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Is Three-Dimensional Virtual Planning in Cranial Reconstruction for Advanced Cutaneous Squamous Cell Carcinoma of the Skull a Feasible Option?

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Background: Cutaneous squamous cell carcinoma (cSCC) is a common type of malignant skin disorder. An uncommon feature is local bony invasion, as can rarely be seen in lesions on the scalp. The optimal treatment strategy in these rare cases is still under debate.

Objective: The aim of this case report is to present a 1-stage three-dimensional planned surgical resection and reconstruction of a cSCC with bony invasion into the scalp and to discuss the alternative options and potential pitfalls.

Materials and methods: A patient diagnosed with rT4N0M0 cSCC of the scalp underwent a cranial resection and reconstruction in 1 stage. With the use of computer-assisted design and computer-assisted manufacturing a patient-specific implant (PSI) of poly (ether ether ketone) was manufactured. After the PSI was inserted, it was covered with a latissimus dorsi muscle and a split-thickness skin graft.

Results: Intraoperatively the resection template generated an accurate resection and accurate and fast placement of the PSI. The reconstruction had a clinical satisfactory esthetic result, but was hampered by the development of a small wound dehiscence was observed over the postoperative course.

Conclusion: Three-dimensional planned resection and reconstruction for composite defects of the skull after resection of a cSCC of the scalp with bony invasion may lead to an accurate and predictable resection and accurate and fast placement of the PSI. However, patient specific characteristics should be considered to assess potential risks and benefits before opting for this one-stage treatment strategy.

Key Words: cranial reconstruction, craniectomy, cranioplasty, cutaneous squamous cell carcinoma, implant, latissimus dorsi flap, poly (ether ether ketone)

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Actinic keratosis is a high prevalence premalignant skin disorder. Commonly, the affected area shows multiple undefined erythematous scaling papules or plaques of 1 to 3 mm. Due to the variable and nonspecific clinical presentation, diagnosis and treatment are frequently delayed. Untreated actinic keratosis may develop into malignant cutaneous squamous cell carcinoma (cSCC).[1]

Cutaneous squamous cell carcinoma is a common type of skin cancer with a high prevalence, especially in elderly and in immunosuppressed patients.[2–4] Cutaneous squamous cell carcinoma presents mostly on sun exposed surfaces of the skin such as the underarm, face, and scalp. The preferred location is the external ear and lower lip.[3,5] Cutaneous squamous cell carcinoma initially starts with an asymptomatic painless, rough patch of the skin which may progress into an ulcerated tumor with radial spread at diagnosis.[6,7]

For cSCC in general, but also for lesions located on the scalp, local bony invasion remains an uncommon feature. When the cranium is affected, there is no consensus about the optimal treatment strategy (radiotherapy vs. surgery).[8] In case of surgery, reconstruction of these composite defects by cranioplasty in addition to soft tissue reconstruction may be recommended because of better protection of the brain, increase of psychosocial aspects, and improvement of esthetic outcome.[9–13] Time interval between diagnosis and surgery in case of craniectomy for cSCC, allows for preoperative digital surgical planning. This gives the surgeon the opportunity for three-dimensional (3D) planned cranial resection and symmetric reconstruction of the cranial vault in 1 stage. Besides the most important advantage of saving the patient additional

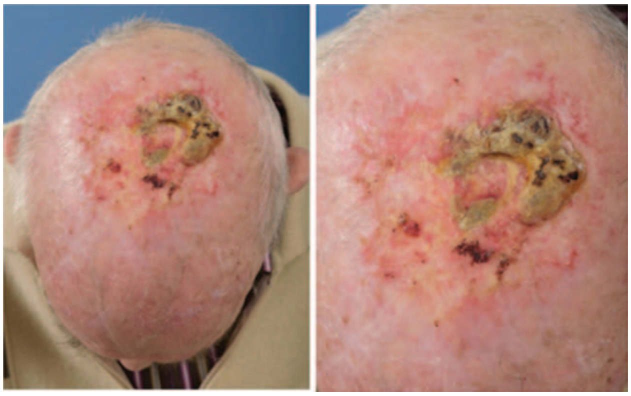

FIGURE 1. Clinical presentation of the ulcerated and crusted lesion on the scalp with a diameter of 7 cm and centrally exposure of the underlying cranial bone.

surgical procedures, it may also help to achieve more accurate and predictable resection margins.

