



The Most Human Form of Wound Healing

We provide Mother
Nature's most natural gift
of healing. At BioTissue,
science meets nature.


Meeting the Clinical and Financial Challenges of Wound Healing

Time heals wounds. Diabetes doesn't know time.

In the United States, every 17 seconds someone is diagnosed with diabetes, and every day 230 Americans with diabetes will suffer an amputation.¹



Diabetic Foot Health

Up to **25%** of those with diabetes will develop a foot ulcer²⁻³ 



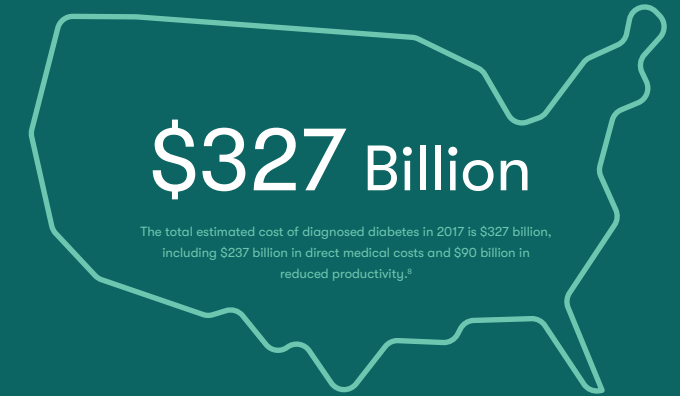
Annual incremental payer burden ranges from **\$9.1 - \$15 Billion.**⁴

More than half of DFUs develop infection, often with osteomyelitis, and up to 20% of infected DFUs require major or minor amputations. One recent study demonstrated that excess health care costs of diabetic foot ulcers (DFU) are approximately twice that attributable to the treatment of diabetes alone, with annual incremental per-patient medical costs ranging from \$11,710 to \$16,883⁴



\$1 Million are spent on diabetic foot complications in the USA every 30 minutes⁷

Cost of Diabetes in the U.S.



\$237 Billion
direct medical costs

\$90 Billion
indirect medical costs
(disability, reduced productivity, premature death)

Wound Epidemiology

14.5% of Medicare beneficiaries in 2014 (8.2 million patients) were diagnosed with at least one type of wound or wound-related infection.⁶



Listed by prevalence:

1. Surgical wound infections, the largest category, at 4%
2. Diabetic wound infections 3.4%
3. Non-healing surgical wounds 3%

Outsmart Diabetes



Podiatric medical care can reduce amputation rates up to **80%**¹⁰

The use of Advanced Treatments improved outcomes in lower extremity diabetic ulcers as demonstrated in a recent clinical study. In the clinical use of NEOX as an advanced treatment, 79% of patients with Wagner 3-4 DFUs achieved closure in an average of 16 weeks with an average of 1.2⁴ graft applications.¹¹

The inclusion of care provided by podiatrists for those with diabetes alone will save the healthcare system **\$3.5 Billion** per year.¹²



Managing the Complexities of Human Healing



Together we are on a journey to solve unmet patient needs by helping to improve healing and reducing patient suffering.

We share your dedication to knowing more about the disease process and trying to understand if there is a better way to treat difficult diseases.

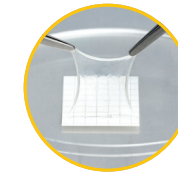
Our goal has been and always will be solving patients' unmet clinical needs through the relentless pursuit of new solutions to complex problems. Everything we do to discover, develop, and bring to market products and applications is centered on helping you as healers and improving the lives of patients.

Biological Tissue Provides the Most Human Form of Healing

We are in a race against time to heal chronic wounds. BioTissue Surgical products provide the natural healing properties of human birth tissue to the wound.



Neox 1K is a cryopreserved ultra-thick human amniotic membrane derived from umbilical cord used as an adjunct treatment for chronic and acute, partial and full-thickness wounds.^{11,13-15} This allograft helps promote healing in complex diabetic foot ulcers complicated with osteomyelitis, comparing favorably to the Standard of Care.^{11,15,16} It's up to 10 times thicker than amniotic membrane alone,¹⁷ which may increase longevity in the wound bed, potentially reducing applications and cost of care.



Neox 100 is a thinner cryopreserved version of our human amniotic membrane allograft, ideal for shallow wounds or for larger wound areas. The allograft is delivered on a non-implantable, gridded paper backing for easier handling and application.



Neox RT is a sterile, ultra-thick human amniotic membrane allograft derived from umbilical cord, for chronic and acute partial and full thickness wounds. Neox RT delivers the benefits of human amniotic allograft in a shelf stable product with room temperature storage. It is manufactured, using the SteriTek® preservation process, stored in saline (0.9% w/v NaCl) and terminally sterilized via gamma irradiation yielding a hydrated shelf stable product.

