Current status of radiation therapy and radiosurgery in the treatment of intracranial meningiomas

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Complete surgical removal, including resection of involved bone and dura, is curative of intracranial meningiomas in approximately 90% of cases. However, complete removal may entail unwarranted risk if the tumor involves or is adjacent to critical vascular or neural structures. In addition, it is possible for fragments of tumor to "evade" resection, even with the use of meticulous microsurgical technique. Because of this, clinicians may be faced with the decision of whether to offer or recommend radiation therapy or radiosurgery to a patient with a residual or recurrent meningioma. For many years, it has been recommended that external-beam radiation therapy be considered in the treatment of incompletely resected or malignant meningiomas. More recently, the role of radiosurgery as adjuvant or even primary therapy for meningiomas has attracted considerable attention. This article presents a review of the literature on postoperative radiotherapy of intracranial meningiomas.

Key Words * brain tumor * meningioma * radiation therapy * radiosurgery

The definitive treatment for an intracranial meningioma continues to be complete surgical resection, including removal of the involved dura and bone.[13,14,35] However, complete resection may not always be advisable if it entails an unacceptable degree of risk to the patient. Because of this, there are situations in which an incomplete resection of a meningioma may occur, or indeed, is even anticipated. In general, the more complete the resection of a meningioma, the less the chance for its recurrence.[14] After macroscopically complete removal of a meningioma with excision of the dural attachment and abnormal bone, the recurrence rate still is approximately 10%.[13,14] Macroscopically complete removal and simple coagulation of the dural attachment results in a recurrence rate of approximately 20%.[14,45] Recurrence rates of up to 74% have been reported after subtotal excision.[5,50] Sphenoid wing and parasagittal meningiomas recur most frequently because of their location and sinus attachments, which make them difficult to remove (Table 1). The cavernous sinus, peritrochlear, and tentorial locations are also very difficult to treat successfully with surgery alone, but meningiomas occur less frequently in these locations. En plaque meningiomas and those involving bone also have higher recurrence rates. Recurrence is also higher in meningiomas with a papillary, hemangioblastic, or hemangiopericytic pathological appearance.[14]

TABLE 1 MENINGIOMAS: RECURRENCE ACCORDING TO LOCATION AND EXTENT OF RESECTION*				
Location	Total Tumors	Extent of Resection		Recurrence Rate (%)
		Radical Subtotal	Subtotal	
parasagittal	39	4	0	7
falx	12	1	1	0
cerebral convexity	65	1	0	1.5
olfactory groove	18	1	0	0
tuberculum sellae	10	8	3	14
sphenoid wing				
hyperostosing	0	0	16	25
middle	7	0	0	0
medial	0	3	14	17.6
optic sheath	10	5	0	0
middle fossa	7	3	2	0
cavernous sinus	0	1	5	50
intraventricular	5	0	0	0
* Modified from Cjemann [36] and reproduced with permission.				

Treatment options for patients with incompletely resected meningiomas include: 1) follow up with serial neurological examinations and magnetic resonance (MR) imaging; 2) radiation with standard external-beam therapy; 3) treatment with radiosurgery; or 4) additional surgery. Which choice is most appropriate depends on the patient. Treatment options are similar when a meningioma that was thought to be completely resected recurs. Since the 1970s, the linear accelerator (LINAC) has been the principal external-beam radiation machine, delivering photons (x-rays) or electrons at various energies.[34] Brachytherapy and charged-particle therapy may also be used in the treatment of residual or recurrent meningiomas,[1,16,22,32] but are not discussed in this article.

POSTOPERATIVE EXTERNAL-BEAM RADIATION THERAPY

For many years, it has been recommended that external-beam radiation therapy be considered as a treatment for incompletely resected, recurrent, and/or malignant meningiomas (Fig. 1).[5,9,44,50] This view opposed an earlier belief that there was minimal benefit to radiation therapy and that meningiomas were relatively radioresistant.[17] In 1987 an article was published by Barbaro, et al.,[3] reporting the results of a retrospective analysis of 84 patients with meningiomas, treated at the University of California, San Francisco. Thirty of 84 patients underwent subtotal resection of a meningioma and did not receive postoperative radiation therapy, whereas 54 patients underwent subtotal resection followed by radiation therapy. The median time to tumor recurrence was found to be significantly longer in the group that received radiation than in the group that did not: 125 months versus 66 months. The patients received a mean total dose of approximately 5000 rad; none was reported to have suffered deleterious effects from the radiation during an average follow-up period of 78 months. The authors concluded that "radiation therapy is beneficial in the treatment of partially-resected meningiomas".[3] Similar conclusions were reached in a smaller study of incompletely resected tumors reported by Taylor, et al.[47]

Fig. 1. Magnetic resonance imaging demonstrating a recurrent medial sphenoid wing meningioma. This patient was treated with standard external-beam radiation therapy.

