Cavernous sinus meningiomas: a radiosurgical pathology

Meningeomas do seio cavernoso: uma patologia neurocirúrgica

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ABSTRACT

Introduction: Tumors of the cranial base arising from or partially involving the cavernous sinus have represented a formidable challenge to neurosurgeons. Stereotactic radiosurgery represents an alternative to microsurgery for the management of cavernous sinus meningiomas. The present study aims to evaluate the results of radiosurgery in a large series of patients treated with a linear accelerator with a long-term follow-up.

Patients and Methods: From 1993 through 2007, 462 patients with meningiomas underwent radiosurgery at the Chaim Sheba Medical Center LINAC radiosurgery unit. Of those, 117 had tumors involving predominantly the cavernous sinus. A mean follow-up of 67 months was obtained in 102 patients (range: 12 to 180 months). Patients' age ranged from 31 to 86 years (mean 57). Seventy two (70%) were females. Thirty five patients (34.3%) were initially submitted to microsurgery and 67 (65.6%) underwent stereotactic radiosurgery as the first treatment option. Patients were treated using a linear accelerator with cylindrical collimators in 44 patients (43.1%) and a minmultileaf collimator in 58 patients (56.8%). The prescription dose was delivered to the 60 to 80% isodose line (mean, 68%) in patients treated with cylindrical collimators, and to the 80% in those treated with a single conformal isocenter. Doses ranged between 12 and 17.5 Gy (mean, 13.5 Gy). Median tumor volume was 7.2 cm³ (range 0.61–23 cm³).

Results: All patients were available for follow-up at 12 to 180 months after treatment (mean, 68 months; median, 60 months). The actuarial control rate was 98%. Fifty nine patients (58%) had a volume reduction and forty one (40%) had stable tumor volumes at the end of follow-up. Two tumors grew. Overall, 4 patients had a new lasting neurological deficit (facial hypesthesia or pain in two, trochlear neuropathy in two, and visual defect in one), for an incidence of 4% in persistent neurological complications.

Conclusions: This series of linear accelerator radiosurgery confirms that in the short and long term, radiosurgery affords excellent control for cavernous sinus meningiomas with a very low incidence of complications. Radiosurgery can thus be regarded as the treatment of choice for cavernous sinus meningiomas.

Key-Words: meningiomas, stereotactic radiosurgery, cavernous sinus.

SUMÁRIO

Introdução: Tumores da base do crânio surgindo ou invadindo o seio cavernoso tem representado um desafio formidável aos neurocirurgiões. A radiocirurgia estereotáxica representa uma alternativa à microcirurgia para os meningeomas do seio cavernoso. O presente estudo tem por objetivo avaliar os resultados da radiocirurgia em uma grande série de pacientes tratados com acelerador linear e seguidos por longo prazo.

Casuística e métodos: De 1993 a 2007, 462 pacientes com meningeomas foram submetidos à radiocirurgia no Chaim Sheba Medical Center. Destes, 117 apresentavam tumores envolvendo predominantemente o seio cavernoso. Um seguimento médio de 67 meses foi obtido em 102 pacientes (variação: 12 a 180 meses), com uma variação de idade entre 31 a 86 anos (média 57). Setenta e dois pacientes (70%) eram do sexo feminino. Trinta e cinco pacientes (34.3%) foram inicialmente submetidos à microcirurgia e 67 (65.6%) submetidos à radiocirurgia com o acelerador linear, sendo 58 pacientes (56.8%) tratados com um colimador multielementar e 44 pacientes (43.1%) com um colimador cilíndrico. A dose prescrita foi aplicada para a linha de isodose de 60 a 80% (média 68%) em pacientes tratados com colimadores cilíndricos e para 80% em pacientes tratados com um colimador conformacional.

Resultados: Todos os pacientes estavam disponíveis para avaliação a 12 a 180 meses após o tratamento (média 68 meses; mediana 60 meses). O controle atuarial foi de 98%. Cinquenta e nove pacientes (58%) tiveram um volume de redução e quarenta e um (40%) tiveram um volume de estabilização no final do seguimento. Dois tumores cresceram. No total, quatro pacientes tiveram um novo déficit neurológico persistente (hipestesia facial e dor em dois, neuropatia troclear em dois, e defeito visual em um), para uma incidência de 4% em pacientes com déficit neurológico persistente.

