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(CASE REPORT)

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The use of Acellular Dermal Matrix (Dermacell) in diabetic chronic wounds

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Abstract

The extracellular matrix (ECM) is an intricate network composed of an array of multidomain macromolecules organized in a cell/tissue-specific manner. Components of the ECM link together to form a structurally stable composite, contributing to the mechanical properties of tissues. The ECM is also a reservoir of growth factors and bioactive molecules. It is a highly dynamic entity that is of vital importance, determining and controlling the most fundamental behaviors and characteristics of cells such as proliferation, adhesion, migration, polarity, differentiation, and apoptosis.[1][2]

The ECM provides a structural scaffold via a network of protein–protein and protein–proteoglycan interactions. These interactions are involved in the formation of supramolecular assemblies such as collagen fibrils and elastic fibers, in tissue architecture, and in cell-matrix interactions that regulate cell growth and behavior.

The cells and the ECM have a two-way reciprocal relationship.[3][4] Cells produce, secrete, deposit, and remodel ECM to mediate ECM composition and topography. The ECM in turn transmits signals through ECM receptors to influence cell characteristics and activities.[5] Such a feedback mechanism is essential for rapid response of cells to surrounding environmental changes.

Human acellular dermal matrices (ADMs) are used successfully in a variety of procedures, including sports medicine related, wound repair, and breast reconstructions,

Current treatment strategies for skin wounds/tissue support mostly aim to replace lost tissue rather than support intrinsic self-healing mechanisms. However, new developments within the area of tissue-engineered scaffolds are leading to an ultimate goal of tissue regeneration rather than replacement.[6][7][8][9][14][15]

Keywords: Dermacell; ADM; Wound Healing; Diabetes; Chronic Wounds; Skin Substitutes; Skin Dressings; Matrices

1. Introduction

Wound healing is a complex and coordinated cascade of events that helps to maintain homeostasis within the integument [10][11] and subsequently protect the whole organism. When considering dermal wound healing, the longer a wound takes to heal, the greater the opportunity for foreign agents to enter the body and have pathological effects. To help mitigate the duration of the wound, implanting materials into the integumentary can alter the wound healing cascade of events.[12][13] Historically, large and/or complex soft-tissue defects have been treated with techniques including full and split-thickness skin grafts, local flap coverage and free tissue transfer. Each of these has

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disadvantages such as donor site morbidity, risk of lap/graft complications or even failure. In some cases, such as excessive wound depth or specialized function of tissue needing repair, patient and/or wound characteristics may preclude the use of traditional techniques for soft-tissue overage. Successful wound healing depends largely on the interactions of proliferating cells with the extracellular matrix (ECM) in a process known as dynamic reciprocity.[16] The ECM, composed of proteoglycans, hyaluronic acid, collagen and elastin, directs tissue regeneration and differentiation via mechanical cues and signaling molecules.2 In traumatic or chronic wounds, the ECM is often damaged to the extent that it no longer adequately supports healing. Acellular Dermal Matrices (ADMs) were developed in an attempt to capitalize on the properties of native ECM and promote organized regeneration of host tissue in a wide variety of clinical contexts. When ADMs are placed, host cells are incorporated into the matrix and directed by preserved growth factors and mechanical cues in the matrix structure.[17] A variety of cells invade the ADM, including fibroblasts, myofibroblasts, lymphocytes, macrophages, granulocytes, mast cells and others. After inflammatory cell infiltration, the matrix undergoes remodelling, collagen and elastin levels increase, and revascularisation is initiated. Essentially, the ADM acts as a scaffold to promote host tissue growth. ADMs were initially used to treat burn wounds in the 1990s and have since become a valuable addition to reconstructive algorithms as they are available off the shelf. All ADMs are decellularized and antigenic components have been removed to prevent immune rejection.

The pronounced effect of decellularized ECM scaffolds in supporting tissue regeneration is based on two major characteristics: first, the maintenance of the 3D structure, providing support, tensile strength, and attachment sites for cell surface receptors; and second, the availability of bioactive components that modulate angiogenesis, cell migration, and cell proliferation and orientation in wound healing.[18][19]

Cell-Extracellular Matrix interactions not only guide and regulate cellular morphology, but cellular differentiation, migration, proliferation, and survival during tissue development.

Large or complex wounds present unique reconstructive and healing challenges. In normal healing, the extracellular matrix (ECM) provides both structural and growth factors that allow tissue to regenerate in an organized fashion to close the wound. In difficult or large soft-tissue defects, however, the ECM is often compromised. Acellular dermal matrix (ADM) products have been developed to mimic the benefits of host ECM, allowing for improved outcomes in a variety of clinical scenarios.

The restoration of dermis requires three-dimensional (3D) scaffolds to provide elasticity and strength to the epidermal graft and to feed the keratinocytes in the epidermal layer. Among the essential noncellular components, the ECM is a heterogeneous, connective network composed of fibrous glycoproteins, proteoglycans, and small molecules that coordinate in vivo to provide the physical scaffolding, mechanical stability, and biochemical cues necessary for tissue morphogenesis and homeostasis.[8] Dermacell contains both the reticular and papillary compartments with a basement membrane. Upon application, the reticular site is placed against the surgical wound. The patented preparation process for Dermacell includes the use of anionic detergents and endonucleases to eliminate more than 97% of the nucleic acids. It is preserved and stored at room temperature and thus can be delivered hydrated. Dermacell acts as extracellular matrix. Dermacell is human dermis processed using Matracell® Technology, a validated and patented process which renders the Dermacell graft acellular, without compromising its biomechanical and biochemical properties.[20][21][22][23][24][25][26][27][28][29]

- This process is robust yet gentle enough to protect the native scaffold.
- Vascular channels, growth factors, and proteins are preserved to assist in the healing of the wound.
- Retains growth factors, native collagen type I and III scaffold and elastin.

