One-stage Reconstruction of Soft Tissue Defects with the Sandwich Technique: Collagen-elastin Dermal Template and Skin Grafts

Background: A full-thickness soft tissue defect closure often needs complex procedures. The use of dermal templates can be helpful in improving the outcome. **Objective:** The objective was to evaluate a sandwich technique combining the dermal collagen–elastin matrix with skin grafts in a one-stage procedure. **Materials and Methods:** Twenty-three patients with 27 wounds were enrolled in this prospective single-centre observational study. The mean age was 74.8 ± 17.2 years. Included were full-thickness defects with exposed bone, cartilage and/ or tendons. The dermal collagen–elastin matrix was applied onto the wound bed accomplished by skin transplants, i.e. 'sandwich' transplantation. In six wounds, the transplants were treated with intermittent negative pressure therapy. **Results:** The size of defects was ≤875 cm^2. The use of the dermal template resulted in a complete and stable granulation in 100% of wounds. Seventeen defects showed a complete closure and 19 achieved a complete granulation with an incomplete closure. There was a marked pain relief. No adverse events were noted due to the dermal template usage. **Conclusions:** Sandwich transplantation with the collagen–elastin matrix is a useful tool when dealing with full-thickness soft tissue defects with exposed bone, cartilage or tendons.

KEYWORDS: Dermal template, sandwich technique, skin grafts, soft tissue defects

INTRODUCTION

Full-thickness wounds often need complex procedures for defect closures, in particular when bone, cartilage or tendons are exposed. In recent years, the spectrum of flaps and grafts has been expanded by dermal templates and tissue engineering.[1,2]

Matriderm™ (Dr. Suwelack Skin and Healthcare Ltd., Billerbeck, Germany) is a dermal substitute consisting of a non-cross-linked collagen matrix supplemented by elastin hydrolysate of bovine origin. In experimental models, this dermal template reduced wound contractures.[3] Clinical trials with a long-term evaluation demonstrated no difference in the scar elasticity between the described dermal template and split-thickness grafts alone. The healing rate was improved.[4]

The major advantage of dermal templates results from the coverage of bone, cartilage or tendon allowing an immediate skin grafting in the same session.[5-7]

We present herein a series of patients treated with the collagen–elastin matrix and split-skin mesh graft transplantation in a one-stage procedure.

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MATERIALS AND METHODS

Twenty-three patients (15 males and 8 females) with 27 wounds were enrolled in this prospective single-centre observational study (including 5 patients previously reported).[8] The age range was 21–89 years, with a mean of 74.8 ± 17.2 years. The wounds were either acute (after surgery) or chronic (like leg ulcers). All wounds were characterized by exposed bone, cartilage and/or tendons. In the majority of patients, previous transplants (sometimes multiple) had failed. Wound healing could

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not be improved by non-surgical methods.

Patients with acute wounds were those who underwent delayed Mohs surgery for facial or scalp non-melanoma skin cancer (NMSC) and defects where standard surgical procedures like flaps or grafts were impossible due to morbidity, surgical reasons or due to patient's wishes (n = 9). The tumour diagnosis was basal cell carcinoma (BCC) in four and squamous cell carcinoma (SCC) in two patients. All facial tumours were localized on the nose, with two NMSC cases of the scalp.

One patient suffered from calcifying prepatellar bursitis and another patient presented with a longstanding burn scar of the lower leg suggestive of malignant transformation. Fortunately, the malignancy was not confirmed by histopathology in this case.

Fourteen patients suffered from 16 chronic wounds of the lower extremities. The aetiology of the wounds was venous (3), mixed arterio-venous (7), post-necrotizing fasciitis (1), post-surgical (2), pressure sores due to paraplegia (2) and pyoderma gangrenosum (1). In all of these wounds, tendon and/or bone was exposed not allowing simple split-skin mesh graft transplantation. The location of wounds was either the foot (n = 6) or the lower leg (n = 10).

The size of the wounds was between 4 and 875 cm^2. Before sandwich transplantation, all other measures to improve perfusion had been tried to the bottom of the matter. In five ulcers, wound bed preparation was supported by negative pressure treatment (VAC™; KCI Licensing, Inc., San Antonio, TX, USA) before to shorten the time to surgery.

