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Meningioma

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Benign meningiomas are well managed with total excision if achievable with minimal morbidity, resulting in 5-, 10-, and 15-year progression-free survival (PFS) rates of 93%, 80%, and 75% and 5-, 10-, and 15-year cause-specific survival (CSS) rates of 95%, 93%, and 88%, respectively [1]. Approximately one in three meningiomas is not fully resectable [2], however, because of tumor location, size, and proximity to adjacent critical central nervous system (CNS) and vascular structures. In the skull base, total resection is accomplished approximately half of the time [2] and is less likely in the setting of prior irradiation, vessel encasement, multiple fossa involvement, and cranial nerve palsies [3]. Although subtotal resection is an appropriate goal when decompression is expected to result in amelioration of symptoms, it is inadequate as a sole modality, with inferior 5-, 10-, and 15-year PFS rates of approximately 50%, 40%, and 30% and CSS rates of 80%, 66%, and 50%, respectively [4,5].

Fractionated radiotherapy [4] or single-fraction radiosurgery [6] as primary management without surgery or after subtotal resection of benign meningioma yields long-term PFS superior to subtotal resection and comparable to total excision, with low morbidity.

Fractionated radiotherapy

Technique

Meningiomas selected for fractionated radiotherapy include well-circumscribed and diffuse and/or irregular tumors of all sizes and intracranial locations, including those abutting the optic nerve or chiasm. Patients may be irradiated after subtotal resection or recurrence or as primary management without surgery when diagnosed by imaging criteria (eg, homogeneously enhancing dural-based tumor without rapid growth and no metastatic disease).

Optimal radiation therapy requires meticulous attention to tumor volume as delineated by the neurosurgeon's description as well as by CT and MRI findings. MRI is superior to CT, with its exquisite resolution, absence of bone artifact, intense tumor contrast enhancement, and coronal and sagittal viewing advantages. In a comparison study by Khoo and colleagues [7], however, MRI-defined meningioma volumes were larger but not inclusive of CT-defined volumes, suggesting complementary spatial information and a role for treatment planning with composite CT/MRI volumes. Pre- and postoperative studies should be used in treatment planning when available. The planning tumor volume (PTV) consists of the clinical tumor volume (CTV) plus a margin of 5 mm for conventional mask immobilization or 2 to 3 mm for a stereotactic frame–based immobilization technique [8–10]. For benign (World Health Organization [WHO] grade I) meningioma, the CTV includes the composite CT/MRI gross tumor volume (GTV) in the setting of primary radiotherapy and the residual composite CT/MRI GTV in the adjuvant setting. After surgery, the CTV may be expanded beyond the remaining radiographic GTV to encompass microscopic residua based on the neurosurgeon's description of intraoperative findings and an appreciation of the preoperative dural base. Because (1) most benign meningioma recurrences after stereotactic

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fractionated radiotherapy [10] are not marginal and (2) microscopic involvement of the adjacent dura is typically confined to a distance 1 or 2 mm beyond the gross tumor, routine inclusion of the entire dural tail in the CTV has not been demonstrated to be necessary [11–13]. Atypical and anaplastic meningiomas also rarely fail marginally when treated with a CTV 10 mm beyond the GTV, an operative bed, hyperostotic bone, and dural thickening [14]. For anaplastic tumors, the CTV also includes peritumoral edema if present or a rim of adjacent normal brain parenchyma if not.

Five-millimeter setup error precision is achieved by use of an immobilization system, consisting of a head support, a thermoplastic mask that is molded to the patient's head, and a frame that locks the mask and head in a reproducible position. Fused CT/MRI computerized treatment planning should be used, with treatment-planning scans obtained with the patient in the treatment position and wearing the immobilization device with radiopaque fiducials. The use of such careful tumor localization and immobilization techniques has been shown to have greater prognostic importance than tumor size or radiotherapy dose and has been associated with a 5-year PFS, which is significantly better (98% versus 77%; $P = .002$) than that achieved without such techniques [15]. With the addition of a stereotactic frame and localization system, setup error is reduced to 2 mm, allowing for a tighter PTV and less normal tissue irradiation [9,10].

