Title

Intraoperative Extracorporeal Irradiation for the Treatment of the Meningioma-Infiltrated Calvarium

Journal

Journal of Neurological Surgery Reports, 76(01)

ISSN

2193-6358

Authors

Kerr, Edward E

Fragoso, Ruben

Schrot, Rudolph J

et al.

Publication Date

2015-07-01

DOI

10.1055/s-0035-1554908

Peer reviewed

Intraoperative Extracorporeal Irradiation for the Treatment of the Meningioma-Infiltrated Calvarium

Edward E. Kerr[1] Ruben Fragoso[2] Rudolph J. Schrot[1] Kiarash Shahlaie[1]

[1] Departments of Neurological Surgery, University of California, Davis School of Medicine, Sacramento, California, United States
[2] Departments of Radiation Oncology, University of California, Davis School of Medicine, Sacramento, California, United States

Address for correspondence Kiarash Shahlaie, MD, PhD, Department of Neurological Surgery, UC Davis School of Medicine, 4860 Y Street, Suite 3740, Sacramento, CA 95817, United States (e-mail: kiarash.shahlaie@ucdmc.ucdavis.edu).

J Neurol Surg Rep 2015;76:e173–e179.

Abstract

Objectives Complete removal of infiltrated bone is required to achieve a Simpson Grade 1 meningioma resection. Reconstruction of the resulting bone defect is typically achieved with a nonnative implant that can result in poor cosmesis, foreign body reaction, or infection. Extracorporeal irradiation and reimplantation of tumorous bone has been used for limb-sparing surgery with excellent results, but this treatment option is not routinely considered in meningioma surgery. We present a case of anterior fossa meningioma with tumorous overlying calvarium that was successfully managed with intraoperative extracorporeal irradiation and reimplantation.

Design, Setting, and Participant A 37-year-old woman with persistent chronic headaches was found to have an anterior skull base meningioma with extension into the forehead frontal bone. Concurrently with mass resection, the bone flap was irradiated intraoperatively with 120 Gy. After resection of the tumor, the bone flap was replaced in its native position.

Main Outcome Measures and Results Twenty-nine months postoperatively, the patient had an excellent cosmetic outcome with no radiographic evidence of tumor recurrence or significant bone flap resorption.

Conclusion Intraoperative extracorporeal irradiation of tumorous calvaria during meningioma surgery is an effective, logistically feasible treatment option to achieve local tumor control and excellent cosmetic outcome.

Keywords
- extracorporeal irradiation
- meningioma
- tumorous calvarium
- skull reconstruction

Background

In his landmark series, Simpson demonstrated that gross total resection (GTR) of meningioma, including the involved meninges and bone, results in lower recurrence rates than subtotal resection.[1] Although they arise from arachnoid cap cells, meningiomas often transgress the periosteal layer of the dura and involve local calvaria via infiltration of the Haversian canals.[2,3] To achieve gross total tumor resection in these scenarios, involved bone is resected and often reconstructed with a nonnative implant. An alternative option to bone resection is extracorporeal irradiation and reimplantation, a strategy that has been reported extensively as a successful limb-sparing treatment option for tumors involving bone.[4–7] We present a case of anterior fossa meningioma with tumorous overlying calvarium that was successfully managed with intraoperative extracorporeal irradiation and reimplantation.

received
January 8, 2014
accepted after revision
April 9, 2015
published online
June 26, 2015

DOI http://dx.doi.org/10.1055/s-0035-1554908.
ISSN 2193-6366.