The dermal collagen–elastin matrix (Matriderm™; Dr. Suwelack Skin and Healthcare Ltd., Billerbeck, Germany) was used in sheets of 74 × 52 × 1 mm. Matriderm™ was cut to size and regenerated using Ringer's solution for a couple of minutes until the sheets became translucent. The template was applied directly onto the clean wound bed. Full-thickness skin transplants were used for facial defects. For all other types of wounds, split-skin mesh grafts were obtained. The grafts were placed above the dermal template (therefore the term 'sandwich' transplantation has been coined). The transplants were fixed with non-absorbable sutures (face) or staples (all other regions). As a dressing, silicone sheets (Mepitel™; Mölnlycke Health Care, Gothenburg, Sweden) and cotton swaps or compresses were applied. In addition, compression bandages were used for leg ulcers. The first dressing was allowed to stay for 6 days. Regular dressing changes followed.

In six wounds, the transplants were covered by silicone sheets, microporous foam (GranuFoam™) and treated with intermittent negative pressure (-125 mmHg) using the VAC™ therapy system for 7 days. We used this technique in cases were due to anatomical and pathophysiological reasons, transplant survival was critical.

Perioperative antibiosis was chosen in all facial wounds and in patients with previous severe infections (like necrotizing fasciitis) or immunocompromising disorders like serious diabetes mellitus. The usual duration of antibiosis was 7 days. The drugs were chosen according an antibiogram for leg ulcers. For facial defects, cefuroxim 500 mg was given twice daily.

RESULTS

The size of soft tissue defects was between 3 and 875 cm^2. All patients had one or more comorbidities including diabetes, chronic ischaemic heart disease, hypertension, ankylosis, paresis and depression treated by appropriate drug therapy.

The use of the dermal template resulted in a complete and stable granulation in 100% of wounds. In the case of complete graft take, wounds healed within 9–14 days [Figures 1 and 2). Three of four facial defects healed completely. The follow-up for 6–20 months demonstrated not only stability of the wound closure but also a very good aesthetic outcome [Figures 3 and 4]. Of the two scalp lesions, one healed completely while the other one – a very large wound (375 cm^2) – showed only a partial graft take after 2 weeks.

From all soft tissue defects and chronic wounds treated, 17 showed a complete closure (complete remission, CR) and 19 achieved a complete granulation with an incomplete closure (partial remission, PR; [Table 1]). Of 10 patients with a visual analogue pain score of >6, all reported a marked pain relief, but 5 became pain free. The effect on pain was not restricted to a CR of the soft tissue defects/chronic wounds.

One patient developed a secondary infection 2 weeks after surgery resulting in a loss of the transplant. The final outcome, however, was a complete wound closure after 8 weeks of conventional good ulcer care. The final outcome of the other three patients with incomplete graft take was a complete closure after 8 weeks of conservative treatment (n = 2) and reduction of the wound area by 80% after 8 weeks of good ulcer care (n = 1). The transplants were stable even above the exposed Achilles tendon. The transplants did not show any significant shrinkage during follow-up. In a single patient with a surgical wound on the tip of the nose, the transplant failed, but granulation was good and the wound area decreased about 50% in