Optic nerve sheath (ONS) meningiomas require precision conformal therapy, as described by Eng and colleagues [16]. The patient is positioned supine with the head rotated laterally so that the affected optic nerve is approximately perpendicular to the horizontal plane. The appropriate angle of lateral head rotation can be estimated from diagnostic CT scans. In the series from Eng's group, this value ranged from 15° to 27°. Neck flexion should establish an imaginary vertical line on the lateral simulation film from the center of the orbit to a point just superior to the pituitary fossa. In this position, the patient's head is immobilized with a head support, thermoplastic mask, and locking frame as just described. The treatment planning CT scan is then obtained with the patient in this position and wearing the immobilization mask. Three small half-beam blocked fields are set up isocentrically with axes lying in the horizontal plane. Treatment table rotation is used to produce a vertex field and two superior-lateral fields. The superior-lateral fields are angled to avoid the contralateral eye and optic nerve. The beams are split perpendicular to the vertical axis, and the anterior half is blocked to prevent anterior divergence toward the globe. Differential field weighting is used to optimize the isodose distribution, and the prescribed isodose volume (with 5% or less heterogeneity) should encompass the PTV. Stereotactic technique is particularly appropriate in this setting to minimize setup error and PTV and to maximize organ-at-risk (OAR) sparing [17,18].

For other intracranial sites, multiple static fields should be selected to minimize the dose to the uninvolved CNS tissues. Opposed lateral fields should be avoided in practically all cases to prevent unnecessarily irradiating lateral CNS structures, such as the temporal lobes. Intensity-modulated radiotherapy (IMRT), consisting of objective weighting, inverse planning, and fluence modulation, yields target coverage, target conformity, and OAR sparing superior to conventional radiotherapy, particularly for complex tumor volumes, at the expense of larger volumes of normal tissue receiving a low dose [19,20]. Careful conformal technique should limit inhomogeneity of dose to less than 10% (ideally, less than 5%). No portion of the optic nerve or chiasm should receive greater than 54 Gy at 1.8 Gy per fraction [21]. A dose of 54 Gy at 1.8 Gy per fraction for 5 days a week is generally given to benign (WHO grade I) meningiomas, and for atypical and anaplastic (WHO grade II and III) lesions, the dose is increased to 59.4 to 61.2 Gy [4,22]. Dose-response relations have been demonstrated [14,15,23,24], with 54 Gy and 60 Gy conventionally fractionated yielding a significantly better PFS than lower dose schedules for benign [24] and atypical or anaplastic [14] meningiomas, respectively Aggressive fractionated radiotherapy beyond 60 Gy is more toxic and has not been demonstrated to improve local control [22,25]. Anaplastic lesions may be considered for radiosurgery boost after external beam radiotherapy if the tumor volume is well defined and small [26].

Outcome

Fractionated radiotherapy as primary management without surgery [4,27] or after subtotal resection [4,15] of benign meningioma yields a 5-year PFS rate between 91% and 98%, which is superior to subtotal resection and comparable to

total excision, and symptom improvement in 43% to 72% of cases (Table 1). Note that Table 1 excludes reports published before 1994 because those series did not use CT- or MRI-based targeting and dose planning, in contradistinction to all contemporary single- or multifraction radiation treatments of meningiomas). Multivariate analyses demonstrate no relation between PFS and degree of resection or tumor size [10].

Mendenhall and colleagues [4] treated 101 patients with skull base meningiomas between 1984 and 2001 with fractionated radiotherapy alone (n = 66) or after subtotal resection (n = 35). The median dose was 54 Gy. After a median follow-up of 5 years, 5-, 10-, and 15-year PFS rates were 95%, 92%, and 92%, respectively, and the corresponding CSS rates were 97%, 92%, and 92%, both independent of prior surgery.

