

### Hyalomatrix<sup>®</sup> Bibliography

Hyalomatrix<sup>®</sup> is a sterile, flexible wound device consisting of two layers: a non-woven pad of esterified HYAFF and a semi-transparent silicone membrane.

Upon contact with the wound bed, the HYAFF layer transforms into a hydrophilic gel and integrates with the surrounding tissue. This biodegradable matrix acts as a 3-D scaffold for cellular invasion and capillary growth, which facilitates the colonization of fibroblasts and vascular cells.

1. Kozusko SD, Hassouba M, Hill DM, Liu X, Dadireddy K, Velamuri SR. Esterified Hyaluronic Acid Matrix in Lower Extremity Reconstruction With Exposed Tendon and Bone: A Retrospective Review. J Burn Care Res. 2020 Jul 3;41(4):828-834. doi: 10.1093/jbcr/iraa044 Full Article:

#### https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7333675

Purpose: This article evaluates the use of Hyalomatrix in 15 patients with lower extremity wounds with exposed bone and tendon featuring specific clinical outcomes of 3 patients. Conclusion: 13 of the 15 patients were treated successfully with Hyalomatrix and achieved definitive coverage with split-thickness skin grafting. In the 13 successful cases, the mean time to split-thickness skin graft was 22.9 ± 7 days. Given the success rate in these challenging patients Hyalomatrix can be treatment option for similar cases.

2. Aballay A, Hermans MHE. Neodermis formation in full thickness wounds using an esterified hyaluronic acid matrix. Journal of Burn Care & Research 2019. irz057,\_

https://doi.org/10.1093/jbcr/irz057

Abstract: https://academic.oup.com/jbcr/advance-articleabstract/doi/10.1093/jbcr/irz057/5430850

Purpose: This article focusses on clinical aspects, morphology, and histology, observed in the treatment of different ulcers and wounds treated with Hyalomatrix.

**Conclusion**: The long-term histological observations in the reconstruction of scars in combination with the reduction of scarification after scar excision and the provision of a dermis to the fresh wound indicate that Hyalomatrix supports and stimulates for the creation of a neodermis.

3. Schneider HP, Landsman A. Preclinical and Clinical Studies of Hyaluronic Acid in Wound Care: A Case Series and Literature Review. Wounds 2019 Feb;31(2):41-48. Full Article: https://www.woundsresearch.com/article/preclinical-and-clinical-studies-hyaluronicacid-wound-care-case-series-and-literature

Purpose: The purpose of the retrospective case series was to assess the effect of Hyalomatrix on 6 patients with DFUs and 3 patients with VLUs.

**Conclusion**: During the 55-day evaluation period, the average change in wound size decreased by  $6.43 \text{ cm}^2$  (SD = 7.55 cm<sup>2</sup>), from 7.93 cm<sup>2</sup> (SD = 8.12 cm<sup>2</sup>) to 1.50 cm<sup>2</sup> (SD = 0.92 cm<sup>2</sup>). The presented case series supports the contention that hyaluronic acid is a critical component in wound healing.

## Hyalomatrix<sup>®</sup> Bibliography

 Kapp DL, Rogers M, Hermans MHE. Necrotizing Fasciitis: An Overview and 2 Illustrative Cases. Int J Low Extrem Wounds 2018 Dec;17(4):295-300. doi: 10.1177/1534734618804037. Epub 2018 Nov 13.

Abstract: <a href="https://www.ncbi.nlm.nih.gov/pubmed/30422020">https://www.ncbi.nlm.nih.gov/pubmed/30422020</a>

**Purpose**: This article reviews the symptoms and treatment of two necrotizing fasciitis cases treated with Hyalomatrix to "fill in" the wound with neodermis for the lost dermis and create a wound bed most suitable for grafting.

5. Cheung T, Laidley Z, Jones J, Wu S. Outcomes of an Esterified Hyaluronic Acid Matrix in the Treatment of Chronic Lower Extremity Wounds: A Case Series. *Wounds* 2018 Dec;30(12):367-371. <u>Full Article</u>: <u>https://www.woundsresearch.com/article/outcomes-esterified-hyaluronic-acid-matrix-treatment-chronic-lower-extremity-wounds-case</u>

**Purpose**: This case series evaluates the use of Hyalomatrix in patients with chronic lower extremity wounds.

**Conclusion**: In the 20-week evaluation period, 85.7% of wounds measuring a mean of 2.32 cm<sup>2</sup> healed in a mean of 8.9 weeks. Hyalomatrix may be a useful adjunct in the treatment of chronic, non-infected, non-ischemic wounds.

