

Endoform[®] helps to improve the outcome and reduce the cost of STSG and CTP treatments

- **Endoform[®]** is rapidly vascularized, providing a nurturing scaffold that underlies the grafted tissue or CTP
- Early establishment of vascular networks provides the healing graft or skin substitute with nutrients and growth factors resulting in robust remodelling and regeneration of the dermis.¹
- **Endoform[®]** can be used before and after the application of a CTP or STSG. Application of Endoform beforehand reduces matrix metalloproteinase (MMP) activity in the wound bed, promoting constructive remodelling.² Application of **Endoform[®]** after STSG/CTP encourages wound closure by promoting granulation tissue formation and epithelialization.^{3,4,5}
- Preparation of wound bed with **Endoform[®]** can reduce the cost of CTP by increasing the likelihood of success and reducing the number of applications required for wound closure.^{4,5,6}



Week 0:

Wound measurement:
24 cm x 6.0 cm x 0.5 cm



Week 8:

Wound measurement:
14.5 cm x 2.5 cm x 0.2 cm

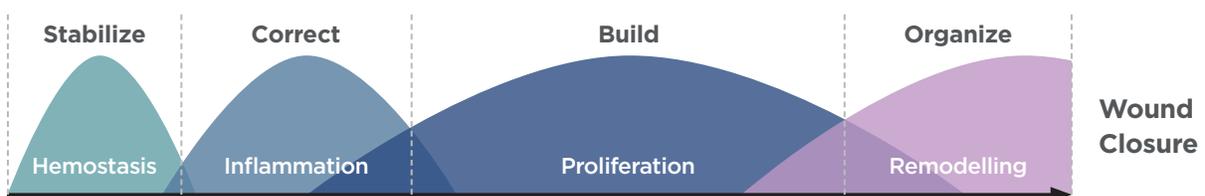


Week 16:

Wound measurement:
Wound closure

Leg wound closure by treatment with Endoform before and after use of skin substitute²

Endoform[®] can be used at all phases of wound management



*For use with Split Thickness Skin Grafts (STSG) and Cellular and/or Tissue-Based Products (CTP)


Natural Dermal Template

Antimicrobial Dermal Template


*For use with Split Thickness Skin Grafts (STSG) and Cellular and/or Tissue-Based Products (CTP)

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Ovine Forestomach Matrix as a Substrate for Single-Stage Split-Thickness Graft Reconstruction

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Keywords: biomaterial, carcinoma, ovine forestomach matrix, reconstruction, split-thickness graft

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Objective: Split skin graft reconstruction of scalp defects often leaves an obvious contour defect. Here, we aimed to demonstrate the use of a decellularized extracellular matrix biomaterial, termed ovine forestomach matrix (OFM), as a substrate for split-thickness skin grafts (STSGs) for scalp reconstruction. **Methods:** Following full-thickness tumor excision, OFM was applied directly to skull periosteum, and then an STSG was applied. Participants were monitored for graft take, epithelialization, and cosmetic outcomes. **Results:** Participants responded well to the procedure with more than 95% graft take in 4 participants, and 100% epithelialization of the grafts after 2 weeks. A 30% graft take was observed in the fifth participant due to local infection and partial necrosis of the graft. Ovine forestomach matrix was remodelled with time and the regenerated dermis was well vascularized and had robust and ordered collagen deposition. **Conclusions:** This series demonstrates that OFM can serve as a temporary dermal scaffold to support an overlying STSG and allow for a single-stage grafting procedure.

Reconstruction of skin defects may be performed by skin grafting procedures. Full-thickness skin grafts result in a more durable reconstruction due to the larger proportion of dermis placed into the defect than split-thickness skin grafts (STSGs). Because of limited full-thickness skin graft donor sites, STSGs are used in larger defects. Two-stage grafting procedures have been developed whereby a dermal substitute is grafted into the defect under an artificial epidermis, which is subsequently replaced by an STSG. There is a clinical need to replace the relative complexity of 2-stage grafting procedures with robust single-stage procedures without compromising clinical outcomes. However, the feasibility and success of single-stage procedures is dependent on the vascularity of the underlying tissue. To overcome these limitations, collagen-based dermal substitutes have been investigated as temporary substrates for an overlying STSG. This approach creates a composite graft, whereby the underlying dermal substitute is rapidly vascularized and therefore can

support epithelial proliferation of the STSG, leading to closure of the defect and dermal regeneration. The dermal substitute, human acellular dermal matrix (eg, AlloDerm) has been investigated for STSG composite grafting in the treatment of burns,¹⁻³ traumatic skin loss,^{2,4,5} and tumor excision.⁶⁻⁸

Ovine forestomach matrix (OFM) is a decellularized extracellular matrix biomaterial developed for wound healing and tissue regeneration applications and is cleared by the US Food and Drug Administration for dermal indications. Ovine forestomach matrix comprises mainly collagens I and III arranged as native fibres that retain the 3-dimensional architecture seen in tissue ECM.⁹ Additional structural (eg, collagen IV, fibronectin, and elastin), signalling (eg, glycosaminoglycans and heparin sulphate), and adhesion molecules (eg, laminin) are also present. Ovine forestomach matrix is nonantigenic, and it undergoes cellular infiltration and subsequent remodelling leading to regeneration of missing or damaged tissues. In preclinical models, OFM has been shown to be angiogenic and is rapidly revascularized,¹⁰ and in clinical studies, OFM treatment resulted in well vascularized granulation tissue in chronic venous ulcers.¹¹ These previous findings suggested that OFM may be suitable for composite grafting with STSGs, where clinical success is reliant on the ability for the substrate to rapidly revascularized and provide the requisite nutrients and immune components to the overlying STSG.