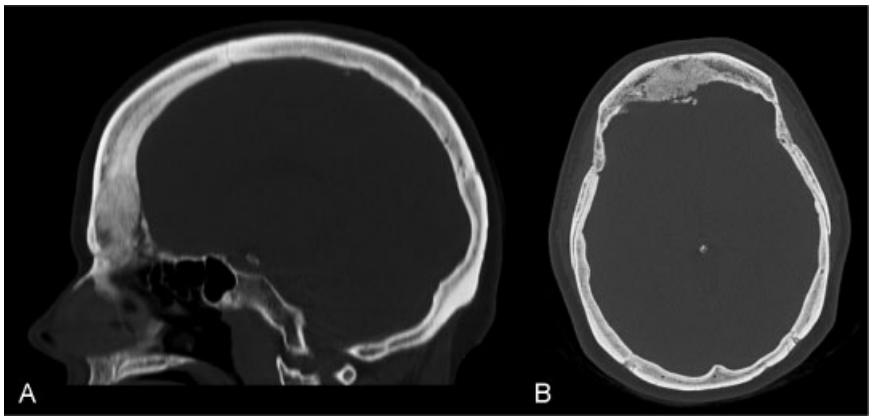

Fig. 1 Preoperative (A) sagittal and (B) axial computed tomography scan demonstrating extensive bony involvement of the meningioma.

Methods and Results

Clinical History

A 37-year-old woman with a 6-month history of persistent chronic frontal headaches was found to have a dural-based anterior skull base meningioma (►**Fig. 1**). The lesion involved the anterior falx cerebri and measured 4 cm in the coronal plane and 3.5 cm in the craniocaudal dimension. The lesion was 11 mm in the anteroposterior dimension and extended through the orbitofrontal dura, with abnormal expansion of the forehead frontal bone. The patient had no cosmetic abnormalities as a result of this frontal bone prominence.

Surgery

A hair-sparing bicoronal incision was made (►**Fig. 2A**), and the underlying pericranium was elevated as a separate flap with an anteriorly based vascular pedicle. A bifrontal craniotomy was performed to encompass the area of forehead frontal bone involvement. Tumor was partially resected from the inner table of the bone flap with a high-speed drill. The flap was sterilely packed with saline-soaked gauze to form a "brick" (►**Fig. 2B–D**) in a sterile tissue storage bag. This was subsequently packed into four additional serial sterile tissue storage bags and then transported to the radiation oncology suite.