- 6. Simman R, Mari W, Younes S, Wilson M. Use of Hyaluronic Acid–Based Biological Bilaminar Matrix in Wound Bed Preparation: A Case Series. *ePlasty* 2018 Feb 22;18:e10. eCollection 2018.
  Full article: <a href="http://www.eplasty.com/images/PDF/eplasty18e10.pdf">http://www.eplasty.com/images/PDF/eplasty18e10.pdf</a>
  Purpose: This case series analyzes the use of Hyalomatrix in the treatment of 12 surgical wounds where the extracellular matrix was lost, many with exposed muscle, tendons, and/or bone.
  Conclusion: Three wounds healed by secondary intention, and nine wounds closed with a split-skin autograft, with no graft failure. All wounds completely reepithelialized. Hyalomatrix may a useful tool in supporting wound healing in complex, surgical wounds.
- Alvarez OM, Makowitz L, Patel M. Venous Ulcers Treated With a Hyaluronic Acid Extracellular Matrix and Compression Therapy: Interim Analysis of a Randomized Controlled Trial. *Wounds* 2017;29(7):E51–E54.

**Full article**: <u>http://www.woundsresearch.com/article/venous-ulcers-treated-hyaluronic-acid-</u><u>extracellular-matrix-and-compression-therapy-interim</u>

**Purpose**: In this interim analysis of a prospective, parallel, randomized, single-center study, Hyalomatrix was evaluated for the treatment of venous leg ulcers in 16 subjects. **Conclusion**: At week 12 and week 16, the incidence of wound healing was 66.6% for the Hyalomatrix group and 14.2% for the control (P = 0.066) and 87.5% for the Hyalomatrix group and 42.8% for the control (P = 0.059), respectively. For the Hyalomatrix group, the mean time to healing was 41 days compared with 104 days in the control (P = 0.029).

8. Litwiniuk M, Krejner A, Grzela T. Hyaluronic Acid in Inflammation and Tissue Regeneration. *Wounds* 2016;28(3):78-88.

**Full article**: http://www.woundsresearch.com/article/hyaluronic-acid-inflammation-and-tissueregeneration

**Purpose**: The purpose of this review is to describe the role of different molecular weight HA polymers in tissue regeneration and in wound healing, particularly inflammation and angiogenesis. The review further summarizes the main cellular receptors involved in HA signaling and examines the antioxidative properties of HA the associated clinical implication.

### Hyalomatrix<sup>®</sup> Bibliography

9. Vaienti L, Marchesi A, Palitta G, Gazzola R, Parodi PC, Leone F. Limb Trauma: the use of an advanced wound care device in the treatment of full-thickness wounds. *Strat Traum Limb Recon* 2013;8:111-115.

Full article: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3732675/

**Purpose**: The purpose of this 15 patient observational case series was to evaluate the clinical efficacy and safety of Hyalomatrix on dermal reconstruction in full thickness traumatic wound defects.

**Conclusion**: All patients went on to successful repair, and the mean average time to complete healing was 26.8 days.

 Motolese A, Vignati F, Brambilla R, Cerati M, Passi A. Interaction between a regenerative matrix and wound bed in nonhealing ulcers: results with 16 cases. *Biomed Res Int* 2013; 2013:849321.
 Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/23971047</u>

**Purpose**: The purpose of this 16 patient case series was to evaluate the use of a Hyalomatrix grafting for reconstructive surgery of venous leg ulcers.

**Conclusion**: Four patients did not require the epidermal graft since they showed a quick and satisfying reepithelialization. The combination of wound bed preparation with application of Hyalomatrix can be a useful approach for treatment of partial thickness ulcers.