The aim of this case presentation is to demonstrate a 1-stage 3D planned surgical resection and reconstruction of a recurrent cSCC of the scalp with bone invasion, followed by discussion of alternative options and potential pitfalls.

MATERIALS AND METHODS

Clinical Presentation

An 82-year old Caucasian fair skinned male visited the department of Head and Neck Surgery and Oncology with complaints of an itchy and tender red, scaling, and nonhealing skin of the scalp since 4 months.

The patient had undergone multiple surgical procedures for a cSCC of the scalp, after which he underwent external beam radiation therapy (20 × 3 Gy) 2 years before presentation because of a recurrent lesion. Furthermore, the medical history of the patient included hypertension and Waldenstrom macroglobulinemia.

At physical examination a crusted and ulcerated lesion with a diameter of approximately 7 cm was observed. Centrally of the ulceration the underlying bone of the tabula externa was visible (Fig. 1). The principal clinical diagnosis was osteoradionecrosis of the skull; however, biopsy demonstrated a recurrent cSCC.

Standard work-up included a computed tomography (CT) scan and magnetic resonance imaging (MRI), demonstrating an osteolytic defect of the tabula externa and interna suspected of bony invasion without dural involvement (Fig. 2). Regional and distant metastasis were excluded by an ultrasound of the regional lymph nodes and 18-fluorodeoxyglucose positron emission tomography - computed tomography. Extension of the radial spread was evaluated by dermatoscopy combined with mapping by multiple histological tissue sampling. The tumor was staged as a rT4aN0M0 cSCC according to the AJCC Cancer Staging Manual, 8th edition.[14]

FIGURE 2. (A) Axial and (B) coronal slides of the computer tomography demonstrating bone invasion. (C) Magnetic resonance images excluded dural involvement.

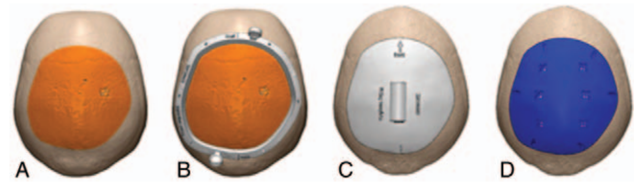

FIGURE 3. The 3-dimensional virtual planned resection and reconstruction with a poly (ether ether ketone) cranioplasty. (A) Segmentation of the tumor; (B) design of the resection template; (C) design of the control template; and (D) design of the cranioplasty.

A total resection was indicated with direct reconstruction of the cranial defect. The reconstruction was planned with a cranioplasty of poly (ether ether ketone) (PEEK) covered by a free latissimus dorsi (LD) muscle-only flap and a split skin graft of the anterolateral thigh to cover the muscle.

Preoperative Planning

For the preoperative planning a CT scan of the neurocranium using the Siemens Somatom Definition Flash (Siemens Healthcare, Erlangen, Germany) (AS +, 120 kV, 179 mAs, 512 × 512 matrix size, 0.6 mm slice thickness, kernel D [hard-tissue]) was performed. On the CT-scan segmentation of the tumor, including a bony margin of 1 cm around the osteolytic defect was performed (Fig. 3A). Using MedX (Xilloc Medical B.V., Geleen, The Netherlands) software, a resection template and cranioplasty were designed (Fig. 3B and D). For final intraoperative adjustments and to ensure a perfect fit of the cranioplasty, a control template was also constructed (Fig. 3C).

In the design, navigation landmarks for positioning of the resection template were incorporated. The resection template and control template were 3D printed in nylon using selective laser sintering. The cranioplasty was milled of PEEK (Xilloc Medical BV, Geleen, the Netherlands).

Surgical Procedure

Preoperatively 2 g cefalozin was administered intravenously and continued during the surgical procedure 1 g every 4 hours. The patient was placed in right lateral position with the head fixated with the Mayfield clamp. Navigation (Brainlab, Munich, Germany) for the perfect position of the resection template was calibrated and installed. After this, a sterile operation field was created according to normal procedures.