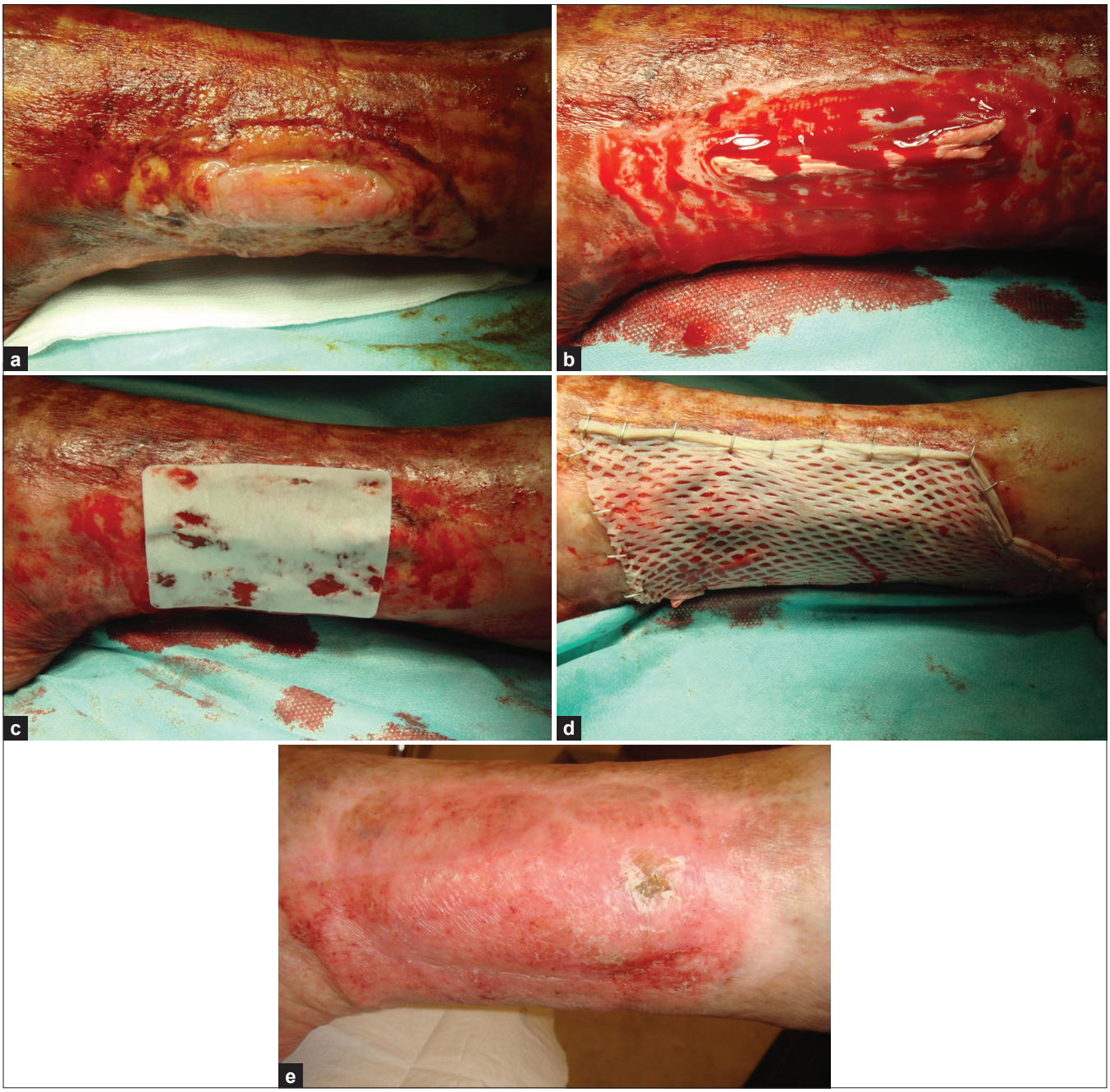

Figure 1: Patient 14, arteriovenous leg ulcer with exposed tendons; (a) Before treatment; (b) Shave excision; (c) Matriderm™ on the wound; (d) Split-skin mesh graft; (e) One year later with stable healing