Despite these reports, the use of radiation therapy in the treatment of residual or recurrent meningiomas has continued to be somewhat controversial.[13,14,39] The hazards of radiation therapy are generally divided into the acute "early delayed" and "late delayed" reactions.[4] Acute reactions have been rare unless very large doses of radiation have been given.[21] Early delayed reactions usually appear a few weeks to months after radiation treatment and are characterized by the sudden onset of neurological symptoms such as somnolence, nausea, vomiting, ataxia, and nystagmus.[4] Corticosteroid administration may help relieve the symptoms, which usually, but not always, resolve within a few weeks.[4] Late delayed reactions (radionecrosis) are the major hazard of central nervous system radiation, usually presenting 4 months to many years after therapy as a space-occupying lesion that may even be fatal.[4,34] Optic neuropathy after radiation therapy for meningioma has also been reported.[12] Other risks include pituitary dysfunction and the development of secondary neoplasms.[25,51] Sekhar, et al.,[43] have been concerned that definitive microsurgical removal of a progressing meningioma might be more difficult after radiation therapy.

In 1994, Goldsmith, et al.,[13] reported further on the experience from the University of California, San Francisco, with respect to the results of postoperative irradiation for subtotally resected meningiomas. By this time, 140 patients had been treated during the period from 1967 to 1990. For patients with a subtotally resected benign meningioma, the 5-year progression-free survival rate with radiation was 89%, which compares very favorably with the 43 to 59% rate without radiation.[13] These data showed further improvement for patients treated after 1980, probably because of better treatment planning. Of these patients, 3.6% experienced morbidity associated with the radiation treatment. Maire, et al.,[30] also recently reported on the efficacy of radiation therapy for incompletely resected, recurrent, totally resected but aggressive (such as angioblastic or anaplastic), and inoperable meningiomas. In 91 patients, six late delayed reactions were encountered; the median follow-up time was 48 months. Interestingly, 43 of 60 symptomatic patients were thought to have improved neurologically as early as 15 to 20 days after beginning therapy.[30] Residual meningiomas may be more susceptible to radiation therapy than recurrent ones.[5,13,25]

Reports have been published recommending radiation therapy for meningiomas in particular locations,

notably the cavernous sinus and torcular herophili.[15,49] Peritorcular meningiomas are usually subtotally resected because interruption of the venous sinus flow and/or attempts at torcular reconstruction are particularly hazardous. It has been recommended that residual tumor in the torcular area be irradiated using external-beam therapy if the remaining tumor volume is greater than 10 cm³. [15] Similarly, external-beam radiation should be considered in diffuse residual tentorial and large residual skull base meningiomas.[41,42] The histological subtype of most benign meningiomas has not been found to relate to the success of radiation therapy in preventing recurrence, although there has been some indication that very vascular tumors may respond more favorably.[39]

Conventional external-beam radiotherapy is generally administered once daily, 5 days per week, over a 5- to 6-week period to deliver a total dose of 50 to 55 Gy in 1.7 to 2 Gy fractions.[30,39] The patient with a meningioma is treated through fields that cover the known area of disease plus a 1 to 2 cm margin.[39] Chamberlain[6] has recently reported the use of a 3 cm margin (and chemotherapy) for the treatment of malignant meningiomas. For tumors other than meningiomas, accelerated fractionation, in which two or three fractions per day are given, or hyperfractionation, in which a larger number of smaller-sized fractions are given, have been studied.[23] No reports of these types of studies for conventional beam irradiation for meningioma patients were found. Tumor control rates for meningiomas treated with conventional external-beam fractionated radiation therapy have been reported to range from 50 to 90%. [5, 9,13, 25,47]

RADIOSURGICAL TREATMENT

The role of radiosurgery in the management of meningiomas has attracted considerable attention over the past 7 to 8 years.[8,19,20,26] The term "radiosurgery" was coined by the late Lars Leksell as early as 1951.[24,33] The term describes a procedure in which ionizing radiation is used to destroy a circumscribed volume of tissue in a single session.[2,24] Reports on "fractionated stereotactic radiotherapy," which is distinct from radiosurgery, have also been published, including its use in the treatment of meningiomas.[10] The first meningioma was treated by gamma knife radiosurgery in 1975.[24] Meningiomas can be accurately imaged with current modalities, and possess a discrete nature. These features make them particularly suitable for radiosurgical treatment.[25] Studies of radiosurgical treatment for incompletely resected, recurrent, aggressive, and/or inoperable meningiomas have been reported for both the gamma knife and LINAC-based units. The rationale for using radiosurgery instead of external-beam radiation is that it is more accurate and should therefore minimize the risks involved with irradiating brain adjacent to tumor.[24,25] Stereotactic radiosurgery may also play a role in patients who are considered unsuitable for craniotomy because of their age or medical condition.[2,20,33] The complications of dementia and the induction of secondary neoplasia have not been reported with use of the gamma knife.[24] The single-session treatment is also very convenient for the patient.[24]