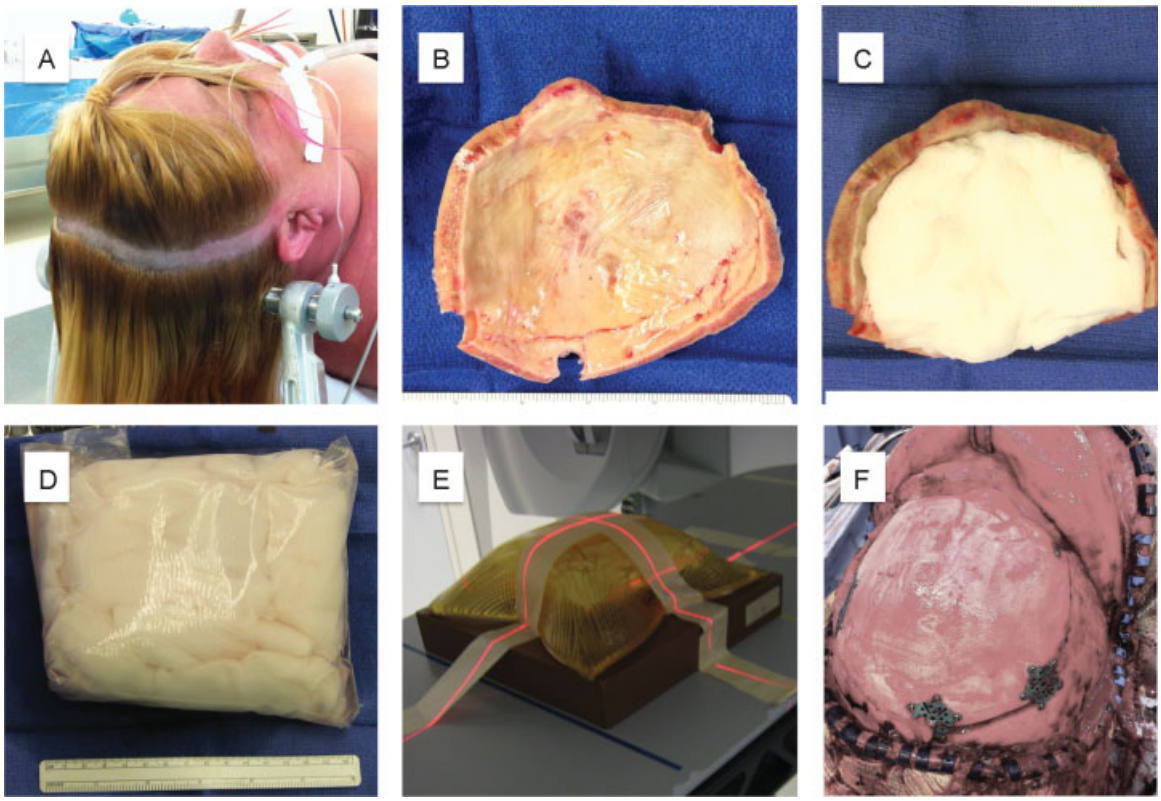

Fig. 2 Intraoperative photographs depicting the bicoronal incision (A) and the removed calvarial flap before (B) and after (C) gauze packing to facilitate a homogeneous extracorporeal radiation dose. The fully packaged flap (D) was transported to the radiation suite, treated in the linear accelerator (E), and reimplanted in the native position (F).

Due to the flap's concavity, it was not practical to add more gauze at the extremes of the flap for dosing purposes. Therefore, the packaged flap was placed on top of 5 cm of buildup material (a water-equivalent block) to deliver a homogeneous radiation dose to the entire flap. Additionally, bolus material was placed on top of the flap to enhance backscatter dose and to reduce underdosing of the extremes of the convexity (the most lateral portions of the bone flap). A clinical linear accelerator was used to irradiate the bone flap to a total dose of 120 Gy using six megavoltage X-rays with an expected dose in homogeneity of $\pm$ 5% (►**Fig. 2E**). The package was then irradiated from below and flipped over halfway through treatment to deliver a homogeneous dose to the flap. Once treatment was completed, it was returned to the operating room, $\sim$ 90 minutes later. The irradiated bone flap was stored in a bacitracin-containing normal saline bath until reimplantation.

After GTR of the frontal meningioma, the resected dura was repaired with a suturable collagen matrix. Tumor was resected from the anterior skull base using a high-speed drill, both frontal sinuses were exenterated, the nasofrontal ducts were obliterated, and the entire area was covered with the pericranial flap. The irradiated bone flap was affixed to the calvarium in its native position using titanium plates and screws (►**Fig. 2F**), taking care to prevent strangulation of the pericranial flap's vascular pedicle. The scalp was then closed in a routine fashion.

Postoperative Course

The patient's postoperative course was uneventful, and she was discharged home 3 days after surgery. The final histopathologic analysis of the mass was consistent with a World Health Organization grade 1 meningioma. She was seen 10 days postoperatively for a wound check and skin staple removal, at which time she had a normal forehead contour with no palpable step-offs. She was seen again at 3, 6, 12, 19, and 29 months after surgery, with serial imaging and repeat clinical examination. Her cosmetic outcome was excellent throughout the follow-up period (►**Fig. 3**), and her postoperative imaging demonstrated radiodense feathering of the kerf edges suggestive of fibrous union (►**Fig. 4**); there was no evidence of tumor recurrence in the bone flap. Contrast-enhanced magnetic resonance imaging obtained preoperatively and 29 months postoperatively demonstrates absence of dural enhancement and expansion of the cerebrum into the space previously occupied by tumorous bone (►**Fig. 5**).

Discussion

GTR of meningioma with invasion into the local calvarium can be achieved using one of two general approaches: resection of the involved bone with subsequent reconstruction or sterilization of the native bone flap during surgery with immediate reimplantation. There are many described strategies for the reconstructive or sterilization techniques, each of which has particular advantages and disadvantages that warrant careful consideration. A thorough understanding of allograft and biological skull reconstructive options is important in developing patient-specific treatment plans for managing meningiomas that involve adjacent bone structures.

