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1 **Custom surgical management of invasive malignant tumors of the scalp**

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Short running head: Surgery of invasive cancers of the scalp

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28 **ABSTRACT**

29 **Background:** There is no universal management protocol concerning invasive malignant tumors of
30 the scalp with bone and dura mater invasion. The aim of this study was to report and discuss our
31 experience in the management of these forms of tumors.

32 **Methods:** We retrospectively reviewed all consecutive patients of microsurgical scalp reconstruction
33 performed after resection of invasive cutaneous malignancies of the scalp, calvarium and dura mater
34 from 2017 to 2019, at Pitié-Salpêtrière University Hospital (Paris, France).

35 **Results:** Five patients met inclusion criteria. There were 3 squamous cell carcinomas and 2
36 undifferentiated sarcomas. Mean age at surgery was 63.6 years. The sex ratio male/female was 4. Two
37 received radiation prior to resection and 2 patients had a history of prior scalp tumor surgery. All the
38 patients underwent craniectomy and the mean cranial defect size was 41cm². Cranioplasty was
39 performed in one patient. Soft tissue coverage was provided by free tissue transfer of latissimus dorsi
40 muscle in all patients. In 4 patients, split-thickness skin graft was performed in a second surgical stage
41 few weeks later. There were no intraoperative complications and no complications into the donor site
42 for the tissue transfer or the skin graft. Two patients had flap necrosis that healed after a new free flap
43 of latissimus dorsi.

44 **Conclusions:** Wide resection with craniectomy, and reconstruction with microvascular free tissue
45 transfer provides safe and reliable treatment of recalcitrant invasive scalp skin cancers. The surgical
46 management of these complex patients is a challenge that must be conducted by trained, experienced
47 and multidisciplinary teams.

48

49 **KEYWORDS**

50 craniofacial microsurgery,

51 cranioplasty,

52 cutaneous malignancy,

53 free tissue transfer,

54 microsurgical reconstruction,

55 neurosurgery.

56 INTRODUCTION

57 Few data are available in the literature concerning scalp invasive malignancies and their
58 surgical care (excision and reconstruction after large and complex resection of calvarium). Tumor
59 excision with scalp and bone invasion can be a surgical challenge due to the size and the invasiveness
60 of the tumor. Likewise, calvaria reconstruction after excision can be also challenging and is generally
61 performed using skin grafts or large flap depending on the defect size. However, there is no universal
62 management protocol for these forms of tumors. When they are invasive, craniectomy and dura mater
63 excision may be required to obtain full tumor excision, which exposes the patient to a risk of
64 cerebrospinal fluid leak and infection. After these procedures, there is no consensus on the need of
65 cranioplasty after microsurgical reconstruction of the skin.

66 Reconstruction scalp and skull defect resulting from tumor excision present most difficulties
67 for the surgeon. Wide excision may include skin, periosteum, skull and dura mater, creating a complex
68 wound. The use of radiation therapy and chemotherapy can compromise healing and scalp's
69 vascularization. Flaps used for reconstruction should be durable to support adjuvant treatment. In
70 1972, free tissue transfer for reconstruction of large scalp defect was used for the first time, with an
71 omentum flap to cover the defect [15]. Since then, other series have demonstrated the efficacy of this
72 approach [16, 23]. The aim of the present study was to report and discuss our experience in the
73 management of invasive malignant tumors of the scalp with bone and dura mater invasion.

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76 PATIENTS AND METHODS

77

78 *Patients recruitment*

79 We retrospectively reviewed all consecutive patients of microsurgical scalp reconstruction
80 performed after resection of invasive cutaneous malignancies of the scalp, calvarium and dura mater
81 from February 2017 to July 2019, at Pitié-Salpêtrière University Hospital (Paris, France).

82 Presurgical evaluation included: complete general and neurological examination, brain MRI
83 and CT-scan, body scanner and in some cases body positron emission tomography (PET). These data

84 were analyzed by a multidisciplinary team, including plastic surgeon, neurosurgeon, anesthetist,
85 oncologist, radiotherapist, dermatologist and radiologist, to determine whether surgical treatment was
86 indicated and whether a postoperative treatment would be required.