Built on a foundation of relentless clinical pursuit, discovery and cost-effective solutions



36 Years
of National Institute of Health (NIH) funding



680,000+
human clinical applications



380+
peer-reviewed publications studying our technology



1st
to establish Level 1 CPT Codes or reimbursement of amniotic membrane used on the ocular surface



6 IND
(Investigational New Drug) products with three in Phase 2 & 3 Clinical trials for BLA approvals

Preserving as Much of Nature as Possible

For over 36 years, our pioneering scientists have focused on understanding the regenerative features of human birth tissue—ultimately identifying HC-HA/PTX3 as a key orchestrator in human birth tissue regenerative healing.¹⁸⁻²²

The BioTissue CryoTek cryopreservation process is the only tissue processing method shown to produce a matrix comparable to the native tissue.^{17,23} In conventional dehydration processing, critical biological components—including the majority of HC-HA/PTX3 naturally found in

birth tissue—are degraded, which may limit the processed tissue's healing capabilities.¹⁷

CryoTek cryopreservation technology utilizes controlled deep freezing to effectively preserve the functional and structural integrity of the birth tissue.^{17,23}

CryoTek preserves the functional components of the extracellular matrix.

BioTissue Surgical human birth tissue products are aseptically processed, devascularized and cell devitalized to deliver the innate properties of human birth tissue to the wound environment.

The Proof is in the Evidence

The number of non-healing wounds is dramatically increasing, this poses extreme challenges to the U.S. healthcare system. Diabetic wound healing is one of the most prevalent complications. Healing in the diabetic patient is more crucial than ever, as the 5-year mortality rate is 31% - the same rate as all reported cancer.



Healing complex wounds in less time with fewer applications:

	Neox UC ¹¹ Caputo DPM 2016	Neox UC ¹⁴ Raphael DPM 2016	Neox UC ¹⁵ Raphael DPM 2017	AM+Chorion ²⁵	Placenta ²⁶	AM+Chorion ²⁷
#Patients/ #Wounds	31/33	29/32	13/14	63/63	31/31	13/13
Indications	Complex DFU with Osteomyelitis	DFU	Complex DFU with Osteomyelitis	DFU	Complex DFU without Osteomyelitis	DFU
Avg Wound Area	15.6 cm ²	10.6 cm ²	33.2 cm ²	5.2 cm ²	14.6 cm ²	2.6cm ²
Healing Rate	78.8% Avg: 16 weeks	87.5% Avg: 13.8 weeks	100% (+NPWT*) Avg: 24 weeks	Week 24: 47%	Week 16: 59.7%	Week 6: 92%
Avg # Applications	1.24	1.68	3.2	3.5	9.0	N/A
Wagner Grade	Wagner 3-4	Wagner 1-4	Wagner 3-4	N/A	Wagner 2	Wagner 1

*Negative Pressure Wound Therapy

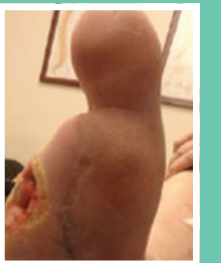
Proven Outcomes

Clinical Use of Neox 1K as an Adjunct Therapy In Promoting Healing of A Complex Wound Resulting from Necrotizing Fasciitis

Thomas Fusco, DPM, FACFAS - Orthopedic Associates, Fort Walton Beach, FL

Wound closure in 10 weeks

2 Neox 1K graft applications



Clinical Use of Neox 1K as an Adjunct Therapy in Promoting Healing of a Complex Wound

Wayne Caputo, DPM Clara Maass Medical Center, Newark, NJ

Wound closure in 28 weeks

2 Neox 1K graft applications

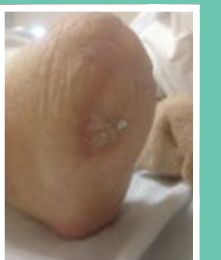


Clinical Use of Neox 1K as an Adjunct Therapy in Transmetatarsal Amputation with Recurrent Ulceration of the Lateral Column

Allen Raphael, DPM, Village Podiatry Center, Smyrna, GA

Wound closure in 13 weeks

2 Neox 1K graft applications





The time is now to achieve a new standard of care. Together we can make a difference in complex wound management.

