Utilizing an Innovative 3D Electrospun Synthetic Polymer Matrix (I3DESPM) as a *First Line of Defense* in Winning the War on Chronic Activity

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RENOVODERM

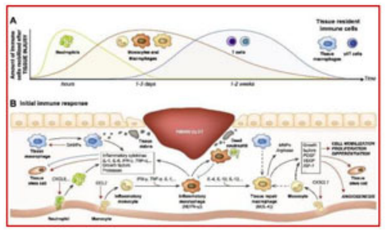
INTRODUCTION

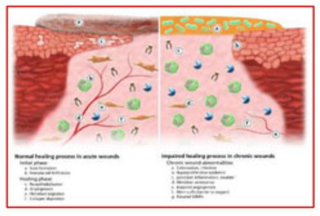
The body's ability to maintain a homeostatic microbiome throughout the phases of wound healing allows for natural pro-regenerative cellular action and interaction to occur, for the tissue regeneration and repair of acute and chronic wounds, and burns. Through science, we know a disruption in the cellular makeup of a wound can alter the body's ability to regenerate and repair the tissue within a normal and predictable period of time. This loss of microbiome homeostasis, often results in healing dysfunction manifested by chronicity and sustained/stalled inflammation [1-2] that greatly challenges our ability to heal wounds in an acceptable period of time.

The focus of this case series is to evaluate the role and impact a new bioresorbable 3D electrospun synthetic polymer matrix (I3DESPM) may represent in the battle against chronicity, helping to restore a homeostatic microbiome and facilitate the body's natural wound healing process.

ADDRESSING CHRONIC CELLULAR ACTIVITY IS CRITICAL TO RESTORING A HOMEOSTATIC MICROBIOME FOR WOUND HEALING

Cutaneous wound healing involves complex independent and dependent pathways which employ numerous cell lineages, tissues, and intrinsic and extrinsic mediators.[3,4] If wound healing continues through the "normal" series of biological events, then effective healing occurs, and homeostasis is restored. However, any interruption or interference to these pathways results in a nonhealing or "stalled" wound, rendering the wound chronic. [3-8]





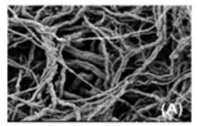
Many healing processes are affected by changes in pH including angiogenesis, collagen formation, and macrophage activity. [7-9] A change in pH has also been shown to influence the toxicity of bacterial end products and affect enzyme activity. [11] In particular, the matrix metalloproteinases (MMPs), which are important for wound healing and extracellular matrix remodeling. [11-14] Studies have also reported that variations in pH may affect wound closure, graft take, microbial infection rates, bacterial virulence, and biofilm formation.[15-16]

Additionally, lactate has several aerobic sources in wounds, being a consequence of the aerobic glycolysis that is associated with rapid cell growth, and also a by-product of the oxidative burst of leukocytes, which is also an aerobically glycolytic process. [18-20] When macrophages are exposed to hypoxia (PO2 ¼ 10–15 mmHg), VEGF is released. On the other hand, lactate alone also enhances collagen-prolyl hydroxylase activity and procollagen synthesis.[17] When, after a period of hypoxia during which lactate rises, oxygen is re-introduced, collagen deposition is enhanced.[17-20]

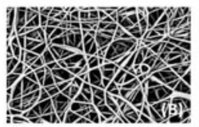
BREAKTHROUGH TECHNOLOGY - AN INNOVATIVE 3D ELECTROSPUN SYNTHETIC POLYMER MATRIX

Scientifically engineered to mimic native extracellular matrix (ECM) morphology, I3DESPM provides a multi-dimensional solution to wound healing. The 3D electrospun synthetic polymer scaffold acts as a stimulus to facilitate pro-regenerative cellular adhesion, infiltration and proliferation for the tissue regeneration and repair of acute and chronic wounds, and burns.

Additionally, comprised of polymers which naturally biodegrade to α-hydroxy acids and fatty acids known by the body to stimulate pro-regenerative cellular activity for wound healing, I3DESPM acts as a protective barrier to quickly support a pro-healing wound environment by representing low pH and lactate mediated effects that address chronic activity and chronic inflammation, helping to restore the wound healing process.