Fragments of the following proteins were found by LC-MS/MS to be present in DermACELL:

Collagens	GF-binding ECM	Additional ECM	Matrikines	Growth Factors	Cytokines
Type I	Heparan Sulfate Proteoglycan (HSPG)	Elastin	Tenascin-C	BMP6	IL1a
Type III	Chondroitin Sulfate Proteoglycan (CSPG)	Nidogen (Entactin)	Laminins	CTGF	IL1b
Type IV	Perlecan (HSPG2)	Keratin	Decorin	EGF	IL2
Type V	Aggrecan		Endostatin	HGF	IL5
Type VI	Lumican		Pentastatin	PDGFD	IL9
Type VII	Versican		Tumstatin	TGFB1	IL22b
Type VIII	Glypican		Elastokines	VEGFA	IL25
Type XII	Syndecan			VEGFD (FIGF)	IL27
Type XIV	Tenascin (C & N)				IL32
Type XVII	Thrombospondin 2				TNF
Type XVIII	Dermatopontin				
Type XX	Decorin				
Type XXI	Vitronectin				
Type XXIII	Laminin (α1-5,β1-3, γ1&3)				
Type XXVII	Fibrinogen (Fibrin precursor)				
Type XXVIII					

Figure 1 Proteim present im Dermacell after Matracell® processing

From Bornstein P, Sage EH, Matricellular Proteins: Extracellular Modulator of Cell Function Curr Opin Cell Biol; 2002;608-16

2. Clinical cases

2.1 Case #1 - I.E

72-year-old Caucasian male patient.

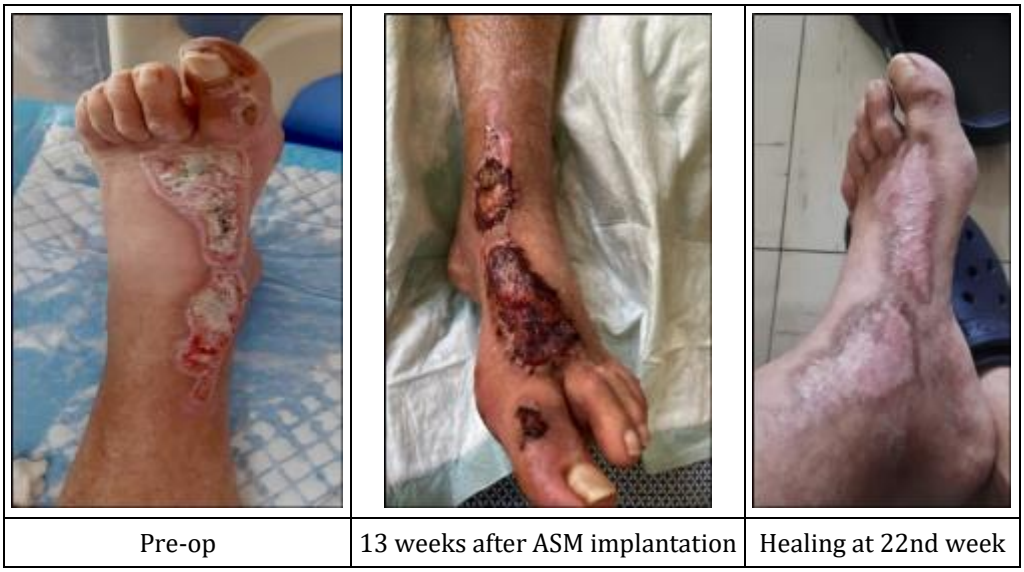
Pre-implantation	73days Post ADM implantation	Healing at 32n weeks post-op

Figure 2 Ulcer after transmetatarsal amputation

Right leg gangrene of toes. His medical history includes Type-1 DM, Dyslipidemia and Hypertension. The patient was endovascularly treated with balloon angioplasty of the tibial arteries due to concomitant diabetic PAD. After successful revascularization of the arteries, a transmetatarsal amputation and wound debridement have been done. Due to late wound healing a 3x3cm meshed Dermacell was placed after WBP. The microbiologic wound specimens revealed a multi-resistant Proteus and the patient received IV antibiotics for 14 days. Healing in 32 weeks.

2.2 Case #2 - K.C

47-year-old Caucasian male patient with left leg ulcer due to insect bite. His medical history includes Type-1 DM, Dyslipidemia, Obesity, CKD, COPD and Hypertension. The patient was endovascularly treated with balloon angioplasty of the tibial arteries due to concomitant diabetic PAD. After successful revascularization of the arteries and WBP, a 4x4cm meshed Dermacell was placed. The microbiology wound specimens revealed multi-resistant p. aeruginosa and the patient received IV antibiotics for 14 days. Healing in 22 weeks.