Alloplastic Reconstructive Options

Several alloplastic materials are commercially available for calvarial reconstruction, and their physical properties determine their most suitable clinical applications. Titanium mesh is a commonly used highly biocompatible and widely available material suitable for intraoperative reconstruction of defects $<$ 25 cm.[2,8] However, its malleability and lack of osteoinductivity or osteoconductivity render it unsuitable for stand-alone reconstruction of larger defects, for which structural support and protection of underlying cerebrum is paramount.[8] In these cases, it is more suitable for use as a scaffold and calvarial anchor for other reconstructive materials.[8,9]

Space-occupying alloplastic implants are more suitable for large defects and generally constructed of one of four materials. Polymethylmethacrylate (PMMA) is among the most commonly used modern alloplastic implants for cranioplasty[10] and can be used in one of three ways: intraoperative formation with adherence to the defect, intraoperative

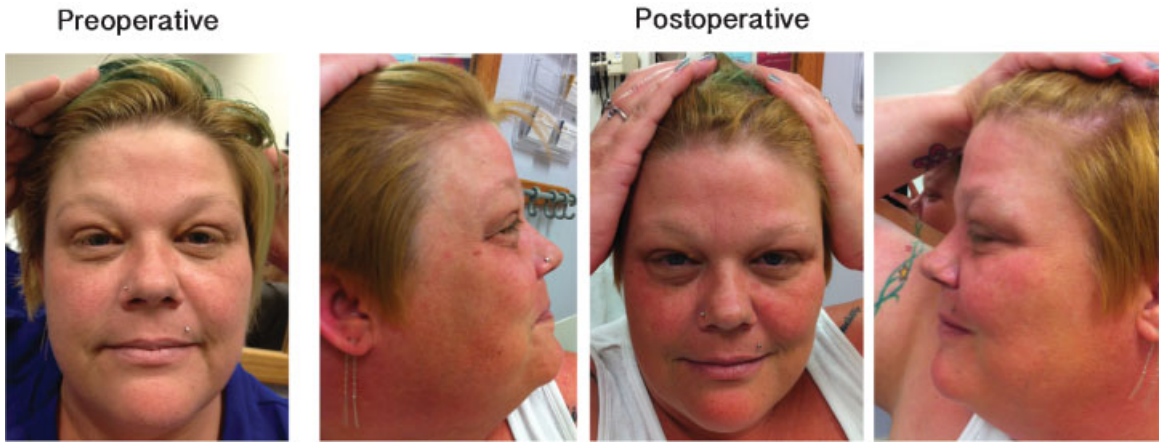

Fig. 3 Preoperative and 19-month postoperative photographs depicting cosmetic outcome.

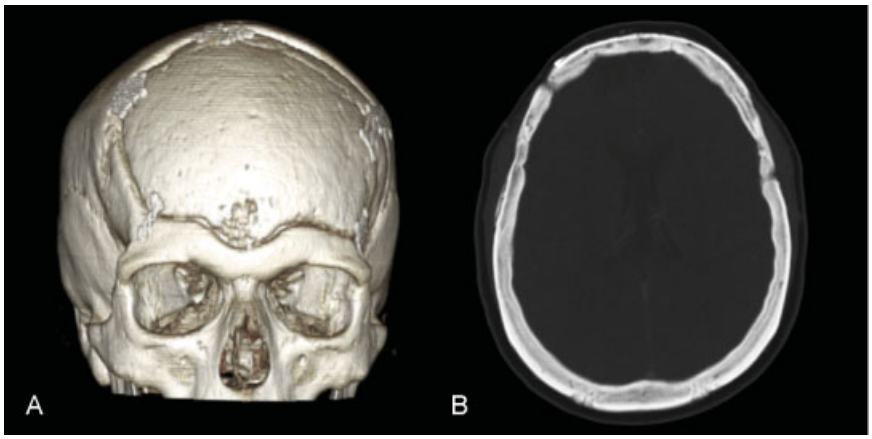

Fig. 4 (A) Three-dimensional and (B) axial computed tomography scans 19 months after surgery, demonstrating feathering of bone edges with preservation of normal contours.

formation and reinforcement with metallic fixation, and preoperative formation based on preoperative three-dimensional imaging.[9,11] PMMA implants offer numerous advantages to other alloplastic materials: they are lightweight, rigid, relatively low cost, lack thermal conductivity, are not ferromagnetic, and are biologically inert.[10,12–14] However, PMMA is not vascularized by or subsequently incorporated into adjacent bone, so it presents an infection risk. It also exposes the patient to a potentially toxic monomer when cold polymerized and may cause exothermic thermal injury to the cerebrum when polymerized in situ.[11,14]

