Post-surgical scalp wounds with exposed bone treated with a plant-derived wound therapeutic

• **Objective:** To evaluate the efficacy of a plant-derived wound dressing, a mixture of hypericum oil (*Hypericum perforatum*) and neem oil (*Azadirachta indica*), in scalp wounds with exposed bone.
• **Method:** A retrospective review was conducted of all patients presenting with scalp wounds with exposed bone following the excision of skin tumours and treated with a plant-derived wound dressings (1 Primary Wound Dressing; Phytoceuticals AG), from January to July 2011. Time to healing, wound size, area of exposed bone, ease of handling, pain and complications were evaluated.
• **Results:** Nine consecutive patients were analysed retrospectively. The patients' mean age was 81.2 ± 8.5 years (63–90 years), with a mean wound size of 13.2 ± 6.8cm^2 (0.4–22.6cm^2) and 6.8 ± 6.5cm^2 (0.3–20.7cm^2) of exposed bone. The time to complete healing by secondary intention was 4–20 weeks. A rapid induction of granulation tissue was observed, which covered the entire exposed bone surface in six out of nine cases (67%) after 4 weeks, and showed a reduction in the mean area of exposed bone of 95%. Dressing change was easy and without pain and there were no complications.
• **Conclusion:** This retrospective, non-controlled analysis suggests that ONE is a very simple to use, safe and potentially effective therapy for the treatment of scalp wounds with exposed bone.
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scalp wounds; exposed bone; secondary intention healing; wound spray; neem oil; hypericum oil

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Tumours of the scalp, such as squamous cell carcinoma and dermal sarcoma, which require surgical treatment, are becoming increasingly common in an elderly patient population.[1] Surgical treatment often creates large defects that need to be covered with flaps, skin grafts or left to heal by secondary intention.

Healing by secondary intention is a good treatment alternative in cases where the periosteum remains intact. However, if the periosteum has to be removed, or if it dries out in the healing process of a skin graft or flap, wounds with exposed calvarial bone develop, which show no, or very slow, granulation tissue formation and, therefore, are almost refractory to healing by secondary intention.[2]

Current conservative treatment options to enhance healing by secondary intention typically involve a moist wound-healing environment.[3] The primary dressings that enable moist wound healing are hydrocolloids, hydrogels, alginates, foam and Hydrofiber dressings, and paraffin gauzes.

Even with the correct moisture balance, most wounds with exposed bone do not heal and require advanced treatments, such as bioengineered skin substitutes, surgical treatment or negative pressure wound therapy (NPWT) in combination with skin grafts.[4] There are two common surgical options. The first consists of establishing a connection between the inner bone structures and the surface by drilling holes in the tabula externa,[5] through which granulation tissue can expand. In the second, the tabula externa is sanded, in order to obtain capillary bleeding, or removed and the resulting defect can be covered with a dermal substitute, such as a dermal regeneration template or a split-thickness skin graft.[6,7]

The major disadvantages of these surgical treatment options are the need for general anaesthesia, thus excluding a proportion of this often elderly and medically compromised population, and the high costs of the inpatient surgical intervention, as well as of other advanced therapies, such as tissue-engineered skin substitutes or NPWT, which may be applied concurrently.

Recently, a new plant-derived wound therapeutic was introduced to the Swiss market (1 Primary Wound Dressing [ONE]; Phytoceuticals AG). It consists of a mixture of hypericum oil (*Hypericum perforatum*) and neem oil (*Azadirachta indica*), designed to create a moist wound healing environment, with the oil layer preventing the secondary dressing from adhering to the wound. Furthermore, it is thought to have an antimicrobial effect,[8] and promotes the regeneration of the epidermis.