11. Caravaggi C, Grigoletto F, Scuderi N. Wound Bed Preparation with a Dermal Substitute (Hyalomatrix PA) Facilitates Re-epithelialization and Healing: Results of a Multicenter, Prospective, Observational Study on Complex Chronic Ulcers (The FAST Study). Wounds 2011;23(8):228-235. Note: Hyalomatrix PA is the European equivalent of US FDA Hyalomatrix. The study is conducted in Europe so the description of the product which varies from US FDA cleared description is used. <u>Full article</u>:

http://www.woundsresearch.com/article/wound-bed-preparation-dermal-substitutehyalomatrix%C2%AE-pa-facilitates-re-epithelialization-and

**Purpose**: The study evaluated the performance and safety of Hyalomatrix in the treatment of chronic wounds of different etiology in 262 elderly patients from 70 Italian centers. **Conclusion**: Hyalomatrix stimulated the healing process in 217 (83%) of the treated ulcers. Twenty-six percent of wounds achieved 75% re-epithelialization within the 60-day follow-up period using only Hyalomatrix treatment.

 Vindigni V, Cortivo R, Iacobellis L, Abatangelo G, Zavan B. Hyaluronan Benzyl Ester as a Scaffold for Tissue Engineering. *International Journal of Molecular Sciences* 2009; 10: 2972-2985.
 Full article: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738906/

**Purpose**: The article discusses the properties of a benzyl ester of hyaluronan (HYAFF<sup>®</sup>) scaffolds for tissue engineering and regenerative medicine.

**Conclusion**: HYAFF scaffolds have been found to be highly biocompatible and have been cultured with human hepatocytes, dermal fibroblasts and keratinocytes, chondrocytes, Schwann cells, bone marrow derived mesenchymal stem cells and adipose tissue derived mesenchymal stem cells without eliciting any adverse reactions.

### Hyalomatrix<sup>®</sup> Bibliography

 Osti E. Skin pH Variations from the Acute Phase to Re-Epithelialization in Burn Patients Treated with New Materials (Burnshield, Semipermeable, Adhesive Film, Dermasilk, and Hyalomatrix). Non-invasive preliminary Experimental Clinical Trial. *Annals of Burns and Fire Disasters* 2008; 21(2):73-77.

**Full article**: <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3188158/</u>

**Purpose**: The aim was to measure the pH value of the skin of two burn patients, one treated with Burnshield and Hyalomatrix and one treated with Burnshield and Dermasilk, from the acute phase through to complete re-epithelialization.

**Conclusion**: For both patients, the pH was alkaline from the day of the burn until day 12, with an alkaline pH peak on day 4 with gradual return to normal (pH=5.5) from day 13 onwards. The mean re-epithelialization time was similar in the two patients, equivalent to 24.5 days.

#### **Additional Studies**

Request additional resources from Medical Affairs.

#### **Pediatric Studies**

Request additional resources from Medical Affairs.

#### HYAFF and Hyaluronic Acid

1. Aya KL, Stern R. Hyaluronan in wound healing: Rediscovering a major player. *Wound Repair Regen* 2014;22:579-593.

Full Article: http://onlinelibrary.wiley.com/doi/10.1111/wrr.12214/epdf

- Frenkel JS. The role of hyaluronan in wound healing. *Int Wound J* 2014; 11:159-163.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/22891615</u>
- Vazquez JR, Short B, Findlow AH, et al. Outcomes of hyaluronan therapy in diabetic foot wounds. Diabetes Res Clin Pract 2003;59(2):123-7.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/12560161</u>
- Price RD, Berry MG, Navsaria HA. Hyaluronic acid: the scientific and clinical evidence. J SurgRecon 2007 March; 60: 1110-1119.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/17466613</u>
- Price RD, Das-Gupta V, Leigh IM, Navsaria HA. A comparison of tissue-engineered hyaluronic acid dermal matrices in a human wound model. *Tissue Engineering* 2006;12(10):2985-95.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/17518666</u>
- Price RD, Myers S, Leigh IM, Navsaria HA. The role of hyaluronic acid in wound healing: assessment of clinical evidence. *Am J Clin Dermatol* 2005;6(6):393-402.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/16343027</u>
- Caravaggi C, De Giglio R, Pritelli C, et al. HYAFF-11 based autologous dermal and epidermal grafts in the treatment of noninfected diabetic plantar and dorsal foot ulcers: a prospective, multicenter, controlled, randomized clinical trial. Diabetes Care. 2003;26:2853-2859.
   Full article: http://care.diabetesjournals.org/content/diacare/26/10/2853.full.pdf
- Chen WYJ, Abatangelo G. Functions of hyaluronan in wound repair. Wound Repair and Regeneration 1999;7:79-89.
   Abstract: <u>http://www.ncbi.nlm.nih.gov/pubmed/10231509</u>