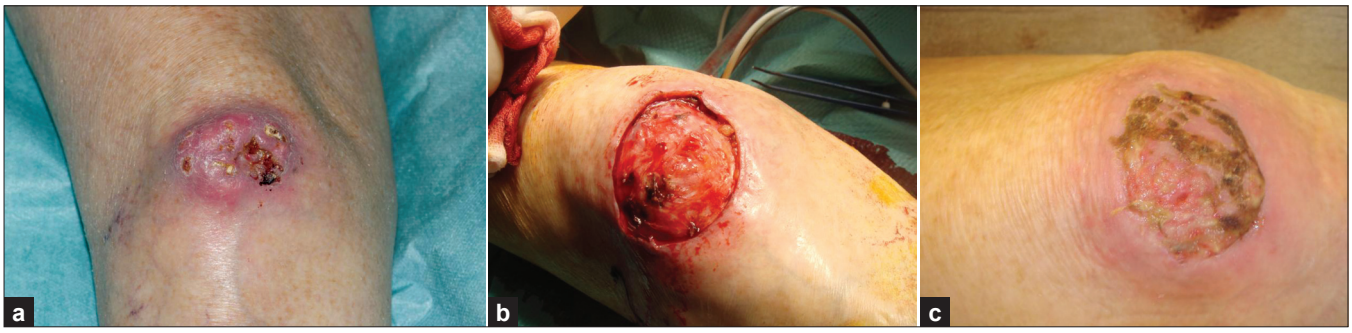

Figure 2: Patient 2. Calcifying prepatellar bursitis; (a) Before surgery; (b) Soft tissue defect after complete excision; (c) After three weeks

3 weeks. Because there was a partial sorption of the soft tissue resulting in a 2-mm defect, second surgery with a primary wound closure by sutures was performed 4 weeks later. No necrosis of the underlying tissue was noted in the case of transplant failure.

The aesthetic outcome was very good or good in 17 patients. No adverse events were noted due to the dermal template usage like biocompatibility problems or granuloma formation. The volume of the template and, in particular, the thickness, does not seem to diminish during the healing process. Skin elasticity was clinically not different from the surrounding tissue. The operation time was not prolonged by the use of the 'sandwich' technique. The technique can be easily used in conjunction with intermittent negative pressure when necessary.

DISCUSSION

In soft tissue defects, a wound closure often is possible by transplants or flaps. In other cases, the use of dermal templates has become an alternative.

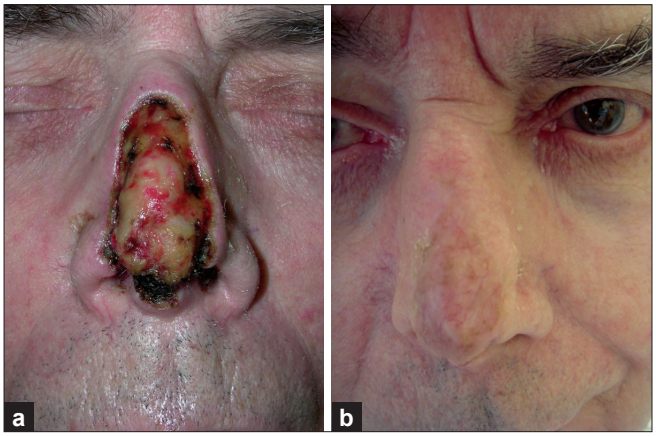

Figure 3: Patient 7. (a) After Mohs surgery of basal cell carcinoma, larger nasal defect with exposed cartilage; (b) One year after sandwich transplantation

A variety of acellular dermal templates have been developed. AlloDerm™ (KCI LifeCell Corp., San Antonio, TX, USA) is a human allogeneic dermal matrix with an intact basement membrane. Integra™ (Integra Life Sciences Corp., Plainsboro, NJ, USA) is a bovine collagen –glycosaminoglycan (chondroitin-6-sulphate) copolymer with silicone backing. Oasis™ consists of a collagen matrix from porcine small intestinal submucosa (Cook Biotech, West Lafayette, IN, USA).[8]

There are several products with a combination of matrix components that have been evaluated *in vitro* and *in vivo*. Scaffolds composed of different ratios of type I comb collagen and chitosan with added hyaluronic acid have been investigated by Lin *et al*. (2009). The microstructural observation of the composite scaffolds demonstrated a high pore interconnectivity with the pore size negatively influenced by chitosan.[9] Combined dermal matrix structures using collagen, chondroitin sulphate and hyaluronic acid have been developed by Wang *et al*.[8] Morphological observation showed that the novel scaffold had uniform and widely interconnected pores and an adequate porosity of about 94%.[10] A porous pullulan–collagen hydrogel matrix has been developed recently by Stanford University that supports the early phases of wound healing. Pullulan is a linear glucosic polysaccharide produced by the polymorphic fungus *Aureobasidium pullulans*, which has long been applied for various applications from food additives.[11]