METHODS

Case studies

The case series was approved by an institutional review board (Upper South A Regional Ethics Committee, New Zealand) and registered with the Australian New Zealand Clinical Trials Registry (<http://www.anzctr.org.au/>). Five participants were selected on the basis of the inclusion and exclusion criteria listed in Table 1 and all tumors were confirmed by pathology prior to the procedure. The procedure was conducted under either local or general anesthetic. A full-thickness excision down to but not including the pericranium was used to remove the tumor and a 5- to 10-mm margin (Fig 1a). Ovine forestomach matrix (Endoform, Mesynthes Limited, New Zealand) was meshed by either hand or a skin graft mesher at a ratio of 1.5:1 (Zimmer) and then trimmed to fit the excisional defect. The material was rehydrated in sterile saline for a minimum of 5 minutes and placed into the defect to contact the underlying periosteum (Fig 1b). An STSG (approximately 0.25-mm thick) was harvested from the thigh of each participant, using either a dermatome (Zimmer Machinery Corporation, Cowpens, South Carolina) or a hand knife. The graft was meshed by hand, cut to fit the defect, and then placed over the OFM, making sure the OFM and STSG were in contact (Fig 1c). A nonadherent dressing (Mepitel, Mölnlycke Health Care, Sweden) was placed over the graft, then a bolster of foam was sutured in place to ensure close contact between the STSG, OFM, and underlying periosteum (Fig 1d). The secondary dressing was removed 7 days following surgery and the graft imaged and evaluated for percentage graft take and epithelialization, based on the total area of the defect. A silver-based hydrogel (Silvasorb; Medline Industries, Inc, Mundelein, Illinois) was used to treat any suspected bacterial infection. The defect was re-dressed using a nonadherent dressing, as required,

and reevaluated weekly for the first fortnight, then monthly or as required. At final review, the healed wounds were assessed for contour defect and scalp mobility by palpation.

Table 1. *Inclusion and exclusion criteria*

Inclusion criteria	Exclusion criteria
> 18 years old	Any cutaneous malignancies with metastatic disease
At least 1 nonmelanoma skin cancer without metastatic disease	Diagnosed with malignant melanoma
Malignancies that require full-thickness excision	Systemic malignancy
Postexcision wounds that would normally be reconstructed with a split skin graft	Under suspicion of metastatic disease
Compliant	Pregnant or lactating
Competent	Clinically significant cardiac, pulmonary, renal, hepatic, neurologic, and/or immune dysfunction that may affect wound healing
Tumor located on the scalp, neck, or upper limbs	Known allergy to collagen or ovine (sheep) materials; any previous reaction to a collagen product
	Family or personal history of severe allergies (including asthma, hay fever, and atopic dermatitis)
	Allergies to foods, especially meat products
	Unable to remain in study for 6 mo
	Diabetes mellitus
	Declined, unable, or unwilling to make informed consent
	Not fluent in English or Maori—requires interpreter
	Religious or ethical objections to sheep-derived product
	Previous radiotherapy at the defect site
	Immunosuppressant medication (prednisone >5 mg/d or equivalent)

Histology and immunohistochemistry

Excised tissues were fixed with 4% formalin, paraffin embedded and stained. Gomoris' Trichrome staining was conducted as previously described.¹⁰ Anti-CD34 immunohistochemistry was conducted as previously described¹⁰ using a mouse antihuman CD34 (Abcam Plc, Cambridge, England) monoclonal antibody. Slides were imaged using a CX-31 microscope (Olympus Imaging America Inc, Center Valley, Pennsylvania) fitted with a DP12 digital camera (Olympus).

RESULTS

Participants (B001 through B005) enrolled in the study were all male, 61 to 83 years old, presenting with either an squamous cell carcinoma (SCC) (n = 4) or basal-cell carcinoma (BCC) (n = 1), located on the scalp (Table 2). The tumor size, estimated at enrolment, ranged from 1.2 to 4.6 cm², and tumors had been present for approximately 2.5 to 9

months. Following tumor excision, the full-thickness wounds were approximately 5 to 10 cm². Ovine forestomach matrix could be meshed using a surgical skin graft mesher and once rehydrated was easy to handle and conformed well to the underlying periosteum. One week postsurgery, 4 of the participants had more than 95% graft take (B002, B003, B004, and B005), while the fifth participant, B001, had a 30% graft take. The low graft take in participant B001 resulted from a local infection and partial necrosis of the graft (Fig 2b), which was managed with a silver-containing hydrogel. Complete epithelialization of all grafts occurred in 2 weeks, except for participant B001 where infection delayed complete epithelialization to 8 weeks.

Table 2. Summary of participant details and outcomes

Participant	Sex	Age	Tumor location	Age, mo	Type	Area, cm ²
B001	Male	83	Left vertex scalp	4	SCC	1.5
B002	Male	83	Left anterior scalp	9	BCC	1.2
B003	Male	73	Vertex scalp	8	Previous SCC	16.0
B004	Male	81	Left vertex scalp	2.5	SCC	2.9
B005	Male	61	Left vertex scalp	6	SCC	4.6

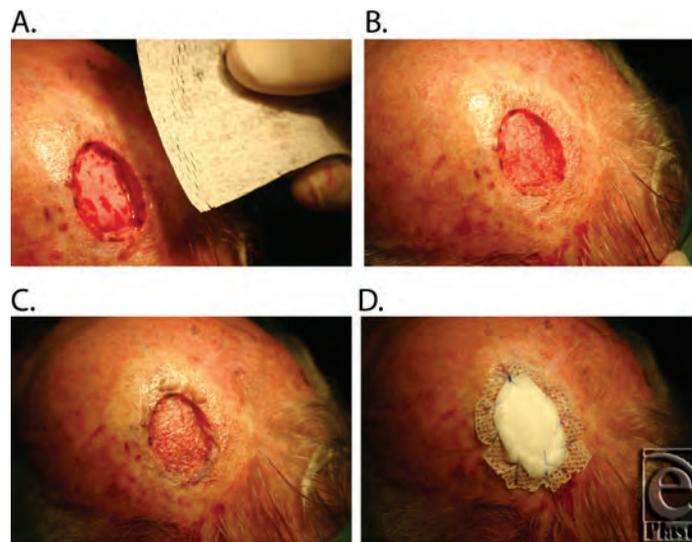


Figure 1. Representative images of the tumor resection and single-stage split-thickness grafting. (a) Excisional defect following tumor resection and meshed OFM prior to rehydration. (b) Rehydrated OFM cut to size and placed within the defect to conform to the underlying periosteum. (c) Meshed STSG in contact with the underlying OFM. (d) Secondary dressings secured to the perimeter of the excision.

