



REPRESENTATIVE REPORTS USING DERMACELL AWM®

Documents available upon request.

Clinical Reports using DermACELL AWM in Advanced Wound Management

Published & Peer-Reviewed Articles, Posters, & Abstracts from the DermACELL AWM Randomized, Controlled Trial (RCT)

Clinical Trial Highlights

The Largest Multi-Center, Randomized, Controlled Trial to Date Using Human ADM in Chronic Wound Management

- Over 200 Patients Enrolled
- 13 Trial Sites
- 12 Investigators

Comparing Complete Healing Rate & Percent Wound Area Reduction Between:

- Dermacell AWM (D-ADM)
- Conventional Care (CC)
- GraftJacket® (GJ-ADM)

Published & Peer-Reviewed Clinical Articles from the DermACELL AWM RCT:

Diabetic Foot Ulcer (DFU) 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.

- The Dermacell AWM patient group had a significantly higher percentage of completely healed ulcers by the 16-week follow-up compared to the conventional care group (67.9% vs. 48.1%; $P=0.0385$) and a non-significantly higher percentage than the GraftJacket patient group (67.9% vs. 47.8%; $P=0.1149$). The Dermacell AWM treatment arm also had a greater average percent reduction in wound area than the conventional care arm (91.4% vs. 80.3%; $P=.0791$) and the GraftJacket arm (91.4% vs. 73.5%; $P=.0762$).

Posters and Abstracts from the DermACELL AWM RCT: Diabetic Foot Ulcer (DFU)

Walters J. A multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management in the treatment of diabetic foot ulcers: An updated interim analysis. (CR-039) Fall SAWC: September 26-28, 2015.

- "At 12 weeks, mean reductions in wound size were; D-ADM (89.5%), GJ-ADM (71.9%), and CC (67.6%), with statistical significance for D-ADM vs. GJ-ADM ($p=0.0417$) and D-ADM vs. CC ($p=0.0071$)."

Walters J. A multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management in the treatment of diabetic foot ulcers: An interim analysis. (CR-038) Spring SAWC: April 29-May 3, 2015.

- "At 12 weeks, mean reductions in wound size were; D-ADM (91.3%), GJ-ADM (89.3%), and CC (74.3%)... These preliminary results show a strong trend of improved wound closure using D-ADM supporting further study."

Posters and Abstracts from the DermACELL AWM RCT: Venous Stasis Ulcer (VSU)

Cazzell S. A multicenter, randomized study to assess a sterile, hydrated acellular dermal matrix versus conventional care wound management in subjects with venous stasis ulcers: An interim analysis. (CR-006) Spring SAWC: April 29-May 3, 2015.

- “At 12 weeks, D-ADM treated wounds exhibited 79.1% average wound reduction versus 41.5% average wound reduction for CC treated wounds. At 20 weeks, D-ADM treated ulcers had demonstrated an average 88.5% closure, while the CC group remained at 41.5%.”

Cazzell S. A multicenter, randomized study to assess a sterile, hydrated acellular dermal matrix versus conventional care wound management in subjects with venous stasis ulcers. (CR-004) Fall SAWC: September 26-28, 2015.

- “Single application D-ADM treated ulcers displayed significantly improved wound closure over CC at 20 weeks (89.7% vs. 22.5%, $p=0.0363$).”

Other Clinical Reports and Publications using DermACELL AWM in Advanced Wound Management

Atzei A, Bertasi G. Repair of distal triceps tendon rupture with [DermACELL]. Data on File, LifeNet Health (68-20-097).

- A case study of a 42 year old male who underwent treatment of a tendon rupture of the distal triceps with Dermacell. Distal triceps tendon ruptures can cause long-term disability, complicated by difficulties for the surgeon in developing a diagnosis and prognosis. These are often caused from a fall onto an outstretched hand, or trauma to the posterior of the arm. Treatment of these ruptures typically includes surgery to reattach the ruptured triceps tendon to the olecranon of the elbow. This is commonly achieved with the use of sutures that are passed through tunnels in the olecranon. Surgeons often augment the tendon with an allograft in patients with chronic tears, or undergoing revision surgery. Excellent augmentation of the distal triceps brachialis tendon was achieved in the case presented, and by 6 months, the patient had regained 87% range of motion and 70% strength.