Phase I: Tumor Resection

The soft tissue outline of the cSCC including at least 1 cm free margin was marked and the skin incision was performed. After the skin incision, a careful subperiosteal dissection was performed to allow proper positioning of the resection template (Fig. 4A). Periosteal attachment around the region of bony invasion was maintained.

The resection template positioning was controlled with the use of navigation and fixed with 4 screws of 6 mm into the skull. Four burr holes, 2 frontal and 2 parietal, were prepared and the craniectomy was performed guided by the resection template (Fig. 4B and C). With the use of the control template adjustments were made to allow a proper fit of the patient-specific implant (PSI) of PEEK in a later stage of the surgical procedure.

Phase II: Dissection of Temporal Artery and Vein Simultaneous with Harvesting of the LD Flap

After tumor resection, dissection of a free LD flap with the thoracodorsal artery as vascular pedicle was performed. Simultaneously, the superficial temporal artery and external jugular vein

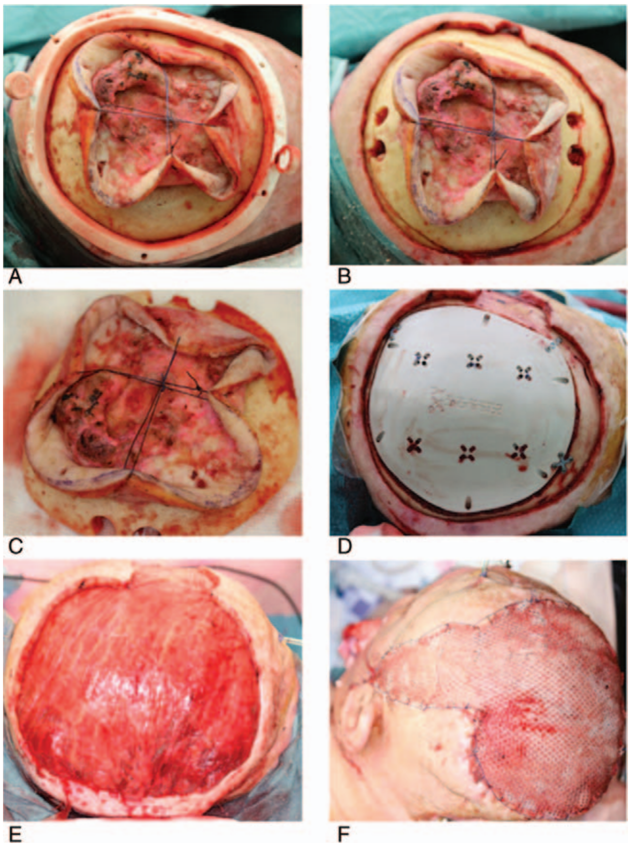

FIGURE 4. (A) The navigation guided positioning of the resection template.(B and C) The craniectomy performed guided by the resection template with 2 burr holes anterior and posterior.(D) Definite placement of the patient-specific implant.(E) Vest-over-pants inset of the free latissimus dorsi muscle-only flap covering the implant and implant-bone interface.(F) Coverage of the latissimus dorsi muscle with a meshed split-thickness skin graft of the anterolateral thigh to allow for epithelization.

were dissected and prepared as recipient vessels for arterial and venous anastomosis of the vascular pedicle after free tissue transfer.

Phase III: Reconstruction of the Skull

Before definite placement of the PSI, 6 absorbable dural suspension sutures were placed to fix the dura to the PSI. Thereafter, the PSI could be positioned and fixed to the skull with osteosynthesis material (KLS Martin Group, Tuttlingen, Germany) and 10 screws of 5 mm (Fig. 4D).

After fixation of the PSI, the free LD flap could be detached from its vascular pedicle and transferred to the skull. It was ensured that the PSI was completely covered by the LD flap. A vest-over-pants inset[15] was used to prevent bone exposure at the flap–scalp junction and increase the distance between the implant and wound edges (Fig. 4E). The vascular pedicle was anastomosed to the recipient vessels and perfusion of the flap was controlled with Doppler ultrasonography.