Native Dermal ECM

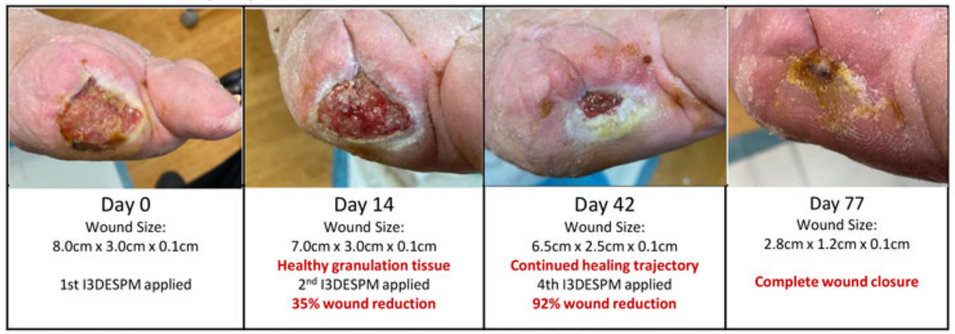


I3DESPM SEM Image

I3DESPM cellular adhesion, infiltration and proliferation

CLINICAL OBSERVATIONS & OUTCOMES:

Case 1: Charcot Arthropathy Left Foot Ulceration



Day 0	Day 14	Day 42	Day 77
Wound Size: 8.0cm x 3.0cm x 0.1cm	Wound Size: 7.0cm x 3.0cm x 0.1cm	Wound Size: 6.5cm x 2.5cm x 0.1cm	Wound Size: 2.8cm x 1.2cm x 0.1cm
1st I3DESPM applied	**Healthy granulation tissue** 2nd I3DESPM applied **35% wound reduction**	**Continued healing trajectory** 4th I3DESPM applied **92% wound reduction**	**Complete wound closure**

78 y/o male with DM II, neuropathy, charcot arthropathy presented post left foot, partial 1st ray resection, 2 months earlier. Amniotic was applied as patient had adequate blood flow however, wound healing stalled.

Case 2: Plantar Hallux Ulceration

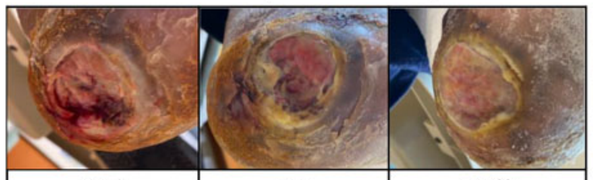
Wound 18 months in duration prior to utilization of I3DESPM

Day 0	Day 28
Wound Size: 1.8cm x 0.2cm x 0.5cm **1st I3DESPM applied**	Wound Size: 0.4cm x 0.1cm After 3rd Application of I3DESPM **92% reduction in wound size**

54 y/0 male with DM II, mild neuropathy, pedal pulses are palpable DP & PT ¼ bilateral, presented a left foot plantar hallux ulceration, 18 months in duration.

Case 3: Diabetic Foot Ulcer of the Right Heel

Wound 3 months in duration prior to utilization of I3DESPM



Day 1	Day 7	Day 30
Wound Size: 3.0cm x 3.0cm x 1.0cm **1st I3DESPM applied**	Wound Size: 3.0cm x 2.5cm x 1.0cm **Healthy granulation tissue** **2nd I3DESPM applied**	Wound size: 3.2cm x 3.2cm x 0.2 cm **70% wound closure**

62 y/o male with DMII, morbid obesity presented with a right heel DFU, 3months in duration. I3DESM was introduced into treatment strategy. Considerable reduction in drainage, odor and pain was observed with signs of healthy granulation tissue by Day 7.

Study results: *Three highly chronic and complex wounds were chosen to evaluate the dynamics of I3DESPM on chronicity and wound healing.*

It was consistently observed and documented that when selecting I3DESPM ***as a first-line treatment strategy:***

- *a visible change in the tissue and the* ***appearance of healthy granulation tissue was achieved with 7 to 14 days***
- *wounds achieved* ***>70% reduction in size within 4 to 5 weeks*** *an* ***average of 3 applications*** *of I3DESPM*

Addressing chronic cellular activity and establishing a pro-healing homeostatic microbiome helped to put these complex chronic wounds on a consistent healing trajectory. We observed remarkable progress with these wounds as a result of incorporating I3DESPM into the treatment plan.

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