Due to the simple mode of application (spray) and the broad mode of action, it is indicated in the treatment of scalp wounds with exposed bone, with the intention to find an effective alternative to the existing treatment options. This study was designed to

Table 1. Case reports of patients treated with ONE

Patient no.	Sex	Age (years)	Diagnosis	Wound size (cm^2)				Area of exposed bone (cm^2)				Treatment (weeks)
				0 weeks	2 weeks	4 weeks	6 weeks	0 weeks	2 weeks	4 weeks	6 weeks	
1	M	63	SCC	17.1	7.7	0.0	0.0	6.9	0.0	0.0	0.0	4
2	M	90	BCC	13.8	6.3	4.5	0.0	7.9	0.4	0.0	0.0	7
3	M	89	Atypical fibroxanthoma	10.2	8.4	0.75	0.4	0.5	0.0	0.0	0.0	10
4	M	89	Lentigo maligna	16.5	7.4	1.5	0.0	3.4	1.5	0.0	0.0	10
5	F	84	BCC	11.0	6.2	1.0	0.2	3.0	0.9	0.0	0.0	7
6	M	81	SCC	21.5	12.4	6.9	5.6	20.7	9.0	4.1	2.9	20
7	M	74	SCC	0.4	0.3	0.0	0.0	0.3	0.0	0.0	0.0	4
8	M	75	SCC	5.9	4.1	3.2	1.5	3.4	1.9	0.7	0.0	8
9	F	86	BCC	22.6	21.9	19.6	13.8	15.2	13.2	0.5	0.0	14

M=male; F=female;
SCC=squamous cell carcinoma; BCC=basal cell carcinoma

References

1 Donaldson, M.R., Coldiron, B.M. No end in sight: the skin cancer epidemic continues. Semin Cutan Med Surg. 2011; 30: 1, 3–5.

2 Becker, G.D., Adams, L.A., Levin, B.C. Secondary intention healing of exposed scalp and forehead bone after Mohs surgery. Otolaryngol Head Neck Surg. 1999; 121: 6, 751–754.

3 Winter, G.D. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. Nature. 1962; 193: 293–294.

4 Hurvitz, K.A., Kobayashi, M., Evans, G.R. Current options in head and neck reconstruction. Plast Reconstr Surg. 2006; 118: 5, 122e–133e.

5 Meissner, M., Kaufmann, R. Surgical wounds of the scalp. Methods of closure [in German]. Hautarzt. 2011; 62: 5, 354–361.

6 Komorowska-Timek, E., Gabriel, A., Bennett, D.C. et al. Artificial dermis as an alternative for coverage of complex scalp defects following excision of malignant tumors. Plast Reconstr Surg. 2005; 115: 4, 1010–1017.

7 Corradino, B., Di Lorenzo, S., Leto Barone, A.A. et al. Reconstruction of full thickness scalp defects after tumour excision in elderly patients: our experience with Integra dermal regeneration template. J Plast Reconstr Aesthet Surg. 2010; 63: 3, e245–247.

8 Desbois, A.P., Smith, V.J. Antibacterial free fatty acids: activities, mechanisms of action and biotechnological potential. Appl Microbiol Biotechnol. 2010; 85: 6, 1629–1642.

9 Snow, S.N., Stiff, M.A., Bullen, R. et al. Second-intention healing of exposed facial-scalp bone after Mohs surgery for skin cancer: review of ninety-one cases. J Am Acad Dermatol. 1994; 31: 3 Pt 1, 450–454.

10 Bickels, J., Kollender, Y., Wittig, J.C. et al. Vacuum-assisted wound closure after resection of musculoskeletal tumors. Clin Orthop Relat Res. 2005; 441: 346–350.

11 Schintler, M.V., Prandl, E.C., Wittguber, G. et al. The impact of the VAC-treatment for locally advanced malignancy of the scalp [in German]. Zentralbl Chir. 2004; 129: (Suppl. 1), S141–146.

retrospectively evaluate the effectiveness of this product in this challenging wound healing situation.

Method

A retrospective review was performed on all patients with postoperative scalp wounds with exposed calvarial bone following excision of skin tumours, at the Department of Dermatology of the University Hospital of Zurich, Switzerland, from January to July 2011. All wounds had initially been treated with a split-thickness skin graft, which did not take due to insufficient blood supply after removal of the periosteum or desiccation of the tissue in the healing process.