87

88 *Classification of comorbidities and outcomes*

89 Patient's data were collected through review of medical records. Current smoking was defined
90 as smoking within 2 months of surgery. Hypertension and hyperlipidemia were defined by the use of
91 antihypertensive and cholesterol-lowering drugs, respectively. Diabetes was defined by the use of oral
92 hypoglycemic drugs or insulin. Immunosuppression was defined by use of immunosuppressive drugs
93 or diagnosis known to cause an immunocompromised state. Patient's preoperative physical status was
94 classified using the American Society of Anesthesiologists (ASA) score. Patients with a mild systemic
95 disease were classified as ASA II. Patients with a systemic disease which is not incapacitating were
96 classified as ASA III, and patients with an incapacitating systemic disease which is life-threatening
97 were classified as ASA IV.

98 Measurement of skull defects were performed on postoperative CT-scans. Patients were
99 carefully followed to ensure that no complications were missed. Cerebral spinal fluid (CSF) leak was
100 defined by the presence of fluid collected from the operative site. Partial flap loss was defined as flap
101 necrosis that resulted in subtotal loss of flap, while complete flap loss was defined as requiring total
102 flap replacement.

103

104 *Standard Protocol Approvals, Registrations and Patient Consents*

105 The database is registered with the *Commission Nationale de l'Informatique et des Libertés* (n°.
106 2214386). In accordance with the ethical standards of our hospital's institutional review board, the
107 Committee for the Protection of Human Subjects, and French law, written informed consent was not
108 needed for demographic, physiological and hospital-outcome data analyses because this observational
109 study did not modify existing diagnostic or therapeutic strategies; however, patients were informed of
110 their inclusion in the study. The manuscript was prepared in accordance with the Strengthening the
111 Reporting of Observational studies in Epidemiology (STROBE) statement.

112 RESULTS

113

114 *Patient characteristics*

115 We found 5 patients who underwent resection followed by reconstruction surgery for invasive
116 malignant tumors of the scalp extending into the calvarium and the dura mater. Mean age at surgery
117 was 63.6 ± 9.2 years (range 35-84). The sex ratio male/female was 4. Preoperative patient
118 comorbidities are summarized in [Table 1](#). The mean follow-up period was 19 (range 7-36) months.

119

120 *Tumor characteristics and surgical management*

121 Of the 5 patients included in the study, 3 had stage IVA squamous cell carcinomas and 2 had
122 sarcomas (one grade III undifferentiated sarcoma and one low-grade myofibroblastic sarcoma). The 3
123 patients with squamous cell carcinomas presented both clinical and histological poor prognostic
124 factors according to the National Comprehensive Cancer Network (NCCN, USA) classification [18].
125 Two patients were treated by radiation therapy prior to resection (#1 and #2) and 2 patients had a
126 history of prior scalp tumor surgery (#1 and #5). None of the patients had adjuvant lymph node
127 excision.

128 Two patients had active scalp infections at the time of presentation: one had methicillin-
129 resistant *Staphylococcus aureus* (MRSA) plus *Proteus mirabilis* plus *Enterococcus Faecalis* extra- and
130 subdural empyema with skull necrosis that required surgical evacuation and intravenous antibiotics
131 prior to reconstruction surgery (#1, [Fig. 1 a, b](#)), and the second one had methicillin-susceptible
132 *Staphylococcus aureus* superficial infection treated with oral antibiotics (#4, [Fig. 2 a-c](#)). Three patients
133 had tumor-related cerebral venous thrombosis before surgery: two had partial superior sagittal sinus
134 thrombosis (#2 and #4, [Fig. 2 a](#)) and had one cortical vein thrombosis (#1, [Fig. 1 A](#)) that needed
135 postoperative anticoagulation therapy.

136 All patients underwent wide scalp resection, craniectomy and dural electrocoagulation ([Table](#)
137 [2](#)). The mean cranial defect size was 41 cm^2 (3.4 - 155). The 3 patients who had a dural resection
138 required primary dural repair. Cranioplasty was performed on the same surgical stage in one patient
139 (#2, [Fig. 3 c](#)). Soft tissue coverage was provided by free tissue transfer of latissimus dorsi muscle in all

140 patients (#1, Fig. 1 c, e; #2, Fig. 3 d; #3, Fig. 4 e). The recipient vessels were the superficial temporal
141 artery and vein in all patients. Mean surgical duration was 7.3 (range 5 - 10.5) hours. Mean
142 intraoperative blood loss was 780 (range 400 - 1500) ml. In 4 patients (80%) split-thickness skin graft
143 was performed in a second surgical stage few weeks later (Fig. 1 d, e; Fig. 3 d; Fig. 4 e).

