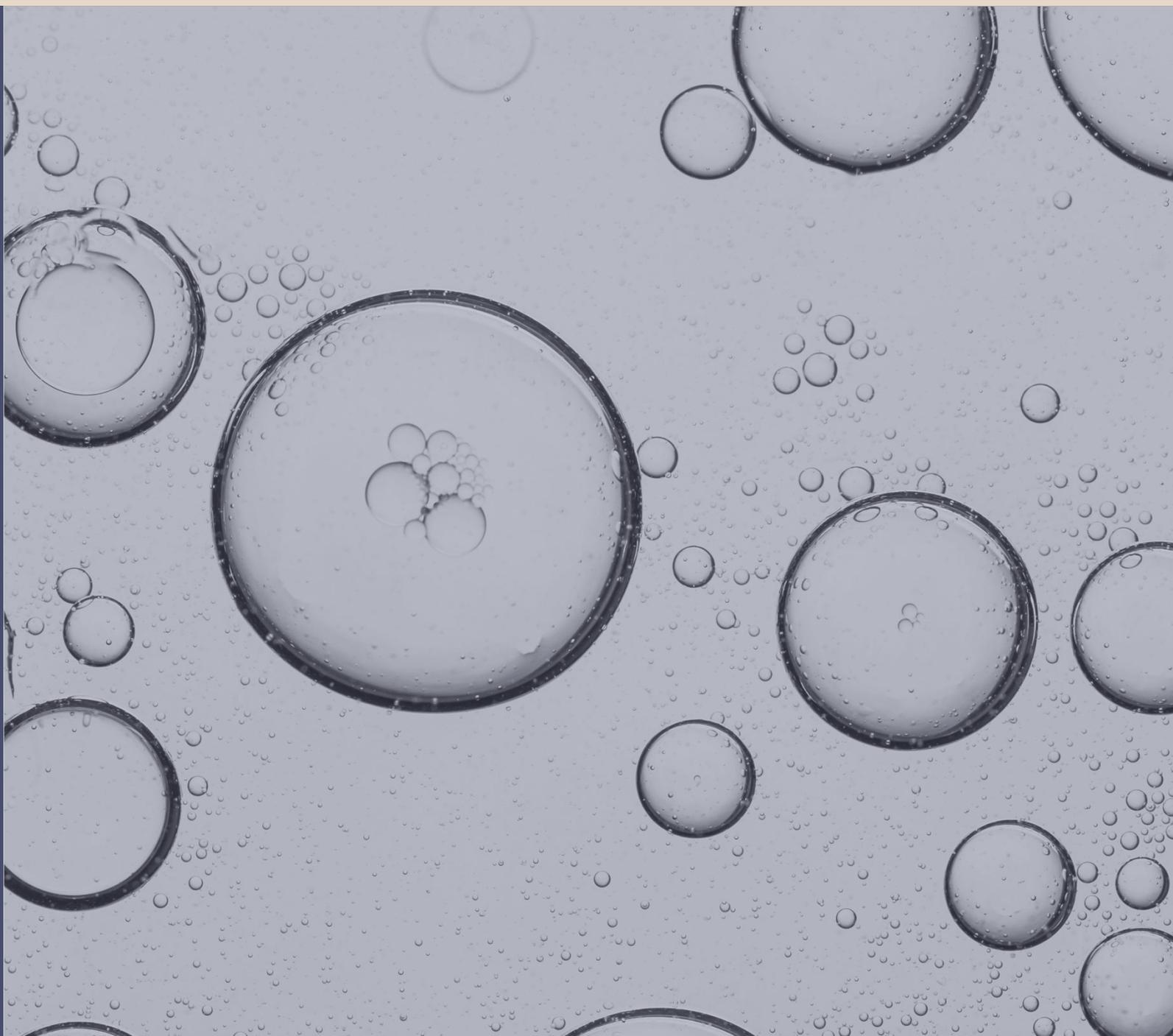


**A Case-Based Approach to
Managing Complex Chronic
Wounds with Borate-Based
Bioactive Glass Fiber**

Supported by an educational grant from
Engineered Tissue Solutions



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Faculty Disclosures

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Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the U.S. Food and Drug Administration)
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Learning Objectives

- Explore the role of synthetics in wound healing and their importance in creating an optimal healing environment
- Assess the benefits of integrating synthetic materials into the wound care treatment armamentarium
- Examine the science and mechanism of action (MOA) of a borate-based glass fiber matrix
- Navigate challenging cases utilizing a borate-based glass fiber matrix in managing challenging complex cases in the OR setting and chronic wound cases in the outpatient setting

Q&A

Please submit your questions anytime
via the question box.

