REPRESENTATIVE REPORTS USING DERMACELL® FOR BREAST RECONSTRUCTION

Documents available upon request

Clinical Reports using DermACELL in Breast Reconstruction

Bullocks J, Nelson J. Dermacell: A novel and biocompatible acellular dermal matrix in tissue expander and implant-based breast reconstruction. Eur J Plast Surg. 2014; 37(10):529-38.

Bullocks J, Nelson J. The new alternative for breast reconstruction post mastectomy: Case study series parts 1-3. Data on File, LifeNet Health (68-20-059-01 – 68-20-059-03).

- A case study series performed by Bullocks and Nelson evaluated the efficacy of Dermacell used in immediate bilateral breast reconstructions. This was a 3 part series. Breast reconstruction may be necessary in cases of congenital or acquired breast absence; this includes defects of the breast, partial or full. Case 1 was a 33-year-old female with a strong family history of breast cancer and positive for BRCA-1. The patient's mother died of breast cancer in her early 30s. Her sister developed cancer in her 30s and has had a mastectomy with reconstruction. The patient was tested for the BRCA-1 gene mutation, and this was positive. The patient elected to undergo a prophylactic mastectomy and desired to have immediate breast reconstruction. Case 2 was a 43-year-old female recently diagnosed with breast cancer and no significant past medical history. The patient received neoadjuvant chemotherapy for a left locally advanced breast cancer that was discovered in June 2010. The patient responded well to chemotherapy and was counseled by her surgical oncologist to have a mastectomy. The patient agreed, and requested a contralateral prophylactic mastectomy with immediate breast reconstruction. Case 3 was a 52 year-old female recently diagnosed with breast cancer and no significant past medical history. The patient had multi-centric DCIS in the left breast, and after extensive consultation with a surgical oncologist, agreed to undergo a left mastectomy and right prophylactic mastectomy. The patient also desired to have immediate breast reconstruction. All patients underwent successful breast reconstructions and the Dermacell was found to be well incorporated into the surrounding tissues.

Chang E, Liu J. Prospective unbiased experience with three acellular dermal matrices in breast reconstruction. J Surg Oncol. 2017.

Hanna K, Yu D, LeGallo R, Colen D, Drake D. MatrACELL processed, sterilized acellular dermal matrix in implant-based breast reconstruction: Clinical and histologic outcomes. J Am Coll Surg. 2013;217(3S):S91.

- Hanna et al. clinically evaluated Matracell processed ADM, Dermacell, in 28 patients (42 tissue expanders). The histologic properties of Dermacell (vascularity, inflammation, and fibrosis) were compared to native breast capsules biopsied at the time of implant exchange. Seroma and infection rates, as well as wound separation, were noted. Dermacell complications were compared to an AlloDerm cohort group consisting of 37 patients (51 tissue expanders). The rate of major infection, seroma rate, and wound separation was found to be 7%, 2.4%, and 5%, respectively. Wound separation was similar among the two groups; however infection and seroma rates were lower in the Dermacell group, though not statistically significant. "Histologic evaluation of inflammation, vascularity and fibrosis was significantly less in the Dermacell incorporated capsule than native capsule ($p<0.05$)." Overall, the authors concluded that "Matracell processed ADM may have an advantage over AlloDerm in terms of seroma and infection rates in breast reconstruction. Histologic analysis confirms Matracell processed ADM to have desirable properties of low immunogenicity, low levels of fibrosis, and minor inflammation."

Ortiz JA. Clinical outcomes in breast reconstruction patients using a sterile acellular dermal matrix allograft. Aesth Plast Surg. 2017;41(3):542-550.

Ortiz JA. Poland's breast reconstruction with decellularized human dermal allograft. Mil Med. 2014;179(2):e249-52.

- A case report by Ortiz evaluated the use of decellularized human dermal allograft, Dermacell, in the breast reconstruction of a 27 year old female with severe left breast hypoplasia secondary to undiagnosed Poland's syndrome, or abnormalities of multiple muscles of the thoracic wall. A 350 cc Medium Height tissue expander and two 4x16 cm pieces of Dermacell were used in the procedure. The procedure, along with subsequent expansions, was uneventful. The authors concluded that "it [Dermacell] allows for improved results in the indicated patient. The successful use of DHDA [Dermacell] such as the case presented here shows another promising indication for its use. Aesthetically pleasing result with minimal morbidity and tissue sacrifice was obtained in the case on hand."

Park JS, Lee TJ. Abstract: Comparison of two different acellular dermal matrices sling (AlloDerm, DermACELL) for implant-based immediate breast reconstruction. Milan Breast Cancer Conference, June 23-26, 2015.

