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The cavernous sinus meningiomas' dilemma: Surgery or stereotactic radiosurgery?

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ABSTRACT

Despite the advances in techniques and technologies, the management of cavernous sinus (CS) meningiomas still remains a challenge for both neurosurgeons and radiation oncologists.

On the other hand, the improvement of the anatomical knowledge and the microsurgical techniques together with diffusion of radiosurgery are currently changing the treatment strategy, opening new perspectives to the patients which are suffering from such lesions.

The authors reviewed here the literature data. A multidisciplinary treatment algorithm is also proposed.

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1. Introduction and historical remarks

The cavernous sinus (CS) region, due to its complex anatomy and its particular position in the antero-lateral skull base, has always been a challenge for neurosurgeons. The treatment of malignant diseases has presented over the past few decades a number of developments, particularly with the progress of the techniques of radiotherapy and radiosurgery. Even today however, it is still a controversial and debatable subject, and the best multimodal treatment is yet to be defined.

In 1965 Parkinson[1] was the first to realize an anatomical study and to propose a surgical approach to the CS. Despite the development of the microsurgical technique in the seventies, it was thought that microneurosurgery was reaching its furthest limits in the approach of lesions in and around the CS. The extremely high risk of damaging nervous structures, as well as causing uncontrollable haemorrhage or postoperative CSF leak seemed to be an unavoidable and insuperable obstacle. Thanks to the anatomical work of Dolenc and his surgical experiences, a rational surgical approach was eventually developed and the different relations between the lesion and the neurovascular structures were defined. In Dolenc's book preface, Yasargyl states that "there is no doubt that this type of microsurgical anatomical study is a new step in the 100 year history of neurosurgery".[2]

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Once this frontier was opened the experiences of other groups of skull base surgeons were added and we started to develop different approaches and new techniques to address these tumours.[3,4] More recently, new and less invasive endoscopic routes started to flourish. These approaches are less invasive and allow to address the tumour combining two complementary corridors, one antero-lateral and one transsphenoidal.

Still, a complete radical removal or the attempt of near total excision with anatomo-functional preservation is a very arduous exercise or even an illusion. The intimacy between tumour, nerves and vessels can be hardly overcome and represents the main unfavourable prognostic factor.

The role of both radiotherapy and radiosurgery to treat the recurrent tumours of the skull base is well known.[5]

However, it was with the gradual evolution of stereotactic radiosurgery that the method of dealing with the CS pathology has really changed. A multimodal treatment strategy combining surgery with radiotherapy, as well as radiotherapy alone in selected cases, have become the main practice to handle these tumours.

2. Anatomy

Cavernous sinus is constituted of paired venous structures located in the middle cranial fossa.[2,6]

These structures are surrounded by dural layers, which contain neurovascular structures, and face the sella turcica, the pituitary gland, the sphenoid bone on the medial side and the temporal lobe on the lateral side.

A cavernous sinus is roughly arranged in four walls, the lateral, medial, anterior and posterior walls, and a roof.

The lateral wall faces the temporal lobe. The medial wall is mainly arranged by the sella turcica and the pituitary gland together with the sphenoid bone. The posterior margin is limited by the posterior cranial fossa. Anteriorly the cavernous sinus reaches the superior optic fissure and the near inferior surface of the anterior clinoid process. The roof faces the basal cisterns, extending anteriorly from the anterior clinoid process to the posterior clinoid process posteriorly.

The dura completely surrounds the cavernous sinus. From the floor of the medial cranial fossa the dura curves rostrally along the lateral edge of the sella and then it turns laterally to shape the lateral wall of the cavernous sinus.

The lateral dural wall of the cavernous sinus is composed of two layers, the outer dural layer (dura propria) and the inner membranous layer. The inner layer of the lateral edge of the cavernous sinus contains the critical structures, it separates the lateral wall and its contents form the venous spaces. The outer layer faces the mesial temporal lobe.

The lateral wall meningiomas usually grow between the inner and the outer layer. In this sense these lesions are substantially extra cavernous tumours. This particular condition has to be considered in surgical planning and an accurate dissection of these layers has to be performed in order to obtain a total removal of these tumours.