Patients with meningiomas who are chosen for radiosurgery usually harbor tumors less than 3.5 cm in average diameter located at least 5 mm from the optic chiasm or nerve, presenting as well-demarcated tumors on contrast-enhanced computerized tomography or MR imaging.[28] Many meningiomas treated with radiosurgery have shown a reduction in tumor volume.[11,18,19,28,37] Several short-term reports have stated, in general, that radiosurgical treatment of meningiomas is safe and well tolerated.[19,20,26, 28] Most of these data come from Lunsford's group at University of Pittsburgh, which was the site of the first North American gamma knife unit.[26] Long-term results (up to 20 years) from Stockholm have also indicated that control of tumor growth using the gamma knife unit is excellent.[24] While controversy has existed regarding the relative merits of the gamma knife versus LINAC-based systems,

few hard data regarding this subject as it pertains to the treatment of meningiomas are available in the literature. As with conventional radiation therapy, highly vascular meningiomas may be particularly susceptible to radiosurgery.[2] The most common acute complication in patients undergoing radiosurgery is seizure.[2] Alopecia, hypopituitarism, visual loss, other cranial nerve deficits, weakness, sensory loss, brain edema leading to herniation, and other problems have been reported to occur weeks, months, or even years after therapy, depending on the radiation dose and location of the lesion .[2,8,18,33,40] Corticosteroid therapy may help; symptoms may resolve but recovery is variable.[2,33] What constitutes a "safe" radiation dose for radiosurgery has been questioned.[31]

Concerning specific sites, radiosurgery has been used to treat petrous ridge meningiomas and anterior skull base tumors, with encouraging initial results.[27,29,38,46] Radiosurgery has been evaluated as an addition or alternative to microsurgery for cavernous sinus meningiomas by Duma, et al.[7] Of 34 patients treated, no patient had tumor progression demonstrated on MR imaging during a median follow-up period of 26 months. Tissue confirmation of meningioma was not obtained in six of the 34 patients; however, they were treated based on imaging criteria alone.[7] Valentino, et al.,[48] found that tumor progression occurred in only four of 72 patients with residual, recurrent, or previously untreated middle fossa meningiomas treated with radiosurgery and followed for 2.5 to 8 years. For peritumoral meningiomas in which the residual tumor volume is less than 10 cm³, radiosurgery has been recommended.[15]

CONCLUSIONS

Both external-beam radiation therapy and stereotactic radiosurgery have been advocated in the treatment of residual or recurrent meningiomas. Radiation therapy has also been used in the postoperative treatment of malignant meningioma. Many investigators believe that the precision of radiosurgery makes it the preferred technique for use when dealing with a discrete tumor mass. Radiosurgery has also been used as a primary treatment (without surgery) when studies have indicated that the diagnosis of meningioma is extremely likely or when the patient has been judged unable to withstand surgery.[7,48] Radiation therapy is recommended for the treatment of larger residual (postoperative) tumor volumes. Both techniques have the potential for causing neurological deficits. Because radiosurgery usually involves a single treatment, it is convenient for the patient and potentially less expensive. Control rates for tumor growth after radiosurgery, primarily in shorter-term studies, have been excellent;[33] however, prospective studies specifically designed to answer questions concerning efficacy and the incidence of complications have not been conducted. Although postoperative radiation therapy has been used as an adjuvant therapy for many years in numerous centers, stereotactic radiosurgery has been offered as a potentially effective alternative treatment for small-to-moderate sized meningiomas in many anatomical locations.[25]

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References

1. Austin-Seymour M, Munzenrider J, Linggood R, et al: Fractionated proton radiation therapy of cranial and intracranial tumors. **Am J Clin Oncol** 13:327-330, 1990
2. Bakay RA: Stereotactic radiosurgery in the treatment of brain tumors. **Clin Neurosurg** 39:292-313,

