

# Integra in Scalp Reconstruction After Tumor Excision: Recommendations From a Multidisciplinary Advisory Board

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**Abstract:** Integra is a dermal regeneration template used in the reconstruction of burns, traumatic injuries, or excision lesions in patients who present particular risk factors for traditional surgical procedures. A multidisciplinary advisory board of expert dermatologists and plastic surgeons have discussed the use of Integra in the reconstruction of scalp defects after tumor excision, focusing on the evidence derived from literature and on their experience in the treatment of approximately 400 patients. In this position paper, the authors summarize the main evidence discussed during the board, and the common practice guidelines proposed by the experts. The use of Integra is recommended in elderly patients with multiple comorbidities who have a higher risk for potential complications in traditional surgery; these patients may in fact benefit from a lower anesthetic risk, a less complicated postsurgical care and limited morbidity at the donor site obtained with the dermal template. Integra should also be used in the reconstruction of large and complex wounds and in case of bone exposure, as it helps to overcome the challenges related to wound healing in difficult areas. Notably, Integra has proven to be effective in patients who have undergone previous surgical procedures or adjuvant radiation therapy, in which previous incisions, scarring and radiation damages may hamper the effectiveness of traditional procedures. Finally, Integra is recommended in patients with recurrent and aggressive tumors who need closer tumor surveillance, as it gives easy access to the tumor site for oncologic follow-up examination.

**Key Words:** Dermal matrix, Integra, scalp reconstructive surgery, tumor excision

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The reconstruction of scalp defects after tumor resection represents a difficult surgical challenge, especially considering the mounting incidence of skin cancer among elderly patients.<sup>1</sup> Standard reconstructive techniques follow a step-wise approach that incorporate principles of the reconstructive ladder. Free tissue transfers, local flaps, or skin grafts are usually used in cases of smaller-medium wounds, while larger or infected or previously irradiated wounds can be treated by free tissue transfer.<sup>2,3</sup> Each of these options has advantages and limitations, and is chosen based on anatomical characteristics of the lesion, as size, depth, and quality of regional tissue, and patient-related factors, including physical and mental health, comorbidities, and patient preferences.<sup>4</sup>

Traditional surgical approaches have a limited application in elderly patients, which may present additional risk factors due to comorbidities (eg, diabetes and cardiac disorders), concomitant medications, problems at donor site, and anesthetic tolerance.<sup>5</sup> Moreover, the peculiar anatomy, mobility, and poor vascularization of the scalp poses additional challenges in surgical reconstruction, especially in cases of wide local excision leading to bone exposure. In fact, the exposure of the skull bone leads to slow formation of granulation tissue and wound healing by secondary intention, increasing the risk of flap necrosis, especially in older patients.<sup>6</sup> Lastly, cancer patients may present additional complications, such as the extent of resection, especially in advanced stages, need for preservation of original surgical margin orientation, possibility of tumor recurrence, and requirement for adjuvant radiation therapy.<sup>3,7</sup>

Patients at higher risk for traditionally reconstructive procedures may benefit from the use of biologically engineered materials, also called dermal matrix, that help generate a new dermis, offering major improvements in the coverage of complex and larger defects.<sup>8</sup> Integra is a dermal regeneration template composed of a layer of bovine collagen crosslinked with glycosaminoglycan covered by a silastic membrane. The silicone layer temporarily closes the wound to ward off infections and control fluid and heat loss, while the collagen matrix promotes infiltration of host cells, which eventually form a neodermis in 3–6 weeks. The generation of the new dermis provides a reliable recipient bed for split-thickness skin grafting, which replaces the silicone layer.<sup>8–10</sup>

Integra has been widely used in reconstructive procedures to treat burns, ulcers, traumatic injuries, or excision lesions all over the body, leading to long-term engraftment and excellent cosmetic and functional results.<sup>11–13</sup> Multiple retrospective studies and case reports have also reported the successful use of Integra in the reconstruction of scalp defects after excision of different types of tumors.<sup>6,14–16</sup> However, common guidelines on the use of Integra after tumor excision on the scalp is still lacking and variance in patients and defect characteristics leads to a highly individualized treatment.

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A multidisciplinary team of expert dermatologists and plastic surgeons has recently discussed the use of Integra in the surgical reconstruction of scalp defects after tumor excision, with the aim to define some common practice guidelines. This position paper summarizes the main findings of the discussion and the final recommendations provided by the experts.