Participants B001, B002, and B003 were available for long-term follow-up (Fig 2). The epithelium remained stable throughout follow-up (minimum follow-up of 6 months, range 7-9 months). Regenerated dermal tissues were well vascularized, elastic, and mobile over the underlying periosteum. Contour defects were judged to be mild via subjective observation.

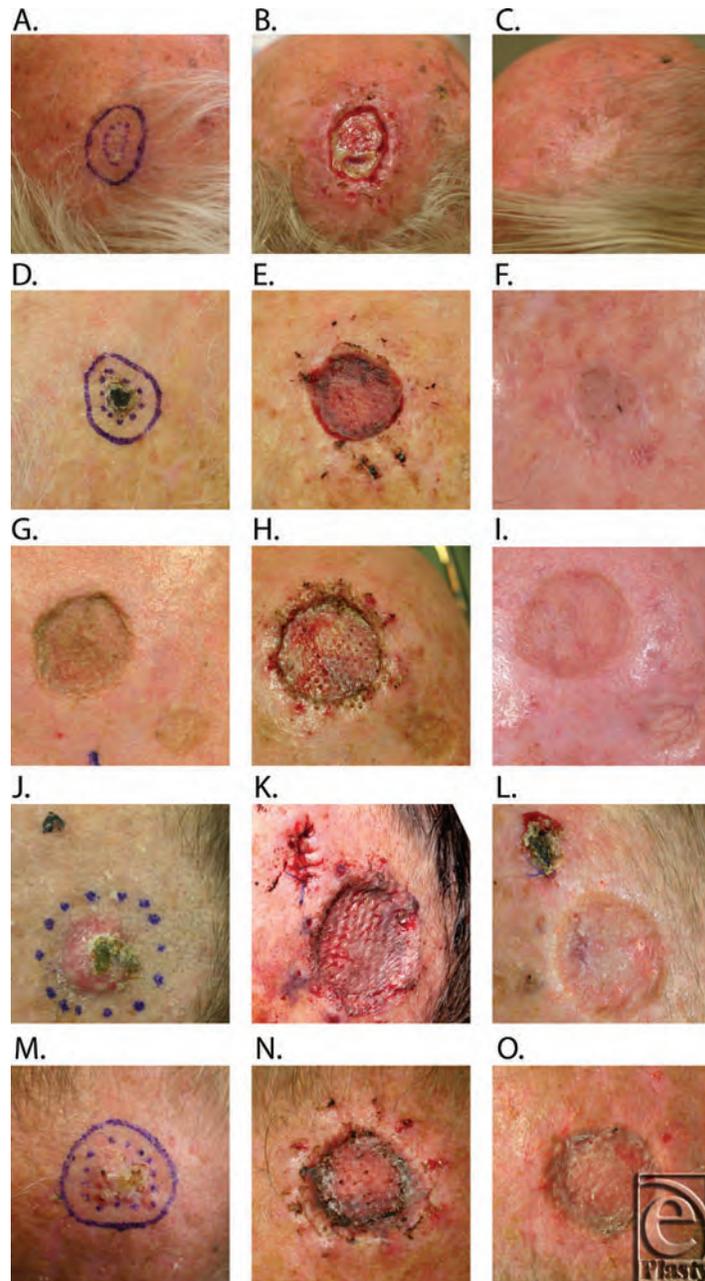


Figure 2. Representative images of the study participants B001 (2.A., 2.B., 2.C.), B002 (2.D., 2.E., 2.F.), B003 (2.G., 2.H., 2.I.), B004 (2.J., 2.K., 2.L.), and B005 (2.M., 2.N., 2.O.), prior to tumor excision (2.A., 2.D., 2.G., 2.J., 2.M.) and 1 week following surgery (2.B., 2.E., 2.H., 2.K., 2.N.). Surgical site following healing; 2.C., 40 weeks; 2.E., 16 weeks; 2.I., 16 weeks; 2.L., 4 weeks (prior to reexcision); 2.O., 4 weeks (prior to reexcision).

Two of the participants (B004 and B005) had the original surgical site further excised 4 weeks postsurgery to gain adequate (>1 mm histological margin) excision of the tumors at the deep margin. The subsequent procedure excised the original graft as well as the margins and underlying periosteum leaving exposed skull. Therefore, the defects were closed with scalp rotation flaps. The excised tissues containing the original graft were fixed, stained, and imaged (Fig 3a). Remnants of the matrix was evident in both B004 and B005 appearing as compact blue collagen fibers that were distinct from collagen of the regenerating dermis. The matrix was evident in the upper sections of the regenerating dermis, immediately beneath the superficial dermis from the STSG. Matrix fragments were infiltrated with fibroblasts and immune cells, including multinuclear giant cells (MNGCs) macrophages and lymphocytes. The immune response in B005 was greater than that in B004, with mononuclear cells and MNGCs associated with the remodelled matrix. Both patients had a well-vascularized dermal layer with dense well-organized collagen bundles and spindle-shaped fibroblasts (Fig 3a). A fully formed keratinized stratified squamous epithelial layer was present and dermal papillae extended into the epithelial layer. An extensive network of blood vessels was present within the regenerating dermis, as evidenced by anti-CD34 immunohistochemistry (Fig 3b).