We want to hear from you!

Borate-Based Glass Fiber Matrix (BBGFM): The Importance of Synthetics in Creating An Optimal Environment for Wound Healing

Cyaandi Dove, DPM

Director of Clinical Research

University of Texas Science Center San Antonio

San Antonio, TX

What Is Bioactive Glass?

- Bioactive glass is a synthetic, inorganic material that is biodegradable and composed of elements naturally found in the body
 - These essential elements, such as boron and calcium, have been proven to support many healthcare applications (ie, orthopedics, spine, dentistry) for ≈ 30 yrs

How is bioactive glass made?

- Pure ingredients are mixed and heated at extremely high temperatures
- State-of-the-art processes are used to make the material into desirable shapes, such as powder, beads, fibers



Where Has Bioactive Glass Been Used?

Bioactive glass has proven biocompatibility and been widely used in a range of biomedical applications, including

- Tissue engineering
- Bone grafting
- Dental reconstruction
- Wound healing

Some bioactive glass compositions have been shown to promote soft tissue regeneration and enhance vascularization to ensure healthy blood flow to the newly regenerated tissue



What Differentiates Borate-Based Bioactive Glass in the Wound Care Market?

Borate-Based Bioactive Glass Fiber Matrix (BBGFM)



Facilitates quality tissue formation



Without the infection risk associated
with tissue-based products



Easy-to-use versatile form factor

Quality Tissue Formation

1

GRANULATION

- **Well-vascularized:** Development of a robust network of blood vessels in the newly formed tissue
Importance: Ensures adequate delivery of oxygen and nutrients, essential for tissue health and healing
- **Well-organized:** Deposition of tightly packed collagen fibers
Importance: Provides strength and durability to newly formed tissue, ensuring it can withstand normal physiological stress

2

RE-EPITHELIALIZATION

- **Regeneration of the epithelium** via the migration and maturation of keratinocytes
Importance: Restores protective barrier, prevents infection, seals the wound

How Does Borate-Based Bioactive Glass Fiber Matrix Do This?

MOA Behind Borate-Based Bioactive Glass Fiber Matrix

1

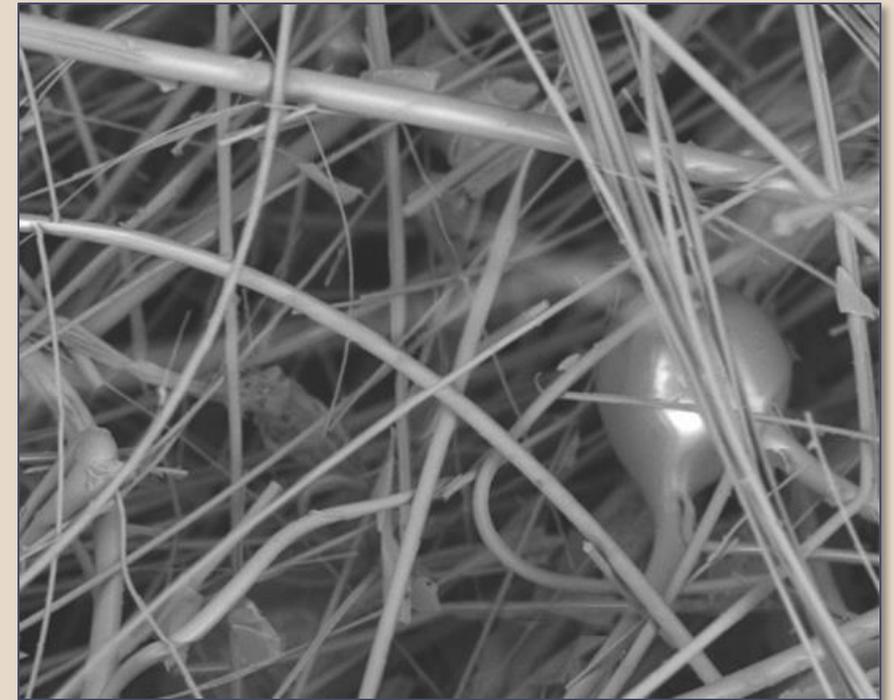
Scaffold Effect of Borate-Base Bioactive Glass Fiber Matrix