## INTEGRA IN SCALP RECONSTRUCTION AFTER TUMOR EXCISION: EVIDENCE FROM THE LITERATURE

Various retrospective studies and case reports have reported the efficacy and safety of Integra in the reconstruction of scalp defects after tumor excision.<sup>17</sup> A detailed description of these studies goes beyond the scope of this position paper and can be found in 2 recent papers published by Johnson et al and by Watts et al,<sup>18</sup> who conducted very interesting systematic reviews on the use of Integra in the reconstruction of complex full thickness scalp defects.<sup>14</sup> Notably, while these reviews primarily focus on the main evidence available in literature, in this position paper we aimed at discussing more in depth the positioning of Integra in clinical practice, reporting the experience and recommendations of clinical experts.

The most important retrospective studies and case reports discussed during the multidisciplinary board are summarized in Table 1 (Supplemental Digital Content, <http://links.lww.com/SCS/A590>).

### Elderly Patients With Comorbidities

Integra has been extensively used in the reconstruction of scalp defects in elderly patients presenting with multiple comorbidities, for whom traditional surgical procedures are deemed inappropriate.

In 2011, Corradino et al reported the successful use of Integra in eight elderly patients (mean age: 81.5 years) with scalp malignant tumors, for which a traditional surgical reconstruction was deemed not tolerable. Patients underwent a 2-step procedure under local anesthesia, initially consisting of tumor removal and Integra positioning, and followed, 3 weeks later, by the removal of Integra silicone layer and covering of the defect with a split-thickness graft. The procedures were successful in all the patients with no complications and led to satisfactory cosmetic and functional results; moreover, in 2 cases, Integra allowed the detection of an early tumor recurrence 2 months after the first operation.<sup>19</sup>

Positive results in older patients (mean age: 85.5 years) were also reported in a small series of 4 subjects treated at the University Hospital Coventry and Warwickshire (UK) for squamous cell carcinoma (SCC;  $n=2$ ), basal cellular carcinoma (BCC;  $n=1$ ), and angiosarcoma ( $n=1$ ) of the scalp. Of note, the series comprises a 93-year-old man with SCC of the scalp, who suffered from multiple comorbidities including diabetes, hypertension, and chronic renal failure; he reported a 100% graft take with Integra and no complications.<sup>20</sup>

In 2015, another retrospective analysis was published on 20 elderly patients with multiple comorbidities and extended defects of the scalp, treated with Integra. Mean age was 80 years and the most common tumor type was BCC (16 cases), followed by SCC (4 cases). Patients also had multiple comorbidities, including arterial hypertension, coronary heart disease, atrial fibrillation, use of antiplatelet drugs, chronic renal failure, diabetes mellitus type II, smoking habits, and chronic lymphocytic leukemia. Integra reconstruction was successful with 100% engraftment rate and only minor complications occurred in 2 cases. Of note, while in most of the studies the Integra-based reconstruction is performed in a 2-step procedure, in this study, a single-step procedure was chosen and the neodermis formed after Integra positioning was not covered with skin graft after silicon removal. The procedure was successful,

with healing by secondary intention occurring within 35–50 days, and with the additional advantage of avoiding a 2nd surgical intervention.<sup>17</sup>

### Complex Wounds and Bone Exposure

Several studies have reported the use of Integra in reconstruction of complex wounds located in the scalp, an anatomical site that poses additional challenges in surgical reconstructive procedures.

In 2005, Wilensky et al conducted a retrospective study on 23 elderly patients treated with Integra for the reconstruction of complex full-thickness defects of the scalp, with exposed cranium. The majority of the patients ( $n=13$ ) were diagnosed with melanoma either as primary diagnosis or after recurrence; additional tumor types included SCC ( $n=5$ ), angiosarcoma ( $n=2$ ), BCC ( $n=1$ ), spindle cell carcinoma ( $n=1$ ), and malignant pilar tumor ( $n=1$ ). Traditional surgical procedures were deemed unsuitable due to the complexity of the defect, higher risk of tumor spreading with immediate or transposition flaps, and additional risks of general anesthesia for elderly patients. The authors opted for radical resection with generous margins, and the average defect size requiring reconstruction was 51 cm<sup>2</sup> (range: 9–169 cm<sup>2</sup>). Integra led to successful engraftment in 100% of the patients with minimal morbidity and no mortality. The only complications reported by the authors were infection, which was observed in 21.7% of the patients, and delayed healing reported in 5 patients.<sup>15</sup>