Alloplastic alternatives to PMMA include hydroxyapatite, polyethylene, and bioactive glasses. Hydroxyapatite used in the cement form offers the advantages of malleability before hardening, osteoconductivity, and relative resistance to infection; however, it carries the disadvantages of being relatively expensive and does not fully convert to bone, so it is frequently used in conjunction with a structural support such as titanium mesh.[11] Polyethylene is osteoconductive in its porosity and composed of biologically inert aliphatic hydrocarbons. It is frequently used as the benchmark material in biocompatibility testing, so it offers a clear advantage in biocompatibility.[11] However, it has been shown to have a substantially higher infection rate than its alternatives, variously reported between 7% and 10%.[11,15,16] Bioactive glasses are available as custom-formed hardened implants or as particulate material that is malleable intraoperatively. They are inherently osteoinductive and osteoconductive but are more expensive and very difficult to reshape after hardening.[11]

Irrespective of allograft material, all stereolithographically preformed implants share the common disadvantage of requiring ionizing radiation exposure for high-resolution computed tomography scans to direct their construction. Preformed implants also are generally more expensive than biological reconstructions and require a second surgery for cranioplasty.[9,11]

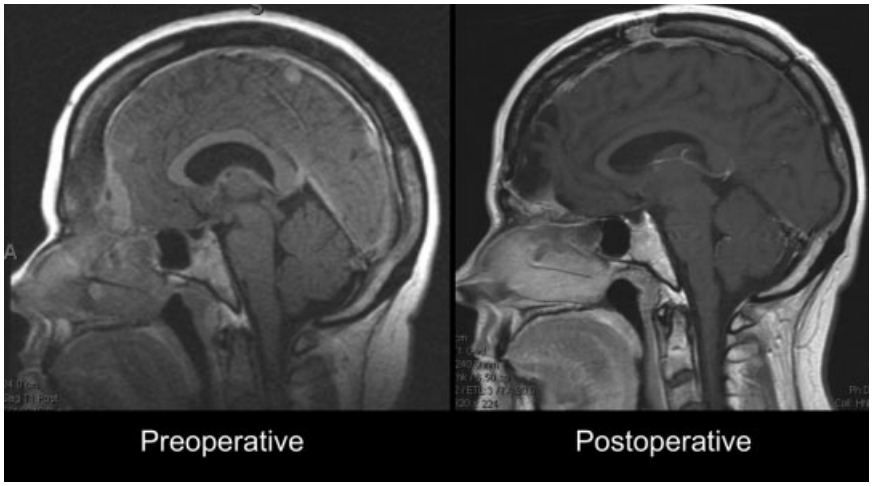

Fig. 5 Preoperative and 29-month postoperative sagittal contrast-enhanced magnetic resonance imaging of the head demonstrating postoperative absence of dural enhancement and expansion of the cerebrum into the space previously occupied by tumorous bone.

Biological Reconstructive Options

Various biological reconstructive options are available, none of which offer an uncompromising reconstructive solution. Heterotopic autograft, obtained from split-thickness local calvaria, rib, mandible, iliac crest, or tibia, eliminate the risk of immunologic reactivity or foreign body reaction.[11,14] However, donor site morbidity, increased surgical complexity, and graft site resorption render this option less desirable.[11,14,17] Calvarial allografts[18] and xenografts[14] eliminate the risk of donor site morbidity but offer suboptimal cosmesis and risk infection and immunologic reactivity that are unacceptable in light of the available alternatives. Demineralized bone matrix represents a newer option for custom in situ cranioplasty that offers the advantages of osteoconductivity and minimized infectious and immunologic reactivity risks.[11] However, it is relatively expensive and structurally weak until bony ingrowth is complete, so it is more suitable as an adjunct to a structural implant.[11] ►**Table 1** compares the various options used for calvarial reconstruction.