The fiber matrix provides a physical structure – similar to a fibrin clot after hemostasis – **for native cells to live, thrive, and rebuild tissue.** Those native cells include:

- Endothelial cells that build blood vessels for proper vascularization
- Fibroblasts that deposit collagen to form granulation tissue
- Keratinocytes that rebuild the epithelium

The scaffold's fibers dissolve over 1-2 wks, creating space for native collagen deposition and blood vessel formation, which are essential for granulation tissue

The scaffold's microspheres can persist up to 3 wks or longer, continuing to create a sustainable environment conducive to wound healing



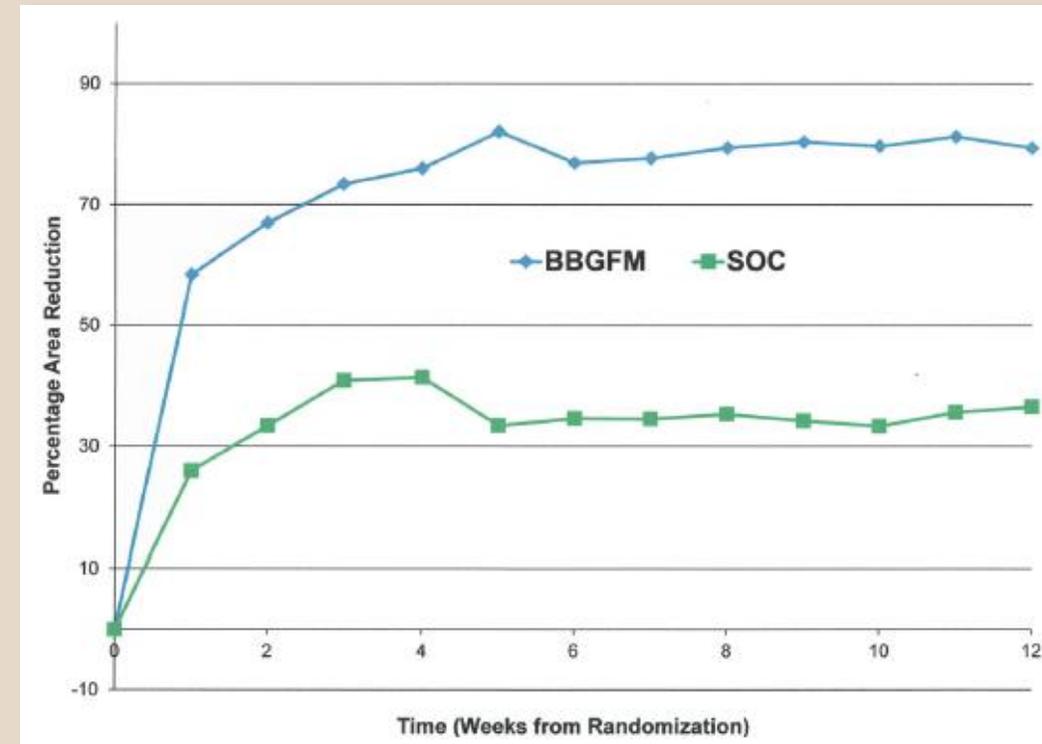
MOA Behind Borate-Based Bioactive Glass Fiber Matrix

2

Environmental Effect of Borate-Base Bioactive Glass Fiber Matrix

Bioactive glass facilitates a wound healing environment conducive to **angiogenesis**