The cavernous sinus contains vascular and nervous structures.

The vascular structures include the cavernous segment of the internal carotid artery (ICA) and multiple venous tributaries (superior and inferior petrosal sinuses, the basilar sinus, the intercavernous sinus) as well as various draining veins of the skull base, sylvian fissure, and middle cerebral vein.

The nervous structures include the sympathetic plexus, the oculomotor nerves (III, IV, VI) and the first and second branch of the trigeminal nerve (V1, V2). According to a craniocaudal direction, the cranial nerves III and IV as like as V1 and V2 travel inside the lateral wall of the cavernous sinus. The cranial nerve VI occupies a more medial position, behind and lateral the ICA.

According to their anatomy it is possible to identify meningiomas which arise from cavernous sinus dura itself (the strictly speaking cavernous sinus meningiomas) and meningiomas arising from the dura of the sphenoid ridge, clinoid processes and petroclival region extending to or infiltrating the cavernous sinus.

3. General considerations

In CS tumours management histological type, biological behaviour, location, extent of dural attachment and particularly relationship and encasement of neurovascular structures have to be considered. Biological behaviour can be schematically categorized into three groups: benign, intermediate malignancy and high malignancy. This subdivision is probably too simplistic, but it may facilitate decision making and the most appropriate treatment strategy. Among the most common benign oncotype, we find meningiomas, pituitary adenomas and schwannomas. These tumours may invade and encase nearby structures. Tumours of intermediate malignancy include chordomas, chondrosarcomas, adenoid cystic carcinomas and low grade esthesioneuroblastomas. Highly malignant tumours include cranial base carcinomas, sarcomas, high grade esthesioneuroblastomas and lymphomas.[7]

Meningiomas represent 41% of all CS tumours. They can either start in areas outside the CS and subsequently invade it, or start into CS and then spread to the surrounding structures. The CS is frequently invaded by tumours (meningiomas) of the orbital apex, sella, medial sphenoid wing, middle fossa, Meckel's cave, petrous apex and tentorium. This behaviour is mostly to be found in en plaque meningiomas. On the other hand, meningiomas arising within the CS can extend and involve the same above mentioned areas, infiltrating extra or subdural spaces and bone.

Sekhar in order to assess the surgical technical difficulties and risks, and to compare different patients' series, created a classification based on the CS areas involved by the tumour, on its volume and on carotid artery involvement.[3,8] According to this point, the most important variable influencing risks and patients outcome in the management of such lesions is the grade of involvement-encasement of nerves and vessels.

The natural history of meningiomas is still partially unknown. Although the growth rate is estimated to be between 2 and 24 mm per year, some authors found that about 23% of the meningiomas (particularly the calcified ones) did not grow.[9]

4. Surgical management

The modern approach to CS meningiomas arises in particular from the anatomical studies and surgical experiences of Dolenc.[10]

According to his experience the drilling of the temporal floor up to the carotid canal, together with the partial removal of the orbital roof with opening of optic canal and with the clinoidectomy provide an optimal approach to the sellar and cavernous region, almost without brain retraction. In addition, clinoidectomy and unroofing of optic canal allow a good and early control of the carotid artery and of the optic nerve.

Variations to this approach have been proposed and mainly consist in removing the orbito-zygomatic arch and extending in different directions the skull base drilling.[3,4,11–15]

In 1997 Dolenc[16] published a very large surgical series of 1050 patients operated because of tumours or vascular lesions of the CS. He described very encouraging results: 7 patients died, 9 lost vision in ipsilateral eye, 25 had a visual deterioration, 15 transient emiparesis (3 persistent), 6 needed a reoperation for CSF leak, 820 had a partial transient oculomotor paresis. Overall 770 patients regained the preoperative clinical function.

This study represented a milestone in the CS surgery. Mainly basing on this positive experience new and amazing improvements in the microsurgical technique have been made. Unfortunately the results in terms of complete tumour removal, post-operative cranial nerves deficit and patient quality of life not always corresponded to the expectations. In addition, the rate of recurrences was not negligible.