The wounds were treated with the wound therapeutic (ONE), applied daily on the wound and peri-wound skin. The wound and peri-wound skin was then covered with a simple secondary dressing (non-woven gauze [Vliwasoft; Lohmann & Rauscher] or absorbent dressing [Primapore; Smith & Nephew]), without any active compound. The choice of the secondary dressing was based on the amount of wound exudate. Debridement and cleansing of the wound was only performed when necessary. Necrotic and fibrinous tissue were mechanically removed with scissors or a curette.

Outcomes

Treatment was continued until the soft tissue defect was covered by granulation tissue and secondary epithelialisation. Wound healing was defined as complete closure by secondary epithelialisation. The treatment period was defined as the time between the first application of the wound therapeutic and complete wound closure. Informed consent for their data to be submitted for publication was obtained from all patients.

Patients were seen at least every 2 weeks, by a wound-care specialist. Before starting treatment, and at every clinical visit, the wounds were photographed together with a ruler (Fig 1) and the wound size, as well as the area of exposed bone, was determined from the photographs using measuring software (Synedra View). At each follow-up visit, pain (assessed by open-ended questions), clinical signs of infections, as well as any side effects, were recorded.

Results

Over the study period, nine patients presented with postoperative scalp wounds with exposed calvarial bone following the excision of skin tumours; all were treated with ONE. All patient records included the required information. The patients' mean age was 81.2±8.5 years (range 63–90 years). In four patients, the excised tumours were squamous cell carcinomas. The diagnoses of the five remaining patients were lentigo maligna (n=1), atypical fibroxanthoma (n=1) and basal cell carcinoma (n=3; Table 1).

The soft tissue defects, following the surgical removal of the tumours, were all located on the scalp. Secondary diagnoses included arterial hypertension (n=5), allergies (n=1) and non-skin malignant tumours (n=2). The mean size of the skin and soft tissue defect on presentation was 13.2±6.8cm^2 (range 0.4–22.6cm^2). All defects showed exposed bone with a mean area of exposed bone of 6.8±6.5cm^2 (range 0.3–20.7cm^2).

All nine soft tissue defects were completely healed by secondary intention, without any further surgical or other intervention (Table 1; Fig 1). The mean treatment period until total re-epithelialisation of the wounds was 9.3±4.8 weeks (range 4–20 weeks; Table 1). The mean wound size reduction after

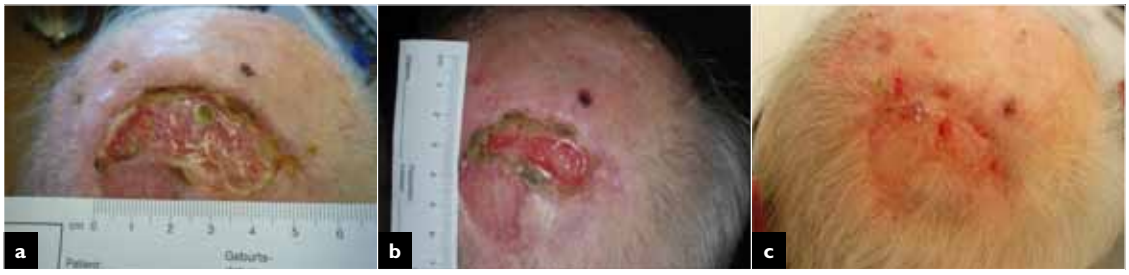


Fig 1. Patient 2, a 90-year-old male, presented with a 13.8cm² wound with exposed bone at the vertex, 40 days after excision of basal cell carinoma and skin grafting, (a). The same wound after 3 weeks of treatment, with near-complete granulation of the wound bed and partial re-epithelialisation, (b), and after 8 weeks of treatment, with 90% of the wound covered by epithelium and a small island of granulation tissue remaining at the centre, (c)

4 weeks' treatment was 9.04cm², from a mean of 13.2cm² to 4.2cm² (69%) and the mean reduction of the exposed bone area was 6.2cm², from a mean of 6.8cm² to 0.6cm² (97%; Fig 2 and 3).