Atzei A, Bertasi G. Reconstruction of finger flexor tendon and pulley repair with [DermACELL]. Data on File, LifeNet Health (68-20-098).

- A case study of a 16 year old male who underwent treatment of an injured finger flexor tendon with Dermacell. These types of injuries often require immediate surgical intervention to preclude more lasting damage. Autografts are sometimes used, but they have inherent disadvantages, such as second site morbidity and limited material for use. In addition, autograft harvest can increase operating time.

Atzei A, Bertasi G. [DermACELL] augments finger extensor tendon reconstruction. Data on File, LifeNet Health (68-20-159).

- Case study describing the surgical technique and outcomes using Matracell processed dermis to augment the extensor tendon in a 40 year-old male who presented 8 months after sustaining an open crushing injury to the middle finger with damage to the dorsal skin, the extensor apparatus at both the proximal and middle phalanges, and the proximal interphalangeal joint (PIP-j). Six months after replacing the PIP-joint with a polycarbon implant, tendon reconstruction was performed using Matracell-processed dermis. There were no post-operative complications, and the patient achieved 10° to 90° range of motion at 3 months post-operative.

Bertasi G. Case study: Treatment of diabetic foot ulcer with human acellular dermal matrix (ADM). Data on File, LifeNet Health (68-20-108).

- Bertasi presented a case study of a 52 year old male who underwent treatment of a diabetic foot ulcer with the use of Dermacell AWM. Diabetes is a metabolic disorder leading to hyperglycemia. One of the long term complications of uncontrolled blood sugar is neuropathy. When it occurs in the extremities, poor sensation results, and this contributes to the formation of ulcers. These are typically observed on the feet of diabetic patients. Current treatment includes wound dressing, hyperbaric oxygen therapy, negative pressure therapy, and, in advanced cases, amputation. The wound closed by 3 months postoperative follow-up and there was no swelling or major exudates. [Dermacell] has proven to be an effective method of treatment in selected cases.

Buchbaum EJ. Case study: Treatment of plantar diabetic ulcer with human acellular dermal matrix (ADM). Data on File, LifeNet Health (68-20-067).

- A case study by Buchbaum assessed the effectiveness of Dermacell AWM in the treatment of plantar diabetic ulcers. Diabetes is a group of disorders leading to hyperglycemia. One of the long term complications of this disease is neuropathy. When it occurs in the extremities, it leads to poor sensation, and this contributes to the formation of ulcers. These are typically observed on the feet of diabetic patients. Current treatment includes wound dressing, hyperbaric oxygen therapy, negative pressure therapy, and, in advanced cases, amputation. A 41 year old male, who presented with a left plantar diabetic ulcer, was treated with Dermacell AWM and experienced a 92.4% size reduction in the area and volume of his wound. These dermal matrices support cellular and vascular in-growth and have unique characteristics, providing advantages for the treatment of diabetic ulcers.

Chen S-G, Tzeng Y-S, Wang C-H. Case report: Treatment of a severe burn with DermACELL, an acellular dermal matrix. Int J Burn Trauma. 2012;2(2):105-9.

- Chen et al. reported on the use of Dermacell AWM in the treatment of a severe scar that was the result of second- and third-degree burns. Three years after initial treatment with antibiotic ointment and wound dressings, the patient had poor range of motion and hypertrophic scarring from the elbow to the hand. After excision of the scar, meshed Dermacell AWM was applied, and the wound was resurfaced with a

split-thickness graft. Postoperative care included application of a pressure garment and silicone sheet, along with range of motion exercises and massage. After 30 days post-application of dermis, the authors reported that the patient's wound appeared well-healed, with no significant scar formation. After 180 days, the patient continued to heal well without significant scar formation and an improvement in the patient's range of motion was noted.

Deanesi W, Reitano R, Cogo A. Case report: Treatment of a venous leg ulcer using DermACELL, a human acellular dermal matrix (ADM). Data on File, LifeNet Health (68-20-099).