Matriderm™ is composed of elastin and native collagen (types III, IV, and V) of bovine origin. Elastin and collagen are two major types of fibrous structures found in the human dermal tissue. In an experimental head-to-head

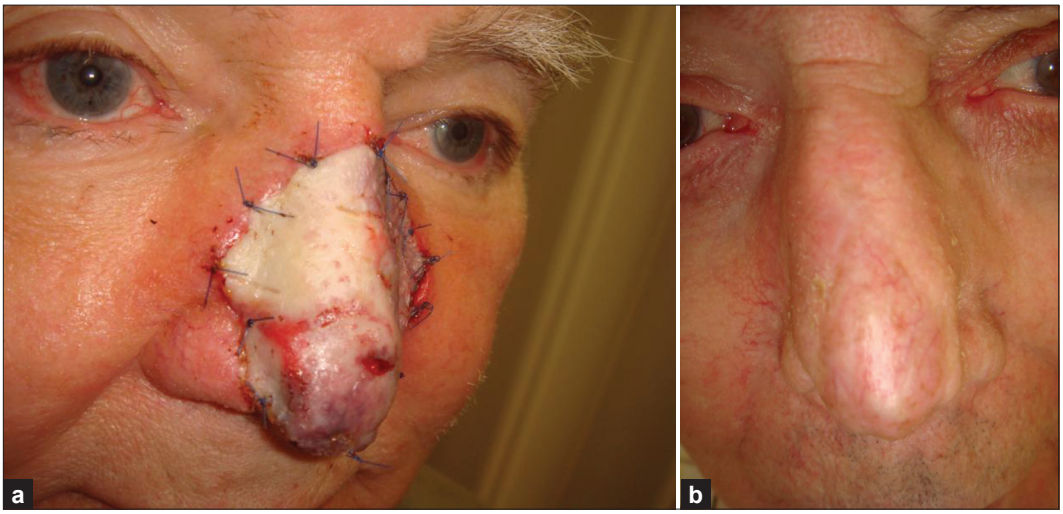

Figure 4: Patient 8. (a) Sandwich transplant after Mohs surgery for basal cell carcinoma of the nose. (b) About one year later

Table 1: Patients demographics, underlying disease and outcome after sandwich transplantation