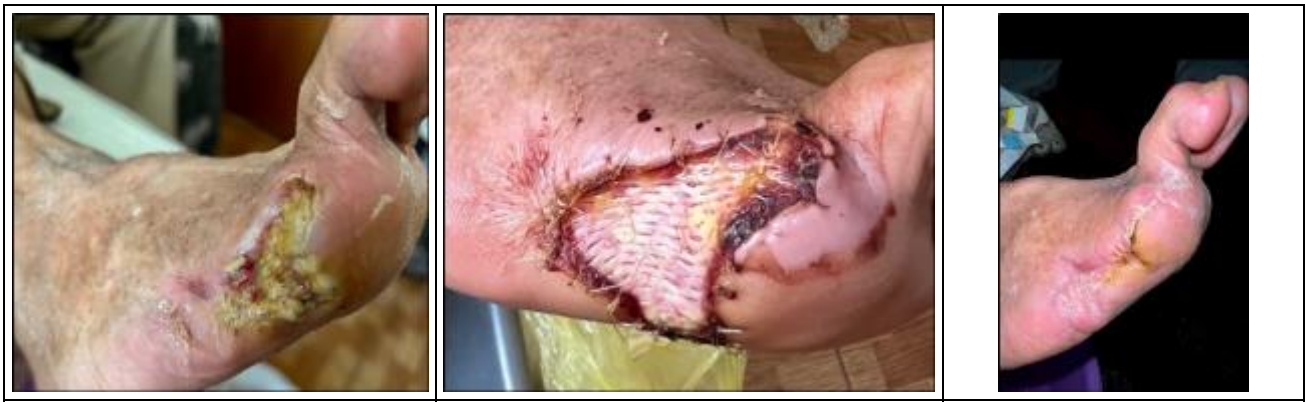


Pre-op	13 weeks after ASM implantation	Healing at 22nd week

Figure 3 Ulcer after insect bite

2.3 Case #3 - M.I

63-year-old Caucasian male patient with left leg ulcer after amputation. His medical history includes Type-1 DM, Dyslipidemia, Obesity, and Hypertension. The patient was endovascularly treated with balloon angioplasty of the tibial arteries due to concomitant diabetic PAD. After successful revascularization of the arteries and WBP, a 3x3cm meshed Dermacell was placed. The microbiologic wound specimens revealed multi-resistant proteus and the patient received IV antibiotics for 14 days. Healing in 24 weeks.

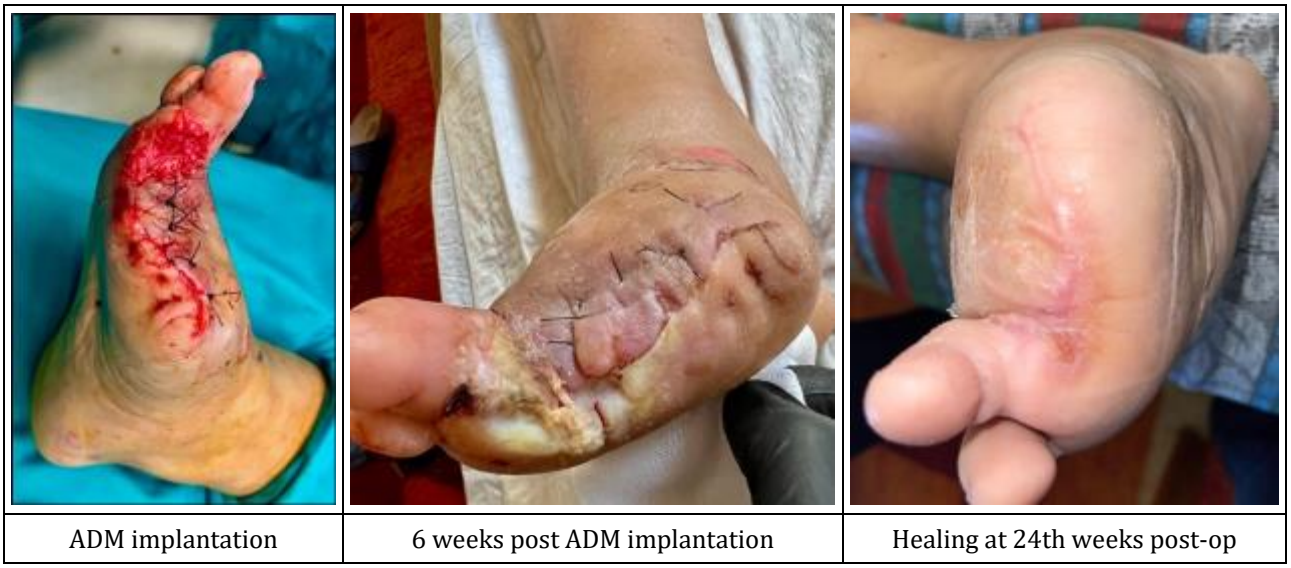


Pre-implant	1 week Post ADM implantation	Healing at 24th weeks post-op

Figure 4 Ulcer after amputation

2.4 Case #4 - T.P

58-year-old Caucasian male patient with gangrene of the first three toes (Rutherford Class 5) in the right leg. His medical history includes Type-1 DM and dyslipidemia. The patient was endovascularly treated with stent angioplasty of the SFA and PTA angioplasty of the tibial arteries due to simultaneous SFA PAD and BTK diabetic PAD. After successful revascularization of the arteries and WBP, primary closure of the wound combined with a 3x3cm meshed Dermacell was placed. The microbiologic wound revealed multi-resistant Proteus and the patient received IV antibiotics for 14 days. Healing in 24 weeks.