- A case study performed by Deanesi et al. involved treating a venous leg ulcer with Dermacell AWM. Leg ulcers often form secondary to hyperglycemia associated with diabetes. Venous leg ulcers, like diabetic foot ulcers, are very difficult to treat. A variety of treatment options exist, including, but not limited to, hyperbaric therapy, negative pressure and wound dressings. In all cases, poor response to treatment can cause more severe complications including amputation. The patient was a 65 year old male whose wound closed by three months post-operative

Mulder G. Tissue augmentation and replacement of a heel fat pad with a decellularized sterile human dermal matrix. Wounds. 2012;24(7):185-9.

- Mulder reported on the use of Dermacell AWM for tissue augmentation in 3 patients who had damage to the heel fat pad due to motor vehicle accidents and had difficulty ambulating without pain. The patient in case 1 suffered near complete loss of the plantar heel fat pad, and also presented with a full-thickness ulcer on the posterior calcaneus. During an initial examination, the patient rated pain with palpation on the right heel as a 6, and pain with ambulation was rated between 6 and 8 (on a 1-10 scale with 0 = no pain and 10 = unbearable pain). The heel wound was addressed by placing Dermacell AWM directly under the calcaneus. The ulcer was treated with bone marrow aspirate and a xenograft. All surgical sites were covered with dressings, which were changed weekly. The patient remained on crutches, and was non-weight bearing until 3 weeks postoperatively, when the patient was placed in a walking boot. At week 6, the patient was in normal shoes and was able to ambulate without pain. The patient remained pain free at both the 3 month and 1 year follow-up. Cases 2 and 3 in this series were reported as supplements to the first case. Both patients had similar wounds and were treated with the application of Dermacell AWM in the affected area. After 5 weeks, the patients in Case 2 and Case 3 reported an 80% and 75% reduction in pain, respectively. The author concluded that the cases presented the successful use of an allograft to correct a plantar defect that had been associated with pain on ambulation.

Robb GL, Gurtner GC. Letter to the Editor: 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:e27.

Roussalis J. Novel use of an acellular dermal matrix allograft to treat a chronic scalp wound with bone exposure: A case study. Int J Burn Trauma. 2014;4(2):49-52.

- Meshed Dermacell AWM was used to treat a chronic scalp wound with an exposed frontal bone. The 58 year-old male patient developed the chronic wound from lichen simplex chronicus (neurodermatitis), and previous standard treatment was ineffective. A non-meshed skin graft was applied to the wound area 8 weeks after placement of Dermacell AWM, and full granulation was achieved in 6 weeks post-operative. The wound had completely healed 10 weeks after placement of Dermacell AWM, with no complications.

Shitrit SB, Ramon Y, Bertasi G. Use of a novel acellular dermal matrix allograft to treat complex trauma wound: A case study. Int J Burn Trauma. 2014;4(2):62-5.

- Dermacell AWM was used to treat an open arm fracture of a male in his thirties whose wound involved exposure of tendons in the wound bed. Initial treatment included surgical fixation of the fracture and connection of the wound to a VAC machine. Two months after the initial injury, the

Walters J. A multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management in the treatment of diabetic foot ulcers: An interim analysis. (CR-038) SAWC April 29-May 3, 2015.

Walters J. A multicenter assessment of a sterile, room temperature, acellular dermal matrix versus conventional care wound management in the treatment of diabetic foot ulcers: An updated interim analysis. (CR-039) SAWC September 26-28, 2015.

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).

Yonehiro L, Bursleson G, Sauer V. Use of new acellular dermal matrix for treatment of non-healing wounds in the lower extremities of patients with diabetes. Wounds. 2013;25(12):340-4.

- Yonehiro et al. reported a case study involving 15 patients who underwent treatment of chronic, diabetic foot ulcers using Dermacell AWM. Dermacell AWM was secured to the wound by either a suture, Steri-strip™ or non-adherent dressing. Patients were clinically evaluated at each visit, on a weekly basis, for up to 12 weeks (based on wound healing rates). Dressings were left in place for a minimum of 5 days (up to 7 days) and were changed by the clinician at follow-up visits. Single applications were employed, except in 3 cases, where a second dermis graft was applied. This second application was due to either non-compliance or clinician preference. Wound closure was observed in 7 of the 12 ulcers treated within the study, for a 58% wound closure rate. Substantial wound healing (95% or greater) was noted in 10 of the 12 ulcers, for a rate of 83%. The average duration to wound closure was 10 weeks, and integration of Dermacell AWM with the surrounding tissue was evident. The presenters concluded that the results from this case series compared favorably with other methods of advance wound care.