Mainly basing on the critical review of the results, the combined surgical, radiosurgical approach is nowadays widely accepted. Indeed, by combining less aggressive surgical approach with adjuvant radiosurgery, this strategy may limit the patients risk while maintaining the tumour control.[17–19]

This new philosophy opened the way to endoscopic approaches: through a transnasal route it is possible to safely perform a partial debulking, to decompress the optic canal or to do a biopsy in cases where no clear diagnosis can be established.[20–24]

Furthermore, in case of small asymptomatic meningiomas, considering the very slow (or even absent) growth rate of these tumours, a “wait and scan” approach appears to be a safe and more than reasonable strategy.[25]

Despite the real benefit of an aggressive intracavernous surgery is actually debated, some selected circumstances may still require more aggressive approach. This is the case of there are some rare eveniences (mainly recurrences resistant to all treatment attempts) in which a very aggressive surgery of complete CS resection with carotid revascularization can be seen as a “salvage therapy”.[26]

5. Radiotherapy

The intrinsic limit of microsurgery in the treatment of CS meningiomas was overcome with the advent of radiosurgery in Leksell era. The use of gammaknife and, in the most recent period, of dedicated linac and Cyberknife systems gave the possibility to obtain excellent results in terms of local control and reduction of possible injuries. From a radiobiological point of view meningiomas are classically considered as late responding tissue and can be better controlled with a higher dose/fraction rather than conventional fractionation. Radiation injury to the cranial nerves is probably secondary to damage of small vessels and protective Schwann cells.[27]

Major radiosurgery (RS) series report progression-free survival rates at 5 and 10 years of 80–100% and 73–98% respectively and a radiographic response in a rate of 29–69% (Table 1).[28–46]

This technique has obtained a large consensus in the medical community of neurosurgeons but the validation of these results is limited by the paucity of randomized and controlled studies.[19] The other limit is related to a technical point: the application of the RS is reserved only to lesions of small volume (range 7–15 cc). Given the proximity of CS meningiomas to radiosensitive structures, the choice of RS is usually based on a balance between the risk of delayed toxicity and delayed loss of control over the growth of the meningioma.

The peripheral dose of 12–14 Gy is accepted in most cases for CS meniongiomas radiosurgery.[28–46] The total dose is a little bit lower than the total dose in other sites’ meningiomas (tentorium, falx) but it is considered safe in terms of local neurotoxicity. The proximity of the tumour to optic pathways can determine the reduction of the dose to 12 Gy in order to keep the dose to organs at risk lower than 10 Gy. In the situation of a parasellar meningioma, the distance between nerve and tumour must be carefully considered. The risk of visual impairment is related to the volume of the optic apparatus receiving high doses. A distance of 5 mm between the meningioma and the optic nerve is considered safe in single shot RS.[39,45]

In RS technique the target volume (TV) is the contrast enhanced lesion without margin. MR and TC images are usually acquired and fusions images used to obtain a better definition in drawing both the volume that has to be irradiated and the organs at risk (OARs) to be spared. The necessity to include the dural tail in the TV is in debate among the physicians:[47–49] It is true that the 75% of the recurrences involve the dura outside the treatment field[31] but it is difficult to correctly define its extension and in fact the evaluation of the infiltration is totally related to the skill of the specialists involved in the contouring phase of the treatment. Importance has to be given to the verification in future trials of the importance of this issue in local control and efficacy of radiosurgery. In case that the decision to insert the dural tail in target definition is adopted, care has to be observed in dose distribution when an irregular shape of TV is dominant.

RS can be used alone or in combination with previous surgery. In the series where RS is used as first line treatment a rate of 3–15% of new or preexisting cranial nerve deficits is reported. A meta-analysis of more than 2000 CS meningiomas retrospectively evaluated and treated with either RS or surgery followed by radiotherapy or RS showed a significantly higher rate of neurological morbidity in patients undergoing surgery and RS as compared with those undergoing RS alone (59.6% vs 25.7%).[50] This fact could be explained by the negative impact of resection on micro-vascular support therefore contributing to reinforce the effects of radiosurgery and consequently,

Table 1 – Radiosurgery series.