Milker-Zabel and coworkers [28] reported the University of Heidelberg's experience in treating 317 patients (153 benign tumors, 26 atypical tumors, and 138 unbiopsied tumors) between 1985 and 2001 with stereotactic fractionated radiotherapy to a median dose of 57.6 Gy. After a median follow-up of 5.7 years, 5- and 10-year PFS rates were 91% and 89%, respectively, for benign and unbiopsied tumors. Pretreatment neurologic deficits improved in 43% of patients and worsened in 8%. Improvement was seen in diplopia in 39 (37%) of 106 patients, exophthalmos in 17 (38%) of 45 patients, trigeminal hypo- or dysesthesia in 20 (24%) of 82 patients, and trigeminal neuralgia in 9 (33%) of 27 patients. Twenty-two percent of patients with preexisting cranial nerve deficits experienced complete resolution. A previously published analysis of University of Heidelberg patients with skull base meningiomas [10] (a subset of those described by Milker-Zabel's group) found no difference in PFS between primary radiotherapy without surgery and postoperative radiotherapy.

Maire and colleagues [29] have described the Hôpital Saint-André experience with radiotherapy alone for 44 inoperable or unresectable patients between 1981 and 1993. The median dose was 52 Gy. After a median follow-up of 3 years, the crude PFS rate was 93%. When reported in combination with 51 patients treated for other indications (subtotal resection, salvage after recurrence, and total resection with unfavorable histology), the overall neurologic performance improved in 72% of patients.

ONS meningioma is frequently irradiated without prior surgery. Narayan and coworkers [27] described 14 such patients treated (12 without surgery) between 1986 and 2001 with three-dimensional conformal fractionated radiotherapy to a median dose of 54 Gy and followed for a median of 4 years. The radiographic PFS rate was 100%. Visual acuity significantly improved, remained stable, and worsened in 36%, 50%, and 14% of patients, respectively. Of 9 patients with complete baseline and follow-up visual fields testing, all significantly improved.

Goldsmith and colleagues [15] reported on 117 patients irradiated after surgery to a median dose of 54 Gy for benign meningioma. After a median follow-up of 3 years, the 5-year PFS rate for patients treated after 1980, when CT or MRI imaging was used for treatment planning, was 98%. Local control of orbital, parasellar, and posterior fossa tumors, which are notoriously difficult to resect completely and thus associated with higher recurrence rates in the surgical literature [2], did not differ significantly from local control of tumors from all other sites.

Toxicity

Common acute toxicities of fractionated radiotherapy for meningioma are, in general, mild and include fatigue, skin erythema, and varying

Table 1
Fractionated radiotherapy for benign meningiomas

Authors	Year	Median dose (Gy)	PFS at 4–5 years (%)	PFS at 10 years (%)	PFR at 15 years (%)	Symptom improvement	Complication rate (%)
Mendenhall et al [4]	1984–2001	54	95	92	92	NS	6%
Milker-Zabel et al [28]	1985–2001	57.6	91	89	NS	43%	2.5%
Maire et al [29]	1981–1993	52	93	NS	NS	72%	5%
Narayan et al [27]	1986–2001	54	100	NS	NS	36% (VA) 100% (VF)	0% grade 3+
Goldsmith et al [15]	1980–1990	54	98	NS	NS	NS	4%

Abbreviations: NS, not stated; PFS, progression-free survival; VA, visual acuity; VF, visual fields.

degrees of dose-related alopecia (which may be transient or permanent). If the external auditory canal and middle ear are not excluded from the prescription volume, an irradiated field, external otitis, and serous otitis media may result. Rarely seen are acute transient symptoms suggestive of increased intracranial pressure (eg, headache, nausea, vomiting) and exacerbation of preradiation therapy neurologic deficits [30]. The risk of radiation-induced edema is low [4].