DISCUSSION

Scalp reconstruction is especially challenging given the limited blood supply of the underlying calvaria, the relatively thin cutaneous tissue, and the lack of redundant skin. Split-thickness skin grafts take well on the underlying periosteum; however, this leaves an obvious contour defect. Skin flaps and expanders have been traditionally used, but these approaches are complicated by the minimal laxity of the scalp and the complexity of these multistage procedures. As an alternative, collagen-based biomaterials that function as temporary dermal scaffolds have become increasingly useful as part of a single- or 2-stage procedure for surgical reconstruction. These materials allow direct grafting to the underlying calvaria, usually following removal of the outer portion of exposed bone to allow vascularization of the dermal scaffold.^{7,12,13} There are a few examples in the literature where dermal scaffolds have been used directly in contact with exposed pericranium to support an STSG,⁸ and to our knowledge this is the first report of a xenogenic dermal scaffold being used in this fashion. The current composite grafting procedure allows for a single-stage procedure to be completed, therefore reducing increased costs associated with multiple procedures and longer term wound management. Results from the 5 participants enrolled in the current study indicate that clinical outcomes from this approach were not compromised, though further controlled studies are warranted.

Previous preclinical studies have shown OFM is remodelled, and importantly the remodelling phenotype resolves with time, with concomitant deposition of new tissues.¹⁰ This is consistent with the known inflammatory response invoked by decellularized extracellular matrix-based biomaterials, namely remodelling as characterized by an immunomodulatory M2 macrophage phenotype rather than acute inflammation.¹⁴ The current study provided a rare opportunity to microscopically examine a snapshot of the remodelling of OFM following human implantation, be it with a limited sample size. As has been seen previously in *in vivo* studies,^{10,15} the inflammatory response to OFM included the recruitment of a number

of immune modulatory cells, including lymphocytes, macrophages, and MNGCs. Long-term resolution of the remodelling inflammatory response in participants was evidenced by the robustness of the regenerated dermis and absence of any wound breakdown.

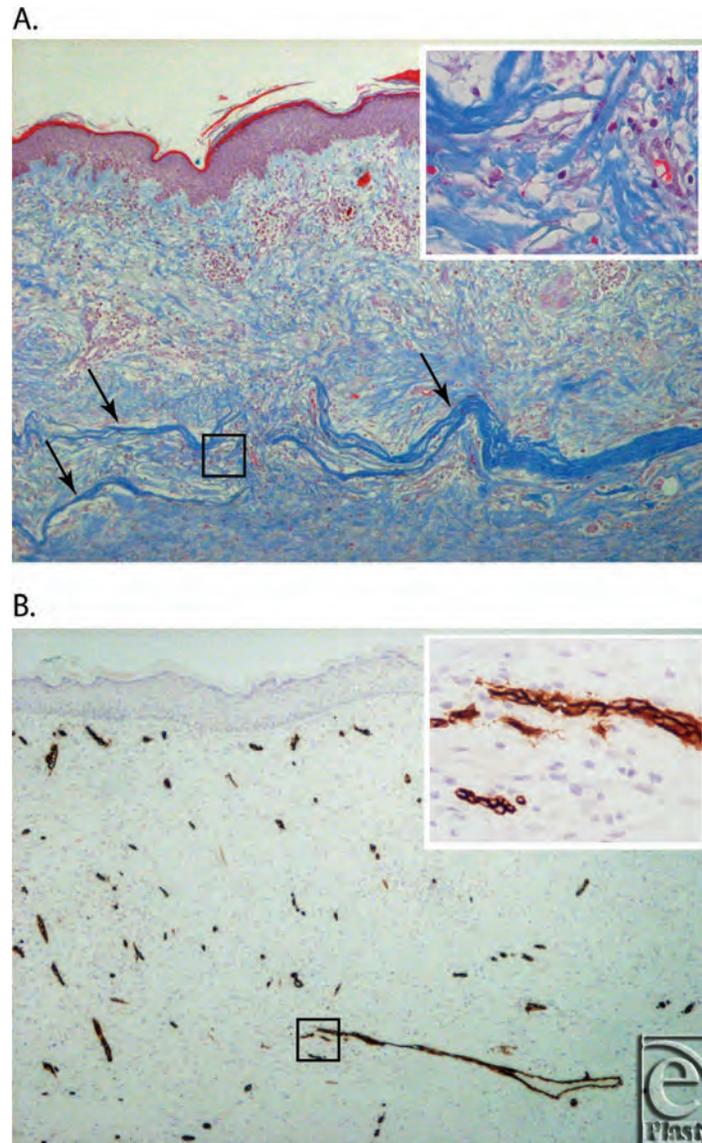


Figure 3. (a) Gomori's Trichome stain of the excised graft from B004, 4 weeks postgraft (4× magnification). Arrows indicate the intact fragments of OFM. Insert shows a 40× magnification of the area indicated by the black square. (b) CD34 immunohistochemistry of the excised graft from B004, 4 weeks postgraft (4× magnification). Insert shows a 40× magnification of the area indicated by the black square.

While the current application of this procedure was in the reconstruction of tissue deficits following tumor resection, there is the potential for this approach to be applied to the treatment of burns and traumatic skin loss. This initial study also suggests OFM as a candidate substrate for autologous cell seeding, whereby suspensions of dermal cells (eg, keratinocytes or fibroblasts) or stem cells (eg, bone marrow or adipose-derived stem cells) are applied to the substrate. This strategy has many similarities to the composite STSG procedure described here, as it relies on rapid vascularization of the underlying dermal scaffold to support the transplanted cells.

Acknowledgements

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CASE STUDY 27 | Left Leg Surgical Wound (Bookending with Endoform)

Patient: 51 year-old female.