Year	First author	Patients (*n*)	Mean f/u (mo)	Prior surgery	SRS alone	PFS 5 years	PFS 10 years	New CN deficits	GK/Linac
1999	Morita	88	35	49	39	95%	–	10.2%	GK
1999	Liscak	67	19	24	43	–	–	3.8%	GK
2000	Roche	80	30.5	30	50	92.8%	–	5.8%	GK
2001	Shin	40	42	28	12	–	82.3%	20%	GK
2002	Spiegelmann	42	36	9	31	97.5%	–	7.5%	Linac
2002	Nicolato	156	48.9	81	75	96.5%	–	1%	GK
2002	Lee	159	35	76	83	93.1%	93.1%	9%	GK
2003	Iwai	42	49.4	22	20	92%	–	4.8%	GK
2004	Maruyama	40	46	23	17	94.1%	–	25%	GK
2004	Kuo	57	42	–	–	97%	–	2.2%	GK
2005	Metellus	36	63.6	13	23	94.4%	–	0%	GK
2005	Pollock	49	58	0	49	80–85%	–	10%	GK
2007	Hasegawa	115	62	66	49	87%	73.0%	12%	GK
2009	Kimball	49	50	12	38	100%	98%	3.5%	Linac
2009	Colombo	199	30	–	99 mSRS	92%	–	3.5%	Linac
2010	Spiegelmann	102	67	33	69	98%	–	4%	Linac
2011	dos Santos	88	86.8	41	47	92.5%	82.5%	12.5%	Linac
2013	Pollock	115	89	46	69	99%	93%	12%	GK
2014	Correa	89	73	26	32	98%	92%	7%	Linac

Abbreviations: CN = cranial nerves; f/u = follow-up; GK = gamma knife; mSRS = multisession radiosurgery; PFS = progression-free survival; SRS = stereotactic radiosurgery.

leading to the neurological deterioration of preexisting symptoms or to the onset of new ones. In the majority of RS series a rate of 15% of new or preexisting cranial nerve deficits is reported; this element could be a support to identify RS as first line treatment in the algorithm for the management of CS meningiomas patients.[36,51]

Another very tough challenge is the therapeutic algorithm of large meningiomas. Single fraction radiosurgery cannot be used because of the high risk of healthy tissue damage and because of a possible reduction of the local control due to the low marginal doses usually used. A complication rate of 21% was observed in patients with large CS meningiomas compared to a 3% in patients with small lesions (volume less than 10 cm^3),[44] on the other hand the local control in these series is near 85% at 5 years.[40,52]

Surgical debulking followed by RS can be an option but only in skilled neurosurgical departments.

Advanced radiotherapy techniques with standard fractionation schedules (56 Gy/28 fractions) can be a good option. At the beginning of 2000 the development of sophisticated devices (MicroMultileafCollimator, pencil beam algorithm, relocatable frame) gave the opportunity to implement better treatment plans. The result in terms of efficacy and tolerance was interesting: the reported local control reached 82–95% at 5 years and a radiological response rate of 29–31% was observed, even if this value is lower respect to the 50% noticed when RS is used.[27,38,53–55]

With the advent of Cyberknife the use of multisession radiosurgery (mRS) in meningiomas has been evaluated.[42,56] Dose selection was based on previous experience with radiosurgery and stereotactic radiotherapy,[57,58] but also on previous studies concerning the dose tolerance of the cranial nerves.[27,28,50,54] Radiobiological data indicate that a hypofractionated schedule should offer benefit in anatomical regions such as the cavernous sinus where the meningioma involves cranial nerves.[59] When a 25 Gy in 5 fractions scheme is adopted, the total dose is theoretically comparable to the doses delivered with conventional fractionated regimens (50.4–56 Gy). In small published studies[42,60] pre-treatment peritumoral oedema and a location adjacent to a large vein were significant risk factors for radiographic post-treatment oedema. Anyway, no major complications have been observed and improvement of pre-existing deficit is noted in 50% of the patients. Our preliminary experience in mRS is in agreement with most of the RS series. The indication for multisession radiosurgery was given by the proximity to optic nerve and chiasma or the dimension of the lesion (>3 cm). The local control rate at 5 years was of 95%. Only 3.5% of patients experienced a deterioration of preexisting symptoms (personal data). The local control is similar to RS series, the critical issues remain the short follow-up and the limited series considered.

