Extracorporeal irradiation of tumorous calvaria: a case series

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OBJECT When intracranial tumors invade the overlying skull, gross resection typically includes removal of the involved bone. Methods used to repair the resulting structural defect in the cranium include artificial prostheses, allogeneic bone grafts, and autoclaving the autologous graft. The authors have previously reported a case involving high-dose extracorporeal ionizing radiation to treat the tumorous calvaria intraoperatively, followed by reimplantation of the treated bone flap. In this paper the authors report the long-term follow-up of that case, as well as results of using extracorporeal irradiation of tumorous calvaria (EITC) for an additional 20 patients treated similarly.

METHODS The decision to undergo EITC was typically anticipated preoperatively, but determined intraoperatively, if upon inspection the bone flap was invaded by tumor. The bone flap was then delivered to the radiation oncology department, where a total dose of 120 Gy was delivered, using a clinical linear accelerator, over a period of approximately 15 minutes. After the intracranial tumor resection was completed, the irradiated craniotomy bone flap was reimplanted and the wound was closed in a standard fashion. A retrospective review of patients who had undergone EITC was performed for evidence of calvarial tumor recurrence or other complications.

RESULTS Since the originally reported case, 20 additional patients have received EITC during craniotomy for invasive tumors. Eighteen (86%) of 21 patients were diagnosed with meningioma: 12 (67%) with WHO Grade I, 5 (28%) with WHO Grade II, and 1 with WHO Grade III (6%). The remaining 3 patients presented with dural-based B-cell lymphoma with extensive adjacent bone invasion (n = 2) and metastatic adenocarcinoma of the lung (n = 1). Follow-up of the 21 patients ranged from 1 to 132 months, with a mean of 41 months and a median of 23 months. No patients have experienced tumor recurrence, infection associated with the treated calvaria, or evidence of bone flap resorption.

CONCLUSIONS Calvaria reconstructions represent an important component in structural and cosmetic outcome following craniectomy for tumorous bone. The authors' long-term experience with EITC has been excellent with no local tumor recurrence or complications. Therefore, EITC represents an excellent and efficient option for cranial reconstruction in such patients.

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KEY WORDS tumorous calvaria; extracorporeal irradiation; meningioma; oncology

WHEN intracranial tumors invade the overlying skull, gross resection typically includes removal of the involved bone. Methods used to repair the resulting structural defect in the cranium include artificial prostheses, autologous and allogeneic bone grafts, and autoclaving the autologous graft.^{8,23,29,31} Although each of these techniques can be well tolerated and produce good

cosmetic results, sterilizing and reimplanting the resected tumorous bone flap may provide optimum cosmetic result without immunological risk.^{29,31,33} The most widely reported technique for sterilizing a tumorous autologous bone graft is autoclaving, which destroys viable tumor cells, but may also denature proteins, increasing the likelihood of bone resorption.^{6,7,24,29–31} We have previously reported

ABBREVIATION EITC = extracorporeal irradiation of tumorous calvaria.

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a case using extracorporeal ionizing radiation to sterilize the tumorous calvaria intraoperatively, followed by reimplantation of the treated bone flap.¹⁷ In this paper we report the long-term follow-up of that case, as well as results of using extracorporeal irradiation of tumorous calvaria (EITC) for an additional 20 patients treated similarly.

Methods

After study approval by the Virginia Commonwealth University institutional review board, a retrospective chart review was performed. Clinical and demographic information was collected, as well as data from the following variables: rates of calvarial tumor recurrence, cosmetic results as determined by clinical examination, and bone resorption via imaging. The decision to perform EITC was typically anticipated preoperatively, but determined intraoperatively, if upon inspection the bone flap was invaded by tumor (Fig. 1). The bone flap was covered in wet gauze, wrapped to maintain sterility, and then delivered to the Radiation Oncology department. The bone flap was then inserted into the tray accessory mount on the clinical linear accelerator. One centimeter of bolus was placed above and below the bone flap and treatment was delivered with 6-MV photons to a total dose of 120 Gy prescribed to D_{max} (the maximum point dose). Treatment time was 7 minutes, with the total process taking approximately 15 minutes. After the intracranial tumor resection was completed, the irradiated craniotomy bone flap was reimplanted and the wound was closed in a standard fashion.