ADM implantation	6 weeks post ADM implantation	Healing at 24th weeks post-op

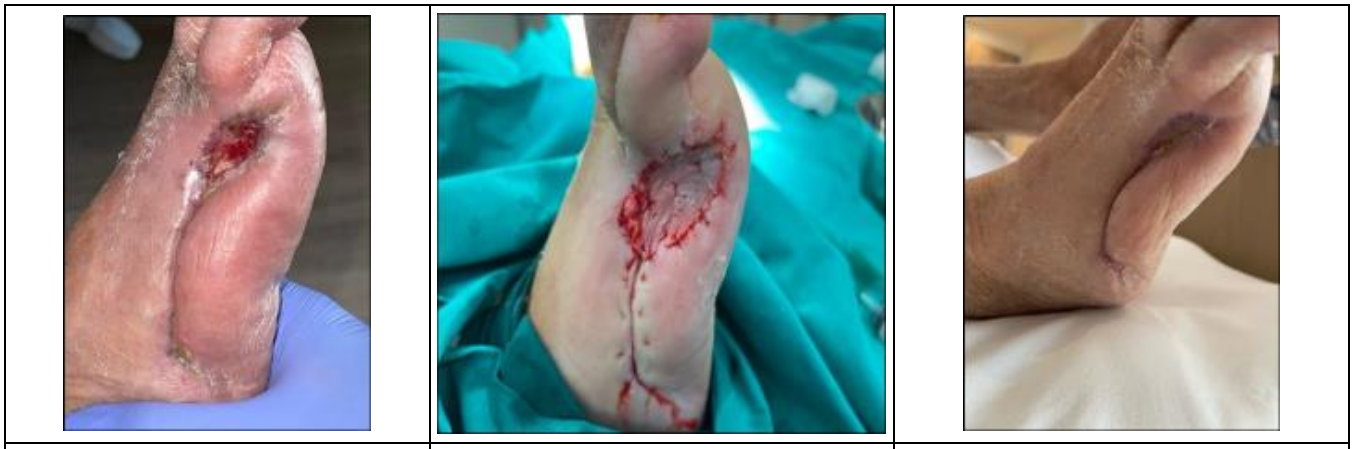
Figure 5 Ulcer after amputation due to gangrene

2.5 Case #5 - T.P

90-year-old Caucasian male patient with gangrene and osteomyelitis of the first toe in the left leg (Rutherford Class 5). His medical history includes Type-2 DM, Hypertension, CKD and Dyslipidemia.

The patient was endovascularly treated with PTA angioplasty of the tibial arteries due to diabetic PAD. After successful revascularization of the arteries and WBP, primary closure of the wound combined with a 3x3cm meshed Dermacell was placed. The microbiologic wound specimens revealed multi-resistant klebsiella and the patient received IV antibiotics for 10 days. The wound healed in 16 weeks.

Seven months later the patient presenting ulcer of the left heel. After wound debridement, primary closure of the wound combined with a 3x3cm meshed Dermacell was placed. The microbiologic wound specimen was sterile so the patient did not receive antibiotics. Due to failure of the first graft a second one placed after 8 weeks. Healing in 42 weeks (in total).



Pre-op	ADM implantation	Healing at 42nd week post op

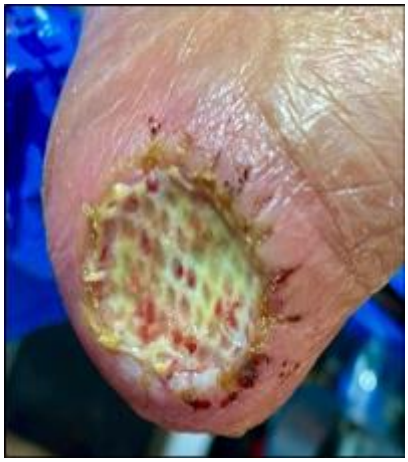
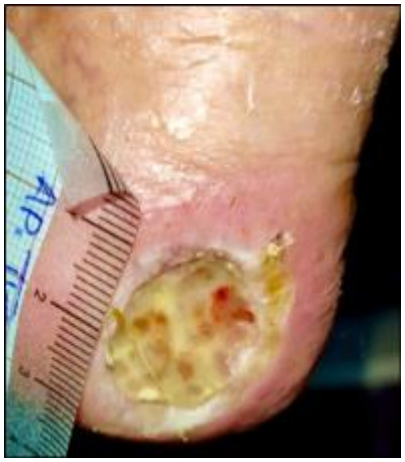
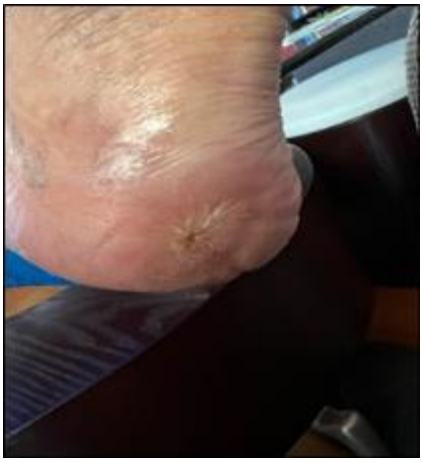
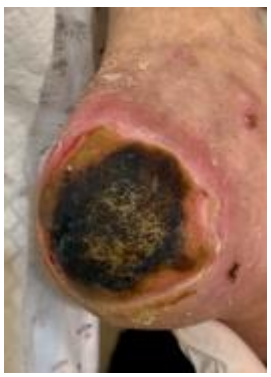
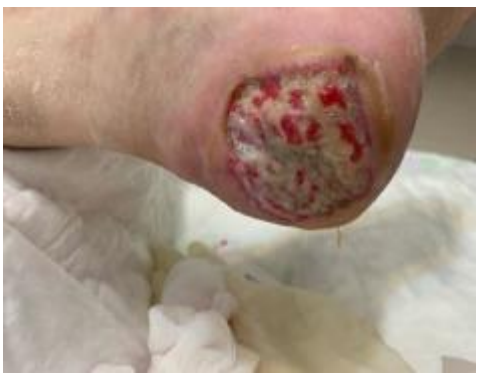
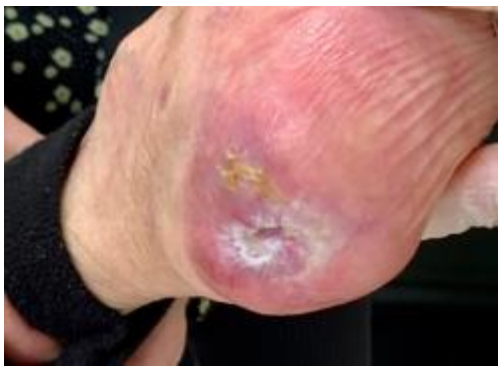
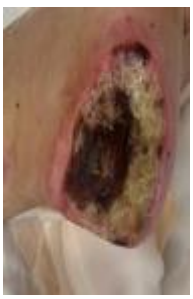
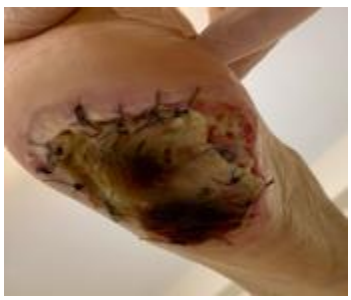
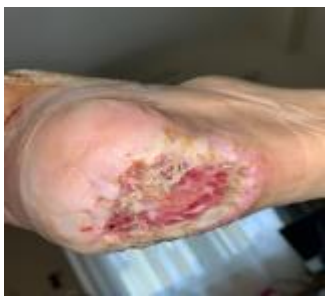
		
