment of meningiomas is total resection of the tumour. The complete removal of skull base meningiomas can be difficult because of the proximity of cranial nerves. Stereotactic radiosurgery (SRS) is an effective therapy, either for adjuvant treatment in case of subtotal or partial tumour resection, or as solitary treatment in asymptomatic meningiomas.

*Method.* Between September 1992 and October 1995, SRS using the Leksell Gamma Knife was performed on 46 patients (f : m = 35 : 15), ranging in age from 35 to 81 years, with skull base meningiomas at the Neurosurgical Department of the University of Vienna. According to the indication of gamma knife radiosurgery (GKRS) the patients (n = 46) were devided into two subgroups. Group I (combined procedure: subtotal resection followed by GKRS as a planned procedure or because of a recurrent meningioma), group II (GKRS as the primary treatment). Histological examination of tumour tissue was available for 31 patients (67%) after surgery covering 25 benign (81%) and 6 malignant (19%) meningioma subtypes.

*Findings.* The overall tumour control rate after a mean follow-up period of 48 months (ranging from 36 to 76 months) was 96% (97.5% in benign and 83% in malignant meningiomas). Group I displayed a 96.7% tumour control rate, followed by group II with 93.3% respectively. Neurological follow-up showed an improvement in 33%, stable clinical course in 58% and a persistant deterioration of clinical symtoms in 9%. Remarkable neurological improvement after GKRS was observed in group II (47%), whereas in group I (26%) the amelioration of symptoms was less pronounced.

*Interpretation.* GKRS in meningiomas is a safe and effective treatment. A good tumour control and low morbidity rate was achieved in both groups (I, II) of our series, either as a primary or adjunctive therapeutic approach. The planned combination of microsurgery and GKRS extends the therapeutic spectrum in the treatment of meningiomas. Reduction of tumour volume, increasing the distance to the optical pathways and the knowledge of the actual growing tendency by histological evaluation of the tumour minimises the risk of morbidity and local regrowth. Small and sharply demarcated tumours are in general ideal candidates for single high dose-GKRS, even after failed surgery and radiation therapy, and in special cases also in larger tumour sizes with an adapted/reduced margine dose.

*Keywords:* Stereotactic radiosurgery; meningioma; skull base; brain tumour.

## Introduction

For intracranial meningiomas, total resection along their dural base is the optimal approach in the surgical management as it provides long-term disease-free survival for more than 90% of patients [1, 4, 6]. Meningiomas tend to recur after surgery, especially if resection of tumour tissue was incomplete, or if the adjacent dura was left in place. In particular, skull base meningiomas, representing 35–50% of all intracranial meningiomas, often are impossible to resect completely. Despite tremendous advances in microsurgical techniques, anaesthetic management, and postoperative intensive care, surgical access to these tumours remains a challenge, and the related mortality and morbidity rates are still high [5, 6, 7, 21].

Two reports provide additional evidence that surgery short of total removal reduces morbidity in meningiomas [10, 16]. Followed by adjuvant radiation techniques (radiotherapy (RT), radiosurgery (RS)), subtotal surgical removal is an efficient method to obtain tumour control while preserving neurological function. Patients with benign histology who underwent subtotal surgery and multiple-port fractionated RT after 1980 had a four-year tumour control rate of 98%, compared to the 87% control rate for those patients treated before 1980 [10]. Other reports, however, fail to demonstrate a benefit of conventional fractionated radiation in preventing recurrences [1, 24].

SRS has been reported as a potentially effective alternative to surgical removal of small-to moderate-sized meningiomas, and as an adjuvant treatment modality to reduce the risk of tumour recurrence after subtotal surgery [8, 13, 15]. Meningiomas are considered an ideal tumour type for SRS due to their clear demarcation from the normal brain, accurate localisation by computed tomography (CT) and magnetic resonance imaging (MRI).