- Park and Lee conducted a study of 137 patients with a total of 157 immediate implant-based breast reconstructions using either Dermacell (n=57) or AlloDerm (n=100). Rates of seroma/hematoma (P=0.354), infection (P=0.535), and wound complications (P=0.531) did not significantly differ between the two groups. Additionally, there was no significant difference in implant removal due to complications between the two groups (P=0.401). Authors concluded that AlloDerm and Dermacell were not different but Dermacell is preferable due to its convenience of storage at room temperature and ready to use without needing to be rehydrated or thawed.

Pittman TA, Fan KL, Knapp A, Frantz S, Spear S. Comparison of different acellular dermal matrices in breast reconstruction: The 50/50 study. Plast Reconstr Surg. 2017;139(3):521-8.

Vashi C. Clinical outcomes for breast cancer patients undergoing mastectomy and reconstruction with the use of DermACELL, a sterile, room temperature acellular dermal matrix. Plast Surg Int. 2014; 2014:704323.

- Vashi reported on the clinical outcomes for breast cancer patients undergoing mastectomy and reconstruction with use of Dermacell. This cohort case series included 9 consecutive breast cancer patients treated with mastectomies and immediate breast reconstruction between August and November 2011. There were 8 bilateral and 1 unilateral mastectomies performed, for a total of 17 breasts. Biopsy specimens were obtained from all patients and submitted in formalin to an independent pathology laboratory for sectioning and staining. General observations for all biopsied patients included presence of fibroblasts, vasculature, and intact ultrastructure, including elastin. Compared to the host tissue, the implant material appeared more organized, with few living cells and less vasculature. This finding is expected for a stable material slowly being incorporated and remodeled after a few weeks to a few months following surgery when the specimens were collected. The author concluded that Dermacell appears to be an appropriate adjunct to reconstruction with expanders. Additionally, he noted that Dermacell appeared to work well with all patients receiving post-operative chemotherapy, postoperative radiation, prednisone, and coumadin.

Yu D, Hanna K, LeGallo R, Drake D. Comparison of the histological characteristics of ADM capsules to no-ADM breast capsules in ADM-assisted breast reconstruction. Plast Reconstr Surg. 2014;133(3 Suppl):113.

- A histological comparison of capsules containing decellularized (Matracell) ADM and capsules without ADM was performed by Yu et al. in ADM-assisted breast reconstruction. In total, 48 biopsies were obtained from 15 women. Histological analysis, including inflammation, capsule fibrosis, vascular proliferation, foreign body giant cell inflammatory reaction and myofibroblasts was collected and analyzed. Additionally, suture granulomas and inflammatory capsules were also assessed. Significantly less inflammation, fibrosis, myofibroblasts, and vascular proliferation were found in the ADM group compared to the no-ADM group. Also, a significantly higher likelihood of the presence of an inflammatory capsule was found in the no-ADM group. No significant differences were found between the two groups in regard to giant cell reaction or suture granulomas. The authors concluded that "when used for staged breast reconstruction, this novel decellularized regenerative matrix processed using Matracell technology appears to induce less inflammation and less myofibroblasts. These results may explain the observed decreased capsular contracture in ADM-assisted breast reconstruction."

Zenn MR, Salzberg CA. A direct comparison of AlloDerm Ready-To-Use (RTU) and DermACELL in immediate breast implant reconstruction. ePlasty. 2016;16:20812.

- Article described a retrospective study of 140 patients who had undergone breast implant reconstructions with either AlloDerm Ready-To-Use (RTU; n=70) or Dermacell (n=70). Authors discovered "no clinical difference between AlloDerm-RTU and Dermacell, and that there is no statistical difference between these ADMs in infection rate, implant loss or need for corrective surgery within 6 months of placement… With equal clinical performance between AlloDerm-RTU and Dermacell, value-based care would dictate that the decision on which product to use will likely be made on nonclinical factors, such as availability and price."

Zenn M, Venturi M, Pittman T, Spear S, Gurtner G, Robb G, Mesbahi A, Dayan J. Optimizing outcomes of postmastectomy breast reconstruction with acellular dermal matrix: a review of recent clinical data. ePlasty. 2017;17;e18.

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 ffl 199.9 N and 532.0 ffl 154.0 N for 2 mm thick Matracell Dermis and 2 mm thick GraftJacket® MaxForce Extreme, respectively. Additionally, suture retention strength of 134.9 ffl 55.1 N and 106.5 ffl 27.9 N was found for Matracell Dermis and GraftJacket MaxForce Extreme, respectively. DNA content was calculated to be 15.97 ffl 4.8 ng/mg of dry weight for Matracell dermis, compared to 134.6 ffl 44.0 and 272.8 ffl 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."

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