In 2009, Koenen et al reported their experience on 13 patients with cutaneous malignancies of the scalp treated with Integra. Patients presented with multiple types of cutaneous tumors including rare and aggressive malignancies. In consideration of the safety margins recommended for the respective type of tumor (ranging from 1 to 3 cm) the authors opted for wide local resection with partial removal of the outer table of the skull to reduce the risk of local recurrence. Within a period of 29 days after the first surgery, all the patients reported sufficient granulation tissue formation and the defect was subsequently covered with an ultrathin graft, which healed within 9–13 days. Only 1 patient reported infection of the template, while no cases of seroma, necrosis, or hematoma were reported.<sup>6</sup>

Positive results with the use of Integra were observed also by Chalmers et al who studied the reconstruction of complex surgical defects in 14 patients with excision up to the bone or tendon. In this series, 6 patients were diagnosed with scalp malignancies and were classified as complex cases due to significant comorbidities, large areas of exposed bone, previous surgery, and/or radiotherapy. Patients were diagnosed with SCC ( $n=4$ ), metastatic melanoma (MM;  $n=1$ ), and sarcoma ( $n=1$ ), and the mean defect area after tumor excision was 163 cm<sup>2</sup> (range: 49–289 cm<sup>2</sup>). Integra was efficient in the reconstruction of these complex and poorly vascularized wounds, graft take ranged from 50% to 100% and registered complications included hematoma (1 case) and delayed healing (1 case).<sup>12</sup>

Of note, the importance of extensive resection of scalp tumors is suggested by a comparative analysis performed in 2012, based on which subperiosteal resection is recommended in patients with node-negative primary scalp melanoma. The authors of the study compared the risk of in-transit/satellite recurrence among 48 patients with scalp melanoma undergoing either subperiosteal (at the level of calvarium, 23 patients) resection with Integra-based reconstruction or subgaleal resection (resection of skin, subcutaneous tissue, and galea, 45 patients) followed by skin graft. The study shows that, although the 2 procedures were similar in terms of engraftment take (97% versus 96%), the recurrence rate was remarkably higher among patients in the subgaleal resection group compared to those in which the resection of the melanoma included

the periosteum (24% versus 8.7%), thus suggesting the importance of complete excision of scalp tumors.<sup>21</sup>

Interestingly, Integra has proven to be safe and effective also in the reconstruction of extremely large scalp defects. Fung et al reported the successful use of Integra in a 69-year-old patient with a history of nonmelanoma scalp tumor who underwent a wide excision of an area of 256 cm<sup>2</sup> including the pericranium. The 2-stage use of Integra, followed by SSG was successful, and after 14 months the patient was fully healed with no recurrence.<sup>22</sup> Similarly, Cunningham et al obtained successful results with Integra followed by negative pressure wound therapy (NPWT) in a 63-year-old man with numerous superficial and invasive SCC of the scalp that required excision of a total area of 400 cm<sup>2</sup>.<sup>23</sup>

### PREVIOUS SURGERY, RADIATION THERAPY, AND TUMOR RECURRENCE

Integra has been used for the reconstruction of scalp defects in patients who had previous surgery, for which the anesthetic risk is higher, and in those suffering from aggressive/recurrent tumors that might need pre- or postsurgery radiation therapy.

In 2005, Komorowska-Timek et al reported their experience on a small population of 7 elderly patients undergoing partial- or full-thickness scalp reconstruction with Integra after removal of a scalp tumor. In detail, 4 patients were diagnosed with BCC, 2 patients with MM, and 1 patient with glioblastoma. Patients presented multiple risk factors for traditional surgical procedures including older age, diagnosis of recurrent malignant tumors (5 cases), preoperative radiation of the scalp (2 cases), and previously failed reconstruction, including local flaps (n = 1), split-thickness skin graft (n = 3), and failed latissimus dorsi (n = 1). The application of Integra was successful in all the patients, with 100% graft and formation of a well-vascularized neodermis before skin grafting. No infection or other complications were noted in this series and patients benefited from satisfactory cosmetic and functional results.<sup>24</sup>