Conclusões: Esta série de radiocirurgia com acelerador linear confirma que a radiocirurgia fornece um controle excelente para meningeomas do seio cavernoso com uma baixa incidência de complicações. A radiocirurgia pode portanto ser considerada como a opção de tratamento de preferência para meningeomas do seio cavernoso.

Palavras-chave: meningeomas, radiocirurgia estereotáxica, seio cavernoso.
únicos. As doses variaram entre 12 e 17,5 Gy (média: 13,5 Gy). O volume tumoral mediano foi de 7,2 cm³ (variação: 0,61–23 cm³).

Resultados: O seguimento obtido em todos os pacientes foi de 12 a 180 meses após o tratamento (média: 68 meses e mediana de 60 meses). A taxa de controle atuarial foi de 98%. Uma redução volumétrica do tumor foi obtida em 59 pacientes (58%) e 41 (40%) mantiveram o volume tumoral estável. Crescimento tumoral foi observado em dois casos após o tratamento. Um total de quatro pacientes desenvolveu um novo déficit neurológico permanente durante o período de seguimento (hipoestesia facial ou dor em dois, neuropatia do nervo troclear em dois e déficit visual em um, com uma incidência de complicações neurológicas persistentes de 4%.

Conclusões: Esta série radiocirúrgica com acelerador linear confirma que tanto a curto como a longo prazo, a radiocirurgia propicia um excelente controle para os meningiomas do seio cavernoso, com uma incidência muito baixa de complicações, devendo assim ser considerada como tratamento de escolha para os meningiomas do seio cavernoso.

Palavras-chave: Meningiomas, Radiocirurgia estereotáctica, seio cavernoso.

INTRODUCTION

Tumors of the cranial base arising from or partially involving the cavernous sinus have represented a formidable challenge to neurosurgeons. For decades, surgery in that area was considered excessively risky or impossible due to brisk bleeding from its venous plexus.

With advances in microsurgical techniques and more precise knowledge of the cavernous sinus anatomy, highly skilled neurosurgeons accumulated experience in removal of tumors from the area. Technical reports and increasingly large surgical series appeared in the literature of the late 1980’s and 1990’s. Still, with time it became clear that even in the most experienced hands, results were less than satisfactory.

Significant surgical morbidity may stem from injury to the carotid artery, resulting in brain infarction, or more frequently from injury to the nerves in the cavernous sinus space. Mortality rates are up to 10%2,3,14,20 and rates of permanent cranial neuropathies range from 6 to 42%2,4,7,15.

Partial injury to the trigeminal nerve may result in severe deafferentation pain, which is among the most treatment-resistant pain conditions.

Moreover, because of tumor infiltration of central structures, such as the carotid artery or nerves15,17, surgical resection of meningiomas in the cavernous space is frequently incomplete1,3,14,20 resulting in a high incidence of recurrence2,3,14. As most tumors in this region are histologically benign, a poor functional outcome after treatment results in a high cost to patient and community.

The impulse for microsurgery of the cavernous sinus was more or less concomitant with the appearance of radiosurgery as an increasingly available treatment technique in the late 1980’s. Although radiosurgery had been in clinical use in a handful of places for more than a decade, its transformation into a mainstream neurosurgical weapon was made possible by the introduction of two important technologies: three dimensional imaging of the brain (first Computed Tomography [CT] and later Magnetic Resonance Imaging [MRI]), and the microcomputer. These inventions fueled the rapid evolution of radiosurgery by enabling the direct visualization of intracranial tumors, and the execution of three-dimensional dosimetry with reasonable speed. Linear accelerator radiosurgery (an invention of the early 1980’s) and gamma knife surgery (developed in the 1960’s) became increasingly available in high-end medical facilities. When we started our service at Sheba Medical Center in 1992, the potential of radiosurgery for treating tumors in the cavernous sinus had already been put forward by pioneers in the field, mainly in the United States. With the information at hand, it became clear to us that radiosurgery could become the treatment of choice for these difficult tumors. In a previous publication from 2002, our preliminary results in a cohort of 44 patients with a mean follow up of 3 years, confirmed that feeling. In the present communication a larger population of patients (117) with a mean follow up of close to 6 years, enlarges the database for analysis.