Late effects are dependent on the region irradiated and uncommon when OAR dose tolerances are respected. Chronic otitis [31] and decreased hearing [32] have been reported after irradiation of the ear. Retinopathy [15,32,33] and optic neuropathy [10,14,15,21,25,31,34,35] have been reported after irradiation of the globe to doses greater than 45 Gy and after irradiation of the anterior visual pathway to doses greater than 54 Gy, respectively. Cerebral necrosis [14,15,25,31,36,37] and focal neurologic deficits suggestive of late brain injury have been seen, particularly after doses greater than 60 Gy, a dose per fraction greater than 1.8 to 2 Gy, and the opposed lateral technique [14,30]. Hypopituitarism manifested by hyposecretion of growth hormone, luteinizing hormone, follicle-stimulating hormone, corticotropin, and thyrotropin (in order of radiosensitivity) is expected after irradiation of the hypothalamic-pituitary axis region and has been reported after radiation therapy for meningiomas [34]. Mechanisms of injury and time-dose analyses for radiation injury to the visual apparatus [21,30,33,35,38,39], brain [30,40], and pituitary gland [30,41] are available to the interested reader.

Goldsmith and colleagues [15] reported a crude incidence of radiation complications of 4% (5 of 140 patients treated to a wide range of target volumes between 1967 and 1990). Two patients experienced retinopathy, and 1 experienced optic neuropathy. One of 2 patients with cerebral necrosis recovered after decompressive craniotomy, and the second died of bronchopneumonia secondary to chronic brain syndrome. As a consequence of the recognition of these complications and a subsequent analysis of optic neuropathy risk [21], the University of California, San Francisco established an institutional policy to avoid using the high-dose opposed lateral technique and exceeding a maximum dose of 54 Gy to the optic nerve whenever possible.

Mendenhall and coworkers [4] described a crude incidence of late radiation complications of 6% (6 of 101 patients treated to a wide range of target volumes between 1984 and 2001). Two patients experienced gradual progressive dementia. One developed edema after radiotherapy as primary management and subsequently underwent resection of the meningioma. Three experienced significant peritumoral edema refractory to steroids, resulting in progressive neurologic compromise and death.

Milker-Zabel and colleagues [28] reported a crude incidence of late grade 3 toxicity of 2.5% (8 of 317 patients treated between 1985 and 1998). Two patients experienced reduced vision, 1 had trigeminal neuropathy, and 5 developed intermittent tinnitus.

The future incidence of complications is expected to decline as modern OAR-sparing treatment techniques become uniformly applied.

Single-fraction radiosurgery

Technique

Meningiomas selected for radiosurgery include discrete small- to medium-sized tumors (generally $\leq$30–35 mm) located in sites that can be treated without exceeding tolerance dose constraints of nearby or encompassed critical structures, such as the optic nerves, chiasm, and brain stem. Patients may be irradiated after subtotal resection or as primary management without surgery when diagnosed by imaging criteria, (eg, homogeneously enhancing dural-based tumor without rapid growth) and when there is little or no surrounding symptomatic vasogenic edema.

For several delivery systems, a stereotactic frame is fixed to the patient's head under local anesthesia and imaging is acquired with a stereotactic localizer to define tumor and normal tissue anatomy relative to the frame. Some robotically controlled radiosurgery systems do not require application of a stereotactic frame but rather rely on thermoplastic mask fixation and plain radiograph/CT scan image coregistration to define stereotactic space for treatment. The necessity of including the entire dural tail within the target volume is unclear. Although recommended by DiBiase and colleagues [42] on the basis of a univariate association between tail inclusion and local control, this factor was also significantly associated with target conformity and was insignificant on multivariate analysis. Patterns of failure were not reported, complicating interpretation. Available data on radiosurgery failure location are conflicting, with Stafford and coworkers [6] and Rowe and colleagues [43] describing

marginal failure as infrequent (3 of 16 cases) and common (12 of 16 cases), respectively. Because microscopic involvement of the dura is typically confined to a distance of 1 to 2 mm beyond the gross tumor [11–13], inclusion of the first several millimeters of adjacent dura within the target volume may be sufficient.