No.	Age (years); gender	Disease, number of defects and indication and size or the dermal template	Exposed structures (cm^2)	Sandwich transplantation	Final outcome
1	89; female	Arterio-venous leg ulcer. Failure of previous	Tendons 37	Lower leg failure due to infection; secondary	CR but secondary transplant transplants CR; marked pain relief
2	89; female	Pretibial calcifying bursitis. Large defect with ex-posed bone and synovial bursa	Bone 96	Knee, with VAC™ above the split-skin mesh graft	CR, complete pain relief
3	88; female	Arterio-venous leg ulcer. Failure of previous grafts	Tendons 33	Lower leg, with VAC™ above a split-skin mesh graft	CR, almost complete pain granulation
4	87; male	Squamous cell carcnoma. Non-elastic tissue and exposed bone, severe cardiac disease	Scull 27	Temporo-occipital scalp	CR
5	85; female	Basal cell carcinoma. Low tissue quality, cardiac and diabetic disorders	Cartilage 4.5	Nose	CR
6	84; male	Posttraumatic ulcer. Cardiac and metabolic disorders, failure of previous transplants	Tendons 18	Foot, with VAC™ above the split-skin mesh graft	CR, marked pain relief
7	83; male	Basal cell carcinoma. Anticoagluation, cardiac disease	Cartilage 5	Nose	CR
8	82; male	Basal cell carcinoma. Metabolic diseases and patient's wish	Cartilage; bone 4.8	Nose	CR
9	78; male	Basal cell carcinoma. Anticoagulation and patient's wish	Cartilage 5	Nose	Transplant failure (necrosis), complete granulation
10	78; male	Diabetic foot ulcers. Failure of previous trans- plants	Achilles tendon 40	Foot, with VAC™ above the split-skin mesh graft	CR
11	76; female	Arterial leg ulcers (2)[a]. Failure of previous transplants with major pain	Achilles tendon 38 + 46	VAC™ before, lower leg	1× CR, 1× PR, total pain relief
12	76; male	Pressure sores (ankles, 2)[a], spinal cord injury, paralysis. Exposed bones, plastic surgeon disapproved flaps	Bones 12 + 7.5	VAC™ before, feet	Transplant failure, complete granulation
13	74; male	Large defect after necrotizing fasciitis. Large defect with an exposed bone, increased risk of re-infection	Bone 375	Lower leg, with VAC™ above the split-skin mesh graft	CR, complete pain relief
14	72; female	Arterio-venous leg ulcers (2)[a]. Previous transplants failed	Tendons 142 + 89	Lower leg	CR, complete pain relief
15	70; female	Peripheral calciphylaxis (2)[a]. Achilles tendon Increased risk of sepsis, metabolic diseases and exposed tendon	Lower leg 72	1× CR, 1× PR, total pain relief	
16	70; male	Diabetic foot ulcer, minor foot amputation. Previous transplants failed	Tendons 27	Foot	PR, complete granulation
17	68; male	Arterio-venous leg ulcer. Previous transplants failed	Tendons 32	Lower leg	PR, complete granulation, marked pain relief
18	67; male	Squamous cell carcinoma. Large scalp defect	Scull 375	Scalp	PR
19	67; male	Rheumatoid arthritis with mixed circumferential leg ulcer. Pretreatments including mesh graft transplants failed, severe pain	Tendons 875	Lower leg, with VAC™ above split-skin mesh-graft	CR; marked pain relief
20	55; male	Burn scar excision. Exposed bone, patient disapproved larger flaps	Bone 25	Lower leg	Partial graft take, but 8 weeks later CR
21	43; female	Pyoderma gangrenosum; combined immuno-suppression (prednisolone + myophenolate mofetil). Immobility due to the painful ulcer, extensive surgery not recommendable due to underlying disease	Tendons 7.6	VAC™ before, foot	PR, but dramatic pain relief
22	32; male	Large scull defect after A traffic accident. Exposed bone interfered with planned rehabilitation, closure of scull defect was planned thereafter	Meninges 200	Temporo-frontal head; only Matriderm™	CR (after 8 weeks)
23	21; male	Multitrauma, post-traumatic foot ulcer. Previous transplants failed	Tendons 58	VAC™ before, foot	CR

[a]Number of defects are given in parentheses

study, Matriderm™ and Integra™ have been evaluated to support split-skin mesh grafting. Both products yielded comparable results.[12]

The collagen–elastin matrix has been used primarily in burn wounds.[13-20] The technique allows skin grafting above exposed tendons and bony structures. The biomechanical properties of the transplanted skin seem to be much improved compared to grafts alone that may lead to contractures and diminished elasticity. The sandwich transplant technique may contribute in preventing joint contractures. More recently, the same technique has been employed for cranial defects after traffic accidents,[21] defects in skin tumour surgery,[8,22-24] defects after various injuries of the hand,[17] painful plantar callosities[25] and various other chronic and postoperative soft tissue wounds.[8]

Nasal tip defects are challenging. In a comparative study, Riml *et al*.[23] observed better outcome with a perichondrodermal composite graft and reported two patients developing fistulae after Matriderm™-aided skin transplantation.[23] We observed a complete graft take in three of four patients, but further studies are necessary.

Even if complete graft take is not always possible with our technique, granulation could be improved in all cases. Matriderm™ is a valuable tool when used as a template for split-skin mesh grafts for defect closures when exposed bones, cartilage and tendons would not support a direct transplantation. It is remarkable that the sandwich technique described herein can be combined with intermittent negative pressure to support graft survival.[24]

Another important effect of the elastin–collagen matrix is pain relief. Pain is a major factor in chronic wounds that has a substantial negative impact on quality of life.[25] We suppose that the pain relief is supported by wound dressing-like qualities of the dermal matrix and improved granulation, but further studies would be necessary to better explain the clinical observation.

In conclusion, sandwich transplantation with the elastin–collagen matrix can be used in a variety of clinical situations to support defect closures and pain relief in a simple, reliable and fast way with excellent safety.

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