- As part of the healing process, the body forms new blood vessels (angiogenesis) through a complex process that includes the secretion of pro-angiogenic factors, like VEGF, which facilitates increased migration and proliferation of endothelial cells
- The RCT investigators concluded that angiogenesis in the Borate-Base Bioactive Glass Fiber Matrix-treated group was “probably rapid because wound area reduction, on average, is high over the first week”



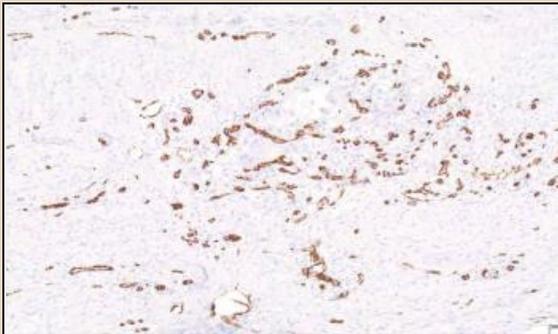
Weekly percentage wound area reduction by treatment group

(From Armstrong, et al. 2021. Figure 4)

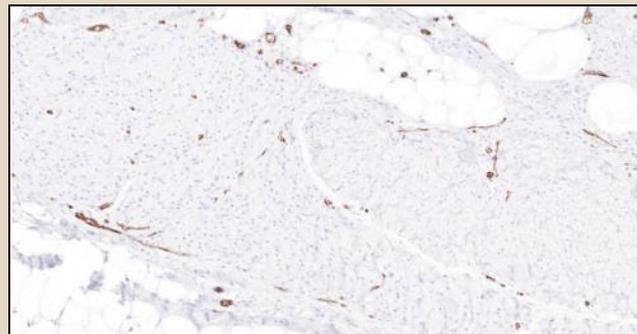
Evidence that Borate-Based Bioactive Glass Fiber Matrix Supports Wound Healing Environment Conducive to Angiogenesis

In a swine study, treatment with BBGFM was associated with increased new blood vessel growth compared to control (no treatment)*