## Methods and Patients

Between September 1992 and October 1995, 46 patients (f : m = 35 : 11) with meningiomas underwent SRS with the 201-source cobalt-60 gamma knife at the University of Vienna, Neurosurgical Department. Their median age was 59 (ranging from 35 to 81). All 46 patients had meningiomas located at the skull base, including 4 falcotentorial, 1 trigonal, 1 optic sheath and 1 olfactory groove meningioma (Table 1). Thirtyone patients (67%) underwent one to three previous operations and in 3 patients (7%) fractionated external beam radiation was performed as additional therapy. In this surgical series, histological examinations revealed in 25 patients (81%) benign, in 4 patients (13%) atypical and in 2 patients (6%) malignant meningiomas.

According to our therapeutic approach in the SRS of meningiomas we devided the series of 46 patients into two groups:

Group I: *31 patients (67%)*, were treated after surgery (partial or subtotal tumour resection) as a planned procedure or because of tumour recurrence after prior surgery.

Group II: *15 patients (33%)*. GKRS was the primary treatment modality in these patients with symptomatic tumours, who had characteristic neurodiagnostic imaging patterns pathognomonic of a meningioma and growing tendency.

The neurological deficits prior to GKRS resulted both, as a symptom of tumour growth, and in the sequel of previous surgical procedures (Table 2).

The Leksell Model "G" stereotactic co-ordinate frame (Elektra Instruments, Atlanta, GA) was attached to the patient under local anaesthesia before high resolution contrast enhanced CT or MRI for tumour localisation was done. The median tumour diameter in this series was 23.5 mm (range, 7 to 53 mm) and was selected from the maximum diameter of the three axis directions, measured on the MRI/CT images (Table 5). Because of irregular meningioma delineation, multiple isocenter planning (median, 9; ranging from 2 to 16 isocenters) with the KULA dose planning system was applied in all patients to cover the tumour margin sufficiently. Treatment isodose, central tumour dose, and tumour margin dose were determined by the neurosurgeon and medical physicist. The dose delivered to the tumours was selected after evaluation of the size, location, and the projected radiobiological risk to adjacent critical cranial nerves. According to the literature, the dose applied to tumour margin ranged from 9 to 25 Gy (mean, 15.9 Gy). Thirtyseven tumours (80%) were prescribed with the 50% isodose line, whereas 8 tumours (18%) were covered with an isodose of 40 or 45% and 1 (2%) with an isodose between 60 and 70%.

Collimator plugging patterns were used to "shift" the radiation dose away from critical areas. In 19 patients, where the tumour was in the proximity of the optic pathways, the single fraction dose to the optic system was restricted to less than 10 Gy [8, 14, 17].

All patients were discharged within 36 hours. Follow-up imaging was requested at 6-month intervals for the first year, and then yearly.

Table 1. *Tumoursite*

| Location | N | % |
|---|---|---|
| Skull base | | |
| – Cavernosus sinus | 17 | 37 |
| – Sphenoid wing | 12 | 26 |
| – Petroclival | 10 | 22 |
| – Other sites | 7 | 15 |
| Total | 46 | 100 |

Table 2. *Neurological Symptoms Pre- and Post-GKRS*

| Neurological deficit | Pre GKRS | | | Post GKRS | | |
|---|---|---|---|---|---|---|
| Group | N (%) | I | II | N (%) | I | II |
| Reduced visual acuity | 13 (28) | 12 | 1 | 8 (17) | 7 | 1 |
| Oculomotor palsy | 13 (28) | 9 | 4 | 9 (20) | 7 | 2 |
| Trigeminal sensory loss | 9 (20) | 7 | 2 | 3 (7) | 3 | 0 |
| Abducens palsy | 9 (20) | 7 | 2 | 4 (9) | 3 | 1 |
| Facial palsy | 4 (9) | 4 | 0 | 4 (9) | 4 | 0 |
| Hemiparesis | 4 (9) | 2 | 2 | 2 (4) | 1 | 1 |
| Seizures | 1 (2) | 1 | 0 | 0 | 0 | 0 |
| Miscellaneous | 22 (48) | 14 | 8 | 11 (24) | 7 | 4 |
| New paresis after GKRS | | | | 3 (7) | 2 | 1 |