If the outer table of the patient's native bone flap is not compromised by erosion or exophytic hyperostosis, it is the option that is most likely to achieve a natural cosmetic appearance. To reimplant tumorous calvaria while achieving a Simpson grade 1 resection, one of four available sterilization

Table 1 Implant options

Category	Implant	Advantages	Disadvantages
Alloplastic			
	Titanium mesh	Commonly used, widely available, highly biocompatible	Unsuitable for large defect reconstruction due to malleability, suboptimal cosmesis
	Polymethyl-methacrylate	Commonly used, widely available, lightweight, rigid, relatively low cost, low thermal conductivity, not ferromagnetic, biologically inert	Not vascularized by or incorporated into adjacent bone (infectious risk), exposes patient to potentially toxic monomer, suboptimal cosmesis
	Hydroxyapatite	Malleable before hardening (cosmetic advantage), osteoconductive, resistant to infection	High cost, does not fully convert to bone (relatively brittle)
	Polyethylene	Osteoconductive, biologically inert	High infection rate
	Bioactive glasses	Available as preformed implant or as malleable particulate material, nearly cosmetically ideal when preformed from preoperative imaging	High cost, difficult to reshape preformed implants intraoperatively, preformed implant requires radiation exposure and second surgery
Biological			
	Xenograft	No donor site morbidity	Unacceptable risk of immune reaction and infectious agent transmission in light of other available options
	Heterotopic autograft	No risk of immune reaction	Donor site morbidity, suboptimal cosmesis
	Native autograft	Cosmetically optimal implant, cost effective, no risk of immune reaction	Requires sterilization of tumor cells

techniques may be considered: autoclaving, boiling, pasteurization, or extracorporeal irradiation.[4,17,19–25]

Autoclaving

The first report of autoclave sterilization of a tumorous calvarial flap was published in 1936.[26] Since then, authors have described autoclaving tumorous bone between 132°C and 135°C for 12 to 20 minutes at pressures between 0.1 and 0.2 MPa to achieve histopathologically proven tumor sterilization.[19,23–25] Autoclaving is a technique that has widespread availability, negligible expense, and logistic ease. It can easily be performed in most operative suites concurrently with tumor resection. Although autoclaving preserves the osteoconductive porous structure of bone,[24] it denatures structural proteins and can lead to substantial bone flap resorption.[24] This can compromise cosmetic outcome due to expansion of the kerf, reduce structural integrity of the flap by up to 23%,[17] and significantly reduce strain-to-failure moduli.[19] Although convenient, autoclaving may not be a prudent strategy for bone flap sterilization in cases where cosmetic outcome and structural integrity are paramount.

Boiling and Pasteurization

Boiling tumorous bone at 100°C has been shown to eliminate tumor cells but can significantly compromise its structural integrity.[19] Pasteurization represents a milder form of boiling the tissue; immersion in normal saline at 65°C for 30 minutes offers similar tumoricidal effects as boiling without the same degree of reduction in mechanical stability.[19,27] Although certainly a cost-effective universally available modality, one long-term study of reimplanted pasteurized femurs and tibias demonstrated 10-year graft survival rates of only 47.6%.[27] Hence for cosmetically important grafts, autoclaving or pasteurization may be inappropriate strategies for tumor eradication.

Extracorporeal Irradiation

Extracorporeal irradiation of tumorous bone offers key advantages over other available modalities. The graft material is native, so there is no risk of immunoreactivity, and the contour is cosmetically ideal. Because radiation does not grossly alter the graft structure, the irradiated material serves as an osteoconductive scaffold for bony healing, as demonstrated histologically in both human and animal studies.[28,29] Furthermore, extracorporeal irradiation does not carry the risks of structural damage and flap resorption associated with other intraoperative modalities of tumor sterilization such as autoclaving.[19]

Intraoperative extracorporeal irradiation for tumor eradication was first described by Spira and Lubin in 1968 as a limb-sparing strategy[30] and has since been further described in larger series for limb-sparing surgery.[7,31] Authors have reported exposing autologous grafts to between 50[7] and 30,000[22] Gy, but the optimal dose for intraoperative extracorporeal irradiation of bone has not been well established. Only two reports exist in the literature of this application to tumorous calvaria, and the authors used drastically different radiation doses (120 versus 30,000 Gy), with substantial resorption documented at the higher radiation dose.[17,22] Singh et al demonstrated in vitro histopathologically complete tumor sterilization at a dose of only 50 Gy, which suggests that lower doses may be adequate for tumor sterilization than have previously been used in vivo.[19] The effects of varying doses of radiation on osteoinductive proteins such as