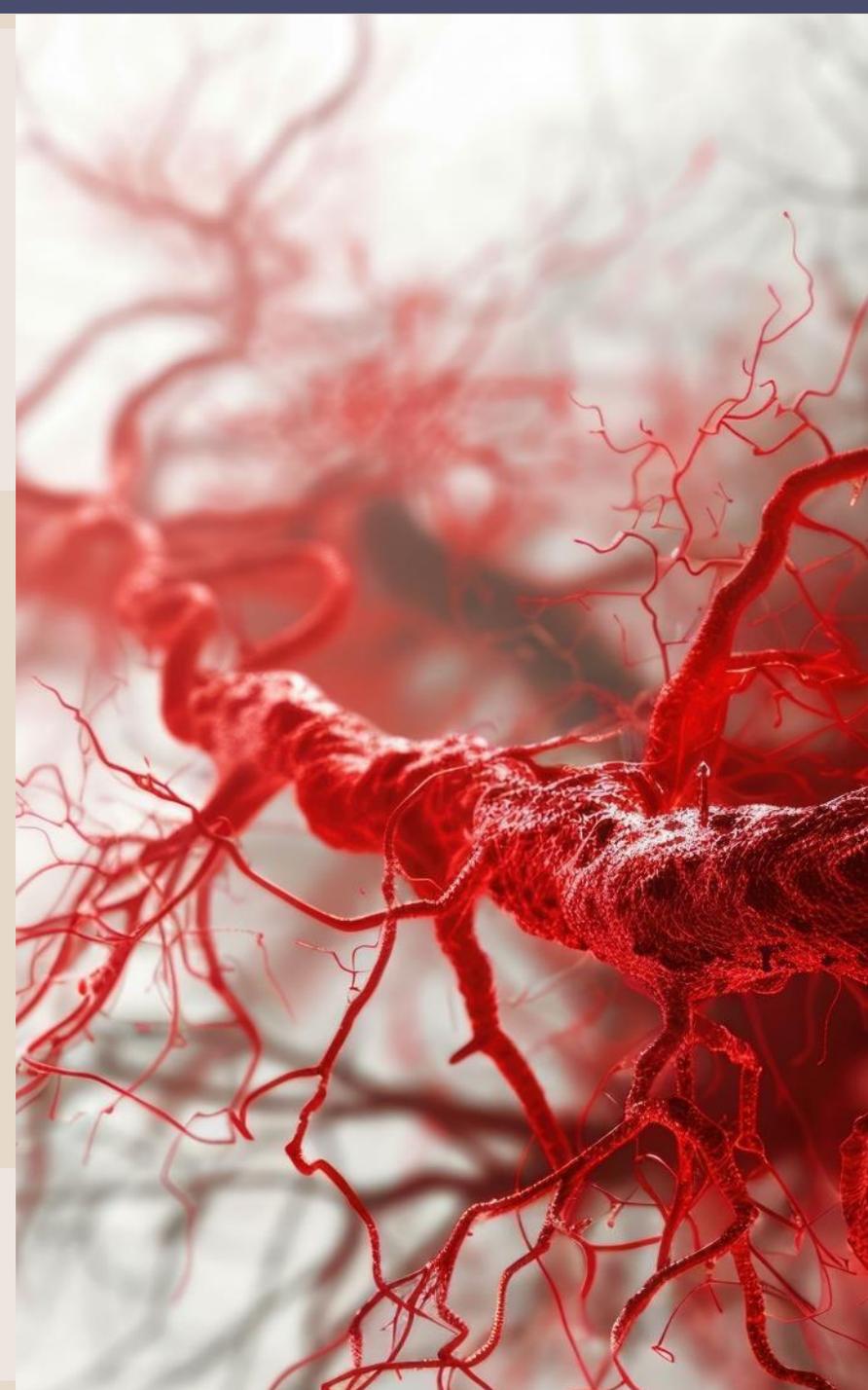
Bioactive Glass



Control



Histology showing blood vessel density at 6 wks in swine study.



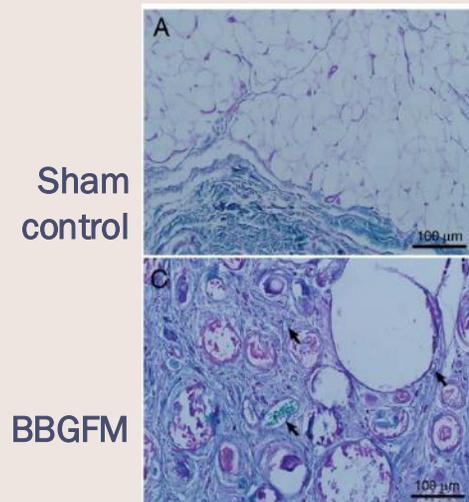
* Data on file.

Statistical analysis not performed for this study. Images are representative of observations made on a Borate-Based Bioactive Glass Fiber Matrix-treated animal with three sample wound sites.

Evidence: Borate-Based Bioactive Glass Fiber Matrix Supports Wound Healing Environment Conducive to Angiogenesis

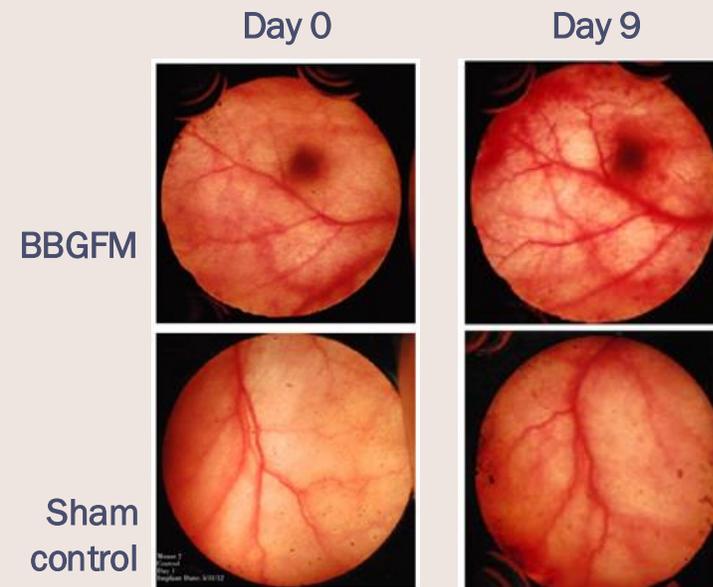
In rodent studies, quantitative histomorphometry results have shown higher microvessel density with bioactive glass than sham controls.