PATIENTS AND METHODS

From 1993 through 2007, 462 patients with meningiomas underwent radiosurgery at the Chaim Sheba Medical Center LINAC radiosurgery unit. Of those, 117 had tumors involving predominantly the cavernous sinus. At the time of this writing, 102 patients who had completed 12 to 180 months of follow up (mean 67 months) were available for analysis, and they represent the body of this series.

Patients’ age ranged from 31 to 86 years (mean 57). Seventy two (70%) were females. Thirty five patients had histological proof of their diagnosis, from tissue obtained during previous attempts at surgical removal. The rest of the cohort was diagnosed by imaging alone. Patients without previous surgery were diagnosed as harboring meningiomas when their MRI scans revealed a lesion with sharp margins that was either isointense or hypointense on T1-weighted images, and showed homogeneous enhancement in postcontrast images. All patients had at least two MRI studies, compatible with a slow growing tumor, before treatment.
PRESENTATION

Twenty seven patients had no neurological deficit attributable to the cavernous sinus meningioma. However, only eight of them were completely asymptomatic at the time of treatment, and their cavernous sinus tumor was detected by cranial imaging done for unrelated complaints. Seventeen patients had moderate to severe chronic headaches, and two other had troublesome dizziness which prompted investigation. Headaches were also a chief complaint in 18 other patients who had previous surgery (2), cranial nerve deficit (6), or both (7).

Sixty four patients (62%) had functional deficit of cranial nerves 2 through 6 (sixth nerve in 39, third nerve in 17, fourth nerve in 7, facial hypesthesia in 11, orbital or facial pain in 9, and unilateral visual loss in 12. One patient presented with inappropriate antidiuretic hormone secretion, and 3 had unilateral proptosis. Of the 35 patients who had undergone previous surgery, 24 (69%) were left with a new neurological deficit.

TREATMENT PARAMETERS

Patients were admitted to the neurosurgical department on the morning of their treatment day. Under local anesthesia, a Brown-Roberts-Wells stereotactic base ring (Radionics Integra, Plainsboro, New Jersey) was applied bedside to the patient’s head, and a stereotactic CT scan was obtained with fine axial cuts (1mm) of the whole head. The imaging data were transferred to the treatment-planning computer. MRI-to-CT fusion software became available at our center in 1998, and since then, MRI has been obtained for all treated patients (n 68) 1 to 2 days before treatment. MRI protocols have changed over the years in pace with evolutionary changes in MRI technology. Currently, our MRI protocol for cavernous sinus tumors includes T1 weighted, contrast enhanced, fat suppressed 1-2mm-thick axial cuts with no gap, and a high resolution T2 weighted axial series, again with 1-2mm cuts. These protocols allow exquisite definition of tumor boundaries within the cavernous sinus and orbit. The T2 images beautifully depict the cranial nerves. Treatment planning was performed with the goal of achieving a complete conformal coverage of the tumor at the highest possible isodose shell. Conventional optimization tools were used for this purpose. Forty four patients were treated with multiple non-coplanar arcs using cylindrical collimators ranging from 10 to 25mm in diameter and with 1 to 9 isocenters (mean, 3 isocenters). The last 58 patients were treated with a single conformal isocenter using a minimultileaf collimator (M3; BrainLab, Munich, Germany). Twenty six of them with multiple (9–11) fixed conformal beams and the last 32 with the dynamic conformal rotation paradigm. Regardless of technique, all doses were normalized to 100%. The prescription dose was delivered to the 60 to 80% isodose line (mean, 68%) in patients treated with cylindrical collimators, and to the 80% in those treated with a single conformal isocenter. Doses ranged between 12 and 17.5 Gy (mean, 13.5 Gy). Median tumor volume was 7.2 cm³ (range 0.61–23cm³). The prescription dose was adjusted whenever necessary to limit the dose to the hypothalamus and functional anterior optic pathways to 10 Gy or less. All patients were discharged immediately after treatment.