144

145 *Postoperative management*

146 In the postoperative period, all patients underwent CT-scan to detect potential early
147 intracranial bleeding and then received subcutaneous heparin. Four patients had been staying for only
148 24 hours in the intensive care unit, and one patient had been staying for 7 days (#1). The median total
149 days of hospitalization was 9 (range 8 – 35) days. Four patients were discharged home and 1 was
150 discharged to a rehabilitation center before returning home.

151 Patients operated on for squamous cell carcinomas did not receive any adjuvant treatment,
152 while adjuvant radiotherapy has been performed in patients with sarcoma. A patient with systemic
153 metastases of sarcoma (#3) received additional chemotherapy (adriamycin 60mg/m²). Of the 5
154 patients, 1 patient who experienced an early local tumor recurrence died 7 months after surgery (#4),
155 and 1 patient died within 10 months of surgery because of multiple systemic metastases (#3). The
156 remaining 3 patients had no recurrence at 12, 34 and 36 months after the surgery, respectively.

157

158 *Complications*

159 There were no intraoperative complications and no complications into the donor site for the
160 tissue transfer or the skin graft. All free tissue transfers achieved 100% soft tissue coverage.
161 Postoperative complications included one CSF leak that required lumbar punctures (#2). Two patients
162 had flap necrosis due to arterial thrombosis (#3 and #5) 7 and 3 days after surgery respectively, that
163 healed after a surgical management consisting of a new free flap of latissimus dorsi. One patient
164 experienced flap dehiscence (#4) which was treated using topical skin care. There were no
165 complications in the 4 patients who had skin grafts.

166

167

168 **DISCUSSION**

169

170 The common cutaneous neoplasms of the scalp (squamous cell carcinoma, basal cell
171 carcinoma, and malignant melanoma) are usually successfully treated with soft tissue excision, and
172 scalp reconstruction using primary repair, local flaps or skin grafting [2, 17]. All of our patients
173 showed invasion of their cutaneous malignancies into the cranium. This was evidenced preoperatively
174 on imaging and confirmed intraoperatively. These patients were first recused by other local or regional
175 hospitals because of the risk of postoperative complications and then referred to our tertiary center.
176 Reconstruction was considerably challenging in these patients given their tumor size, and because the
177 quality of the surrounding tissue was compromised by prior surgery, radiation or infection. Our
178 management of these cutaneous malignancies of the scalp with deep invasion was therefore guided by
179 the balance between obtaining clear surgical margins while avoiding neurological complications. A
180 multidisciplinary approach has been successful in achieving complete surgical excision and immediate
181 single-stage soft tissue reconstruction.

182 Post-operative defect was covered by free tissue transfer of latissimus dorsi muscle with split-
183 thickness skin graft. Other flap techniques such as rectus abdominis muscle or antero-lateral thigh
184 were also eligible. However, free flaps are optimal for reconstruction of large skin defects [9]. In cases
185 which require postoperative irradiation, free flap might be more reliable than local pedicle flaps.
186 Furthermore, the skin graft at the donor site may not tolerate postoperative irradiation [6, 8, 16].
187 Latissimus dorsi muscle is a large, broad and flat muscle providing stable soft tissue coverage,
188 particularly if additional scalp needs to be resected in order to remove substrate for potential tumor
189 recurrence [20]. The thoracodorsal artery and the thoracodorsal vein collected with this flap are of
190 ideal caliber and length to perform the microsurgical vascular anastomosis [19]. The latissimus dorsi
191 muscle flap also has the advantage of mimicking native scalp thickness and contour. Although
192 secondary to the control of the malignancy, the aesthetic result of the reconstruction is an important
193 consideration. Free flaps achieve good aesthetic results both in non-hearing and hearing areas [13].