- As early as 2 wks ($p < 0.05$)¹
- At 3 wks (marginally statistically significant, $p < 0.10$)²



Arrows point to some of the microvessels seen in representative PAS-stained sections of soft tissue recovered after 2 wks.

(Lin, et al. 2014. Fig 3)



Minor halo response visible encircling the bioactive glass plug at day 9; tissue at the sham control site showed no visible halo development.

(Watters, et al. 2015. Fig 4)

Evidence: Borate-Based Bioactive Glass Fiber Matrix Supports Wound Healing Environment Conducive to Angiogenesis

For clinicians, the best visual evidence of this vascularization is the high-quality, red, well-vascularized tissue that forms while using BBGFM as shown in the case report below.*



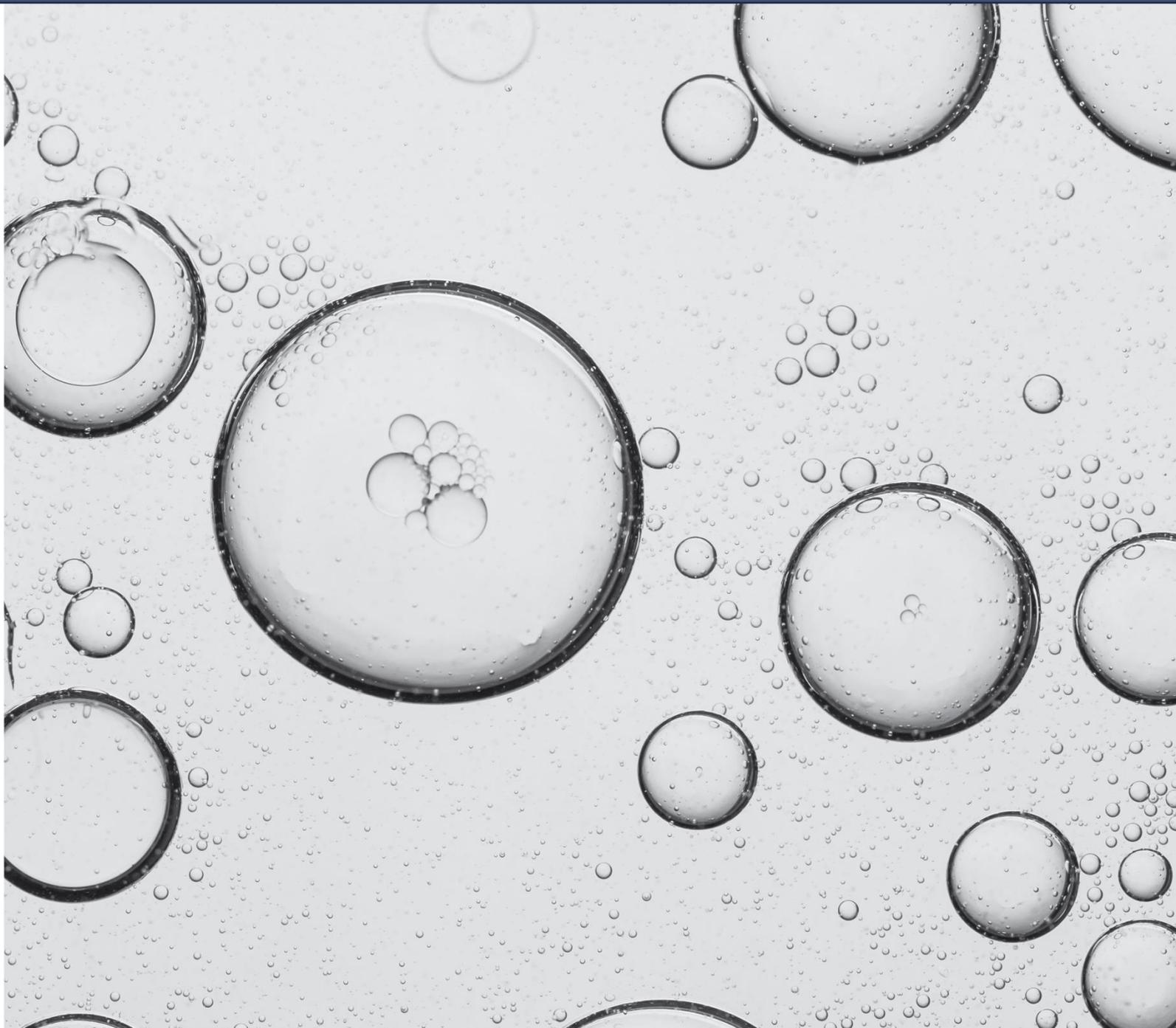
11-19-2023



1-26-2024

Case report courtesy of Stephanie Campbell, DPM, Cyaandi Dove, DPM, and Connor Krowlikowski, DPM. UT Health San Antonio.

**Without the
traditional risk of
infection that
tissue-based
products have**



Lower Risk of Infection Relative to Tissue-Based Products

Borate-Based Bioactive Glass Fiber Matrix does not have the same risk of infection as most biological products because it is synthetic.