Table 2 Tumor sterilization techniques for native autograft

Method	Technique	Advantages	Disadvantages
Heat			
	Autoclaving	Cost effective, easily performed	Compromises structural integrity, leads to resorption and poor cosmesis
	Boiling/Pasteurization	Cost effective, easily performed	Compromises structural integrity, leads to resorption and poor cosmesis
Irradiation			
	Extracorporeal Irradiation	Cosmetically superior to other options, possibly lower likelihood of resorption than with heat sterilization, proven effective since 1968 in orthopedic literature for limb-sparing procedures	Logistically more complicated and less cost effective to perform than heat sterilization

bone morphogenic protein are not understood but warrant further investigation. ►**Table 2** provides a comparison of available means of tumor sterilization from the tumor-laden calvarial flap.

Conclusion

Although expeditious and widely available, alloplastic reconstructive materials have various reconstructive disadvantages including poor cosmesis. Stereolithographically formed alloplastic implants represent a best attempt at approximation of the native calvarial flap's contour, but their cosmetic outcome is sometimes suboptimal, and they are associated with increased costs and added exposure to ionizing radiation. When meningiomas involve craniofacial structures that can significantly impact cosmetic outcome, such as the forehead frontal bone, intraoperative sterilization with immediate reimplantation is a prudent treatment strategy.

Intraoperative extracorporeal irradiation of tumorous calvaria has been nearly completely ignored in the neurosurgical literature despite its demonstrated efficacy in the nonneurosurgical literature. It offers substantial cosmetic and biological advantages over other sterilization techniques and can be performed by the radiation oncology team concurrently with surgical resection of the underlying mass. Extracorporeal irradiation is a prudent treatment strategy that should be considered for management of bone-invasive meningiomas.