FOLLOW-UP

All patients were followed up prospectively yearly with neurological examinations, contrast-enhanced MRI studies, neuro-ophthalmological assessment, and measurement of serum hormonal levels related to the hypothalamic-pituitary axis. Tumor size before and after radiosurgery was assessed by measuring the contrast-enhanced margins in the three standard MRI planes. Tumor size reduction was defined as a decrease of at least 10% in any dimension. Tumor enlargement of more than 10% in any dimension was defined as tumor progression. Tumors of decreased or unchanged size were defined as controlled.

RESULTS

TUMOR CONTROL RATES

All patients were available for follow-up at 12 to 180 months after treatment (mean, 68 months; median, 60 months). The actuarial control rate was 98%. Fifty nine patients (58%) had a volume reduction of 20 to 95%. Forty one (40%) had stable tumor volumes at the end of follow-up. Two tumors grew. In one patient, tumor growth was seen on the MRI performed 36 months after treatment. The patient remained asymptomatic, and the tumor later stabilized until the patient’s death, 54 months after treatment, from complications of acute renal failure. The second tumor growth was detected 84 months after treatment. This patient had bilateral cavernous sinus meningiomas with multiple resections on both sides and gamma knife surgery for the contralateral tumor. After his radiosurgical failure he has recently been retreated with fractionated stereotactic radiation without tissue sampling.

Sixty three patients in this cohort had extended follow ups of 60-180 months (mean 93 months). In this subpopulation, tumor volume reduction was seen in 65%. In the subgroup of patients with less than 5 years follow up (12-48 months, mean 31 months) the volume reduction rate was 43%. This difference was significant (p<0.05 chi square test).
ACUTE SIDE EFFECTS

Acute side effects were rare and mild. A few patients complained of headaches persisting several days, and two had vomiting for up to 24 hours. All the patients returned to their normal activities 2 to 3 days after radiosurgery.

TRANSIENT COMPLICATIONS

One patient had persistent headaches lasting more than 2 years which subsided thereafter. Two patients had transient oculomotor neuropathies during the first year following radiosurgery. In both the deficit lasted for a few weeks and resolved spontaneously. One patient had transient facial hypesthesia.

PERMANENT COMPLICATIONS

One patient developed mild facial hypesthesia. Two patients developed facial pain, one fully controlled with carbamazepine, and another, with deafferentiation pain, is only partially controlled with medication. One patient developed diplopia due to VIth nerve paresis. One patient developed a visual field defect (upper homonymous quadrantopsia) 18 months after radiosurgery.

Two patients developed communicating hydrocephalus (one at 6 months, and one at 2 yr after radiosurgery) which required ventriculoperitoneal shunting. One patient with a partially exophytic tumor involving the temporal fossa, had symptomatic temporal lobe edema 1 year after radiosurgery and required partial resection of her tumor. When seen 6 years after radiosurgery, she had a normal neurological status. Her MRI scan showed a small intracavernous tumor and no residual temporal lobe pathology.

Overall, 4 patients had a new lasting neurological deficit (facial hypesthesia or pain in two, trochlear neuropathy in two, and visual defect in one), for an incidence of 4% in persistent neurological complications. No patient has developed a new pituitary insufficiency.

OUTCOME OF EXISTING CRANIAL NEUROPATHIES

Sixty four patients had cranial nerve deficits attributable to their cavernous sinus tumors. Several of them had multiple neuropathies.

Optic nerve: 12 patients had deficits at presentation, 5 of them had no light perception (all following surgery). Seven had moderate to severe visual loss (five of them following surgery). Of these, 2 improved (fig 2) and one deteriorated.

Third nerve: Deficits were present in 17 patients (partial in 8). Improvement or resolution was seen in 6 (35%).

Trochlear nerve: 7 patients had 4th cranial nerve deficits before radiosurgery. In six of them it was a sequela of surgery, and none of them improved. The only case unrelated to craniotomy resolved following radiosurgery.
Abducens Nerve: this was the most frequent cranial neuropathy at presentation (39 patients). Resolution [7 cases] or improvement [4 cases] was seen in 11 (28%). In one patient a partial deficit deteriorated to full palsy.

Trigeminal nerve: sensory deficit was present in 11 of which 4 (36%) improved after treatment; 9 patients had facial pain, improving in 3 of them (33%). Six patients had paresthesias, which cleared in 5 of them.