Last but not least also proton has been advocated as advanced technique to obtain reduced complication in this specific site. In a recent study by Loma Linda University high overall 5 years local control rate (96%) was observed using 57EGy without major toxicity.[61]

6. Conclusions: evolution of a modern treatment

The comprehension of the CS meningiomas' natural history as well as the knowledge of the treatments results underline the need for a more modern treatment approach.

As we already stressed, a radical removal of the tumour inside the CS is often hard if not impossible and a subtotal removal is associated with a inevitably high recurrence rate.

On the other hand the therapeutic goal should be achieving tumour control while minimizing any treatment related morbidity.[25,51]

Tentatively, in order to respect this assumption we propose the following treatment algorithm.

Small and asymptomatic intracavernous meningiomas can be observed, evolving into good candidates to radiosurgery in case of progression.

Larger meningiomas with the involvement of the lateral wall of the CS may have a safe and radical microsurgical resection.

The large extra-intracavernous meningiomas, could be managed with a combined approach. The extracavernous part can be safely removed while the remnants can be treated by RS. Multisession RS could be also take in consideration as the exclusive treatment.

The role of pre-operative radiosurgery aiming to de-vascularize the tumour and to allow an easier dissection from the CS walls and trigeminal branches is still under debating.[62]

Finally, the giant spheno-petro-cavernous meningiomas represent a lesion likely beyond the possibility of a real treatment. Performing selective, partial resection in order to decompress targeted structures, carefully balancing risks and benefits, seems to be the most appropriate solution if combined with the radiosurgical treatment of the remnants.

All these considerations underline the importance of a real multidisciplinary cooperation.

Conflict of interest

None declared.

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Ethical issues

The manuscript does not contain clinical studies or patient data.