No patient experienced severe pain during the entire treatment period, in particular dressing changes were not reported as painful. No wound exhibited clinical evidence of superficial or deep infection. None of the patients showed signs of allergic reactions and no other side effects were observed. Review of clinical photographs of the healed wounds showed a cosmetically satisfying outcome in all patients.

Discussion

The treatment of scalp wounds with exposed bone is very challenging, particularly when the periosteum is exposed,[9] with moist wound healing often leading to unsatisfying results.

NPWT can be applied to enhance secondary intention healing or graft take.[10–12] Some authors describe treatment of such scalp wounds with other advanced methods, such as tissue-engineered skin substitutes, with good results achieved with the application of acellular dermal matrices.[13,14] However, all these treatment options are limited by availability and costs.

Primary surgical coverage of a scalp wound with flaps or skin grafts is often regarded as the favourite treatment option.[2,15–17] However, donor site mobility, duration of the surgical procedure and general lack of hair growth, especially in free flap reconstruction, remain problematic.

Further surgical options consist of establishing a connection between the inner bone structures and the wound bed by drilling holes in the tabula externa.[5,18] Good closure rates can be achieved with the application of a dermis equivalent on sanded bone, joined by the application of a split-thickness skin graft.[6,7] The major disadvantage of surgical treatments involving the bone is the necessity of general anaesthesia and the risk of treatment-related additional medical problems in this often elderly and medically compromised patient population. All these effective therapies involve considerable costs and significant interference with the patient's daily routine.[19]

Secondary intention healing is commonly considered painful, with a high infection rate, demanding extensive care and resulting in inferior cosmetic outcomes, but this is not substantiated in literature. Our case series shows that secondary intention healing is not associated with infections, pain or poor cosmetic results. No wound exhibited clinical evidence of superficial or deep infection. Snow et al. reviewed 115 wounds that were managed by secondary intention healing. Only 2.7% showed signs of local soft tissue infection as a complication.[9] Other case reports and studies on secondary wound healing at concave locations of the face reported similarly low infection rates.[20,21] None of our nine patients suffered from severe pain.

Further advantages of secondary healing is that it facilitates rapid visualisation and detection of tumour recurrence, thus guaranteeing optimal cancer surveillance.[22] In most cases, it is economic in comparison with surgical treatment methods, and there are no additional scars in donor sites, as with flap or skin-graft techniques.

It is also incorrect that secondary intention healing necessarily results in poor cosmetic outcome. Gohari et al. compared secondary intention healing with wound treatment with tissue-engineered skin substitutes, with patient satisfaction with cosmetic outcome equally positive in both groups.[23] Cosmetically satisfying outcomes were also reported by other authors.[15,22] Disadvantages of secondary intention healing include the prolonged period of wound treatment. Deficient local blood supply caused by previous radiation or additional disease, such as diabetes mellitus, further delaying wound repair.

The present retrospective non-controlled analysis suggests that a plant-derived wound dressing (ONE), is a promising therapy to support the healing process of post-surgical scalp wounds with exposed bone. In six of nine patients (67%), the bone was completely covered by granulation tissue after 4 weeks of treatment. In seven patients (78%), the wound was fully epithelialised after 6 weeks. This appears superior to healing rates commonly seen with moist wound healing for wounds with exposed bone. For example, Becker et al.[2] describe average healing times of 13 weeks, with a simple wound-care regimen of hydrogen peroxide and antibiotic ointment. While the number of patients presented here is too small for a direct statistical comparison, with the exception of one patient who took 20 weeks for complete wound coverage, there seems to be a clear trend to shorter

12 Molnar, J.A., DeFranzo, A.J., Marks, M.W. Single-stage approach to skin grafting the exposed skull. Plast Reconstr Surg. 2000; 105: 1, 174–177.

13 Brunetti, B., Tenna, S., Segreto, F., Persichetti, P. The use of acellular dermal matrix in reconstruction of complex scalp defects. Dermatol Surg. 2011; 37: 4, 527–529.