Clinical and Technical Evidence

- In an RCT, the bioactive glass fiber matrix group experienced no adverse events related to infection of the index ulcer¹
- The SOC group, a collagen alginate, had a 25% infection rate¹

0 infections

SOC had 25% of patients experience infection-related complications, bioactive glass had 0 infection-related complications in the index wound



Lower Risk of Infection Relative to Tissue-Based Products

Tissue-based products may be prone to microbial colonization.

Pathogen Interaction with Collagen-Based Products

Many gram-positive pathogens found in diabetic foot ulcers, such as *Staphylococcus aureus*, *Enterococcus faecalis*, and *Streptococcus equi*, can bind to collagen using collagen-binding adhesins^{2,4,5}

Sources and Vulnerability of Collagen

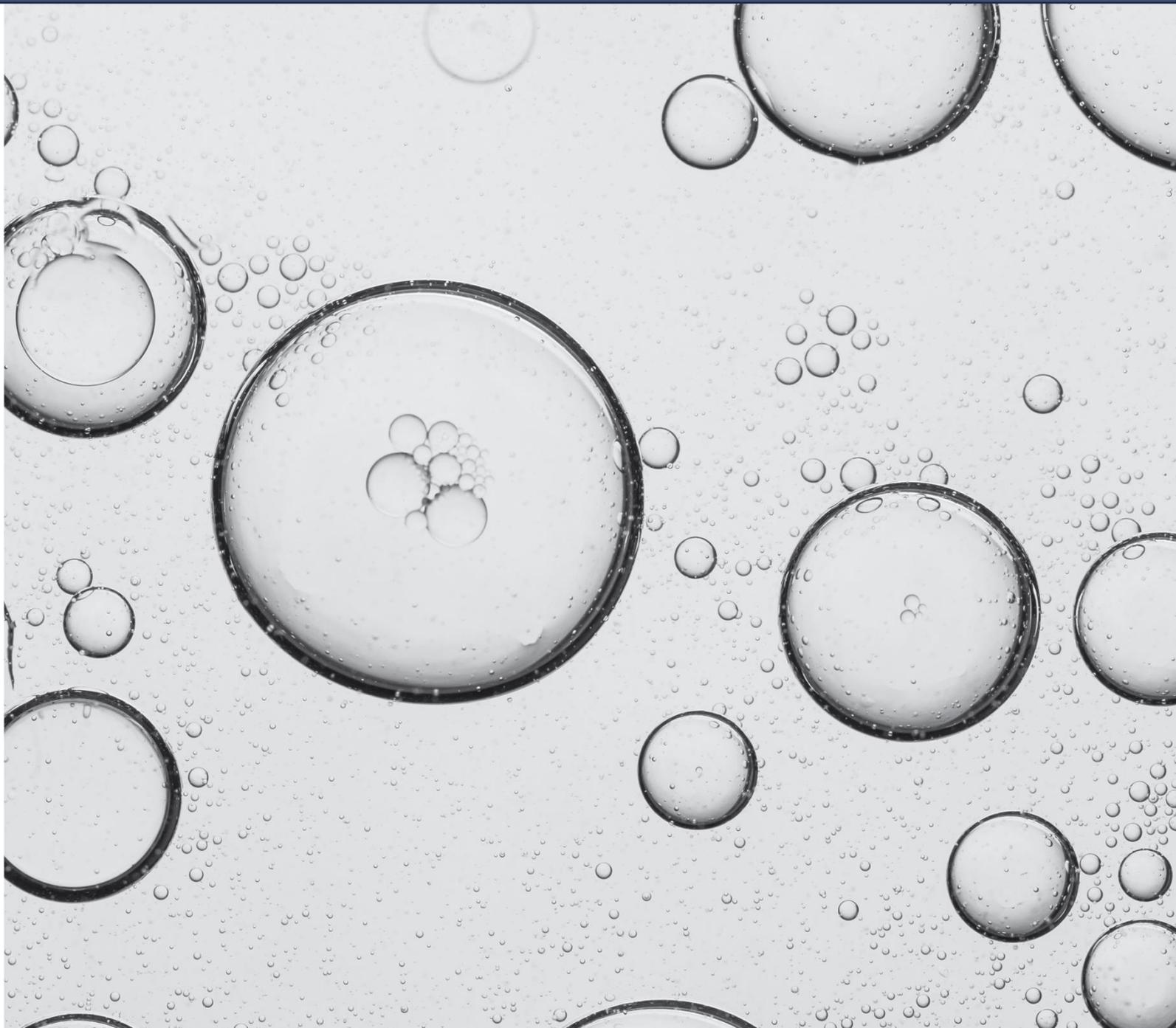
Collagen can be extracted from various sources, such as porcine, bovine, avian, and marine tissues. Despite its useful properties, crude natural collagen can be easily colonized and degraded by bacteria and fungi³