In 2007, Tufaro et al analyzed the use of Integra in 17 patients with soft-tissue tumors located in different anatomical location, including 7 patients with scalp tumors such as MM (n = 3), BCC + SCC (n = 1), dermatofibrosarcoma (n = 1), and others (n = 2). Patients presented with complex defects that needed excision extending to the bone/periosteum, had a history of previous surgery (n = 4) or had received perioperative chemotherapy (n = 1). The authors reported excellent cosmetic and functional results, and less donor-site morbidity. Of note, Integra led to successful reconstruction also in patients treated with pre- and postoperative irradiation at the surgical site, thus suggesting the efficacy of this surgical procedure regardless of the negative effects of radiation therapy on the skin.<sup>25</sup>

Khan et al conducted one of the largest retrospective reviews of 30 cases of full-thickness scalp reconstruction using Integra. Most of the patients were diagnosed with MM (n = 15), followed by SCC (n = 6), BCC (n = 3), basosquamous carcinoma (n = 2), and dermatofibrosarcoma protuberans (n = 2). All the patients included in the series had undergone previous oncology surgery with a wide excision, including 15 cases of primary closure, 11 reconstructions with local flaps, and 4 skin grafts; moreover, nine patients had had neoadjuvant radiotherapy and 3 patients received postoperative radiotherapy. Overall patients reported a 100% graft success, with only 2 minor complications being infection and seroma in 1 case each. Two patients suffered from recurrence while 28 had close margins and aggressive tumors that required further excision and soft-tissue cover, thus underlining the advantages of Integra in terms of tumor surveillance. Moreover, radiotherapy had no adverse effect on Integra take and none of the patients reported radiotherapy-related wound breakdown.<sup>16</sup>

The benefits of Integra in patients receiving radiation therapy for an aggressive tumor has been also reported in a case report published in 2003. Gonyon and Zenn described the case of a 62-year-old man with multiple comorbidities including previous surgery, diagnosed with a large and recurrent SCC of the scalp that required total scalp irradiation. The patient also had an extremely large defect and required the excision of a 400-cm<sup>2</sup> area of almost the entire left scalp, with exposed pericranium and bone. Integra-based reconstruction was successful leading to the creation of an excellent vascularized bed for skin grafting despite heavy radiation damage in the recipient scalp.<sup>26</sup>

### RECOMMENDATION FOR INTEGRA USE IN SCALP RECONSTRUCTION

Overall, the authors of this study have treated 395 patients with Integra, with an overall success rate of 90% and a low number of complications (the most common being infection, 6%). A description of the patients we treated, without any further statistical evaluation, is reported in Table 2 (Supplemental Digital Content, <http://links.lww.com/SCS/A590>).

#### Patients

The use of Integra is recommended in elderly patients with comorbidities that constitute an anesthetic risk (ASA)  $\geq 3$ . Older patients have a higher risk of potential complications associated with general anesthesia and postoperative recovery; moreover, they usually suffer from concomitant conditions that make them unfit to undergo major reconstructive procedures, such as free tissue transfer or regional flaps. Reconstruction with Integra is recommended in these patients as it can be done with local anesthesia and usually requires shorter recovery time. Moreover, Integra requires a less complicated care in the postsurgical phase, and can be followed by thin skin graft, thus reducing the morbidity at the donor site.

#### Tumor Characteristics

In terms of lesion size, Integra is useful in case of cancer or precancerous lesions with a diameter  $\geq 4$  cm localized to the scalp to avoid local flaps or skin grafts. Notably, Integra has reported successful results in the reconstruction of defects up to 400 cm<sup>2</sup>, and the reconstruction of larger scalp wounds does not seem to be associated with significantly increased complication rates.<sup>23,26</sup>

Integra is also recommended in case of full-thickness resection down to the bone surface with the sacrifice of the periosteum. The exposed skull bone is characterized by slow formation of granulation tissue and reduced wound healing by secondary intention, increasing the risk of flap necrosis with traditional procedures. Literature evidence suggests that Integra provides higher quality coverage over wounds with exposed bone, and is efficient in stimulating the creation of a new vascularized dermis.<sup>6,12,15,25</sup> Notably, the panel of authors has reported the use of the dermal substitute directly on periosteum (when present), on well-vascularized exposed bone, and also on non-well-vascularized exposed bone (especially in case of elderly patients or postradiation therapy), which was drilled prior to the positioning of the dermal substitute in order to obtain an efficient vascularized bed.