References

1 Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 1957;20(1): 22–39
2 Pieper DR, Al-Mefty O, Hanada Y, Buechner D. Hyperostosis associated with meningioma of the cranial base: secondary changes or tumor invasion. Neurosurgery 1999;44(4):742–746; discussion 746–747
3 Bonnal J, Thibaut A, Brotchi J, Born J. Invading meningiomas of the sphenoid ridge. J Neurosurg 1980;53(5):587–599
4 Hong A, Stevens G, Stalley P, et al. Extracorporeal irradiation for malignant bone tumors. Int J Radiat Oncol Biol Phys 2001;50(2): 441–447
5 Uyttendaele D, De Schryver A, Claessens H, Roels H, Berkvens P, Mondelaers W. Limb conservation in primary bone tumours by resection, extracorporeal irradiation and re-implantation. J Bone Joint Surg Br 1988;70(3):348–353
6 Ozaki R, Hamada K, Emori M, et al. Limb salvage operation using intraoperative extracorporeal autogenous irradiated bone and tendon graft for myxoid liposarcoma on dorsum of foot. Foot 2010;20(2–3):90–95
7 Araki N, Myoui A, Kuratsu S, et al. Intraoperative extracorporeal autogenous irradiated bone grafts in tumor surgery. Clin Orthop Relat Res 1999;(368):196–206
8 Kuttenberger JJ, Hardt N. Long-term results following reconstruction of craniofacial defects with titanium micro-mesh systems. J Craniomaxillofac Surg 2001;29(2):75–81
9 Bloch O, McDermott MW. In situ cranioplasty for hyperostosing meningiomas of the cranial vault. Can J Neurol Sci 2011;38(1): 59–64
10 Moreira-Gonzalez A, Jackson IT, Miyawaki T, Barakat K, DiNick V. Clinical outcome in cranioplasty: critical review in long-term follow-up. J Craniofac Surg 2003;14(2):144–153
11 Goiato MC, Anchieta RB, Pita MS, dos Santos DM. Reconstruction of skull defects: currently available materials. J Craniofac Surg 2009; 20(5):1512–1518
12 Knöringer P. Long-term results of plastic skull repairs with acrylic resins [in German]. Zentralbl Neurochir 1979;40(3):197–202
13 Luparello D, Bruschi S, Verna G, et al. Cranioplasty with polymethylmethacrylate. The clinico-statistical considerations [in Italian]. Minerva Chir 1998;53(6):575–579
14 Chiarini L, Figurelli S, Pollastri G, et al. Cranioplasty using acrylic material: a new technical procedure. J Craniomaxillofac Surg 2004;32(1):5–9
15 Yaremchuk MJ. Facial skeletal reconstruction using porous polyethylene implants. Plast Reconstr Surg 2003;111(6):1818–1827
16 Cenzi R, Farina A, Zuccarino L, Carinci F. Clinical outcome of 285 Medpor grafts used for craniofacial reconstruction. J Craniofac Surg 2005;16(4):526–530
17 Manning MA, Cardinale RM, Schmidt-Ullrich RK, Kavanagh BD, Wornom IL III, Broaddus WC. Extracorporeal irradiation of tumorous calvaria. Case report. J Neurosurg 2000;93(3):494–497
18 Vanaclocha V, Bazan A, Saiz-Sapena N, Paloma V, Idoate M. Use of frozen cranial vault bone allografts in the repair of extensive cranial bone defects. Acta Neurochir (Wien) 1997;139(7):653–660
19 Singh VA, Nagalingam J, Saad M, Pailoor J. Which is the best method of sterilization of tumour bone for reimplantation? A biomechanical and histopathological study. Biomed Eng Online 2010;9:48
20 Hamaker RC, Singer MI. Irradiated mandibular autografts update. Arch Otolaryngol Head Neck Surg 1986;112(3):277–279
21 Lauritzen C, Alberius P, Santanelli F, Vällfors B, Lilja J, Stephensen H. Repositioning of craniofacial tumorous bone after autoclaving. Scand J Plast Reconstr Surg Hand Surg 1991;25(2):161–165
22 Lauritzen C, Kocabalkan O, Sugawara Y, Sahlin P, Olsson R. Reuse of tumorous calvarial bone after gamma irradiation. J Craniofac Surg 1998;9(5):459–463
23 Osawa M, Hara H, Ichinose Y, Koyama T, Kobayashi S, Sugita Y. Cranioplasty with a frozen and autoclaved bone flap. Acta Neurochir (Wien) 1990;102(1–2):38–41
24 Vanaclocha V, Sáiz-Sapena N, García-Casasola C, De Alava E. Cranioplasty with autogenous autoclaved calvarial bone flap in the cases of tumoural invasion. Acta Neurochir (Wien) 1997; 139(10):970–976
25 Wester K. Cranioplasty with an autoclaved bone flap, with special reference to tumour infiltration of the flap. Acta Neurochir (Wien) 1994;131(3–4):223–225
26 Naffziger HC. The restoration of defects in the skull: with special reference to the management of intrinsic tumors of the skull and certain types of localized osteomyelitis. Ann Surg 1936;104(3): 321–331
27 Koyanagi H, Matsumoto S, Shimoji T, et al. Long-term results from use of pasteurized bone. J Orthop Sci 2012;17(5):605–613
28 Sugimoto M, Takahashi S, Toguchida J, Kotoura Y, Shibamoto Y, Yamamuro T. Changes in bone after high-dose irradiation. Biomechanics and histomorphology. J Bone Joint Surg Br 1991;73(3): 492–497
29 Poffyn B, Sys G, Mulliez A, et al. Extracorporeally irradiated autografts for the treatment of bone tumours: tips and tricks. Int Orthop 2011;35(6):889–895
30 Spira E, Lubin E. Extracorporeal irradiation of bone tumors. A preliminary report. Isr J Med Sci 1968;4(5):1015–1019
31 Sabo D, Bernd L, Ewerbeck V, Eble M, Wannenmacher M, Schulte M. Intraoperative extracorporeal irradiation and replantation (EIR) in the treatment of primary malignant bone tumors [in German]. Unfallchirurg 1999;102(7):580–588