Patient History:

- Peripheral vascular disease and deep vein thrombosis.
- Patient had a popliteal bypass 6 weeks prior. The wound was opened due to infection and allowed to heal by secondary intention.

Previous wound management:

- Wound debridement, collagenase ointment and negative pressure wound therapy (NPWT).



Week 0:

Wound measurement: 24.0 cm X 6.0 cm X 0.5cm
 Wound description: Full thickness wound, moderate drainage and very granular base.
 Wound management: Wound debridement with NPWT twice weekly.



Week 3:

Wound measurement: 20.5 cm X 4.2 cm X 0.2 cm
 Wound description: Decreasing in size.
 Wound management: Wound debridement. Endoform dermal template covered by a non-adherent dressing was applied with NPWT twice weekly.



Week 4:

Wound measurement: 17.0 cm X 4.0 cm X 0.1 cm
 Wound management: Wound debridement. Endoform dermal template covered by a non-adherent dressing was applied with NPWT twice weekly.



Week 6:

Wound measurement: 16.0 cm X 3.3 cm X 0.2 cm
 Wound management: Wound debridement. Endoform dermal template covered by a non-adherent dressing was applied with NPWT twice weekly.



Week 8:

Wound measurement: 14.5 cm X 2.5 cm X 0.2 cm
 Wound management: Wound debridement. Application of an amniotic membrane graft covered with a bordered foam dressing and secured with elastic tubular bandage for compression. Dressing changed once weekly.



Week 9:

Wound measurement: 11.0 cm X 2.5 cm X 0.1cm
 Wound management: Same as previous week 8.



Week 11:

Wound measurement: 9.8 cm X 2.3 cm X 0.1cm
 Wound management: Same as previous week 9



Week 14:

Wound measurement: 2.0 cm X 0.7 cm X 0.1cm
 Wound management: Wound debridement. Application of Endoform dermal template covered with a bordered foam dressing and secured with elastic tubular bandage for compression. Dressing changed once weekly.



Week 16:

Wound measurement: Wound closure.
 Wound management: Continued using elastic tubular bandage for compression.



CASE STUDY 27 | Left Leg Surgical Wound (Bookending with Endoform)

Summary:

Consider a “bookend” approach by using Endoform dermal template before and after skin substitute and graft use, to help reduce matrix metalloproteinases (MMPs) activity with an extracellular matrix (ECM) dressing.

Case provided by:
Patricia McIlrath, DPM Temple University Hospital Wound
Care and Hyperbarics Philadelphia, PA

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Preparing a wound bed before application of cellular tissue based products using an Ovine collagen (CECM) dressing with an intact extracellular matrix.

• Michael Desvigne, MD, CWS, FACS, FAACWS
Plastic & Reconstructive Surgery, Wound Care & Hyperbaric Medicine

Introduction:

With increasing amounts of offerings in dressings for wound closure, the clinician must be careful to choose the best dressing for their patients. There are many clinical reasons for utilizing advanced cellular tissue based products (CTP), but one must weigh the outcomes versus costs. The cost for a standard 2x2 of any of the CTPs can range from the hundreds to thousands of dollars per piece. Healthcare institutions are becoming more cost conscious. Failure of these products can be both costly to the patient and the healthcare system. CECM* provides a broad spectrum MMP reduction¹ before and after CTP utilization. To set up for successful take of a CTP product, one can consider utilizing a CECM both before and after CTP application ("bookend") to help reduce matrix metalloproteinases (MMPs) activity. In addition, CECM provides an intact, native extracellular matrix that helps promotes tissue granulation² and epithelialization for final wound closure.³

Methods:

In this case, CECM was used before, during and after CTP utilization. Both the CECM and CTP were applied per product recommendations. Wounds were assessed weekly.

Conclusion:

CECM provides assistance with MMP reduction, while the CTP provides scaffolding for cellular growth.⁴ Because the exact mechanisms are not known, further research is needed. Early experience of the before and after utilization of CECM with CTP resulted in healing progression and showed positive results in wound closure in this case.

Case Study

Patient: 42 year-old female.

Past medical history:

- Osteosarcoma of the left lower extremity

Previous wound management:

- Tumor resection and free tissue transfer completed after post-operative radiation. Two non-healing wounds, one in the proximal portion of the flap and the other distally at the level of the Achilles tendon. After 14 months, with failed attempts at surgical closure and moist wound therapy. There was no progression toward healing. There was no evidence of recurrent tumor and cultures were negative. The patient then underwent excisional debridement followed by a single application of CTP. The area was covered with gentian violet and methylene blue (GV/MB) polyurethane (PU) antibacterial foam** dressing. The following week, CECM was added to the treatment and reapplied weekly. In 2 weeks, the distal wound had 100% epithelialization and the proximal wound decreased in size by 20% from initial wound size. At 4 weeks, the larger more proximal wound in the area of radiated tissue injury decreased in size by 50% from initial wound size. At 8 weeks, the proximal wound size decreased by 75% from initial wound size. There was notable granulation tissue and new epithelium around and underlying the CTP. The graft remained adherent.
- Despite improvement at 12 weeks, the proximal wound was not completely healed and the distal wound had a recurrent ulceration. The recurring stalled phase of the wounds became apparent although there was no evidence of infection or recurring trauma. At this time, it was elected to proceed with additional placement of CTP with plans to "bookend" the treatment immediately with additional CECM to assist with MMP reduction.



Initial wound
Pre-debridement



Initial wound
Post-debridement



Week 0

Wound management:

Patient initially seen and treated with debridement and placement CTP. Wound improved but stalled after 8 weeks. Bookending management was initiated with placement of CECM (Figure 1) covered MB/GV antibacterial foam dressing (Figure 2). CECM added and reapplied weekly.



Week 12

Wound management:

Despite improvement proximal wound not completely healed and distal wound with recurrent ulceration. CTP placed. CECM applied over CTP to "bookend" treatment to assist with MMP reduction.