Coverage of the LD flap was performed with a split-thickness skin graft from the anterolateral thigh, which was meshed (1:1.5) (Fig. 4F). A local wound dressing was applied.

Postoperative Course and Histology

After 2 days the head bandage was removed. The LD flap remained vital. There were no neurological complications in the direct postoperative course.

FIGURE 5. (A and B) Postoperative situation 4 months after surgery with a symmetric reconstruction of the cranial vault, which will improve as further atrophy of the muscle continues. (C) Unfortunately, there is a stable dehiscence over the implant, showing on the right posterolateral side of the skull. It might be safer to perform the surgery in 2 phases, to prevent this complication.

On the 14th postoperative day, the patient collapsed and sustained direct head trauma without loss of consciousness. Neurological examination was unremarkable. A hematoma between the implant and the LD flap occurred. No surgical intervention was initiated and the hematoma resolved partially. Unfortunately a wound dehiscence of 1 cm $\times$ 2 cm was observed on the most distal aspect of the muscle flap where the hematoma sustained. This area was debrided and wound dressing was applied. After 21 days of hospitalization the patient went home in good condition (Fig. 5A and B). A small area of dehiscence over the implant persisted, which has remained stable during the complete first year of follow-up (Fig. 5C).

The pathologic examination showed a squamous cell carcinoma of the skull with underlying bone destruction and surrounded by actinic keratosis. There were no signs of perineural spread of lymphovascular invasion. Surgical margins were free of tumor.

DISCUSSION

In this case report the feasibility of a 1-stage virtual planned surgical removal and reconstruction of a recurrent and previously irradiated cSCC with invasion into the underlying skull is presented. Also, the potential complications that may occur and management are discussed.

Cutaneous squamous cell carcinoma of the scalp is not uncommon. Predisposing factors include chronic actinic damage, prior treatment with ionizing radiation, immunosuppression, chronic scarring, and certain genodermatosis.[16] They represent approximately 2% of all skin cancers, with a male predominance presumably due to androgenic alopecia.[7,16–18] In contrast, advanced cSCC of the scalp with invasion of the underlying skull has a rare occurrence and clinical decision making is severely hampered by the lack of experience reported in literature.

Nonmelanoma skin cancer of the scalp is most commonly staged according to the tumor, node, and metastases staging system.[14] Staging is an important tool in prognostic stratification. The majority of cSCC is detected at an early stage and classified as low risk. Their prognosis is good with a low incidence (<5%) of metastases.[19,20] Successful treatment is usually achieved with soft tissue excision and scalp reconstruction using primary closure, local flaps, or skin grafting. A small subset of lesions has more unfavorable characteristics, in which the incidence of nodal metastasis is significantly increased (16–47%) and prognosis is worse.[20–27] Although the exact value of negative prognostic factors is still debated, most authors agree that size of the lesion (>2 cm), depth of invasion (>4 mm), incomplete excision, recurrent setting, differentiation grade (poorly differentiated), presence of perineural or lymphovascular invasion, and certain locations (lip, external ear, temple, forehead, anterior scalp) harbor an increased risk for nodal metastasis and/or local recurrence.[21–24] Patients factors (immunosuppression), particularly in the setting of an organ transplantation, may also play a pivotal role in recurrent disease.[21,23,24] It is of utmost importance to identify these patients with high risk cSCC to dictate appropriate work up and management strategy.

Based on best level of evidence, various national and international multidisciplinary guidelines provide treatment recommendations to aid clinicians to obtain best possible locoregional control in case of high risk lesions.[25–29] Although first line treatment is complete surgical excision with histopathological control of excision margins, the optimal surgical margins are unknown. For high-risk tumors, a margin of at least 6 mm is considered necessary, although experts may consider an extended margin of 10 mm to be safer.[25–29] If a R0 resection is not feasible, the patient refuses surgery, or in the adjuvant setting, radiotherapy can be considered.[25–27,29] Data on elective lymph node dissection or sentinel lymph node biopsy are not conclusive.[21,25–27,29] Therefore, strict lymph node examination during follow-up is recommended until more clinical data become available.