Dose prescriptions are based on tumor size, location, and history of prior radiotherapy. At the Mayo Clinic [6], tumor margin doses (TMDs) of 16, 18, and 20 Gy have generally been selected for isodose volumes more than 14.1 cm^3, 4.2 to 14.1 cm^3, and less than 4.2 cm^3, respectively. At the University of Pittsburgh [44,45], TMDs between 12 and 18 Gy have been used and lower doses between 12 and 14 Gy have been more typical since 1993 [45,46]. Shin and coworkers [47] have reported a local failure rate of 20% associated with TMDs between 10 and 12 Gy versus 0% with a TMD greater than 14 Gy. The maximum dose to the optic nerve and chiasm is limited to 8 to 12 Gy to a small portion (Mayo Clinic) [48], 8 Gy (University of Pittsburgh) [49], 10 Gy (Medical University of Graz) [50], and 8 Gy (University of California, San Francisco).

Outcome

Single-fraction radiosurgery as primary management without surgery [5,6,51] or after subtotal resection of benign meningioma yields a 5-year PFS rate between 86% and 98%, which is superior to subtotal resection and comparable to total excision, and symptom improvement in 13% to 42% of patients (Table 2).

Kreil and colleagues [50] treated 200 patients with benign meningiomas (99 after surgery and 101 without prior surgery) between 1992 and 1999 to a median TMD of 12 Gy, with a median isodose volume of 6.5 cm^3. After a median follow-up of almost 8 years, the 5- and 10-year PFS rates were 99% and 97%, respectively. Preexisting neurologic symptoms improved in 42% of patients, with most improvements in visual fields, trigeminal neuralgia, and diplopia.

Stafford and coworkers [6] described radiosurgery for 190 patients with meningiomas treated between 1990 and 1998 to a median TMD of 16 Gy, with a median isodose volume of 8.2 cm^3. Forty-one percent were treated primarily without surgery, and 59% had at least one prior operation. After a median follow-up of 3 years, benign meningioma 5-year PFS and CSS rates were 93% and 100%, respectively, independent of prior surgery. Preexisting neurologic symptoms (diplopia or facial pain) improved in 8% of patients. Subsequently, Pollock and colleagues [5] from the same institution compared contemporary patients managed with primary radiosurgery to a mean TMD of 18 Gy (n = 62) or resection (n = 136; 57 Simpson grade 1, 57 grade 2, and 22 grade 3–4). After a median follow-up of 5 years, tumor recurrence and/or progression was more frequent in the surgical group (11%) than in the radiosurgical group (2%) ($P < .05$). The 7-year PFS rate achieved with radiosurgery (95%) was equivalent to that after Simpson grade 1 excision (all tumor, attached dura, involved bone [96%]) and superior to anything less than this (Simpson grades 2 and 3–4: 82% and 34%, respectively). Symptoms improved in 13% of patients after resection (visual fields, trigeminal neuralgia, and gait) and in 13% of patients after radiosurgery (trigeminal neuralgia, diplopia, facial hypoesthesia, and visual fields). Subsequent tumor treatments were less common after primary radiosurgical management, and there were fewer

Table 2
Stereotactic radiosurgery for meningiomas: selected series since 2000 with 5-year progression-free survival

Author	Year	Number of patients	Median dose (Gy)	PFS at 5 years
Roche et al [55]	2000	92	15	93%
Stafford et al [6]	2001	168	16	93%
Lee et al [45]	2002	159	13	93%
Eustacchio et al [56]	2002	121	13	98%
Kondziolka et al [52]	2003	85	16.5 (mean)	93% (PFS at 10 years)
Pollock et al [5]	2003	62	17.7 (mean)	95% (PFS at 7 years)
DiBiase et al [42]	2004	162	14	86%
Metellus et al [53]	2004	36	15	94%
Malik et al [51]	2005	309	20	87%
Kreil et al [50]	2006	200	12	98%

Abbreviation: PFS, progression-free survival.

complications as well. The authors suggested that if the long-term tumor control rates remain high and morbidity remains low, radiosurgery can be considered as the primary form of treatment for small- to medium-sized meningiomas without symptomatic mass effect.