## Results

### *Radiological Follow-up*

Follow-up MRI studies and clinical analyses of patients were performed in 6-month intervals, followed by 12-month intervals after one year. Mean follow-up of 48 months (ranging from 36 to 76 months) revealed a decrease of the maximum tumour diameter in 24 patients (52%). No change of tumour size was observed in 20 patients (44%), whereas in 2 patients (4%) the meningioma increased in size. The overall tumour control rate was 96% (97.5% in benign and 83% in atypic and malignant meningiomas). Shrinkage or regrowth was postulated when the maximum diameter differed more than 10% compared with the preradiosurgical tumour extension. Group I presented a 96.7% tumour control rate and group II revealed a 93.3% tumour control rate (Table 3). There was no statistical difference of the tumour control rate of skull base meningiomas which were radiosurgically treated directly after microsurgical removal as a planned procedure and those, which received GKRS because of tumour recurrence after prior surgery.

Table 3. *Group Related Postop Tumour Data*

| Group | N (%) | Histological subtype | | Neurological symptoms and signs | | | Tumour diameter | | |
|---|---|---|---|---|---|---|---|---|---|
| | | benign | atypic/malign | improved | stable | worse | decreased | unchanged | increased |
| I | 31 (67) | 25 | 4/2 | 8 | 21 | 2 | 16 | 14 | 1 |
| II | 15 (33) | # | #/# | 7 | 6 | 2 | 8 | 6 | 1 |
| Total (%) | 46 (100) | 25 (81) | 4/2 (19) | 15 (33) | 27 (58) | 4 (9) | 24 (52) | 20 (44) | 2 (4) |

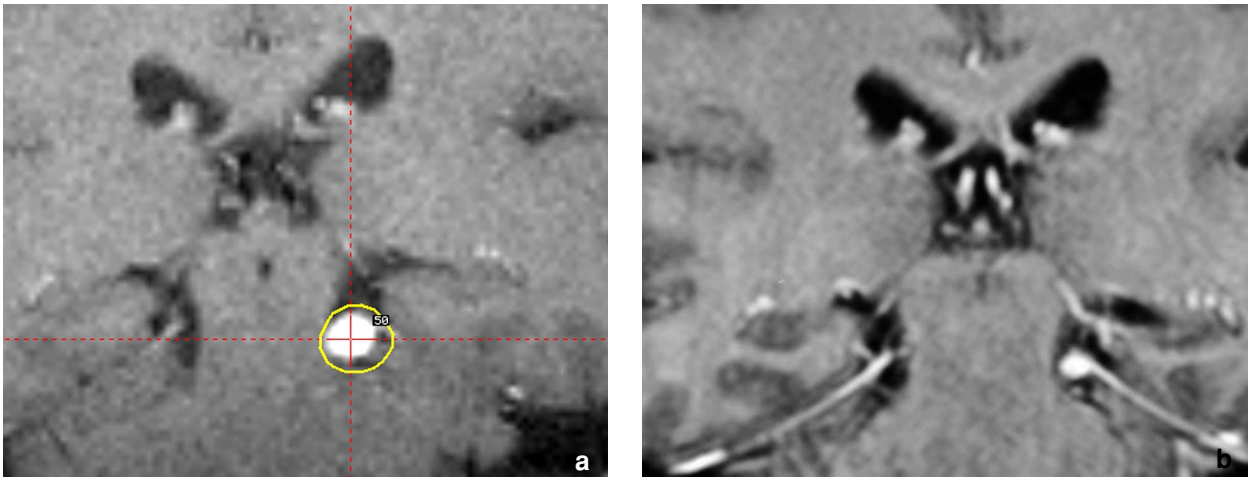


Fig. 1. (a) Coronal dose plan MRI (with 50% isodose line) with contrast medium of a tentorial meningioma touching the brainstem; 7 mm in diameter (group II). (b) 3-yrs post-GKS MRI with contrast medium; shrinking of the tumour; 4 mm in diameter

*Neurological Follow-up*

Neurological follow-up examinations showed the neurological status unchanged in 58%, ameliorated in 33% and worsened in 9% of the patients. Four patients (9%) died during the follow-up period, 2 of whom (4%) died due to tumour progression. No immediate post-operative complications or seizures during the peri-operative period were recorded.