When compared with cSCC in general, scalp lesions may have some complicating characteristics unique to this anatomic site. First, the presence of hair follicles at this location is known to potentially delay accurate diagnosis. Secondly, the microscopic extent of the tumor can be difficult to delineate and exceed clinical apparent margins, as the subgaleal plane offers little resistance to tumor and facilitates radial spread.[6,16] Also, extensive actinic damage with field cancerization and multiple foci of invasive growth, could impede defining clinical margins. Thirdly, accurate diagnosis of minimal invasion into the cranium may be difficult. This accurate diagnosis is of importance, because bone involvement requires resection of the affected bone. In these cases, the surgeon should consider a CT scan or obtain bone chips for microscopic examination, as pitting of bone has not always proven to be reliable.[16] And fourthly, when bone resection is needed, many open questions remain with respect to the optimal reconstructive approach regarding the need for cranioplasty and ideal soft tissue coverage.

Different critical decisions have to be made when addressing composite scalp and calvarial defects after tumor removal of the skull. Various techniques and timing are described in literature for both soft tissue coverage and hard tissue reconstruction. Concerning soft tissue coverage, irradiated wound beds or need of adjuvant radiotherapy, sizeable defects, and prior surgeries make microvascular free tissue transfer frequently unavoidable in their management. Various free flaps have been described to reconstruct scalp defects. These include the LD[30–32] and the anterolateral thigh flap (ALT),[33,34] which have been accepted as the workhorse flaps for reconstruction of large scalp defects. Alternatives include radial free forearm flap,[32] rectus abdominis flap,[32,35,36] and others.[32,37,38] Certain authors consider the LD flap the first choice because of its large surface, predictable blood supply, ease of harvesting, excellent vascularity, and long vascular pedicle.[15,39,40] Others, consider the ALT flap the preferable choice, because of its minimal donor site morbidity, lengthy and sizeable pedicle, and possibility to harvest in supine position.[41–43] It is well known that immobilized denervated muscles are vulnerable to atrophy.[44] The ALT might be associated less with atrophy-related complications compared to LD flaps, although there is lack of evidence to support one superior flap choice over the other.[43]

Some authors have managed composite defects in the same manner as scalp only defects to successfully avoid potential complications and morbidity, with application of a soft tissue flap alone.[8,45] Although they heal satisfactory and demonstrate no major recipient site complications in the postoperative course, the limitations of this strategy are an abnormal cranial contour and absence of protection of cranial contents that is conferred by cranioplasty. These patients have to adhere to the standard precautions of patients who do not have solid protection of their intracranial contents.

Consequently, most authors advise a form of cranioplasty alongside microvascular soft tissue coverage. Biocompatible autologous bone, which has long time been considered the golden standard in neurosurgical and craniofacial literature,[12,34,46–50] has a high complication rate including infection (0–26%) and resorption (1–50%) with a high removal rate.[51] Especially, in case of tumor invasion into the skull, the use of autologous bone is limited by donor sites and finite number and size. Alloplastic materials may overcome these shortcomings and offer a solution for optimal protection of the brain and satisfactory aesthetic outcome. Different materials are developed for cranioplasty, each with their own advantages. The ideal material is biocompatible, radiolucent, resistant to ionizing radiation and heat, MRI compatible, easy to use, and allows a low cost preoperative design and manufacturing to achieve an aesthetic satisfying result.[51] Unfortunately, this material does not exist yet. Titanium, PMMA, PEEK, and hydroxyapatite are the most mentioned materials. Titanium is radiopaque and appears to conduct heat and cold which makes a full cranioplasty of titanium not a good option for cranioplasty.[47] It is well known that a titanium mesh may cause artifacts on a CT or MRI, which could impede follow-up of cranioplasty patients after oncological resection.[52] Also, when inserted directly on the dura, it may cause scalp thinning and penetrate the overlying tissue.[53] Poly (methyl methacrylate) is a radiolucent, relatively cheap and easy to use material. However, this material is manufactured using liquid MMA in combination with PMMA particles. Different studies describe the potentially toxic and adverse effects of MMA.[54] Hydroxyapatite is similar to the mineral phase of human bone and can stimulate bone formation. However, the material itself is very brittle until replaced by bone, the exact time interval is unknown and depends on patient specific factors.[47] The question also remains if hydroxyapatite has any bone formation capability when used in prior irradiated tissues. Poly (ether ether ketone) is a more modern plastic, resistant to high temperatures, has a good biocompatibility and mechanical characteristics comparable to cortical bone. However, the material itself is expensive and without bioactivity.[55] The reported overall complication rates for simultaneous cranioplasty and microvascular free tissue transfer are high (21.0–57.9%).[40,41,43] The main shortcoming and serious complication of using alloplastic materials are the potential for infection and exposure, which might require removal of the cranioplasty. Reported infection and exposure rates reported range from 0% by Lipa et al,[15] up to 14.6% by Chao et al,[40] 25% by Sosin et al,[43] and 38% by Afifi et al.[15,41] Among these studies cranioplasty materials differed. If risk factors, such as radiotherapy or infection are present, some authors advise against the use a 1-stage free flap reconstruction with alloplastic material because of potentially higher recipient site complications.[41] Chao et al (2012) did not find preoperative or postoperative radiation to be associated with development of recipient site complications.[40] However, in patients with a history of infected cranial bone or alloplastic cranioplasty, they did recommend a staged approach with direct free tissue transfer alone and subsequent delayed calvarial reconstruction. The average interval between soft tissue and bone reconstruction was 6.0 ± 1.8 months. Atrophy of the LD flap did not limit the ability to perform a delayed cranioplasty, and no difficulty was experienced in flap elevation from the underlying dura.[40]