First ADM 3 weeks post-implantation ADM	Failure of the first graft after 8 weeks	Heal of the wound after the second (42 weeks in total)

Figure 6 Ulcer due to gangrene at first toe and at left leg

Case #6 - T.N.

82-year-old Caucasian male patient with gangrene of both heels (Rutherford Class 6). His medical history includes Type-2 DM, hypertension, CKD and dyslipidemia. The patient was also obese.

The patient was endovascularly treated with PTA angioplasty of the tibial arteries in both legs due to diabetic PAD. After successful revascularization of the arteries and WBP, two 4x8cm unmeshed Dermacell were placed separately. The microbiologic wound specimens revealed multi-resistant klebsiella and the patient received IV antibiotics for 14 days. The wound in the right leg healed in 40 weeks and in the left in 24.

		
Pre-op (left)	11 weeks post ADM implantation	Healing at 24th week
		
Pre-op (right)	4 weeks post-op	11weeks post-op

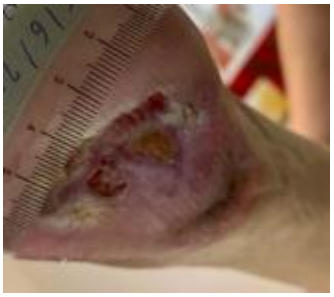

Healing at 40th week post-op

Figure 7 Ulcer due to gangrene

2.6 Case #7 - V.S.

78-year-old Caucasian male patient with gangrene of fingers in the right leg (Rutherford Class 5). His medical history includes Type-2 DM and hypertension.

The patient was endovascularly treated with PTA angioplasty of the SFA and BTK arteries and we transmetatarsal amputation was performed. The wound healing was not satisfied and the doppler revealed biphasic flow in PTA. We did a new revascularization with a femoral-posterior tibial bypass to increase flow, suture and implanted a meshed 4x4 Dermacell graft. The microbiologic wound specimens revealed sensitive Staphylococcus Aureus and the patient received antibiotics (per os) for 10 days. Healing in12 weeks.

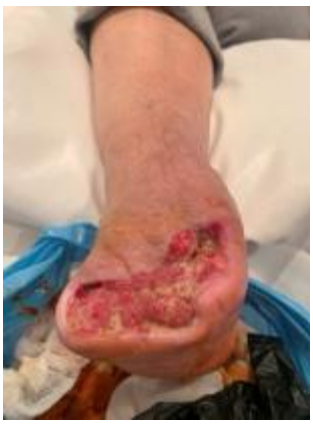
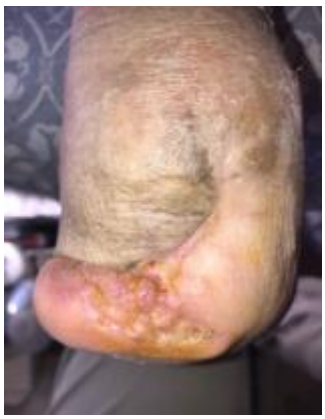
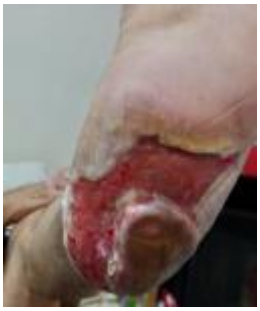
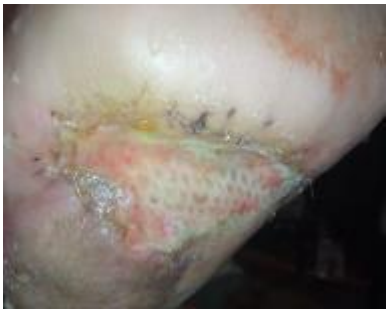
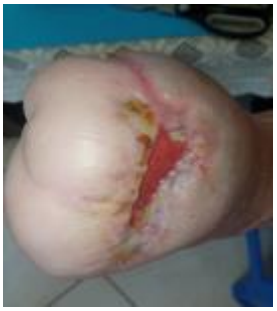
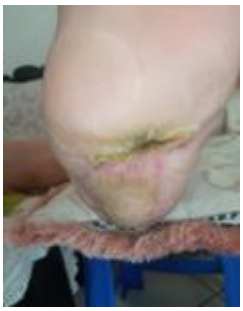
		