In terms of tumor types, Integra has shown successful results after excision of SCC, BCC, and MM<sup>6,12,15,17,20,24,27–29</sup> and, as described in some reports dermatofibrosarcoma protuberans.<sup>16,25</sup> Of note, BCCs are the most common malignancies observed in older patient and require smaller surrounding margins (<5 mm); conversely, in case of more aggressive tumors such as invasive SCC and MM, it is recommended to include wider margins (>5 mm). Additional safety margins (2–4 cm) may be considered to better

control tumor recurrence in particularly aggressive tumors, and subperiosteal resection is recommended in patients with node-negative primary scalp melanoma.<sup>6,21</sup> In this regard, as previously reported, Integra is effective in the reconstruction of both large defects and deep lesions with exposed bones, thus enabling a complete resection that reduces the risk of tumor recurrence.<sup>6,12,15,25</sup>

The use of Integra presents additional advantages in patients with recurrent tumors, as it gives easy access to the tumor site for oncologic follow-up examinations, facilitating the detection of early recurrences and allowing the resection of residual tumors before the final reconstruction step.<sup>12,16,19,24</sup>

Moreover, the possibility to reconstruct the scalp with dermal substitute allows for a more aggressive tumor excision with higher rate of oncologic safety.<sup>21</sup> Traditional reconstructive procedures, such as transposition flaps, might be oncologically unsound in patients with recurrent and aggressive tumors, as they can cause tumor spread beyond the site of the original resection, and they might cover residual or recurring tumors. Oncologic safety can be achieved by a radical excision, demonstrated by clear tumor margins obtained in the histopathology examination. When tumor margins are not clinically well defined, a 2-step procedure might be necessary, with completed tumor excision and delayed definitive reconstruction after the confirmation of histopathology clear margin. In these cases, the dermal substitute can be positioned at the time of tumor excision, as it represents the only surgical option before the histopathology report.

Integra can also be used in patients requiring pre- or postsurgery radiotherapy. Radiation therapy is a known risk factor for wound healing, as it results in reduced blood flow and damage to host fibroblast, eventually limiting the healing potential of the tissue, and increasing the complication rates of traditional surgical procedures. Literature data show that Integra is efficient in creating a vascularized bed also in heavily irradiated scalp.<sup>26</sup> Moreover, postoperative irradiation after Integra-based reconstruction appears to be well tolerated and although some of the patients may experience mild acute radiodermatitis and/or radionecrosis; the outcomes are overall good, with engraftment rates above 95%.<sup>6,12,16,21,24,27,29</sup>

Finally, Integra is recommended in patients who underwent previous surgical procedures, in which previous incisions and scarring make traditional surgery approaches difficult and unpredictable.<sup>16,24,25</sup>

## Steps and Dressings

Although a few case reports and studies have reported the successful use of Integra in healing by secondary intention, the 2-step procedure remains to be the standard approach to Integra-based reconstruction. Secondary healing seems to be sufficient in some cases and has the advantage of avoiding a 2nd procedure for the patient; however, it requires longer time to heal, with mean time to bone epithelization of 13 weeks.<sup>30,31</sup> In addition, the single-step procedure is not feasible for large full-thickness scalp wounds, where bone is devoid of the periosteum.<sup>25</sup> The 2-step procedure is therefore recommended as standard approach, as it provides effective and durable results for all defect size.

In terms of dressing the most commonly used options were bolstered dressing,<sup>15,17,19,22,24,26,32,33</sup> silver-impregnated dressing,<sup>6,16,25</sup> and NPWT,<sup>12,23,28,34,35</sup> which is effective in reducing shearing forces across the surface of the dermal matrix by acting as a splint and forces the material on to the wound bed. The authors recommendation is to perform the dressing with nonadherent wound contact layer (eg, fatty gauze) on top and apply Betadine gel (Braun; B. Braun, Milan, Italy), silver sulfadiazine or other silver dressings to the edge, followed by traditional compressive over the bandage. In selected cases, an NPWT dressing can be used depending upon the site and size of the wound.<sup>36</sup> The only

complications reported by the experts on the use of NPWT are detachment of the dermal substitute from the wound bed and development of infection.

## CONCLUSION

In conclusion, Integra is a safe and effective option in the reconstruction of scalp defects after the excision of multiple types of tumor, including SCC, BCC, MM, and dermatofibrosarcoma protuberans. The use of Integra is recommended particularly in elderly patients with multiple comorbidities, patients with large and complex wounds that lead to bone exposure, and patients with recurrent and aggressive tumors who have undergone previous surgical procedure, and may need adjuvant radiation therapy or for whom a close tumor surveillance is recommended.

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