Week 14

Wound management:

Wounds showed significant improvement with increased granulation tissue and epithelialization.



Week 15

Wound management:

(Figure 3) a reduction of 25% and 44 % in the proximal and distal wounds respectively from wound size in figure 1. (Figure 4) Application of CECM. (Figure 5) CECM covered with a non-adherent dressing and GV/MB PU antibacterial foam.



Week 16



Week 16

Wound management:

A reduction of 55% and 75% reduction respectively from wound size in figure 1. Each week additional CECM was placed followed by GV/MB PU antibacterial foam. Wound treatment is ongoing.

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* Endoform dermal template, Distributed by Hollister Incorporated.
** Hydrofera Blue Ready foam, Distributed by Hollister Incorporated.

Financial disclosure: M. Desvigne received an honorarium from Hollister Incorporated.



Desvigne, M. N. (2016). Preparing a wound bed before application of cellular tissue based products using an Ovine collagen (CECM) dressing with an intact extracellular matrix. Symposium on Advanced Wound Care Fall, Las Vegas, NA.



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Wound Bed Preparation: Is It Time to Up Your Game?

Daniel Ferreras, DPM, FAPWCA, AAWC

Ostomy Wound Management welcomes Wound Care in the First Person to its stable of columns sponsored by leading manufacturers of wound, ostomy, and continence care products. This new column from Hollister Inc, Libertyville, IL, will take a first-person approach to the challenges providers overcome in the care of their patients.

Dr. Ferreras is Lead/Chief Podiatrist, Surgical Services, Carl Vinson VA Medical Center Dublin, GA.

Two years ago, I embarked on a journey to bring 21st century wound healing strategies to a rural veteran's hospital. This journey led to the development of a wound healing center as a pilot program. An important step in this process was the development of an evidence-based, dual-protocol algorithm. The first part (Decision Protocol) honored the fundamentals of wound healing and included optimized perfusion, proper offloading, infection control, diet, and debridement¹⁻³; the second part (Treatment Protocol) guided the clinician with the option of continuing conventional therapy or switching to an advanced graft.⁴

Despite this algorithm, during the first quarter of the 12-month pilot program, 144 advanced grafts (or skin substitutes) were used but only 24 wounds progressed to closure.⁴ Based on 1) the needs of our chronic wound population, 2) growing evidence on the effect of matrix metalloproteinase (MMP) imbalances on wound healing^{5,6}; and a published study⁷ linking dermal graft cellular tissue-based product (CTP) failure to elevated MMP levels in diabetic foot ulcers, I was compelled to refocus efforts on the fundamentals of wound bed preparation. As a result, we altered our algorithm at the start of the second quarter of the pilot program by switching to an alternative collagen dressing, Endoform™ dermal template (Hollister Inc, Libertyville, IL), to be used as a first-line conventional treatment strategy.⁴

Endoform dermal template is a collagen dressing, but more specifically it is an intact extracellular matrix (ECM) dressing that retains the structure and function of the ECM seen in healing tissues.⁸⁻¹⁰ It can assist the body through all phases of wound healing; for example, when placed in an acute wound where the patient's ECM is damaged or missing, the dressing is designed to provide a temporary ECM the patient's body can use to help grow new tissue. In addition, the literature⁶ shows Endoform dermal template provides broad-spectrum MMP reduction. This is useful for chronic wounds in which elevated protease levels are hindering wound advancement.⁵

With the addition of Endoform dermal template to our algorithm, we discovered an interesting trend. From quarter

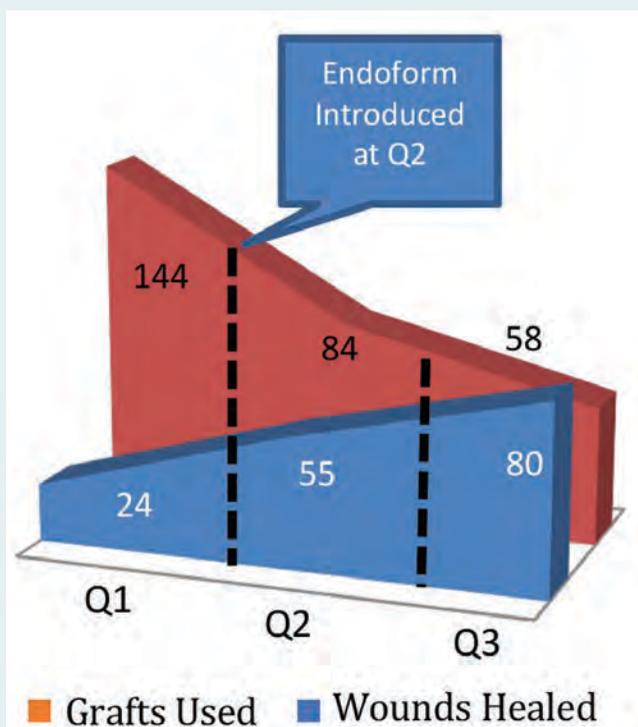


Figure 1. After Endoform dermal template was introduced in Q2, the number of healed wounds increased as the number of advanced grafts used decreased.⁴

1 to quarter 2, our advanced graft usage decreased from 144 to 84 and wound resolution increased from 24 to 55. These dramatic trends continued in quarter 3, with 58 grafts used and 80 wounds resolved. Thus, from the first quarter through the end of the third quarter, graft usage decreased by 59.7% while wound resolution increased by 95.5%⁴ (see Figure 1).