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#### **Posters**

- 1. Lepow, BD. An Esterified Hyaluronic Acid Matrix Used for Severe Diabetic Foot Ulcers and Amputations. Presented at the SAWC Spring Conference, May 13-17, 2020 in San Diego CA
- 2. Hassouba M, Liu X, Walls C, Hill D, Hickerson W, Velamuri SR. Reconstruction of Complex Lower Extremity Wounds With Hyaluronic Acid Based Skin Substitute and Split Thickness Skin Grafting: A Case Series. Presented at the ABA Conference April 2-5, 2019 in Las Vegas NV
- 3. Xu, DH. Limb Salvage in Non-Compliant Type II Diabetic Patients using an Esterified Hyaluronic Acid Matrix without Split Thickness Skin Graft. Presented at SAWC Fall Conference November 4-6, 2020 (Virtual)
- 4. Reardon, B, Blanton, CM, Clougherty, CO. Esterified Hyaluronic Acid Matrix Used Successfully In Nonhealing Chronic Wounds for Patients Who Had Failed All Previous Therapies. Presented at SAWC Fall Conference November 4-6, 2020 (Virtual)
- 5. Wolfe, W. An Esterified Hyaluronic Acid Matrix Provides for Wound Healing of Previously Infected Lower Extremity Wounds with Exposed Bone and Tendon. Presented at the APMA Conference 2020, July 23-26 in Boston, MA.
- Winters, C and Nichols, J. Treatment of Chronic Lower Extremity Wounds in Diabetic Patients using an Esterified Hyaluronic Acid Matrix. Presented at the SAWC Spring Conference, May 13-17, 2020 in San Diego CA.
- Martins, DB, Young, D, Hansen, S. Esterified Hyaluronic Acid Matrix Treatment after Surgical Excision in Patients with Refractory Hidradenitis Suppurativa Promotes Healing and is Associated with Less Post-Operative Pain. Presented at SAWC Fall Conference November 4-6, 2020 (Virtual)
- 8. Brown, D. A Case Series and Reconstructive Burn Surgeon's Experience with an Esterified Hyaluronic Acid Matrix as a Multi-Functional Tool used for Limb Salvage. Presented at the John A. Boswick (JAB) Burn and Wound Symposium, January 25-30, 2020 in Wailea, HI.
- 9. Robertson, T and Benitez, LD. Negative Pressure Wound Therapy in Combination with an Esterified Hyaluronic Acid Matrix Used in Preparation for Split Thickness Skin Grafting in Complex Wounds. Presented at the SAWC Fall Conference, Oct 12, 2019 in Las Vegas, NV
- 10. Xu, DH and Forg, P. An Esterified Hyaluronic Acid Matrix used for Healing Soft Tissue Defect with Exposed Bone and Tendon. Presented at the APMA Annual Conference, July 11 - 14, 2019 in Salt Lake City, UT
- 11. Robertson, T and Benitez, LD. Bone and Tendon Coverage with an Esterified Hyaluronic Acid Matrix. Presented at the SAWC Fall Conference Nov 2, 2018 in Las Vegas, NV
- 12. Alvarez OM, Makowitz L, Patel M. Venous Ulcers Treated With a Hyaluronic Acid Extracellular Matrix and Compression Therapy: Interim Analysis of a Randomized Controlled Trial. Presented at the Symposium on Advanced Wound Care, Spring; San Diego, CA; April 2017.
- 13. Homsombath B, Mullins RF, Abu Zaheed Hassan SM, Craft-Coffman B, Graham PS. Retrospective review of Burns and Chronic Wounds Using a Hyaluronic Acid-Based Matrix Product. Presented at Southern Region Burn Conference; Atlanta, GA; 2016.
- 14. Carpenter S, Brabham R, Shaffet T, Hunt R, Flanagan B. Successful Healing of Complex Wounds using an Esterified Hyaluronic Acid Matrix. Presented at the Symposium on Advanced Wound Care, Fall; Las Vegas, NV; September 2015. (LIT059WC)
- 15. Schneider HP, Landsman AS. Esterified Hyaluronic Acid Matrix Promotes Formation of Granulation Tissue and Facilitates Wound Closure. Presented at the Clinical Symposium on Advances in Skin and Wound Care; New Orleans, LA; September 2015. (LIT061WC)
- 16. Shah S, Saleh P. The Use of an Esterified Hyaluronic Acid Containing Bilayer Matrix in Healing of Chronic and Stalled Wounds, an Outpatient Experience. Presented at the Clinical Symposium on Advances in Skin and Wound Care; New Orleans, LA; September 2015. (LIT057WC)
- Vlad LG, Gumus T, Molnar JA. The Use of an Esterified Hyaluronic Acid Three-Dimensional Scaffold for Treating Chronic Wounds. Presented at the Clinical Symposium on Advances in Skin and Wound Care; New Orleans, LA; September 2015. (LIT060WC)