1992

3. Barbaro NM, Gutin PH, Wilson CB, et al: Radiation therapy in the treatment of partially resected meningiomas. **Neurosurgery** **20**:525-528, 1987
4. Capo H, Kupersmith MJ: Efficacy and complications of radiotherapy of anterior visual pathway tumors. **Neurol Clin** **9**:179-203, 1991
5. Carella RJ, Ransohoff J, Newall J: Role of radiation therapy in the management of meningioma. **Neurosurgery** **10**:332-339, 1982
6. Chamberlain MC: Adjuvant combined modality therapy for malignant meningiomas. **J Neurosurg** **84**:733-736, 1996
7. Duma CM, Lunsford LD, Kondziolka D, et al: Stereotactic radiosurgery of cavernous sinus meningiomas as an addition or alternative to microsurgery. **Neurosurgery** **32**:699-705, 1993
8. Engenhart R, Kimmig BN, Hover KH, et al: Stereotactic single high dose radiation therapy of benign intracranial meningiomas. **Intl J Radiat Oncol Biol Phys** **19**:1021-1026, 1990
9. Forbes AR, Goldberg ID: Radiation therapy in the treatment of meningiomas: the Joint Center for Radiation Therapy experience 1970 to 1982. **J Clin Oncol** **2**:1139-1143, 1984
10. Gademann G, Schlegel W, Debus J, et al: Fractionated stereotactically guided radiotherapy of head and neck tumors: a report on clinical use of a new system in 195 cases. **Radiother Oncol** **29**:205-213, 1993
11. Ganz JC, Backlund EO, Thorsen FA: The results of gamma knife surgery of meningiomas, related to size of tumor and dose. **Stereotact Funct Neurosurg** **61** (Suppl 1):23-29, 1993
12. Goldsmith BJ, Rosenthal SA, Wara WM, et al: Optic neuropathy after irradiation of meningioma. **Radiology** **185**:71-76, 1992
13. Goldsmith BJ, Wara WM, Wilson CB, et al: Postoperative irradiation for subtotally resected meningiomas. A retrospective analysis of 140 patients treated from 1967 to 1990. **J Neurosurg** **80**:195-201, 1994
14. Haddad G, Al-Mefty O: Meningiomas: an overview, in Wilkins RH, Rengachary SS (eds): **Neurosurgery**, ed 2. New York: McGraw-Hill, 1996, pp 833-841
15. Harsh IV GR, Wilson CB: Peritorcular meningiomas, in Wilkins RH, Rengachary SS (eds): **Neurosurgery**, ed 2. New York: McGraw-Hill, 1996, pp 873-890
16. Hug EB, Munzenrider JE: Charged particle therapy for base of skull tumors: past accomplishments and future challenges. **Intl J Radiat Oncol Biol Phys** **29**:911-912, 1994
17. King DL, Chang CH, Pool JL: Radiotherapy in the management of meningiomas. **Acta Radiol Ther Phys Biol** **5**:26-33, 1966
18. Kondziolka D, Lunsford LD: Radiosurgery of meningiomas. **Neurosurg Clin North Am** **3**:219-230, 1992