One case treated under this new algorithm involved a 60-year-old man who presented with diabetic foot ulcers on the hallux and second digit of his left foot (see Figure 2A) and a complex medical history. The wounds were debrided



Figure 2. A) Diabetic foot ulcers on the hallux and second digit of a 60-year-old man's left foot. After wound bed preparation, Endoform dermal template was applied; B) at week 9 of treatment, a bilayered skin substitute was applied; C) the dermal template treatment was continued after an injury interrupted healing; d) both ulcers healed at 6.5 months.

and attention was paid to diet. Noninvasive vascular diagnostic testing was done, wounds were offloaded, vascular intervention was provided, and mental/spiritual counseling were offered. After wound bed preparation, Endoform dermal template was applied with a gentian violet and methylene blue foam as a cover dressing. At week 9, a bilayered skin substitute was applied to the wound to speed resolution (see Figure 2B). After the patient sustained an injury to the foot, setting wound healing back several weeks, Endoform dermal template was continued and a fetal bovine dermal repair scaffold was placed on week 12 to help speed restoration of the collagen-rich wound bed. Endoform dermal template then was continued (see Figure 2C) until both ulcers fully healed at 6.5 months (see Figure 2D).⁴

In summary, we all need a game plan to reach our healing goals. Equally important are the players in that game and how they can work together. This modification to our protocol to incorporate Endoform dermal template was a game changer and greatly impacted wound healing trend in my center.

To learn more about Dr. Ferreras' protocol and data, view his webcast at www.hollister.com/ferrerasbookending.com. ■

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Utilization of an ovine collagen dressing with an intact extracellular matrix (CECM) within a dual-protocol algorithm to improve wound closure times and reduce expenditures in a VA Hospital.

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Alexandria VA Wound Healing Center, Alexandria, LA

Introduction:

Wound healing involves a complex series of biochemical and cellular processes. These sophisticated events can best be orchestrated when careful use of and adherence to an evidence based wound healing algorithm is utilized.² With the evolution and introduction of more costly cellular based biological grafts, which oftentimes have a limited shelf life window, the utilization of a CECM used from the first day of treatment can be a viable option in a wound care treatment plan. The CECM offers clinicians another option in a dual-protocol algorithm to help promote wound closure. When a broad-spectrum MMP reducing CECM₃ was strategically utilized as part of a broader dual-protocol algorithm, it offered positive outcomes to wound closure. It also offers further momentum toward the development of a clinical model that couples organized fundamental wound closure tenets and the use of reasonably priced collagen platforms.

Methodology:

The Alexandria VA Wound Healing Center features state of the art, 21st century technologies that can provide military veterans suffering from diabetic, venous leg and lower extremity pressure ulcers access to some of the most up-to-date wound healing diagnostic and treatment strategies available. The center established consulting protocols and developed a clinically functional, dual-protocol algorithm that can effectively deliver a standardized method of assessing, treating and managing wounds. (See Figure 1).

CECM was introduced in the Wound Healing Center to determine the feasibility of using a unique collagen dressing that combines strength, simplicity and savings. CECM was a first-line treatment strategy in a dual-protocol algorithm that combined both a decision and a treatment protocol. The number of wound resolutions, amount of advanced graft usage and CECM usage was plotted against a function of time. (See Figure 2). Our clinical decision to continue with conservative treatment or bridge to a more advanced product was based on whether there was a 30%-50% wound size reduction over 4 weeks.⁴ If wound size continued to contract after 4 weeks of conservative treatment, CECM remained the primary dressing. If wound contraction stalled or increased after 4 weeks, an advanced biologic was chosen in lieu of CECM to reach our resolution endpoint. Complete and sustained wound resolution was defined as closure by secondary intention,⁵ with repopulation of healthy granular tissue to wound base,⁶ and 100% epithelialization with no drainage.⁷

Conclusion:

This abstract demonstrates two endpoints. First, the use of a comprehensive dual protocol algorithm, utilizing a native MMP-reducing collagen dermal template (CECM) as first line wound management, was a success. Secondly, after the introduction of the CECM in this VA hospital, the number of wound resolutions were increased by 70% and advanced grafts expenditures were reduced by 71.6%.

Figure 1

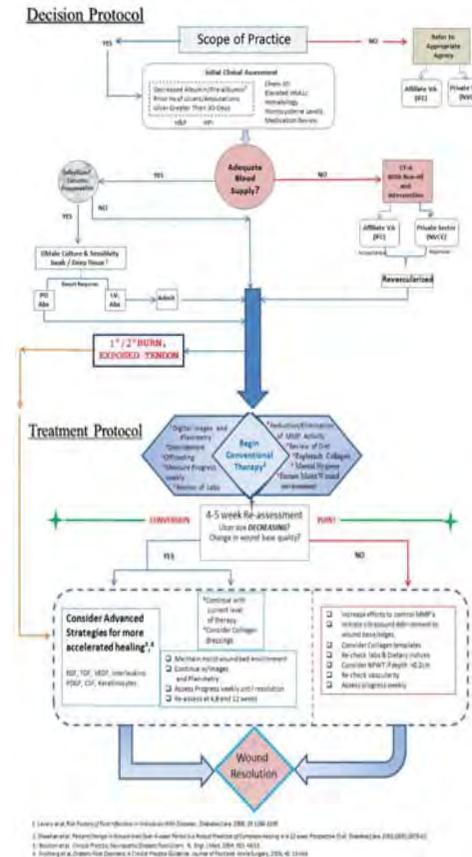
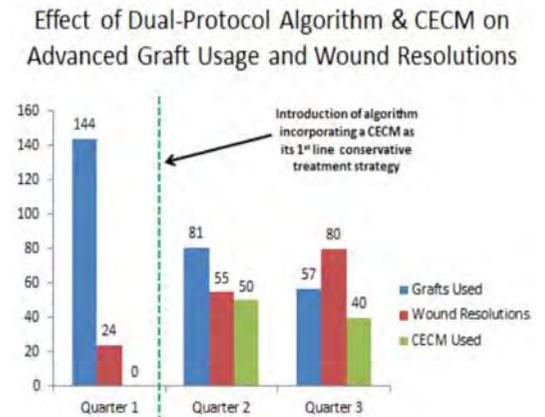


Figure 2



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Effect of Ovine-Based Collagen Extracellular Matrix Dressings on Outcomes in an Outpatient Wound Care Center.