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- Shannon S, Bauerle T, Rayborn A, Wale A, Shannon T. Esterified Hyaluronic Acid Scaffold: A Testing Sample. Presented at the Clinical Symposium on Advances in Skin and Wound Care; New Orleans, LA; September 2015. (LIT074WC)
- 19. Sherman R. Harnessing a Bridge Esterified Hyaluronic Acid Scaffold to Enhance the ECM to Advance the Healing of Diabetic Wounds. Presented at the Clinical Symposium on Advances in Skin and Wound Care; New Orleans, LA; September 2015. (LIT058WC)
- 20. Milne C. The Use of a Novel Hyaluronic Acid Matrix in the Management of Difficult Chronic Wounds. Presented at the Symposium on Advanced Wound Care, Spring; San Antonio, TX; May 2015. (LIT043WC)
- Branigan M, Wu S. Outcomes of a Biologically Derived Hyaluronic Acid Matrix in Treatment of Chronic Lower Extremity Wounds. Presented at the Symposium on Advanced Wound Care, Spring; San Antonio, TX; May 2015. (LIT075WC)
- 22. Livingston M, Chakravarthy D, Roman M. Evaluation of the Use of a Hyaluronic Acid Based Matrix with a Silicone Fluid Transfer Dressing. Presented at the Symposium on Advanced Wound Care, Spring; San Antonio, TX; May 2015. (LIT041WC)
- Livingston M, Chakravarthy D, Roman M. Nine Patient Evaluation of a Hyaluronic Acid-Based Wound Scaffold. Presented at the National Pressure Ulcer Advisory Panel's Conference; Orlando, FL. February 2015. (LIT035WC)
- 24. Huddleston L, Montoya L. The Use of a Hyaluronic Acid Based Matrix in the Management of Extremely Recalcitrant Wounds. Presented at the Symposium on Advanced Wound Care, Fall; Las Vegas, NV; October 2014. (LIT015WC)
- 25. Livingston M, Chakravarthy D, Roman M. Evaluation of the use of a hyaluronic acid based wound scaffold with a silicone fluid transfer dressing. Presented at the Clinical Symposium on Advances in Skin & Wound Care; Las Vegas, NV; September 2014. (LIT003WC)
- 26. Mari W, Younes S, Simman R. The Role of Esterified Hyaluronic Acid Bilaminar Matrix in Wound Healing, a Case Series. Presented at the Symposium on Advanced Wound Care, Spring; San Diego, CA; April 2017.\*
- 27. Pittinger T, Curran D. Side by side comparison of bovine collagen-glycosaminoglycan product and a hyaluronic acid based product in a patient with 56% TBSA. Presented at Southern Region Burn Conference; Atlanta, GA; 2016.\*
- 28. Lintner AC, Kahn SA. Management of Full-Thickness Burns and Wounds with a Bilayer Esterified Hyaluronic Acid Matrix. Presented at JAB Maui Symposium; Maui, HI; 2016.\*