Non-Human Studies using DermACELL

Agrawal H, Tholpady SS, Capito AE, Drake DB, Katz AJ. Macrophage phenotypes correspond with remodeling outcomes of various acellular dermal matrices. Open Journal of Regenerative Medicine. 2012;1(3):51-9.

- Tissue remodeling and macrophage phenotypes of four ADMs, AlloDerm®, Dermacell, DermaMatrix™, and Integra®, were analyzed by Agrawal et al. in a rat model. Samples were “wrapped around the inferior epigastric vessels of a rat and were harvested on 7, 14, 21, and 42 post implantation.” Macrophage surface markers, including CD68 (pan macrophage), CCR7 (M1 profile), and CD206 (M2 profile), were identified using immunohistologic methods. A “bell curve” distribution of CD68+ macrophages was shown for all ADMs, with AlloDerm showing a peak influx on day 21, and DermaMatrix showing peaks at day 14. Integra, a bovine derived matrix, showed increased macrophages over time. The highest influx of macrophages was shown by Dermacell, with Integra having the lowest influx. Quantitative phenotype analysis of macrophages in each ADM showed that cells in AlloDerm were mostly M1 at all time points post implantation. On the other hand, a mixed M1/M2 population of macrophages was found in Integra at all time points. Additionally, Dermacell also had a mixed M1/M2 macrophage population that shifted toward a higher ratio of M2 than M1, which indicated a tissue repair and remodeling environment. Overall, the authors concluded that “the histopathologic evaluation showed that a predominantly M1 macrophage response was associated with a more inflammatory type tissue remodeling outcome in AlloDerm while a mixed M1/M2 macrophage response was associated with a more constructive tissue remodeling response seen in the other substrates.”

Capito AE, Tholpady SS, Agrawal H, Drake DB, Katz AJ. Evaluation of host tissue integration, revascularization, and cellular infiltration within various dermal substrates. Ann Plast Surg. 2012; 68(5):495-500.

- An experimental paper by Capito et al. evaluated and compared four ADMs (AlloDerm, Dermacell, DermaMatrix, and Integra) in regard to revascularization, host tissue integration, and recellularization in an in vivo rat model. Cellular infiltration and revascularization were quantified using immunohistologic assays as well as histology. All products, except Dermacell, experienced a bimodal cellular response. Cellular infiltration was lowest in AlloDerm, and highest in Dermacell (184% higher), and by day 7, angiogenesis was evident. New vessel formation existed in all three ADM products by day 7, with Dermacell demonstrating almost double the new vessel formation of the other ADM products tested. By day 42 both Dermacell and AlloDerm showed statistically greater amounts of new vessels compared to the other ADMs. The authors concluded that “there were clear differences within the various products. It is undetermined whether these differences are advantageous or clinically significant. Future work is needed to define the specific roles of each.”

Rosines E, Lin Q. Analysis of the acellular matrix, growth factors and cytokines present in DermACELL advanced wound management. Data on File, LifeNet Health (68-20-047).

- An in vitro analysis by Rosines et al. evaluated the acellular matrix, growth factors and cytokines in a sterile, decellularized human dermal allograft, Dermacell. Results of the analysis showed that Dermacell retained extracellular matrix, growth factors, matrikines, and cytokines similar to healthy human skin and important to the repair of damaged skin. Dermacell also provided structural integrity where indicated due to its intact extracellular matrix. The authors concluded “the processing of Dermacell preserves many of the structural components, growth factors, and cytokines present in healthy human skin. Applying Dermacell to the chronic wound environment can act to replace the damaged and abnormal skin with a minimally manipulated human dermis containing the same wound repairing factors present in natural healthy skin.”

Process-Related Technologies

Armour AD, Fish JS, Woodhouse KA, Semple JL. A comparison of human and porcine acellularized dermis: Interactions with human fibroblasts in vitro. Plast Reconstr Surg. 2006;117(3):845-56.