Pre-op	4 weeks post-op	4 weeks post-op

Figure 8 Ulcer due to gangrene

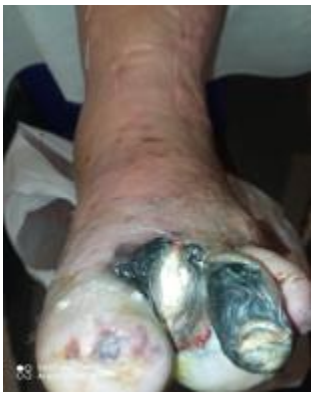
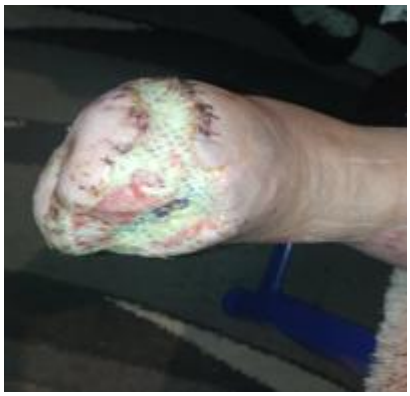
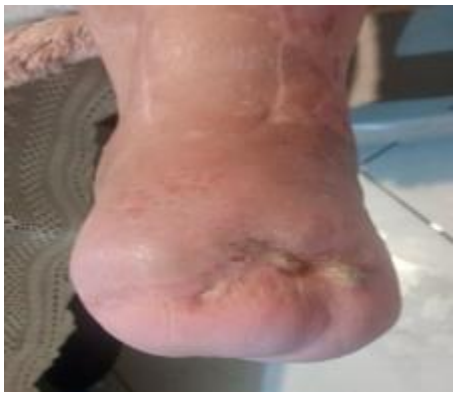
60-year-old Caucasian male patient with gangrene of the first two fingers in the left leg and heel ulcer with osteomyelitis (Rutherford Class 6). His medical history includes Type-1 DM, Hypertension and dialysis for CKD.

The patient as endovascularly treated with PTA angioplasty of the SFA and BTK arteries and we proceed with amputation of the toes and primary closure. WBP of the heel ulcer with partial bone amputation due to osteomyelitis. The healing of the heel wound was not satisfied, and the patient had an important tissue loss of the heel. For this reason, a transposition of muscle graft from a plastic surgeon made and the ulcer improved. We implanted a 3x3 meshed Dermacell graft to improve healing which was at 16th week. The microbiologic wound revealed a multi- resistant Proteus and the patient received IV antibiotics for 50 days.

Two years later the patient presented again with gangrene of the rest fingers (Rutherford Class 5). We proceeded in a new angioplasty of the SFA due to re-stenosis and transmetatarsal amputation. The wound was extensive, and we used a 4x4 meshed graft to cover it. The microbiologic wound revealed again a multi-resistant proteus and the patient received IV antibiotics for 20 days. Healing in 20 weeks.

Pre-op	11weeks post-op	14 weeks post-op	Healing at 16th weeks

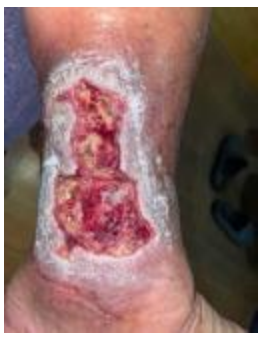
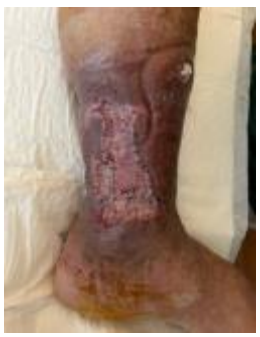
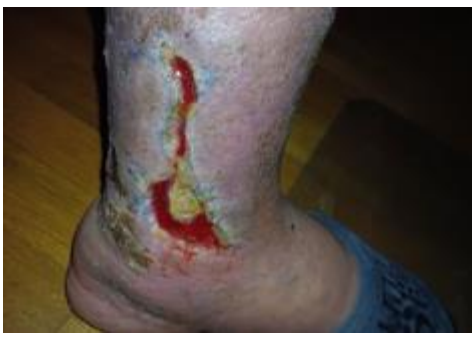
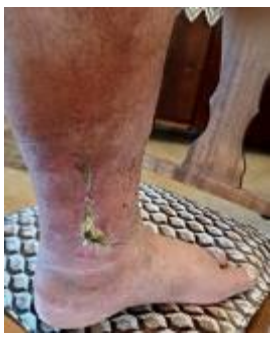
Pre-op	6 weeks post-op	Healing at 20th weeks

Figure 9 Ulcer due to gangrene

2.7 Case #9 - M.G.

71-year-old Caucasian male patient with venous ulcer of the right left (Rutherford Class 5). Past medical history including Type-1 DM, Hypertension and obesity. The patient also suffered from chronic venous insufficiency of the right GSV and insufficiency of perforator vein in calf.