Results

Since the originally reported patient (Case 1), 20 additional patients have received EITC (Table 1). The mean age of these 21 patients was 55 years old (range 24–79 years old), with 8 male and 13 female patients. The follow-up period of the 21 patients ranged from 1 to 132 months,

FIG. 1. Case 6. **Left:** Preoperative axial T1-weighted MR image after contrast administration in a 51-year-old man with an incidentally discovered left temporal meningioma. The arrow indicates contrast-enhancing tissue within the temporal bone. Adjacent images (not shown) demonstrated extracranial growth of tumor with partial invasion of the temporalis muscle, a finding that was confirmed intraoperatively. **Right:** Axial T1-weighted MR image after contrast administration from the analogous location obtained 49 months postoperatively, demonstrating a section of the bone flap (arrow) that had undergone EITC with no recurrence or calvaria resorption.

with a mean of 41 months and a median of 23 months. No patients have experienced calvarial tumor recurrence, infection associated with the treated calvaria, or evidence of bone flap resorption (Figs. 1 and 2). As noted in Fig. 2, cranial flaps were sometimes less calcified than adjacent cranial bone by virtue of the prior presence of tumor involvement with reduction of bone calcium. One patient required reoperation for cranial hardware removal that was not related to EITC. This patient underwent postoperative local external beam radiation therapy for her dural lymphoma and subsequently suffered scalp atrophy, resulting in unacceptable protrusion of the cranial plating hardware. Eighteen (86%) of 21 patients were diagnosed with meningioma: 12 (67%) with WHO Grade I, 5 (28%) with WHO Grade II, and 1 (6%) with WHO Grade III. The remaining 3 patients presented with dural-based B-cell lymphoma with extensive adjacent bone invasion ($n = 2$) and metastatic adenocarcinoma of the lung ($n = 1$).

Discussion

We have performed EITC in 21 patients with a mean follow-up period of 41 months. Our results indicate no calvarial tumor recurrence, bone resorption requiring revision, or infection. The EITC procedure is feasible and can be performed in less than 20 minutes. Calvarial reconstruction in neurooncological surgery is an important component in structural and cosmetic outcome. However, managing tumor invasion of the calvaria can be challenging, especially when it involves the craniofacial or skull base region. Different options have been described, including artificial prostheses, autologous and allogeneic bone graft, and autoclaving the autologous bone graft.^{5,8,23,29–31}

Numerous publications have confirmed that autologous bone grafting is considered the standard means of cranial reconstruction and is associated with lower complication rates and better outcomes.^{4,9,12,13,18,22,27,28,34} The advantages of autologous grafting include the avoidance of foreign material implantation, which may lead to inflammatory response, donor graft rejection, and higher infection rates.^{1,35} Furthermore, because the patient's own calvaria is used, it may lead to better structural and cosmetic outcome, reduced operative time, and lowered cost.^{5,12,29–31,33} Autologous bone grafting options include heterotopic autologous bone graft and sterilized autologous bone graft. Heterotopic autologous bone graft requires harvesting of local unaffected calvaria, which may lead to donor site morbidity and increased operative time.^{29–31,33} The sterilized autologous bone graft technique destroys invaded tumorous cells and allows for reimplantation of the patient's calvaria flap.^{29–31,33} Traditionally, this has been accomplished by autoclaving the tumorous calvarial flap and was first described by Naffziger in 1936.¹⁹ Subsequent follow-up studies of this technique indicated no recurrence of tumor in the treated calvaria, but partial resorption was observed radiologically in 19% of the cases.^{29–31,33} Autoclaving has been shown to reduce torsional strength of up to 23% in mammalian diaphyseal bone.¹⁴ The structural degradation associated with autoclaving may compromise the structural integrity of the reimplanted autoclaved calvarial flap, although this has not been directly studied.