14 Kinsella, C.R. Jnr., Grunwaldt, L.J., Cooper, G.M. et al. Scalp reconstruction: regeneration with acellular dermal matrix. J Craniofac Surg. 2010; 21: 2, 605–607.

15 Sebastian, G., Herrmann, A. Secondary healing of the face [in German]. Hautarzt. 2005; 56: 5, 423–429.

16 Oh, S.J., Lee, J., Cha, J. et al. Free-flap reconstruction of the scalp: donor selection and outcome. J Craniofac Surg. 2011; 22: 3, 974–977.

17 Pitkanen, J.M., Al-Qattan, M.M., Russel, N.A. Immediate coverage of exposed, denuded cranial bone with split-thickness skin grafts. Ann Plast Surg. 2000; 45: 2, 118–121.

18 Koenen, W., Goerdt, S., Faulhaber, J. Removal of the outer table of the skull for reconstruction of full-thickness scalp defects with a dermal regeneration template. Dermatol Surg. 2008; 34: 3, 357–363.

19 Inhoff, O., Faulhaber, J., Rothhaar, B. et al. Analysis of treatment costs for complex scalp wounds. J Dtsch Dermatol Ges. 2010; 8: 11, 890–896.

20 Skaria, A., Adatto, M., Salomon, D. Secondary wound healing with reference to anatomic subunits in operations of the mid-facial area [in German]. Hautarzt. 1997; 48: 2, 110–112.

21 Goldwyn, R.M., Rueckert, F. The value of healing by secondary intention for sizeable defects of the face. Arch Surg. 1977; 112: 3, 285–292.

22 Moreno-Arias, G.A., Izento-Menezes, C.M., Carrasco, M.A., Camps-Fresneda, A. Second intention healing after Mohs micrographic surgery. J Eur Acad Dermatol Venereol. 2000; 14: 3, 159–165.

healing times with the formation of granulation tissue and epithelialisation within 6 weeks in seven out of nine patients. No additional surgery or skin graft was required and no clinical evidence of superficial or deep infection was observed.

The induction of granulation tissue formation was impressive, resulting in progressive filling up even of deep wounds and finally in re-epithelialisation. This effect may be explained by the antimicrobial activity of the fatty acids contained in the spray,[8] the balanced moist environment obtained by the semi-occlusive layer the oil creates[24] and the fact that the oil layer prevents secondary dressings from adhering to the wound.[25] Therefore, cell proliferation is activated and, despite the moist environment, the bacterial load remains under control. In addition, damage of the granulation tissue and regenerating epithelium during dressing change is prevented. This leads to improved epithelialisation and decreased pain during dressing change.

Grafting, artificial skin substitutes, NPWT and surgical options result in considerable costs. Inhoff et al.[19] analysed the treatment costs for complex scalp wounds in 52 patients, comparing three of the four mentioned treatment options (fascia lata, artificial skin substitute and NPWT). The total treatment costs for grafting was estimated as EUR €4475, for the artificial skin substitutes this amounted to EUR €4557, while NPWT generated total treatment costs of EUR €7521.[19] The treatment duration with ONE took on average 9.3 weeks, or 8 weeks if one outlier case is excluded. The treatment duration for grafting, artificial skin substitutes and TNWP was 8.6 weeks, 4.8 weeks and 6.9 weeks, respectively. By comparing these standard treatments with ONE, it can be concluded that the treatment duration does not vary greatly compared with grafting or NPWT. Assuming the same cost for materials and per procedure as those cited by Inhoff, the equivalent average total cost to achieve healing with ONE would be EUR €522. This considerable saving in cost arises from the fact that patients treated with ONE did not require secondary hospitalisation for grafting. This example suggests that use of this wound therapeutic could offer economic advantages over alternative treatments; nevertheless a specific study on the comparative cost-effectiveness of treatments will be required.