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Baptist Medical Center Jacksonville – Center for Wound Care and Hyperbaric Medicine

Introduction:

- Cost efficiency in today's stringent healthcare arena requires appropriate and judicious use of advanced therapies such as cellular and/or tissue based products (CTPs) for chronic wound management.
- Evidence has linked dermal graft (CTP) failure to elevated matrix metalloproteinase (MMP) levels in diabetic foot ulcers (DFUs),¹ thus suggesting that protease balance for the purpose of wound bed preparation prior to CTP placement should be a clinical priority.
- An ovine-based collagen extracellular matrix (CECM) dressing,^{*} available as a HCPCS A-code,² with an intact extracellular matrix has demonstrated broad-spectrum MMP reduction.³ Results from several case series also suggest that CECM dressings may play a positive role in wound healing.⁴⁻⁶
- Considering the high cost of CTP failure - not only in expenditure for the CTP, but also in lengthened time to heal due to the failure - and the fact that there are no visual, clinical signs related to elevated MMPs,¹ we decided to take a proactive approach by implementing a CECM dressing as the first line dressing to treat chronic wounds.

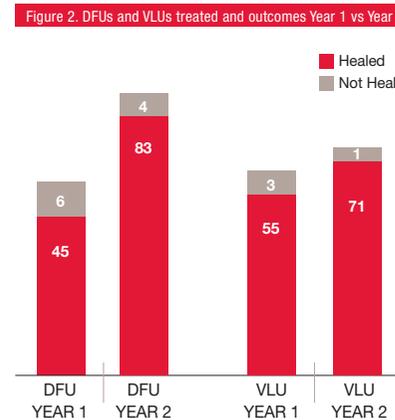
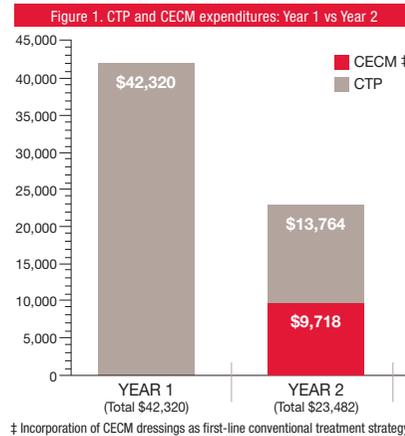
Purpose:

To evaluate the change in CTP usage and wound healing outcomes in chronic wounds, specifically DFUs and VLUs, following the implementation of a CECM dressing as the first-line conventional wound treatment strategy in an outpatient wound care center.

Methodology:

- Records from two years (April 2015 to March 2017) were retrospectively reviewed to determine total number and healing rate of venous leg ulcers and diabetic foot ulcers that were treated by one physician investigator in an outpatient wound clinic.
- Calculations of the actual number of wounds treated by one physician investigator included only DFUs and VLUs since they made up the majority of wounds treated at the center. Additional wound types were treated during the study time frame, but for the sake of simplicity, they were not accounted for in this analysis.
- CECM dressing expenditures were estimated by multiplying the wound center's total CECM dressing expenditures by the percentage of wounds treated by the single investigator compared to the wound center's total number of wounds treated. The investigator's actual CECM dressing unit usage was not recorded or available.

	Year 1	Year 2	Increase/Decrease from Year 1 to Year 2
Total chronic wounds treated (n)	109	159	45.9%
DFUs treated (n)	51	87	70.6%
VLUs treated (n)	58	72	24.1%
DFUs healed	45 (87.3%)	83 (96.2%)	10.2%
VLUs healed	55 (95.8%)	71 (98.8%)	03.1%
Average time to healing DFU (days)	29.5	21	-28.8%
Average time to healing VLU (days)	23.1	27.1	17.3%
CTP use (units)	34	11	-67.6%
CTP expenditure (\$)	42,320	13,764	-67.5%
CECM expenditure (\$)	0	9,718	--
Total CTP and CECM expenditures (\$)	42,320	23,482	-44.5%



A healed wound was defined as 100% re-epithelialized with no drainage; total CTP and CECM dressing expenditures were dollar amounts invoiced to the institution for the dressings.

- Number of wounds treated, wound healing rate, and monthly expenditures for CTP and collagen dressings were compared between the 12 months prior to incorporation of CECM dressings (Year 1: April 1, 2015 - March 31, 2016) versus the 12 months after incorporation of CECM dressings (Year 2: April 1, 2016 - March 31, 2017).

Results:

- A total of 109 chronic wounds (51 diabetic foot ulcers [DFUs] and 58 venous leg ulcers [VLUs]) were treated in Year 1 and 159 wounds (87 DFUs and 72 VLUs) were treated during Year 2.
- Average time to healing for DFUs was 29.5 days during Year 1 versus 21.0 days in Year 2. For VLUs, the average time to healing was 23.1 days in Year 1 and 27.1 days in Year 2.
- Forty-five of 51 (87.3%) DFUs healed in Year 1 and 83/87 (96.2%) of DFUs healed in Year 2, while 55/58 (95.8%) VLUs healed in Year 1 and 71/72 (98.8%) VLUs healed in Year 2.
- CTP unit usage decreased by 67.6% (34 units to 11 units) from Year 1 to Year 2. In regard to total expenditures, in Year 2 the CTP and CECM dressing expenditures totaled \$23,482, which represented a 44.5% decrease from Year 1, despite an increase in number of wounds treated.

Conclusion:

Results of this analysis displayed a trend toward decreased expenditures, while maintaining similar healing rates for DFUs and VLUs with the use of a CECM dressing as the first-line chronic wound treatment protocol in a wound care center.

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*Endoform dermal template, Hollister Incorporated, Libertyville, IL.
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