19. Kondziolka D, Lunsford LD, Coffey RJ, et al: Gamma knife radiosurgery of meningiomas. **Stereotact Funct Neurosurg** **57**:11-21, 1991
20. Kondziolka D, Lunsford LD, Coffey RJ, et al: Stereotactic radiosurgery of meningiomas. **J Neurosurg** **74**:552-559, 1991
21. Kramer S, Lee FL: Complications of radiation therapy: the central nervous system. **Semin Roentgenol** **9**:75-83, 1974
22. Kumar PP, Patil AA, Leibrock LG, et al: Brachytherapy: a viable alternative in the management of basal meningiomas. **Neurosurgery** **29**:676-680, 1991
23. Laperriere NJ, Bernstein M: Radiotherapy for Brain Tumors. **CA- Cancer J Clin** **44**:96-108, 1994
24. Lindquist C, Steiner L: Radiosurgery for Tumors, in Wilkins RH, Rengachary SS (eds): **Neurosurgery, ed 2**. New York: McGraw-Hill, 1996, pp 1887-1907
25. Lunsford LD: Contemporary management of meningiomas: radiation therapy as an adjuvant and radiosurgery as an alternative to surgical removal? **J Neurosurg** **80**:187-190, 1994
26. Lunsford LD, Flickinger J, Coffey RJ: Stereotactic gamma knife radiosurgery. Initial North American experience in 207 patients. **Arch Neurol** **47**:169-175, 1990
27. Lunsford LD, Kondziolka DS, Flickinger JC: Radiosurgery of tumors of the cerebellopontine angle. **Clin Neurosurg** **41**:168-184, 1994
28. Lunsford LD, Kondziolka D, Flickinger JC: Stereotactic radiosurgery for benign intracranial tumors. **Clin Neurosurg** **40**:475-497, 1993
29. Lunsford LD, Witt TC, Kondziolka D, et al: Stereotactic radiosurgery of anterior skull base tumors. **Clin Neurosurg** **42**:99-118, 1995
30. Maire JP, Caudry M, Guerin J, et al: Fractioned radiation therapy in the treatment of intracranial meningiomas: local control, functional efficacy, and tolerance in 91 patients. **Int J Radiation Oncol Biol Phys** **33**:315-321, 1995
31. Marks LB, Spencer DP: The influence of volume on the tolerance of the brain to radiosurgery. **J Neurosurg** **75**:177-180, 1991
32. McDermott MW, Gutin PH: Interstitial brachytherapy of primary brain tumors, in Wilkins RH, Rengachary SS (eds): **Neurosurgery, ed 2**. New York: McGraw-Hill, 1996, pp 1909-1920
33. Mehta MP: The physical, biologic, and clinical basis of radiosurgery. **Curr Prob Cancer** **19**:265-329, 1995
34. Noell KT, Herskovic AM: Principles of Radiotherapy of Central Nervous System Tumors, in Wilkins RH, Rengachary SS (eds): **Neurosurgery, ed 2**. New York: McGraw-Hill, 1996, pp 1837-1848
35. Ojemann R: Meningiomas. **Neurosurg Clin North Am** **1**:181-197, 1990
36. Ojemann RG: Supratentorial meningiomas: clinical features and surgical management, in Wilkins RH, Rengachary SS (eds): **Neurosurgery, ed 2**. New York: McGraw-Hill, 1996, pp 873-890

37. Pendl G, Schrottner O, Friehs GM, et al: Radiosurgery with the first Austrian cobalt-60 gamma-unit. A one year experience. **Acta Neurochir** **127**:170-179, 1994
 38. Pendl G, Schrottner O, Friehs GM, et al: Stereotactic radiosurgery of skull base meningiomas. **Stereotactic Funct Neurosurg** **64 (Suppl 1)**:11-18, 1995
 39. Plunkett SR: Conventional radiotherapy of specific central nervous system tumors, in Wilkins RH, Rengachary SS (eds): **Neurosurgery**, ed 2. New York: McGraw-Hill, 1996, pp 1849-1865
 40. Rocher FP, Sentenac I, Berger C, et al: Stereotactic radiosurgery: the Lyon experience. **Acta Neurochir Suppl** **63**:109-114, 1995
 41. Rostomily RC, Eskridge JM, Winn HR: Tentorial meningiomas. **Neurosurg Clin North Am** **5**:331-348, 1994
 42. Sekhar LN, Babu RP, Wright DC: Surgical resection of cranial base meningiomas. **Neurosurg Clin North Am** **5**:229-330, 1994
 43. Sekhar LN, Lanzino G, Sen CN, et al: Reconstruction of the third through sixth cranial nerves during cavernous sinus surgery. **J Neurosurg** **76**:935-943, 1992
 44. Sheline GE: Radiation therapy of brain tumors. **Cancer** **39 (Suppl 2)**:873-881, 1977
 45. Simpson D: The recurrence of intracranial meningiomas after surgical treatment. **J Neurol Neurosurg Psychiatry** **20**:22-39, 1957
 46. Tanaka T, Kobayashi T, Kida Y: Growth control of cranial base meningiomas by stereotactic neurosurgery with a gamma knife unit. **Neurol Medico-Chirurg** **36**:7-10, 1996
 47. Taylor BW Jr, Marcus RB Jr, Friedman WA, et al: The meningioma controversy: postoperative radiation therapy. **Intl J Radiat Oncol Biol Phys** **15**:299-304, 1988
 48. Valentino V, Schinaia G, Raimondi AJ: The results of radiosurgical management of 72 middle fossa meningiomas. **Acta Neurochirurgica** **122**:60-70, 1993
 49. van Effenterre R, Bataini JP, Cabanis EA, et al: High energy radiotherapy in the treatment of meningiomas of the cavernous sinus. **Acta Neurochir Suppl** **28**:464-467, 1979
 50. Wara WM: Radiation therapy for brain tumors. **Cancer** **55 (Suppl 9)**:2291-2295, 1985
 51. Wilson CB: Meningiomas: genetics, malignancy, and the role of radiation in induction and treatment. The Richard C. Schneider Lecture. **J Neurosurg** **81**:666-675, 1994
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