- An evaluation of acellularized porcine dermis as a scaffold for human fibroblasts was performed by Armour et al. in an in vitro model. Fibroblast adherence, proliferation and migration were analyzed on pig ADM, and compared to human ADM. Overall, the authors noted pig ADM to be an inferior scaffold for human fibroblasts compared to human ADM. Human ADM demonstrated significantly more ADM samples of fibroblast infiltration below the cell-seeded surface and significantly more fibroblasts infiltrated below the surface of the human ADM. Significantly less fibroblast migration was found in the cell-seeded porcine ADM. Additionally, fibroblast proliferation was more rapid in the porcine ADM than the human ADM. No significant difference was found in regard to fibroblast adherence between the two groups. The authors note that “preliminary findings suggest that substantial differences may exist between human fibroblast behavior in cell-matrix interactions of porcine and human acellularized dermis.”

Bio-Implants Brief. Ensuring the safety of allograft dermal tissue. Data on File, LifeNet Health (68-20-006-02).

- An introduction to tissue banking sterility standards including multiple processes (e.g., chemical, mechanical, radiation methods) currently used to reduce bioburden on allograft tissue. Authors included an overview and discussion of potential drawbacks of multiple tissue sterilization techniques, including ethylene oxide gas, e-beam radiation, and gamma irradiation among others. Additionally, the authors described LifeNet Health’s process to prepare its dermal tissue, including decellularization, preservation for room temperature storage, and a final terminal sterilization step to reduce the risk of disease transmission.

Moore M. Inactivation of enveloped and non-enveloped viruses on seeded human tissues by gamma irradiation. Cell Tissue Bank. 2012;13(3):401-7.

- The author studied the effect of low temperature, low dose gamma irradiation on viruses seeded onto both human tendons and cortical bone samples. Human tendons packed in dry ice received irradiation doses within the range of 11.6-12.9 kGy, while cortical bone samples also packed in dry ice experienced gamma radiation in the range of 11.6-12.3 kGy. Enveloped and non-enveloped viruses included: Human Immunodeficiency Virus (RNA, enveloped), Porcine Parvovirus (DNA, enveloped), Pseudorabies Virus (DNA, enveloped), Bovine Viral Diarrhea Virus (RNA, enveloped), and Hepatitis A Virus (RNA, non-enveloped). "While proper donor screening, aseptic technique, and current disinfection practices all help reduce the risk of viral transmission from human allograft tissues, data presented here indicate that terminal sterilization using a low temperature, low dose gamma irradiation process inactivates both enveloped and non-enveloped viruses containing either DNA or RNA, thus providing additional assurance of safety from viral transmission." Dermacell is terminally sterilized in the same manner as the human tendons and cortical bone described by Moore, and the author's work provides evidence for the reduced risk of viral transmission from Dermacell use.

Moore MA, Samsell B, Wallis G, Triplett S, Chen S, Linthurst-Jones A, Qin X. Decellularization of human dermis using non-denaturing anionic detergent and endonuclease: A review. Cell Tissue Bank. 2015;16:2.

- A technical article by Moore et al. evaluated a decellularization method, Matracell, for human dermis. Matracell renders human dermis acellular with >97% donor DNA removal, while retaining biomechanical properties of the tissue. Using an in vivo mouse model, cytotoxicity assays showed Matracell dermis to be biocompatible and to support vascular and cellular in-growth. Biomechanical testing demonstrated ultimate tensile strengths of 635.4 ± 199.9 N and 532.0 ± 154.0 N for 2 mm thick Matracell Dermis and 2 mm thick GraftJacket® MaxForce Extreme, respectively. Additionally, suture retention strength of 134.9 ± 55.1 N and 106.5 ± 27.9 N was found for Matracell Dermis and GraftJacket MaxForce Extreme, respectively. DNA content was calculated to be 15.97 ± 4.8 ng/mg of dry weight for Matracell dermis, compared to 134.6 ± 44.0 and 272.8 ± 168.8 ng/mg dry weight of GraftJacket and AlloDerm, respectively. The authors concluded that "these characteristics indicate the potential utility of [Dermacell] for a variety of wound healing, soft tissue reconstruction, and sports medicine applications."