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REFERENCES

1. Parkinson D. A surgical approach to the cavernous portion of the carotid artery. Anatomical studies and case report. *J Neurosurg* 1965;**23**:474–83.
2. Dolenc VV, Yasargil M. *Anatomy and surgery of the cavernous sinus*. Wien: Springer-Verlag; 1989.
3. Sekhar LN, Janecka IP. *Surgery of cranial base tumors*. New York: Raven Press; 1993.
4. Al-Mefty O. *Meningiomas*. New York: Raven Press; 1991.
5. Krengli M, Apicella G, Deantonio L, Paolini M, Masini L. Stereotactic radiation therapy for skull base recurrences: is still possible a salvage approach? *Rep Pract Oncol Radiother* 2014 (in Press), Available online 4 November 2014.
6. Yasuda A, Campero A, Martins C, Rhoton Jr AL, de Oliveira E, Ribas GC. Microsurgical anatomy and approaches to the cavernous sinus. *Neurosurgery* 2008;**62**(6 Suppl. 3): 1240–63.
7. Bernstein M, Berger MS. *Neuro-oncology the essentials*. New York: Thieme; 2000.
8. Saberi H, Meybodi AT, Rezai AS. Levine-Sekhar grading system for prediction of extent of resection of cranial base meningiomas revisited: study of 124 cases. *Neurosurg Rev* 2006;**29**:138–44.
9. Oya S, Kim SH, Sade B, Lee JH. The natural history of intracranial meningiomas. Clinical article. *J Neurosurg* 2011;**114**:1250–6.
10. Dolenc VV. Surgery of tumors originating in or invading cavernous sinus. In: Long DM, editor. *Surgery of skull base tumors*, vol. 12. Boston: Blackwell Scientific; 1992. p. 211–21.
11. Lemole Jr GM, Henn JS, Zabramski JM, Spetzler RF. Modifications to the orbitozygomatic approach. Technical note. *J Neurosurg* 2003;**99**:924–30.
12. Zabramski JM, Kiriş T, Sankhla SK, Cabiol J, Spetzler RF. Orbitozygomatic craniotomy. Technical note. *J Neurosurg* 1998;**89**:336–41.
13. Rangel-Castilla L, Russin JJ, Spetzler RF. Surgical management of skull base tumors. *Rep Pract Oncol Radiother* 2014 (in Press), Available online 14 October 2014.
14. Diaz Day J, Feng DX, Fukushima T. Tumors involving the cavernous sinus. In: Quinones-Hinojosa A, editor. *Schmidek and sweet's operative neurosurgical techniques: indications, methods, and results*. 6th ed. Philadelphia: Elsevier; 2012. p. 451–67.
15. Couldwell WT, Weiss MH, Rabb C, Liu JK, Apfelbaum RI, Fukushima T. Variations on the standard trans-sphenoidal approach to the sellar region, with emphasis on the extended approaches and parasellar approaches: surgical experience in 105 cases. *Neurosurgery* 2004;**55**: 539–47.
16. Dolenc VV. Approaches and techniques of surgery within the cavernous sinus. In: Torrens M, Al-Mefty O, Kobayashi S, editors. *Operative skull base surgery*. New York: Churchill Livingstone; 1997. p. 207–37.
17. Abdel-Aziz KM, Froelich SC, Dagnew E, et al. Large sphenoid wing meningiomas involving the cavernous sinus: conservative surgical strategies for better functional outcomes. *Neurosurgery* 2004;**54**:1375–84.
18. Dufour H, Muracciole X, Métellus P, Régis J, Chinot O, Grisoli F. Long-term tumor control and functional outcome in patients with cavernous sinus meningiomas treated by radio therapy with or without previous surgery: is there an alternative to aggressive tumor removal? *Neurosurgery* 2001;**48**: 285–96.
19. Pechlivanis I, Wawrzyniak S, Engelhardt M, Schmieder K. Evidence level in the treatment of meningioma with focus on the comparison between surgery versus radiotherapy. A review. *J Neurosurg Sci* 2011;**55**:319–28.
20. Beer-Furlan A, Evins A, Rigante L, Anichini G, Stieg PE, Bernardo A. Dual-Port2D and 3D endoscopy: expanding the limits of the endonasal approaches to midline skull base lesions with lateral extension. *J Neurol Surg B: Skull Base* 2014;**75**:187–97.
21. Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A, De Divitiis E. Extended endonasal approach to the midline skull base: the evolving role of trans-sphenoidal surgery. *Adv Tech Stand Neurosurg* 2008;**33**:151–99.
22. Juanneau E, Simn E, Jacquesson T, et al. The endoscopic endonasal approach to the Meckel's cave tumors: surgical technique and indications. *World Neurosurg* 2014;**82**(6 Suppl.): S155–61.