Compared to the neurological deficits the patients presented before GKRS, an improvement of reduced vision, palsy of the III$^{rd}$, V$^{th}$ and VI$^{th}$ was seen in 39%, 31%, 33% and 44%, respectively. Two of 4 patients with motor deficit showed a significant improvement of their disabilities after GKRS (Table 2).

Comparing both treatment groups, remarkable neurological improvement after GKRS was observed in group II (47%), whereas in group I (26%) the amelioration of symptoms was less frequent, but most of the symptoms remained stable (Table 3). Patients presenting with cranial nerve palsy before GKRS showed good clinical benefit after radiosurgery in both groups (Table 2). Also miscellaneous symptoms like vertigo, cephalea, dysaesthesia, swollowing difficulties, etc. diminished in 50% of group I and II (Table 2).

Transient neurological deficits (seizures, paresis) due to peritumoural edema 6 to 12 months following GKRS was observed in 1 patient (2%), with a recurrent benign meningioma located in the trigonum of the right ventricle (Fig. 3). Under steroid medication the majority of the symptoms disappeared within a few weeks. One late radiosurgical side-effect was observed in a patient with an invasive petroclival meningioma extending into the pituitary fossa. Six months after RS increasing hypopituitarism was observed, requiring permanent medical substitution therapy.

*Tumour Recurrence*

Tumour recurrence was defined as a local regrowth which occured within the radiosurgical treatment volume. In 2 patients (4.3%) tumour recurrence was seen 12 and 34 months after RS. One patient, both in group I and group II presented with a tumour regrowth. In one case it was a tumour with a benign histology of a meningotheliomatous meningioma and 1

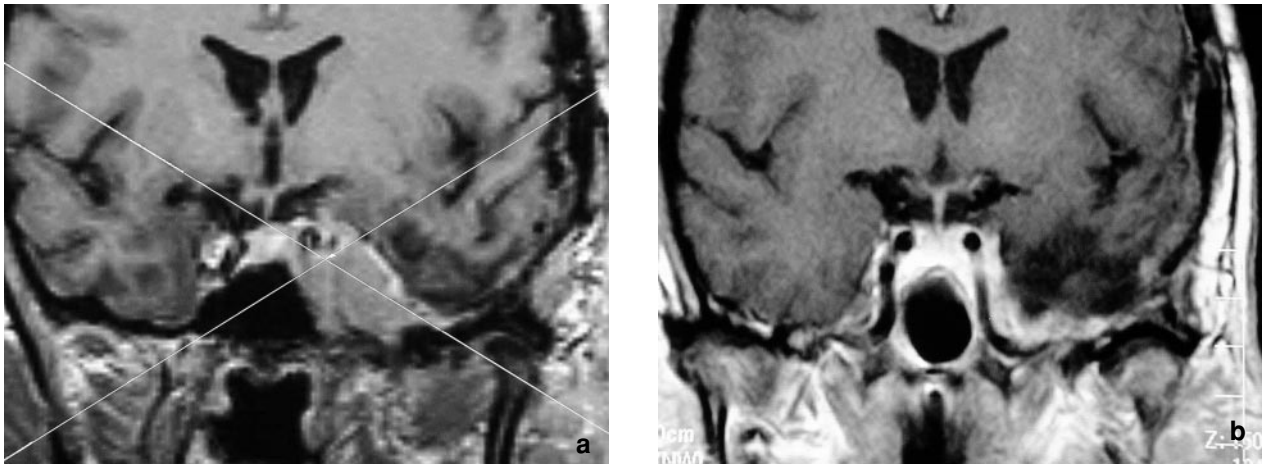


Fig. 2. (a) Pre-GKS coronal MRI with gadolinium; meningioma of the sphenoid wing invading the right sinus cavernosus after several subtotal surgeries because of regrowth; maximum diameter of 24 mm (group I). (b) 4-yrs post-GKS; coronal MRI with gadolinium; reduced tumour mass on the floor of the left middle fossa