Nowadays, with the use of CAD-CAM techniques, preoperatively the resection outline can be marked keeping a safe margin to the tumor and a resection template can be manufactured. During the operation, the resection template can be positioned and fixed accurately to the skull guided by navigation. This helps the surgeon to follow the planned resection outline. It results in a highly accurate and predictable resection of the tumor which may potentially minimize future recurrences. The PEEK cranioplasty implant can be designed accordingly to the shape of the predicted defect and allow a perfect fit.[56] Because of the nonbioactive nature of PEEK, it will not securely adhere to the surrounding bone. To improve the stability of the cranial implant, a good edge contact is necessary. A sawing edge of 45° during the craniectomy would allow the eventual implant (also with a 45° edge) to be supported across the entire bone-implant contact surface. Such design features could easily be incorporated in the preoperative design phase.

In the described case, there were multiple factors making this a high risk cSCC, including recurrent setting and size of the lesion. Local wound problems and pain had severe impact on the quality of life of the patient. Accommodated by shared surgical decision-making and not as much the inherent value of human life, a decision to intervene was made through a close dialogue of this frail and elderly patient, family, and health care providers.[57] Nonoperative alternatives were unattractive regarding the exposed bone with tumor invasion and history of prior radiotherapy. A 1-stage surgical treatment was decided upon with the aim to eradicate the tumor and affected tissues, to achieve stable tissue coverage of the defect and enable the patient to return to prior activities with protection of the intracranial content with a cranioplasty. The CAD-CAM produced resection templates allowed for an accurate resection with tumor-free margins as planned and proper fit of the alloplastic cranioplasty. Unfortunately, this digital workflow did not prevent the occurrence of wound dehiscence and implant exposure, which is most feared in this type of surgery. However, it did lead to predictable margins, a more rapid and easy surgical procedure, and accurate fast placement of the cranioplasty. Potentially, a delayed cranioplasty would have prevented wound dehiscence problems, as described by Chao et al.[40]

CONCLUSION

Composite defects of the scalp and cranium resulting from invasive squamous cell carcinoma are known to be a reconstructive challenge and associated with a high rate of complications and morbidity. This first report of a 1-stage 3D virtual resection and reconstruction demonstrates the advantages of an accurate and predictable resection and accurate fast placement of the designed cranioplasty. Unfortunately, this did not overcome the complication of wound dehiscence and implant exposure. The possible benefits and risks should always be assessed in relation to the patient's diagnosis, comorbidity and life expectancy. For high risk cases and unfavorable local conditions such as previous infections, radiotherapy, or exophytic tumors, a multiple staged approach seems to remain the most predictable treatment strategy.

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