194 Complications after surgery for reconstruction of scalp and calvaria in skin cancers are
195 frequent.[24] They are more frequent when skin cancer involves bone and dura mater, and

196 complications include CSF leak, sinus and cortical veins thrombosis, and neurological impairment.
197 Our patients had voluminous and invasive tumors, and had poor general health condition and serious
198 comorbidities, that can explain the high rate of flap necrosis. The two cases of flap loss requiring
199 revision surgery occurred in patients with poor general status and active smoking, the latter being a
200 well-known risk factor for complication after free flap tissue transfer.[3, 7, 22] Special attention
201 should therefore be paid to smoking patients in the postoperative period. We recommend a systematic
202 intervention for smoking cessation before the surgery.[4] Moreover, chronic use of corticosteroids
203 does not increase rates of wound complications, reoperation, or readmission. However, this population
204 of patients may be at increased risk for major bleedings requiring blood transfusion following free flap
205 reconstruction.[25] Superior longitudinal sinus thrombosis can occur especially in patients with
206 tumoral involvement of the dura mater and requires pre- and/or postoperative anticoagulation therapy.
207 Finally, patients whose surgery is delayed have a poor prognosis, suggesting that early detection and
208 treatment are crucial.[1]

209 Despite flap loss in two of our patients, we obtained local healing after surgical revision. The
210 three other patients are currently in remission. Given the severity of the initial clinical presentation,
211 these outcomes can be considered as good. Indeed, oncological and esthetical benefits were major in
212 patients with no other therapeutic resources. Our experienced, shared by other teams, with these
213 advanced lesions is that even when resection is likely to be incomplete because of either sagittal sinus
214 involvement or the magnitude of the lesion, palliative resection and reconstruction are worth
215 considering [10, 14]. We therefore advocate for an aggressive and customized surgical management
216 involving multidisciplinary collaboration and strategic thinking.

217 For patients with large skull defects, the indications for cranioplasty are both functional, in
218 terms of cerebral protection, and aesthetic, to maintain the contour of the calvarium. Nevertheless,
219 performing a cranioplasty during the immediate reconstruction remains controversial, because it
220 increases the risk of postoperative infection while it does not require a second surgery. In our series,
221 we performed immediate cranioplasty in only one patient who experienced no serious postoperative
222 adverse events. The other patients presented exophytic ulcerated tumors with concomitant
223 contamination or infection, that are contraindications for subsequent cranioplasty. In a study

224 evaluating alloplastic cranioplasty, an infection rate of 40% was reported when calvarium was
225 reconstructed with cranioplasty in the same surgical stage [5]. Several studies reported high
226 complication rates (from 33 to 57%), when cranioplasty was performed during the immediate
227 reconstruction, which required in most cases the removal of the prosthesis [1, 3, 21]. However, these
228 studies were not exclusively on patients with cranial defects due to resection of malignant tumors.
229 Regardless of this, the higher complication rates reported in all studies about concomitant cranioplasty
230 and scalp reconstruction have to be considered with caution. Several factors appeared to be important
231 in these complications: the presence of residual devascularized or infected bone after excision,
232 inadequate coverage of the cranioplasty with well-vascularized free tissue, and the nature of the
233 material used for the cranioplasty [11, 14]. Preoperative and intraoperative recognition of the extent of
234 the bony abnormality appears therefore fundamental to guide both tumor resection and cranioplasty.
235 Cho et al. reported 11 cases of reconstruction without cranioplasty for recalcitrant invasive skin cancer
236 of the scalp and proposed to avoid cranioplasty during the immediate reconstruction [5]. Moreover, in
237 the Bethesda Cranial Facial Reconstruction Protocol delayed skull reconstruction resulted in a lower
238 complication rate than previously described [12]. This approach is based on the two major advantages
239 theoretically provided if cranioplasty is avoided at first excision. First, as seen in patients without
240 dural repair, having a vascularized graft immediately on the dura mater can limit the creation of
241 epidural fluid collections [12]. The second advantage of delaying cranioplasty is evidenced in patients
242 who underwent dural repair using xenograft material and in whom the contact with a well-vascularized
243 flap seemed to aid in healing and decreased CSF leaks [5]. Finally, although experience with
244 cranioplasty is limited, the use of titanium mesh satisfies our requirements of a malleable but sturdy
245 implant, which can be fixed rigidly.