In summary: of 101 cranial neuropathies, improvement or resolution was seen in 32 (32%). Deficits of early onset (less than 1 year before radiosurgery) had a significantly higher rate of resolution: in 43 cranial neuropathies of early onset, 21 improved or resolved (49%), whereas of 57 deficits lasting for more than one year, improvement was seen in only 11 (19%). This difference was statistically significant (p < 0.03 chi square test).

Previous surgery affected negatively the chance to recover from cranial nerve deficits: of 47 deficits in patients who had surgery, 9 improved (19%). Conversely, of 54 deficits in patients without surgery, 23 improved (43%, p=0.012, chi-square test).

It could be argued that post surgery patients arrived to radiosurgery with greater delay due to the need to recover and get reassessment. Nonetheless, in 12 post-surgical deficits lasting for less than one year, improvement was seen in just 3 (25%). Of 35 post surgical deficits lasting for more than one year, improvement registered in 6 (17%). Conversely, in patients without surgery, deficits lasting less than one year improved in 58% (18 of 31), whereas deficits lasting for > 1 year improved in 23% (5 of 22).

This results strongly support the notion that early radiosurgery greatly increases the chance of improving cranial nerve deficits in patients whose deficits are not related to surgery. Post surgical deficits had a much reduced chance of improvement, even after early radiosurgical intervention.

**DISCUSSION**

Microsurgery of the cavernous sinus peaked in the late 1980’s and early 1990’s, following the seminal efforts by V. Dolenc.

Early enthusiasm chilled when over time it became clear that complete removal of intrinsic cavernous sinus meningiomas is relatively rare, tumor re-growth is the rule with incomplete resection, and that surgery takes a high toll in terms of cranial nerve deficits. Proof of this is the meager number of series on resection of cavernous sinus meningiomas published in the last years. Two series appearing in this decade merit attention due to their scope: Al Mefti reported in 2003 on his personal series of 163 patients.

This series is of importance since it provides contemporary information on what can be expected from microsurgery in the hands of one of the most respected specialists in the field. Total removal was achieved in 71 cases (44%). In the latter group, tumor recurrence was observed in 7%. In the cases with partial resection re-growth was registered in 57%. The authors put forward the case for microsurgery since “no other treatment can achieve total [tumor] removal or disappearance consistently”. They do not provide information on the incidence of neurological deficits in their own series, but proclaim that “the majority of neuropathies in these patients exist at presentation, whereas a minority develops permanently after surgery, and many of those affect sensory function or can be treated with strabismus surgery”. Strabismus surgery, however, does not correct oculomotor deficit. It can only improve in some cases its cosmetic effect. Facial sensory deficits are a minor deficit only when not complicated by deafferentation pain.

Sindou et al reported in 2007 on a series of 100 patients with cavernous sinus meningiomas with extrasinus extension (supra, lateral, or posterior). Follow up ranged from 3 to 20 years (mean 8.3 years). The appearance or aggravation of disorders in vision, ocular motility, or trigeminal function occurred in 19, 29, and 24% of patients respectively, with a significantly higher rate of complications when resection was performed inside the cavernous sinus. Gross-total removal of both the extra and intracavernous portions was achieved in 12 patients, removal of the extracavernous portions with only a partial resection of the intracavernous portion in 28 patients, and removal only of the extracavernous portions was performed in 60 patients. Mortality occurred in 5%. Interestingly, tumor re-growth was observed only in 11 of the 82 surviving patients with subtotal removal. The authors concluded that there is no oncological benefit to resection of intracavernous tumor components. It is of note that their low re-growth rate is in conflict with data from other surgical series.

The data presented in these contemporary series reaffirm the
high cost in terms of mortality and morbidity of microsurgery of cavernous sinus meningiomas.

In a previous publication by our group\textsuperscript{23} the excellent results afforded by radiosurgery of cavernous sinus meningiomas were documented in the short term (mean follow up of 36 months). We stressed the need for more extended follow up to assess the ultimate significance of radiosurgery in the definitive control of these difficult tumors. Would the early promise hold ground after many years?

Our current series has a mean follow up of 67 months. In 59 patients, follow up has reached 5 to 15 years (mean 107 months). This cohort allows for analysis of late results and is certainly one of the series with the longest follow up so far reported.