Kondziolka and coworkers [44] reported the treatment of 99 patients with benign meningiomas with a median volume of 4.7 cm^3 between 1987 and 1992. Forty-three percent of these patients were treated primarily, and 57% had at least one prior operation. Patients received a single-fraction median TMD of 16 Gy (range: 9–25 Gy). After a median follow-up of 4 to 6 years, the 5-year PFS rate was 95%. A subsequent publication on the long-term follow-up of 85 meningiomas confirmed their earlier results [52]. For 85 meningiomas treated between 1987 and 1992 with a median follow-up of 10 years, 53% had a decrease in size, 40% were unchanged, and 7% grew. No patient developed a radiation-induced tumor. New or worsening deficits developed in 5 (5.8%) of the 85 patients and resolved completely in 2.

Malik and colleagues [51] treated 309 meningiomas (44% without prior surgery and 56% after surgery) with a mean volume of 7.3 cm^3 between 1994 and 2000 with single-fraction radiosurgery. The median TMD was 20 Gy, but in 52% of cases, part of the tumor received less than the prescribed dose to safeguard neurologic, most commonly visual, function. After a mean follow-up of almost 4 years, 5- and 8-year benign meningioma PFS rates were 87% and 75%, respectively. Neither conformity nor the volume of tumor receiving less than 5, 10, or 15 Gy influenced outcome.

Although no randomized trial of radiotherapy treatment techniques for meningiomas has been published, Metellus and coworkers [53] reviewed their own experience with a small series of patients with cavernous sinus meningiomas treated with fractionated radiotherapy or radiosurgery at a single institution (Table 3) [53]. Radiosurgery was performed in accordance with commonly accepted techniques, whereas radiotherapy in this retrospective study involved several different fractionation schemes, including some that are associated with a higher risk of complication. The median follow-up was 88.6 months for the fractionated radiotherapy group and 63.6 months for the radiosurgery group. Selection of treatment modality was based on the availability of radiosurgery (after 1992) or on the lesion size, shape, or proximity to critical structures. Although tumor configuration, size, and Sekhar grade were less favorable in the fractionated radiotherapy group, actuarial PFS and clinical improvement rates were no different between the two treatment groups. The radiographic shrinkage was higher in the radiosurgery group (52.7% versus 29%) and was noted to increase in longer follow-up from a subset of patients previously analyzed out to only 30 months (31% shrinkage at 30 months of mean follow-up). In any case, the degree of post-radiation shrinkage does not seem to be correlated with any other outcome variable. The authors concluded that for cavernous sinus meningiomas, fractionated radiotherapy and radiosurgery were both safe and effective techniques for securing long-term tumor control.

Toxicity

Stafford and coworkers [6] described a crude complication rate of 13% (24 of 190 patients) after treatment to a median TMD of 16 Gy, including 15 new or worsened cranial neuropathies with a median onset of 6 months (2 resolved), five cases of symptomatic edema, two internal carotid artery (ICA) occlusions, and two peritumoral cysts (Table 4). Pollock and colleagues [5] reported

Table 3
Retrospective comparison of fractionated radiotherapy and Gamma Knife radiosurgery for cavernous sinus meningiomas

Treatment type	Number of patients	Mean tumor volumes	Sekhar grade III–IV	PFS	Clinical improvement	Tumor reduction
Fractionated radiotherapy	38	13.5 cm^3	68.4%	94.7%	63.2%	29%
Gamma Knife radiosurgery	36	5.2 cm^3	27.8%	94.4%	53.8%	52.7%

Abbreviation: PFS, progression-free survival.

Adapted from 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(5):873–86 [discussion: 878]; with permission.

Table 4
Complication rate after radiosurgery for meningiomas: series of more than 100 patients

Author	Year	Number of patients	Complication rate	Median dose
Stafford et al [6]	2001	168	13%	16 Gy
Lee et al [45]	2002	159	6.7%	13 Gy
Eustacchio et al [56]	2002	121	5%	13 Gy
DiBiase et al [42]	2004	162	8.3%	14 Gy
Malik et al [51]	2005	309	3%	20 Gy
Kreil et al [50]	2006	200	2.5%	12 Gy

complications in 6% (6 of 62 patients) after treatment to a mean TMD of 18 Gy, including diplopia in 1 patient, trigeminal neuralgia and/or hypoesthesia in 3 patients, cyst formation requiring a shunt in 1 patient, and ICA occlusion in 1 patient, respectively.