Even though with ONE a daily dressing change is required, the patients only visit the hospital once a week for a clinical control. The treatments between visits can be performed by the patient, the patient's relatives or a home care organisation, as the dressing change procedure is very simple and rapid.

Limitations

There are a number of limitations of this study. The study included only a small number of patients, recruited from a single centre, with data analysed retrospectively. This makes interpretation of the results challenging; indirect comparison with published data on the management of such wounds has to be undertaken carefully, even if the characteristics of the wounds included in this study, and their prognostic indicators, are similar to those reported in other published trials. Despite this, the results seemingly compare favourably with those from the literature.

Conclusion

The results of this retrospective non-controlled analysis suggest that the plant-derived wound spray is clinically efficacious for soft tissue defects on the scalp that show exposed bone. Further studies, with a larger population, are required to document the effectiveness of this wound spray in a controlled fashion. ■

Fig 2. Reduction in wound surface area in 0–6 weeks

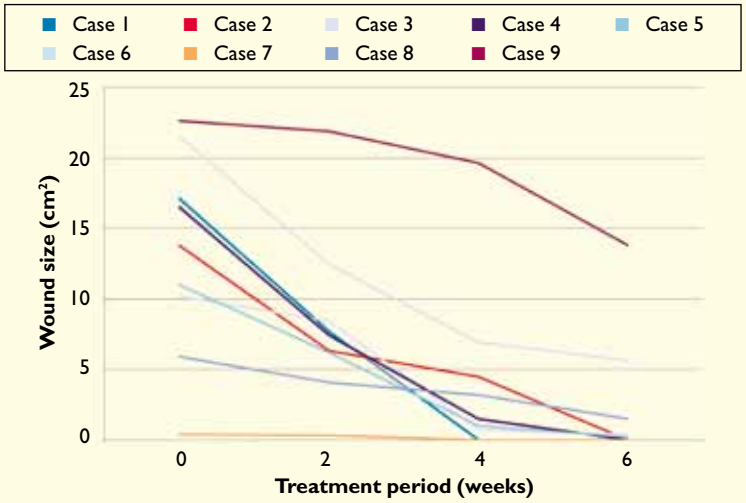
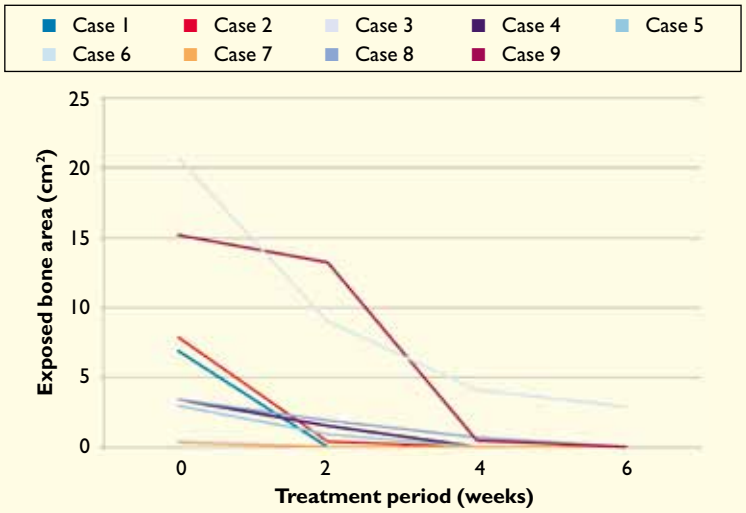


Fig 3. Reduction in the area of exposed bone in 0–6 weeks



23 Gohari, S., Gambla, C., Healey, M. et al. Evaluation of tissue-engineered skin (human skin substitute) and secondary intention healing in the treatment of full thickness wounds after Mohs micrographic or excisional surgery. Dermatol Surg. 2002; 28: 12, 1107–1114.

24 Sharman, D. Moist wound healing: a review of evidence, application and outcomes. Diabetic Foot. 2003; 6: 112–120.

25 Bell, C., McCarthy, G. The assessment and treatment of wound pain at dressing change. Br J Nurs. 2010; 19: 11, S4–S8 passim.