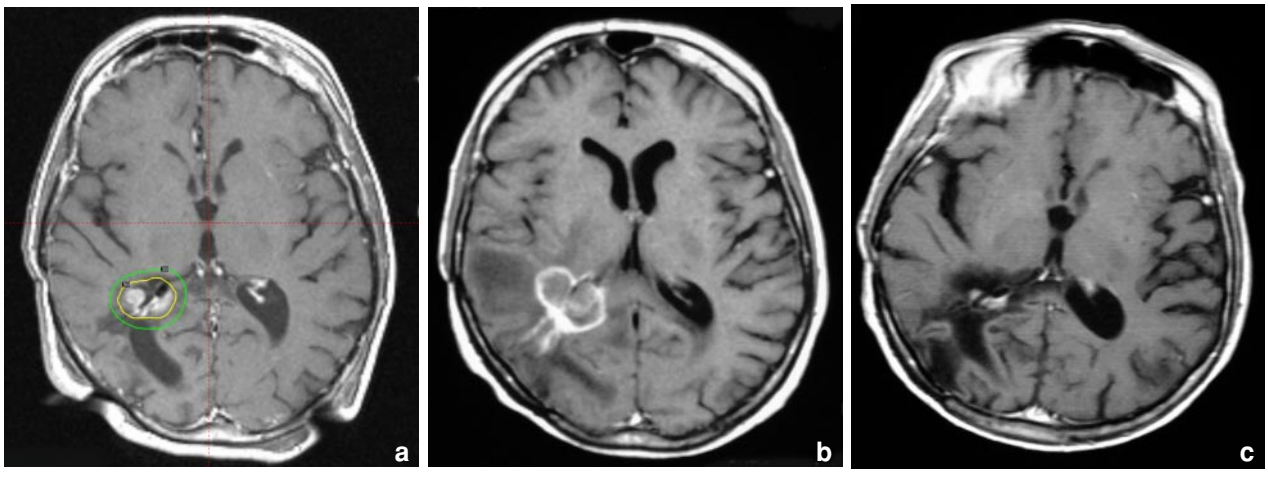


Fig. 3. (a) Axial dose plan MRI (with 50% and 70% isodose line) with gadolinium of a meningioma within the occipital horn of the right lateral ventricle; 16 mm in diameter (group I). (b) 6 month post-GKS; axial MRI with gadolinium; radiation induced contrast enhanced circle around the radiosurgical target and the space occupying perifocal edema. (c) 3 yrs post-GKS axial MRI with gadolinium; showing a tumour shrinking to 9 mm in diameter

patient had an atypical subtype with signs of increased proliferation activity (Table 4). In 2 patients, however, with a recurrence of a malignant meningioma and in 3 patients with an atypical meningioma after failed surgery and RT, a disease-free interval between 34 and 54 months was observed hitherto.

## Discussion

Total resection is the standard aim in the treatment of meningioma. Complete tumour removal can be achieved in nearly all tumours located over the hemispheres. However, management in skull base meningiomas is complicated by the proximity to cranial nerves, thus an incomplete tumour resection as a surgical result is more frequent. After complete resection, Jääskeläinen *et al.* [11] reported a continuing risk of tumour relapse and a median time of recurrence of 7.5 years. Two other series with complete resection of meningiomas report a 5-year progression-free survival rate of 4–7% [3, 19]. Mitotic index and the extent of resection proved to be the most powerful predictors of recurrence within 5 years after tumour resection [18].