23. Qiuhang Z, Hongchuan G, Feng K, et al. Resection of intracavernous sinus tumor using a purely endoscopic endonasal approach. *J Craniofacial Surg* 2014;**25**: 295–302.
24. Yano S, Hide T, Shinojima N, Hasegawa Y, Kawato T, Kuratsu J. Endoscopic endonasal skull base approach for parasellar lesions: initial experiences, results, efficacy, complications. *Surg Neurol Int* 2014;**16**:51.
25. Klinger DR, Flores BC, Lewis JJ, Barnett SL. The treatment of cavernous sinus meningiomas: evolution of a modern approach. *Neurosurg Focus* 2013;**35**:E8.
26. Couldwell VT, Macdonald ID, Taussky P. Complete resection of the cavernous sinus-Indications and technique. *World Neurosurg* 2014;**82**(6):1264–70.
27. Shrieve DC, Hazard L, Boucher K, Jensen RL. Dose fractionation in stereotactic radiotherapy for parasellar meningiomas: radiobiological considerations of efficacy and optic nerve tolerance. *J Neurosurg* 2004;**101**(Suppl. 3): 390–5.
28. Morita A, Coffey R, Foote R, Schiff D, Gorman D. Risk of injury to cranial nerves after gamma knife radiosurgery for skull base meningiomas: experience in 88 patients. *J Neurosurg* 1999;**90**:42–9.
29. Liscák R, Simonová G, Vymazal JJL, Janousková L, Vladyka V. Gamma knife radiosurgery of meningiomas in the cavernous sinus region. *Acta Neurochir* 1999;**141**:473–80.
30. Roche P, Régis J, Dufour H, et al. Gamma knife radiosurgery in the management of cavernous sinus meningiomas. *J Neurosurg* 2000;**93**(Suppl. 3):68–73.
31. Shin M, Kurita H, Sasaki T, et al. Analysis of treatment outcome after stereotactic radiosurgery for cavernous sinus meningiomas. *J Neurosurg* 2001;**95**:435–9.
32. Spiegelmann R, Nissim O, Menhel J, Alezra D, Pfeffer MR. Linear accelerator radiosurgery for meningiomas in and around the cavernous sinus. *Neurosurgery* 2002;**51**(6): 1373–80.
33. Nicolato A, Foroni R, Alessandrini F, Bricolo A, Gerosa M. Radiosurgical treatment of cavernous sinus meningiomas: experience with 122 treated patients. *Neurosurgery* 2002;**51**:1153–61.
34. Lee JYK, Niranjan A, McInerney J, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery providing long-term tumor control of cavernous sinus meningiomas. *J Neurosurgery* 2002;**97**:65–72.
35. Iwai Y, Yamanaka K, Ishiguro T. Gamma knife radiosurgery for the treatment of cavernous sinus meningiomas. *Neurosurgery* 2003;**52**:517–24.
36. Maruyama K, Shin M, Kurita H, Kawahara N, Morita A, Kirino T. Proposed treatment strategy for cavernous sinus meningiomas: a prospective study. *Neurosurgery* 2004;**55**:1068–75.
37. Kuo JS, Chen JC, Yu C, et al. Gamma knife radiosurgery for benign cavernous sinus tumors: quantitative analysis of treatment outcomes. *Neurosurgery* 2004;**54**:1385–94.
38. Metellus P, Regis J, Muracciole X, et al. Evaluation of fractionated radiotherapy and gamma knife radiosurgery in cavernous sinus meningiomas: treatment strategy. *Neurosurgery* 2005;**57**:873–86.
39. Pollock BE, Stafford SL. Results of stereotactic radiosurgery for patients with imaging defined cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys* 2005;**62**: 1427–31.
40. Hasegawa T, Kida Y, Yashimoto M, Koike J, Iizuka H, Ishii D. Long-term outcomes of gamma knife surgery for cavernous sinus meningioma. *J Neurosurg* 2007;**107**:745–51.
41. Kimball MM, Friedman WA, Foote KD, Bova FJ, Chi YY. Linear accelerator radiosurgery for cavernous sinus meningiomas. *Stereotact Funct Neurosurg* 2009;**87**:120–7.
42. Colombo F, Casentini L, Cavedon C, Scalchi P, Cora S, Francescon P. Cyberknife radiosurgery for benign meningiomas: short-term results in 199 patients. *Neurosurgery* 2009;**64**(2 Suppl.):A7–13.
43. Spiegelmann R, Cohen ZR, Nissim O, Alezra D, Pfeffer R. Cavernous sinus meningiomas: a large LINAC radiosurgery series. *J Neurooncol* 2010;**98**:195–202.