The patient was endovascularly treated with PTA angioplasty of the arteries BTK because of stenosis if the anterior and posterior tibial arteries. Then we proceeded in EVLA of the GSV and ligation of the perforator veins. A week later a 4x8 meshed Dermacell graft was implanted. Healing in 16 weeks. The patient did not receive any antibiotics post-op.

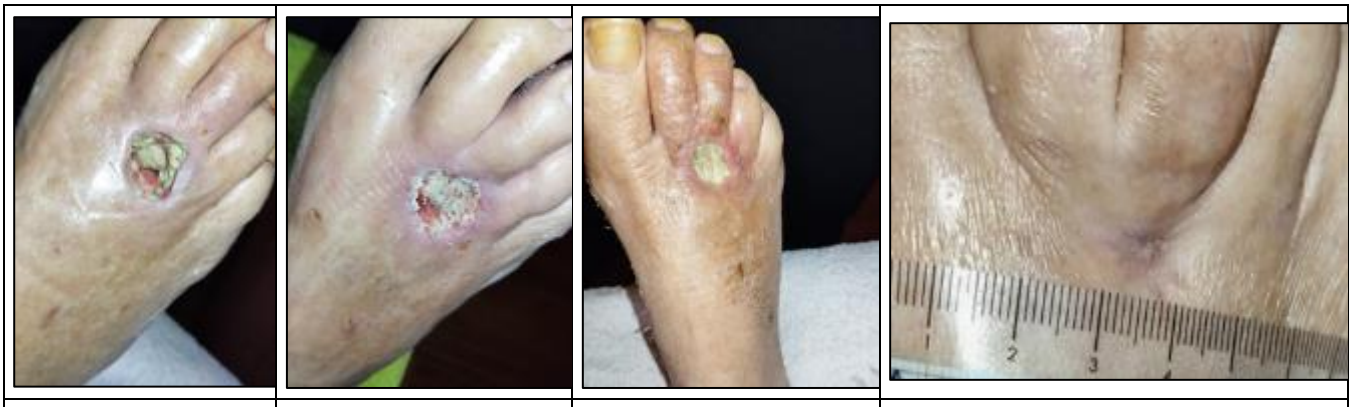
Pre-op	1 - 1 week post-op	13 weeks post-op	Healing at 16th week

Figure 10 Venous ulcer

2.8 Case #10 - P.I.

80-year-old Caucasian male patient with dorsal ulcer at right leg (Rutherford Class 5) after surgical removal of a Morton's neuroma. Medical history including Type-1 DM, Hypertension, dyslipidemia, smoking and COPD.

The patient was endovascularly treated with PTA and stenting in right SFA due to occlusion. One month later a 3x3 meshed Dermacell was implanted due to delay in ulcer healing. Healing in 23 weeks. The microbiologic revealed again a multi- resistant proteus and the patient received IV antibiotics for 30 days.



Pre-op	10 weeks post-op	16 weeks post-op	Healing at 23st week

Figure 11 Ulcer after removal if Morton's neuroma

3. Conclusion

Using ADM in various surgical procedures can yield favorable results in function, aesthetics, and fewer complications. ADM is an acellular graft that protects it against immunogenicity. It also spares the need for extracting the autologous graft, reducing the morbidity of donor-site surgery. ADM is rapidly vascularized and cellularized by the host. The results presented here indicate that Dermacell is an appropriate clinical option in the treatment of chronic ulcers with significant increases in healing rates and rate of percentage of wound closure as compared with conventional care options.

Compliance with ethical standards

Acknowledgments

We thank LifeNet Health, Virginia Beach, Virginia, USA, for providing Decellularized Dermal Matrix (Dermacell)

Disclosure of conflict of interest

The Authors declare that there is no actual or potential conflict of interest in relation to this case study.

Statement of informed consent

Informed consent was obtained from the participant included in the study.

References

[1] Lu P, Takai K, Weaver VM, Werb Z.: Extracellular matrix degradation and remodeling in development and disease. Cold Spring Harb Perspec Biol. 2011;3:a005058. doi: 10.1101/cshperspect.a005058. [DOI] [PMC free article] [PubMed]

[2] Mecham RO.: Overview of extracellular matrix. Curr Protoc Cell Biol. 2012; 57:10.1.1–10.1.16. doi: 10.1002/0471143030.cb1001s57. [DOI] [PubMed] [Google Scholar]

[3] Geiger B, Yamada KM.: Molecular architecture and function of matrix adhesions. Cold Spring Harb Perspect Biol. 2011;3:a005033. doi: 10.1101/cshperspect.a005033. [DOI] [PMC free article] [PubMed]

[4] Daley WP, Yamada KM.: ECM-mediated cellular dynamics as a driving force for tissue morphogenesis. Curr Opin Genet Dev. 2013; 23:408–414. doi: 10.1016/j.gde.2013.05.005. [DOI] [PMC free article] [PubMed]

[5] Gattazzo F, Urciuolo A, Bonaldo P. Extracellular matrix: A dynamic microenvironment for stem cell niche. Biochim Biophys Acta. 2014; 1840:2506–2519. doi: 10.1016/j.bbagen.2014.01.010.[DOI] [PMC free article] [PubMed]

[6] Moore MA, Samsell B, Wallis G,Triplett, S, Chen S, Linthurst Jones A, Xiaofei Qin: Decellularization of human dermis using non-denaturing anionic detergent and endonuclease: a review. Cell Tissue Bank. 2015; 16: 249–259.