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252 **CONCLUSION**

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254 Wide resection with craniectomy, and reconstruction with free tissue transfer with or without
255 cranioplasty provide safe and reliable treatment for invasive malignant tumors of the scalp. The free
256 tissue transfer of latissimus dorsi muscle is the mainstay to cover complex scalp defects and tolerate
257 radiation. The place of cranioplasty during the immediate reconstruction remains controversial and is
258 still debated. Anyhow, the surgical management of these complex patients is a challenge that must be
259 conducted by trained, experienced and multidisciplinary teams comprising neurosurgeons, plastic
260 surgeons and dedicated anesthetists.

261

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264

265 **Conflict of Interest:**

266 All authors certify that they have no affiliations with or involvement in any organization or entity with
267 any financial interest (such as honoraria; educational grants; participation in speakers' bureaus;
268 membership, employment, consultancies, stock ownership, or other equity interest; and expert
269 testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional
270 relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this
271 manuscript.

272

273 **Ethical approval:**

274 All procedures performed in studies involving human participants were in accordance with the ethical
275 standards of the institutional and/or national research committee (name of institute/committee) and
276 with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

277

278 For this type of study formal consent is not required.

279 Informed consent was obtained from all individual participants included in the study.

280 **Patient photographic authorization:**

281 All patients included in this study had given photographic authorization.

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391 **FIGURE LEGENDS**

392

393 **Fig. 1 (patient #1)**

394 A 35-year-old man with a history of sarcoma (diagnosed in 2000 in Algeria with 5 resection surgeries
395 between 2000 and 2017), arrived in France in July 2017. He presented a wide skin, bone and dura
396 mater damage (**a and b**) with a left extra and subdural empyema (**a**). A three-stage surgical
397 management was performed. First, skin and pericranium resection with craniectomy and empyema
398 evacuation have been performed. Postoperatively, intravenous antibiotics and anticoagulation therapy
399 were started to treat both empyema and a cortical vein thrombosis. The second surgical stage was the
400 reconstruction of cranial and skin defects, using a free flap of latissimus dorsi muscle (**c**), performed
401 one month after the first surgical time. Finally, two weeks after the second surgical stage, a skin graft
402 (donor-site was anterior thigh face) allowed to cover the flap (**d**). Lateral view of follow-up at 6 weeks
403 demonstrating stable soft tissue coverage (**e**).

404

405 **Fig. 2 (patient #4)**

406 A 70-year-old man who developed recurrent invasive squamous cell carcinoma after
407 immunosuppression for living-related kidney transplant. Preoperative T1-weighted magnetic
408 resonance imaging (**a**) and CT scan (**b**) show an ulcerated tumor with invasion through the scalp into
409 the cranium with superior longitudinal sinus tumoral involvement (**c**). Scalp and calvarial defect after
410 wide local excision (**d**). A large Surgicel sheet was used to repair the dural defect (**d**). The defect was
411 then reconstructed by a latissimus dorsi muscle free flap.

412

413 **Fig. 3 (patient #2)**

414 A 61-year-old woman, with a long history of recurrent squamous cell carcinoma (diagnosed in 2012,
415 treated by chemotherapy and radiotherapy between 2012 and 2015, with follow-up break between
416 2015 and 2017) arrived in September 2017. She presented a wide skin, bone and dura mater damage
417 with tumor invasion of the superior longitudinal sinus (**a**). We performed skin (**b**), bone (**c**) and dura
418 mater excision. In the same time, the defect was reconstructed with tailored titanium cranioplasty (**c**)

419 and free flap of latissimus dorsi muscle. The patient had a little CSF leak after surgery resolved with
420 lumbar punctures. After three weeks, a skin graft (donor-site was antero-internal thigh face) allowed to
421 cover the flap. View of follow-up after free latissimus dorsi muscle flap with split-thickness skin graft
422 and postoperative radiation (**d**).

423

424 **Fig. 4 (patient #3)**

425 A 68-year-old man presented in February 2018 with a giant retro-auricular left undifferentiated
426 sarcoma (diameter was 29 cm) involving skin, bone and dura mater (**a and b**). A preoperative
427 embolization was performed to limit bleeding during the surgery. Two days after embolization,
428 resection surgery was achieved (**c and d**). The defect was reconstructed in the same time with a free
429 flap of latissimus dorsi muscle. Patient had a flap necrosis, one week after surgery, requiring a revision
430 surgery with a new latissimus dorsi muscle free flap. This second surgery led to local healing (**e**).

431

432