44. dos Santos MA, de Salcedo JB, Gutiérrez Diaz JA, et al. Long-term outcomes of stereotactic radiosurgery for treatment of cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys* 2011;**81**:1436–41.
45. Pollock BE, Stafford SL, Link MJ, Garces YI, Foote RL. Single-fraction radiosurgery of benign cavernous sinus meningiomas. Clinical article. *J Neurosurg* 2013;**119**: 675–82.
46. Correa SF, Marta GN, Teixeira MJ. Neurosymptomatic carvenous sinus meningioma: a 15-years experience with fractionated stereotactic radiotherapy and radiosurgery. *Radiat Oncol* 2014;**9**:27.
47. Rowe JG, Walton L, Vaughan P, Malik I, Radatz M, Kemeny A. Radiosurgical planning of meningiomas: compromises with conformity. *Stereotact Funct Neurosurg* 2004;**82**:169–74.
48. DiBiase SJ, Kwok Y, Yovino S, et al. Factors predicting local tumor control after gamma knife stereotactic radio surgery for benign intracranial meningiomas. *Int J Radiat Oncol Biol Phys* 2004;**60**:1515–9.
49. Rogers L, Jensen R, Perry A. Chasing your dural tail: factors predicting local tumor control after gamma knife stereotactic radiosurgery for benign intracranial meningiomas: in regard to DiBiase et al. (Int J Radiat Oncol Biol Phys 2004;60:1515–1519). *Int J Radiat Oncol Biol Phys* 2005;**62**:616–8.
50. Sughrue ME, Rutkowski MJ, Aranda D, Barani IJ, McDermott MW, Parsa AT. Factors affecting outcome following treatment of patients with cavernous sinus meningiomas. Clinical article. *J Neurosurg* 2010;**113**:1087–92.
51. Pichierri A, Santoro A, Raco A, Paolini S, Cantore G, Delfini R. Cavernous sinus meningiomas: retrospective analysis and proposal of a treatment algorithm. *Neurosurgery* 2009;**64**:1090–101.
52. Skeie BS, Enger PO, Skeie GO, Thorsen F, Pedersen PH. Gamma knife surgery of meningiomas involving the cavernous sinus: long-term follow-up of 100 patients. *Neurosurgery* 2010;**66**:661–8.
53. Milker-Zabel S, Zabel-du Bois A, Huber P, Schlegel W, Debus J. Fractionated stereotactic radiation therapy in the management of benign cavernous sinus meningiomas: long-term experience and review of the literature. *Strahlenther Onkol* 2006;**182**:635–40.
54. Brell M, Villà S, Teixidor P, et al. Fractionated stereotactic radiotherapy in the treatment of exclusive cavernous sinus meningioma: functional outcome, local control, and tolerance. *Surg Neurol* 2006;**65**:28–34.
55. Litré CF, Colin P, Noudel R, et al. Fractionated stereotactic radiotherapy treatment of cavernous sinus meningiomas: a study of 100 cases. *Int J Radiat Oncol Biol Phys* 2009;**4**:1012–7.
56. Marchetti M, Bianchi S, Milanesi I, et al. Multisession radiosurgery for optic nerve sheath meningiomas – an effective option: preliminary results of a single-center experience. *Neurosurgery* 2011;**69**(5):1116–22.
57. Ganz JC, Reda WA, Abdelkarim K. Gamma-knife surgery of large meningiomas: early response to treatment. *Acta Neurochir* 2009;**151**:1–8.
58. Iwai Y, Yamanaka K, Nakajima H. Two-staged gamma knife radiosurgery for the treatment of large petroclival and cavernous sinus meningiomas. *Surg Neurol* 2001;**56**: 308–14.
59. Vernimmen FJ, Slabbert JP. Assessment of the alpha/beta ratios for arteriovenous malformations, meningiomas,

acoustic neuromas, and the optic chiasma. *Int J Radiat Biol* 2010;**86**(6):486–98.
60. Morimoto M, Yoshioka Y, Shiomi H, et al. Significance of tumor volume related to peritumoral edema in intracranial meningioma treated with extreme hypofractionated stereotactic radiation therapy in three to five fractions. *Jpn J Clin Oncol* 2011;**41**:609–16.
61. Slater JD, Loredo LN, Chung A, et al. Fractionated proton radiotherapy for benign cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys* 2012;**83**:e633–7.
62. Kano H, Park KJ, Kondziolca D, et al. Does prior microsurgery improve or worsen the outcome of stereotactic radiosurgery for cavernous sinus meningiomas? *Neurosurgery* 2013;**73**:401–10.