[7] Samsell B, Softic D, Xiaofei Qin, McLean J, Sohoni P, Gonzales K, Moore MA.: Preservation of allograft bone using a glycerol solution: a compilation of original preclinical research. Biomaterials Research. 2019; 23: 5.

[8] M Dussoyer, A Michopoulou, P Rousselle: Decellularized Scaffolds for Skin Repair and Regeneration. Appl. Sci. 2020, 10, 3435; doi:10.3390/app10103435

[9] Walters J, Cazzell S, Pham H, Vayser D, Reyzelman A. Healing rates in a multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management and an active comparator in the treatment of full-thickness diabetic foot ulcers. ePlasty. 2016; 16: e10.

[10] Childs, D.R.; Murthy, A.S.: Overview of wound healing and management. Surg. Clin. 2017, 97, 189–207. [Google Scholar] [CrossRef] [PubMed]

[11] Guo, S.A.; DiPietro, L.A.: Factors affecting wound healing. J. Dent. Res. 2010, 89, 219–229. [Google Scholar] [CrossRef] [PubMed]

[12] Robson, M.C.; Steed, D.L.; Franz, M.G.: Wound healing: Biologic features and approaches to maximize healing trajectories. Curr. Probl. Surg. 2001, 38, 72–140. [Google Scholar] [CrossRef] [PubMed]

[13] Anderson, J.M.: Biological responses to materials. Annu. Rev. Mater. Res. 2001, 31, 81–110. [Google Scholar] [CrossRef]

[14] Decoyer M, Michopoulou A and Rousselle P.: Decellularized scaffolds for skin repair and regeneration. Appl Sci 2020; 10:3435.

[15] Bornstein P, Sage EH: Matricellular Proteins: Extracellular Modulator of Cell Function Curr Opin Cell Biol; 2002;22:608-16

[16] Gregory S Schultz, Jeffrey M Davidson, Robert S Kirsner, Paul Bornstein, Ira M Herman: Dynamic Reciprocity in the Wound Microenvironment Wound Repair Regen. 2011 Mar;19(2):134–148. doi: 10.1111/j.1524-475X.2011.00673.x

[17] Giampietro Bertasi. Windy Cole, Brian Samsell . Xiaofei Qin, Mark Moore: Biological incorporation of human acellular dermal matrix used in Achilles tendon repair, Cell Tissue Bank DOI 10.1007/s10561-017-9628-3

[18] Bornstein P, Sage EH: Matricellular Proteins: an overview, J Cell Com Signal 2009 25;3(3-4):163-165

[19] Yonehiro, et. al.: Use of a New Acellular Dermal Matrix for Treatment of Nonhealing Wounds in the Lower Extremities of Patients with Diabetes, WOUNDS. 2013;25(12):340-344

[20] Bornstein P, Sage EH: Matricellular Proteins: Extracellular Modulator of Cell Function, Curr Opin Cell Biol; 2002;22:608-16

[21] Hanna K; Yu D; LeGallo R; Colen D; Drake DB: "Matracell processed, sterilized acellular dermal matrix in implant-based breast reconstruction: clinical and histologic outcomes". Annals of Plastic Surgery, 2013.

[22] Yonehiro, et. al.: Use of a New Acellular Dermal Matrix for Treatment of Nonhealing Wounds in the Lower Extremities of Patients with Diabetes, WOUNDS. 2013;25(12):340-344

[23] Moore MA, Samsell B, Wallis G,Triplett, S, Chen S, Linthurst Jones A, Xiaofei Qin: Decellularization of human dermis using non-denaturing anionic detergent and endonuclease: a review. Cell Tissue Bank. 2015; 16: 249–259

[24] Samsell B, Softic D, Xiaofei Qin, McLean J, Sohoni P, Gonzales K, Moore MA: Preservation of allograft bone using a glycerol solution: a compilation of original preclinical research. Biomaterials Research. 2019; 23: 5.

[25] Yoursry Abdalaziz and Giampietro Bertasi: Treatment of diabetic foot ulcer with human acellulardermal matrix (ADM) Wound Care Manage. 2018; 1(1): 1 of 2.

[26] S Mazzei, A Sindoni, F Famà, G Bertasi, Nimfa, J Buizo, Mohab. A Shafei: Use of human acellular dermal matrix for wound healing in a patient with necrotizing fasciitis, after failure of autologous dermal / epidermal skin graft: A case report Glob Surg. 2019; 5: 1-3.

[27] Sanjay Sharma and Giampietro Bertasi: An advanced decellularized dermis intended for soft tissue repair: A new surgical approach for DFU. Magna Scientia Advanced Biology and Pharmacy. 2022; 6(1): 012–015.

[28] Vangelis G Alexiou, Stylianos G. Koutsias and Bertasi Giampietro: The use of Dermacell® Allograft in a diabetic patient with critical limb ischemia. Magna Scientia Advanced Biology and Pharmacy. 2022; 6(1): 033–035.

[29] Walters J, Cazzell S, Pham H, Vayser D, Reyzelman A.: Healing rates in a multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management and an active comparator in the treatment of full-thickness diabetic foot ulcers. ePlasty. 2016; 16: e10.