In skull base meningiomas, surgeons have to choose between ''aggressive'' tumour resection, with a substantial risk of neurological sequelae, or partial tu-

Table 4. *Tumour-Recurrence: Patient Data*

| N | Vol | Iso dose | Margin dose | Max. dose | Histology | op | Group |
|---|---|---|---|---|---|---|---|
| 1 | 5,4 ccm | 30–50% | 17,5 Gy | 35 Gy | endoth. | 2× | II |
| 2 | 15 ccm | 30–50% | 11 Gy | 22 Gy | atypic | 2× | I |

Table 5. *Group Related Radiosurgical Data*

| Group | f : m | Age (mean) | Tumoursize (mm) | Margine dose | Iso dose |
|---|---|---|---|---|---|
| I | 24 : 7 | 59 yrs | 10–53 (26.7) | 9–20 (15.3) Gy | 45–50 (50)% |
| II | 11 : 4 | 64 yrs | 7–30 (20.5) | 13–25 (17.3) Gy | 40–70 (50)% |
| Total | 35 : 11 | 61.5 yrs | 7–53 (23.6) | 9–25 (16.3) Gy | 45–70 (50)% |

mour removal with lower morbidity and a higher percentage of tumour progression. In all cases subtotal resection provides the histological evaluation of the tumour tissue and a rapid reduction of the tumour burden. Thus it contributes decisive data to the need of an adjunctive treatment of the tumour remnant and, in particular, optimises the radiosurgical approach by the reducion of the tumour mass.

Fractionated RT of meningiomas imposes risks of long-term side effects, such as loss of vision, pituitary dysfunction, delayed radiation-induced injury of the brain, and the development of secondary neoplasms after irradiation for benign CNS tumours [2]. More recent reports provide additional evidence that conventional RT has relatively few risks [10, 16].

SRS as a primary treatment modality is a potentially effective alternative to surgical removal of small-to moderate-sized benign meningiomas, as documented in several series [12, 13, 15, 20]. The mean age of our patients treated with GKRS alone in group II was 64 years, compared to 59 years in group I (Table 5). In addition, patients in group II showed a small number of neurological deficits before radiosurgery, compared to group I, but, on the other hand, they benefitted most from GKRS and their neurological status improved in 47% (Tables 2 and 3). The tumour control rate was lower (93%), compared to group I, probably due to the unknown histological subtype of the basal meningiomas.

In our series, patients with operated meningiomas and proven histology (benign : atypic/malignant = 25 : 6) showed a tumour control rate of 97.5% for benign and 83% for atypical or malignant meningiomas in a mean follow-up of 4 years. Our overall tumour control of 96% is quite similar to that in other series. There have been several reports on the efficacy and limitations of RS in the treatment of meningiomas [8, 12, 13, 15, 17, 20, 22, 23]. Kondziolka *et al.* [13] found an actuarial tumour control rate of 96% in a follow-up time of 2 years for a series that included all brain locations. Recent papers dealing with SRS of meningiomas at special sites report tumour control rates of 93–98%, depending on the location of the tumour (parasagittal, tentorial, skull base, petroclival) [12, 20, 22, 23]. Pendl *et al.* [22] reported a tumour control rate of 96% in skull base meningiomas in 78 patients with a mean follow-up of 18.5 months. Kondziolka *et al.* [12] reported a tumour control rate of 93% in a multicenter review of parasagittal meningiomas in 203 patients with a mean follow-up of 3.5 years. In 62 radiosurgically treated patients with petroclival meningiomas, Subach *et al.* [23] reported a tumour control rate of 91% with a follow-up of 37 months. The tumour control rate in 41 patients with tentorial meningiomas was 98% after a follow-up period of 3 years [20].

We observed 2 recurrent tumours, 1 with benign and 1 with atypical histology after RS in our series. Two malignant recurrent meningiomas which had been operated on and treated with RT before, did not show any signs of regrowth after radiosurgical treatment.