TABLE 1. Clinical and demographic data of patients undergoing EITC in chronological order of surgery

Case No.	Age at Surgery (yrs), Sex	Diagnosis	Follow-Up (mos)	WHO Grade	Comments
1	59, M	Meningioma	115.7	I	Died of esthesioneuroblastoma not associated w/ flap
2	43, F	Lymphoma	131.5		B-cell lymphoma, required hardware debridement
3	43, F	Meningioma	106.2	I	
4	39, F	Meningioma	111.7	I	
5	65, F	Lymphoma	68.6		Diffuse B-cell lymphoma
6	51, M	Meningioma	48.8	I	
7	67, M	Meningioma	43.9	II	
8	63, M	Meningioma	29.3	I	
9	66, F	Meningioma	32.3	I	
10	66, F	Meningioma	33.5	I	
11	33, F	Meningioma	19.9	I	
12	40, F	Meningioma	23.4	I	
13	24, F	Meningioma	19.3	I	
14	70, F	Meningioma	14.5	II	
15	51, M	Metastatic	13.3		Metastatic adenocarcinoma of the lung
16	67, F	Meningioma	12.4	I	
17	65, F	Meningioma	10.2	II	
18	66, M	Meningioma	3.7	II	
19	79, M	Meningioma	1.1	II	Died 1.1 mos postop
20	42, M	Meningioma	11.2	I	
21	54, F	Meningioma	2.6	III	

An alternative sterilization technique to autoclaving is the use of ionizing radiation. This technique has been described in the maxillofacial and orthopedic literature for malignant musculoskeletal tumors, where the involved tumorous bone is resected, irradiated extracorporeally, and reimplanted.^{3,6,10,11,15,21,25,32} Recently, long-term studies (mean follow-up range of 45–66 months) indicated no local tumor recurrence at the extracorporeally irradiated skeletal bone.^{2,3,6,21} Both animal and in vitro human studies directly comparing autoclaving with irradiation indicated a superior biomechanical profile and better incorporation of

the reimplanted bone with irradiation.^{6,7,24} When cadaveric bone flaps are used for implantation, they are irradiated to extremely high doses in the range of 1000–40,000 Gy to destroy antigens as well as infectious agents.²⁰ However, this can also denature structural proteins, which can impair mechanical integrity and promote demineralization or resorption of the treated calvaria.²⁰ In the setting of autologous bone flaps, a smaller dose of radiation, between 50 and 200 Gy, can provide complete tumor sterilization without the structural degradation caused by high-dose irradiation or autoclaving. Similar low doses between 50 and 300 Gy are also administered in orthopedic cases as described above. Animal studies utilizing intraoperative extracorporeal irradiation with lower doses have demonstrated excellent incorporation of the bone graft without structural integrity compromise.^{7,26,32} Extracorporeal irradiation to sterilize tumorous autologous bone graft has been successfully used in malignant musculoskeletal tumors. However, to our knowledge, there is only 1 report utilizing this technique in neurooncological pathologies,¹⁶ aside from our original prior case report.¹⁷ The study by Lauritzen et al. performed EITC in 4 patients with meningioma with a limited 1-year follow-up.¹⁶ All patients tolerated the procedure well with no recurrence, but 1 patient did require revision of the bone flap due to resorption. The current study is a larger case series of 21 patients with a longer mean follow-up period of 41 months, with no complications or calvarial tumor recurrences. The main limitation of this study is the length of the follow-up period. The majority of the cases (57%) were WHO Grade I meningiomas, which have an inherently low recurrence

Fig. 2. Case 9. Coronal (left) and axial (right) CT scans with bone window settings obtained 24 months after surgery, demonstrating no significant resorption beyond that caused by the original bone invasion. Arrows delineate edges of the bone flap.

rate. Furthermore, calvarial resorption may take multiple years to become apparent. Therefore, a longer follow-up period may be necessary to determine the long-term outcome of EITC. Future studies investigating EITC in more aggressive pathologies and with longer follow-up periods are recommended.

Conclusions

Calvaria reconstruction following craniectomy for tumorous bone represents an important component in structural and cosmetic outcome. Our long-term experience with EITC has been excellent with no local tumor recurrence or complications. We believe that it represents an excellent and efficient option for cranial reconstruction in such patients.

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Administrative/technical/material support: Broaddus, Tavanaiepour. Study supervision: Broaddus.

Supplemental Information

Previous Presentation

Part of the results section of this manuscript was previously presented as an abstract poster at the 2011 CNS Annual Meeting in Washington, DC.

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