**VOLUME**

Early and late tumor control rate were 98%. Tumors shrank in 60% of the patients and remained stable in 38%. Control rates ranging from 87 to 98% have been reported by other large gamma knife series\textsuperscript{8,18,19}.

As would be expected, with longer follow up, more tumors were seen to shrink. In the 36 patients with stable tumor size, mean follow up was 57 months. In those reduced (n 59), follow up was at a mean of 74 months. Two patients showed tumor growth detected at 36 and 84 months post treatment. The early growing tumor remained then stationary until the patient’s demise from unrelated causes 2 years later. The late recurrence is a cautionary event. It occurred in a patient whose tumor, although histologically benign, had a very aggressive course. This male had a bilateral cavernous sinus meningioma. The left sided, larger tumor, was fist partially resected, then treated with gamma knife surgery, and upon massive relapse was completely exenterated with the whole contents of the cavernous sinus (with a concurrent supraclinoid carotid bypass). The right sided tumor treated by us, grew outside of the cavernous sinus into the temporal fossa and retroclival area. We have re-treated it with fractionated stereotactic radiotherapy recently.

After closing this series for analysis, we have observed two patients in whom tumors grew in the temporal fossa adjacent to the cavernous sinus, from untreated infra-temporal extensions of the original cavernous sinus meningioma. The new tumors apparently reentered the cranium from the pterigoid fossa. The infratemporal extensions were present in retrospect at the time of radiosurgery (fig 3).

![Figure 3](https://example.com/figure3.png)

**Figure 3.** (A) This cavernous sinus meningioma was treated with radiosurgery in 2003. (B) In the same patient in 2008 with a slightly smaller tumor. An enhancing node is seen besides the cavernous sinus. (C) In the coronal images show that the enhancing node stems from a previously undetected infratemporal extension of the original cavernous sinus meningioma. In the image on the right it is clear that the new paracavernous tumor does not extend from the lateral cavernous wall. The image on the left shows that the node is continuous with the infratemporal tumor.

Tumor growth outside of the treatment volume is frequently mentioned as a reason for failure of radiosurgery in other series\textsuperscript{8}.

It is of note that tumor control rates have remained unchanged over time in spite of changes in quality of imaging, and radiosurgical dose.

Tumor delineation of our first 34 cases relied on stereotactic CT imaging alone. Since 1998, when MRI to CT fusion became available, tumors have been outlined on MRI (83 cases). It may be argued that MRI has substantially improved our ability to define tumor boundaries within the cavernous sinus only in the last 3-4 years, when high resolution T2 imaging and T1 fat-suppression became available in our center. The main contribution of MRI has been to enable the definition of surrounding anatomy, and particularly the hypophysis, the stalk, the optic apparatus, and the hippocampus, structures to which we try to reduce radiation exposure.

The optic apparatus receives obviously the highest consideration. Since radiation damage to this structure results in irreversible visual loss, radiation exposure of the optic pathways is the main factor potentially limiting the marginal dose to the tumor. The issue of how much irradiation may be safely applied in a single session to the optic nerves and chiasm is not fully settled.

The most widely cited paper dealing with dose limits for radiation induced optic neuropathy is the joint publication by the Harvard and Pittsburgh groups, from 1993\textsuperscript{25}. In that retrospec-
tive analysis, the authors reviewed a total of 62 patients treated for lesions around the cavernous sinus with both a gamma knife and a linear accelerator. They calculated the radiation exposure of the optic nerves and observed a 24% incidence of optic neuropathy in those cases wherein the radiation dose exceeded 8 Gy, as compared to 0% when the dose to the optic apparatus was below 8 Gy. That 8 Gy golden number has hold. However it is to note that all the assessments regarding optic nerve exposure in that paper were done based on CT imaging alone, and consequently were subject to gross errors due to poor visualization of the optic nerves. We have always regarded 10 Gy as our maximal exposure limit to the optic nerves and chiasm. With this limit respected, optic neuropathy has occurred in two cases of pituitary tumors in our series (unpublished data). If we considered the whole cohort of patients with lesions in and around the cavernous sinus, the incidence of optic neuropathy is below 1% (2 cases in 234 patients at risk). Higher doses to the optic nerves (12 Gy) have been given routinely by other groups with reportedly no ill effect10.