Kondziolka and coworkers [44] reported 3 of 99 patients (5% actuarial rate from 31–120 months) with complications after treatment to a median TMD of 16 Gy: visual acuity deterioration (at 6 months, recovered), hemianopsia (at 31 months, permanent), hemiparesis (at 12 months, recovered), and abducens nerve palsy (at 18 months, recovered) in the same patient and worsened preexisting oculomotor palsy (at 3 months, permanent) and hemianopsia (at 30 months, permanent) in the other two patients. Since restricting the optic chiasm dose to less than 8 Gy and conforming the radiosurgery plan with more sophisticated planning software, no subsequent patients developed delayed visual complications.

Malik and colleagues [51] described a crude complication rate of 3% (9 of 277 patients) after treatment to a median TMD of 20 Gy but with part of the tumor receiving less than the prescribed dose in 52% of cases to safeguard neurologic function. One patient experienced trigeminal hypoesthesia exacerbation, and 3 patients developed new transient trigeminal symptoms. Three patients developed new or altered diplopia, and 2 patients experienced motor weakness.

Kreil and coworkers [50] reported a crude complication rate of 3% (5 of 200 patients) after treatment to a median TMD of 12 Gy. Two patients experienced transient increased seizure activity and headache associated with peritumoral edema; 2 developed trigeminal neuralgia at 12 and 16 months, which resolved months later; and 1 had permanent optic neuropathy. Of note in the small series reported by Kim and colleagues [54] on the results of radiosurgery for superficially located meningiomas, 43% of patients experienced the development of new or worsening edema. The volume of increased signal on T2-weighted images was measured in three dimensions and used to define the "edema index" as the ratio of the volume of T2 signal to the volume of tumor. Edema after radiosurgery occurred at a mean interval of 6 months after treatment (range: 2–11 months). In 9 of 11 patients, the edema resolved after a mean period of 11 months (range: 5–23 months). The edema index was 16.6 for parasagittal meningiomas, 2.5 for falx meningiomas, and 1.5 for convexity meningiomas; however, there was no significant relation between location and the development of edema. In univariate analysis, a high integral tumor dose and larger tumor volume were associated with the development of edema. In tumors larger than 4.2 cm^3, edema occurred more frequently. Interestingly, tumor shrinkage occurred more frequently in those patients who had developed edema after treatment.

The incidence of complications after meningioma radiosurgery is low, and these are most frequently cranial nerve injury and symptomatic edema. Generally, over the years, there has been a trend toward using lower TMDs [45,46,50] or compromising conformality to safeguard neurologic function [43,51] for benign meningiomas, with a decrease in complications. Flickinger and colleagues [46] reported a significantly lower (hazard rate ratio of 4.5) complication rate in patients treated after 1991, which was associated with the use of lower doses and MRI for treatment planning. Selection of smaller treatment volumes and restricting maximum dose to the optic nerve and chiasm are also expected to result in a decline in the incidence of radiosurgery complications.

Summary

Total excision is an appropriate treatment option for patients with benign meningiomas

that are resectable with minimal morbidity. It is particularly appropriate for patients with significant mass effect causing symptoms.

Fractionated conformal radiotherapy is an appropriate primary treatment option for patients with benign meningiomas of all sizes and all sites. It is particularly appropriate and preferred for ONS meningiomas, for which there are few alternatives. Single-fraction radiosurgery is an appropriate primary treatment option for patients with tumors measuring 30 to 35 mm or less and located in sites that can be treated without exceeding tolerance dose constraints of nearby critical structures. Control rates and toxicity rates are similar for single-fraction radiosurgery and multifraction conformal radiotherapy for two reasons: both deliver the prescribed dose to the target while minimizing the dose to surrounding tissues, and both deliver similar meningioma biologic equivalent doses (BEDs).

Planned subtotal resection is appropriate if decompression is expected to relieve acute symptoms. After subtotal resection, it is appropriate to offer single-fraction radiosurgery or multifraction radiotherapy, depending on the size, location, and extent of residual tumor, so as to achieve PFS and CSS rates comparable to those of other approaches.

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