References

1. Increasing Awareness This National Diabetes Month Can Save Limbs and Lives. Accessed January 26, 2022. <https://www.ajmc.com/view/increasing-awareness-this-national-diabetes-month-can-save-limbs-and-lives>
2. International Working Group on the Diabetic Foot. Epidemiology of diabetic foot infections in a population-based cohort. Paper presented at: International Consensus on the Diabetic Foot; May 22-24, 2003; Noordwijkerhout, the Netherlands
3. Lavery LA, Armstrong DG, Wunderlich RP, Tredwell J, Boulton AJ. Diabetic foot syndrome: evaluating the prevalence and incidence of foot pathology in Mexican Americans and non-Hispanic whites from a diabetes disease management cohort. *Diabetes Care*. 2003;26:1435-1438. doi:10.2337/14351438
4. Rice JB, et al. *Diabetes Care*. 2014; 37: 651-8.
5. Wu S, Armstrong DG. Risk assessment of the diabetic foot and wound. *Int Wound J* 2005; 2(1):17-24. <https://doi.org/10.1111/j.1742-4801.2005.00085.x>
6. Rankin TM, Miller JD, Gruessner AC, Nickerson DS. Illustration of cost saving implications of lower extremity nerve decompression to prevent recurrence of diabetic foot ulceration. *J Diabetes Sci Technol* 2015; 9(4): 873-880. <https://doi.org/10.1177/1932296815584796>
7. Yang W, Dall TM, Beronjia K et al. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care* 2018; 41(5):917-928.
8. Yang W, Dall TM, Beronjia K et al.; American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care* 2018; 41(5):917-928.
9. Nussbaum SR, Carter MJ, Fife CE, et al. *Value Health*. 2018 Jan;21(1):27-32.
10. Gibson TB, Driver VR, Wrobel JS, et al. Podiatrist care and outcomes for patients with diabetes and foot ulcer. *Int Wound J*. 2014;11(6):641-648. doi:10.1111/iwj.12021
11. Caputo WJ, Vaquero C, Monterosa A, et al. *Wound Repair Regen*. 2016;24(5):885-893.
12. Carls GS, Gibson TB, Driver VR, et al. *J Am Podiatr Med Assoc*. 2011;101(2):93-115.
13. Couture M. *Wounds*. 2016;28(7):217-25.
14. Raphael A. *J Wound Care*. 2016;25(Sup7):S10-17.
15. Raphael A, Gonzales J. *J Wound Care*. 2017;26(Sup10):S38-44.
16. Fife CE, Eckert KA, Carter MJ. *Adv Wound Care*. 2018;7:77-94.
17. Cooke M, Tan EK, Mandrycky C, He H, O'Connell J, Tseng SC. Comparison of cryopreserved amniotic membrane and umbilical cord tissue with dehydrated amniotic membrane/chorion tissue. *J Wound Care*. 2014;23(10):465-476.
18. Tseng SC. HC-HA/PTX3 Purified from Amniotic Membrane as Novel Regenerative Matrix: Insight Into Relationship Between Inflammation and Regeneration. *Invest Ophthalmol Vis Sci*. 2016;57(5):ORS-Fh1-ORSFh8.
19. He H, Li W, Tseng DY, et al. Biochemical characterization and function of complexes formed by hyaluronan and the heavy chains of inter-alpha-inhibitor (HC*HA) purified from extracts of human amniotic membrane. *J Biol Chem*. 2009;284:20136-46.
20. He H, Zhang S, Tighe S, Son J, Tseng SC. Immobilized Heavy Chain-Hyaluronic Acid Polarizes Lipopolysaccharide-activated Macrophages towards M2 Phenotype. *J Biol Chem*. 2013;288:25792-803.
21. Zhang S, He H, Day AJ, et al. Constitutive expression of inter- α -inhibitor (I α) family proteins and tumor necrosis factor-stimulated gene-6 (TSG-6) by human amniotic membrane epithelial and stromal cells supporting formation of the heavy chain-hyaluronan (HC-HA) complex. *J Biol Chem*. 2012;287:12433-44.
22. Zhang S, Zhu YT, Chen SY, et al. Constitutive expression of pentraxin 3 (PTX3) protein by human amniotic membrane cells leads to formation of the heavy chain (HC)-hyaluronan (HA)-PTX3 complex. *J Biol Chem*. 2014;289:13531-42.
23. Tan EK, Cooke M, Mandrycky C, et al. Structural and biological comparison of cryopreserved and fresh amniotic membrane tissues. *J Biomater T Eng*. 2014;4:379-388.
24. Armstrong DG, Swerdlow MA, Armstrong AA, Conte MS, Padula WV, Bus SA. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. *J Foot Ankle Res*. 2020;13(1):16. Published 2020 Mar 24. doi:10.1186/s13047-020-00383-2
25. Kirsner RS et al. *Wound Repair Regen*. 2015 Sept.
26. Frykberg RG et al. *Int Wound J*. 2017 Jun;14(3):569-577.
27. Zelen CM, et al. *Int Wound J* 2013; 10:502-507.

www.biotissue.com
7300 Corporate Drive, Suite 700, Miami, FL 33126 | 888.296.8858
© 2020 BioTissue, Inc. All rights reserved | US-NX-2100044

Neox, CryoTek, SteriTek and BioTissue are registered trademarks of TissueTech, Inc. All other trademarks used herein are proprietary to their respective owners. Amnio Medical, Inc. is now doing business as BioTissue Surgical.

BioTissue Surgical products are authorized under the regulations of the U.S. Food and Drug Administration (FDA) governing the manufacture and distribution of Human Tissue Products. They are marketed as structural tissue products for homologous use and are used by physicians as barriers, wound coverings, conduits, and/or cushions in the treatment of their patients.