Over the years, in an attempt to improve the therapeutic index of radiosurgery, doses have been modified for most pathologies, meningiomas have not been an exception, and in this series we started out with marginal doses as high as 17.5 Gy. In the last 5 years 13 Gy has become our standard dose regardless of the tumor mass. This relatively low marginal dose enables treatment of rather large tumors in the area while preserving the 10 Gy limit to the optic nerves.

Our group was an early adopter of the micro-multileaf collimator (M3, BrainLab, Munich, Germany) as the standard radiation delivery tool (since 1998). The introduction of the M3 profoundly transformed the practice of LINAC radiosurgery. Treatment planning and radiation delivery have been greatly simplified (single isocenter). This is usually accomplished with high reliability in execution, and tight conformity of the treatment dose to the tumor margins.

This apparatus also allows a more homogenous radiation distribution across the target (since in almost every situation the marginal (treatment) dose is the 80-90% of the maximum). Before the introduction of the M3, LINAC radiosurgery for cavernous sinus meningiomas consistently required the use of multiple isocenters with cylindrical collimation to conform the dose distribution to the irregular shape of these tumors. For dosimetric reasons, multiple isocenter treatment demands that the dose to the tumor margin be prescribed to lower isodose shells (typically 50-60%). The lower the marginal dose, the more dose inhomogeneity is created within the tumor. In gamma knife routine, treatment to the 50% isodose line is the rule, with zones of the tumor absorbing twice the marginal dose. In most tumors it is really not relevant how much more radiation is absorbed within the target, since our intention is to eliminate it. In the cavernous sinus however, as the tumor encases normal (functional) tissue (neural and vascular structures) which we want to preserve, radiation definitely has a safety limit. Attesting this, carotid artery occlusion following radiosurgery for cavernous sinus lesions has been documented by gamma knife groups.

Figure 4: T2 CISS (Constructive Interference in Steady State) image of a cavernous sinus tumor, axial cuts, and reconstructed coronal (lower left) and sagittal (lower right) views. The superb anatomic definition obtained with this protocol enables recognition of all the important structures surrounding the cavernous sinus: the stalk and pituitary gland, the optic nerves and chiasm, the temporal lobe and hippocampus.

A report from the Mayo Clinic24 included 60 meningiomas involving the cavernous sinus. Two patients exhibited ischemic events 35 and 60 months after radiosurgery. One of them had a 50% internal carotid artery (ICA) stenosis, and the other had a complete occlusion of the intracavernous ICA. Both patients developed permanent cerebroischemic neurological deficits. Radiation doses were higher than in our series (median tumor marginal dose 16 Gy; median maximal tumor dose, 32 Gy). The authors noted that in both patients, the radiation dose to the carotid vessels exceeded 25 Gy. One case of carotid occlusion was observed by Regis and associates, in a series from 200021.

Because ICA stenosis or occlusion can stem from tumor invading the carotid wall, the causal relationship between radiosur-
gical irradiation and ICA occlusion remains unproven. Nevertheless, it should be noted that external carotid stenosis is not uncommon after high dose fractionated radiotherapy, and its clinical presentation may be delayed.

FUNCTIONAL RESULTS

Radiosurgery stands strong as the only treatment modality that consistently improves functional deficits produced by cavernous sinus meningiomas. As detailed above, cranial neuropathies improved in roughly a third of the patients. When radiosurgery was given early after the onset of the deficit (<1 year) and when surgery was not performed, close to 60% of the deficits improved or resolved. Improvement appeared early after treatment, in some cases in the first few weeks, which cannot be related to changes in the volume of the tumor. Similar functional outcomes have been reported recently by the University of Florida LINAC radiosurgery group.

CONCLUSIONS

This series of Linear Accelerator radiosurgery in more than 100 patients with cavernous sinus meningiomas is the largest in the literature to date. Our experience confirms that in the short and long term, radiosurgery affords excellent control for these difficult tumors, a very low incidence of complications, and a high rate of improvement in pre-treatment cranial nerve impairment.

Radiosurgery can thus be regarded as the treatment of choice for cavernous sinus meningiomas.

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