A transient neurological deterioration occurred 1 in patient with a meningioma located in the trigonum of the right ventricle. The cause for the deterioration was found to be perifocal edema, which appeared 6 months following GKRS. However, Ganz *et al.* [9] reported a high incidence of radiation-induced edema in nonbasal tumours and meningiomas treated with 18 Gy or more at the tumour margin. On the contrary, a recent report on parasagittal meningiomas treated with GKRS found no correlation between edema and tumour margin dose [12]. The presence of a previous neurological deficit revealed to be the most important factor for subsequent symptomatic edema after SRS.

Meningiomas' dural tail should be treated both at microsurgery and SRS in order to prevent tumour recurrences. In 1 patient of our series subsequent tumour growth after GKRS was documented to be due to suboptimal covering of the tumour's ridge. Delayed tumour growth outside the radiosurgical treatment volume occurred 31 months after GKRS. The patient underwent a second radiosurgical procedure without side effects.

## Conclusion

In contemporary surgical management of intracranial meningiomas one must devise a judicious strategy for each individual patient. SRS has gained an important role in the treatment of meningiomas. It proved to be valuable as an adjunct to microsurgical subtotal removal in large tumours, or as an alternative treatment in cases of no-or low-symptomatic benign meningiomas.

SRS also is a primary treatment alternative for patients whose advanced age, medical condition or high-risk tumour location preclude surgical resection.

Because of the often slow and unpredictable growth of meningiomas, it would seem that the evaluation of gamma knife treatment must involve a very long follow-up before any final conclusions can be drawn.

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## Comments

This is a sizable European series of 46 meningioma patients treated by the gamma knife between 1992 and 1995, with a mean follow-up time of four years. It is important that European centers publish their results so that sizable homeground series are formed, to be referred to in national and EANS meetings, not having to be based on North American, Japanese, Korean and Chinese series, collected and analyzed in different atmospheres.

*J. Jääskeläinen*

The authors present their experience in the radiosurgical treatment of intracranial meningiomas. Their follow-up ranges from 36 to 72 months. They achieved a 91% control rate. In 7% of patients with

convexity meningiomas transient neurological worsening occurred due to peritumoral edema. This subsided after corticosteroid treatment.

The radiosurgical treatment of meningiomas has become increasingly popular in the last decade as an adjunct to surgery, in cases of tumor recurrence and even as a replacent for surgery in cases of high-risk patients or in those with lesions in difficult locations. The surge in popularity of radiosurgery came about as the initial enthusiasm for extensive skull base procedures in the therapy of meningiomas has been tempered. Radical surgical procedures in locations such as the cavernous sinus have resulted in ''clean'' postoperative MRIs. The price of this radicality has, however, been a significant morbidity such as cranial nerve dysfunction. With the follow-up period now extending past 5 years, recurrent tumor growth is being increasingly identified, raising doubt about the possibility of cure in certain skull base meningiomas. If surgical cure cannot be achieved in the majority of cases does the high surgical risk for neurological disability justify an aggressive surgical approach? Many neurosurgeons have therefore adopted a more conservative surgical strategy aimed at tumor debulking and treating the remnant with radiosurgery. Whether this strategy is justified will depend on long-term follow-up studies. Results of an up to ten year follow-up show tumor control rates in the 90 percent range being maintained [1]. The authors are encouraged to report their results when a longer follow-up period is available.

The neurological morbidity of radiosurgery is low. Cranial nerves appear quite radioresistant at the doses commonly used. On the other hand the optic nerve apparatus seems to be vulnerable to doses of 10 Gy and above [2]. Studies of lower radiation doses to meningiomas are now underway and may provide similar rates of tumor control with less risk to vision. The incidence of radiation induced brain edema in convexity rather than skull base meningiomas, as reported by the authors, is interesting but remains unexplained.

The authors have treated 18 patient with pathognomonic MRIs by primary radiosurgery without obtaining a prior histological diagnosis. This is an area of controversy as mimicking lesions such as lymphoma are encountered [3]. The risk-benefit ratio of histological verification of a purely intracavernous lesion in a young patient must be established before unhesitatingly recommending primary radiosurgical treatment in these situations. In the author's series, overall results in this subgroup were comparable to cases with verified menigiomas.

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