Photo showing appearance of infected collagen chondroitin-6-sulfate matrix upon arrival to the ICU¹

1. Gonzalez SR, Yuen JC. [JPRAS Open](#) 2020; 25:24–29. 2. Lannergafird J, et al. CNE, a collagen-binding protein of *Streptococcus equi*. Department of Microbiology, Swedish University of Agricultural Sciences, P.O. Box 7025, 750 07 Uppsala, Sweden. Accepted 19 March 2003, First published online 8 April 2003. 3. Warowicka A, et al. Berberine and its derivatives in collagen matrices as antimicrobial agents. *MRS Communications* 2022;12,336–342. 4. Rich RL, et al. Ace Is a Collagen-binding MSCRAMM from *Enterococcus faecalis*. Received for publication, March 30, 1999, and in revised form, May 6, 1999. 5. Patti JM, et al. Identification and Biochemical Characterization of the Ligand Binding Domain of the Collagen Adhesin from *Staphylococcus aureus*. Institute of Biosciences and Technology, Center for Extracellular Matrix Biology, Texas A&M University, Houston, Texas 77030. Received June 1, 1993; Revised Manuscript Received August 10, 1993.

**All in an easy-to-
use, versatile
form factor**





Easy-to-Use, Versatile Form Factor

Borate-Based Bioactive Glass Fiber Matrix easily conforms to wounds with various characteristics.

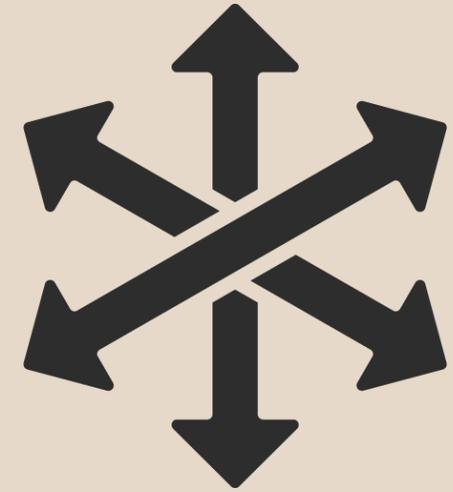
- Can be placed in challenging wound locations
- Contours to different wound topographies
- Customizable for wounds with tunneling or undermining
- Sticks to wounds with moisture and/or punctate bleeding



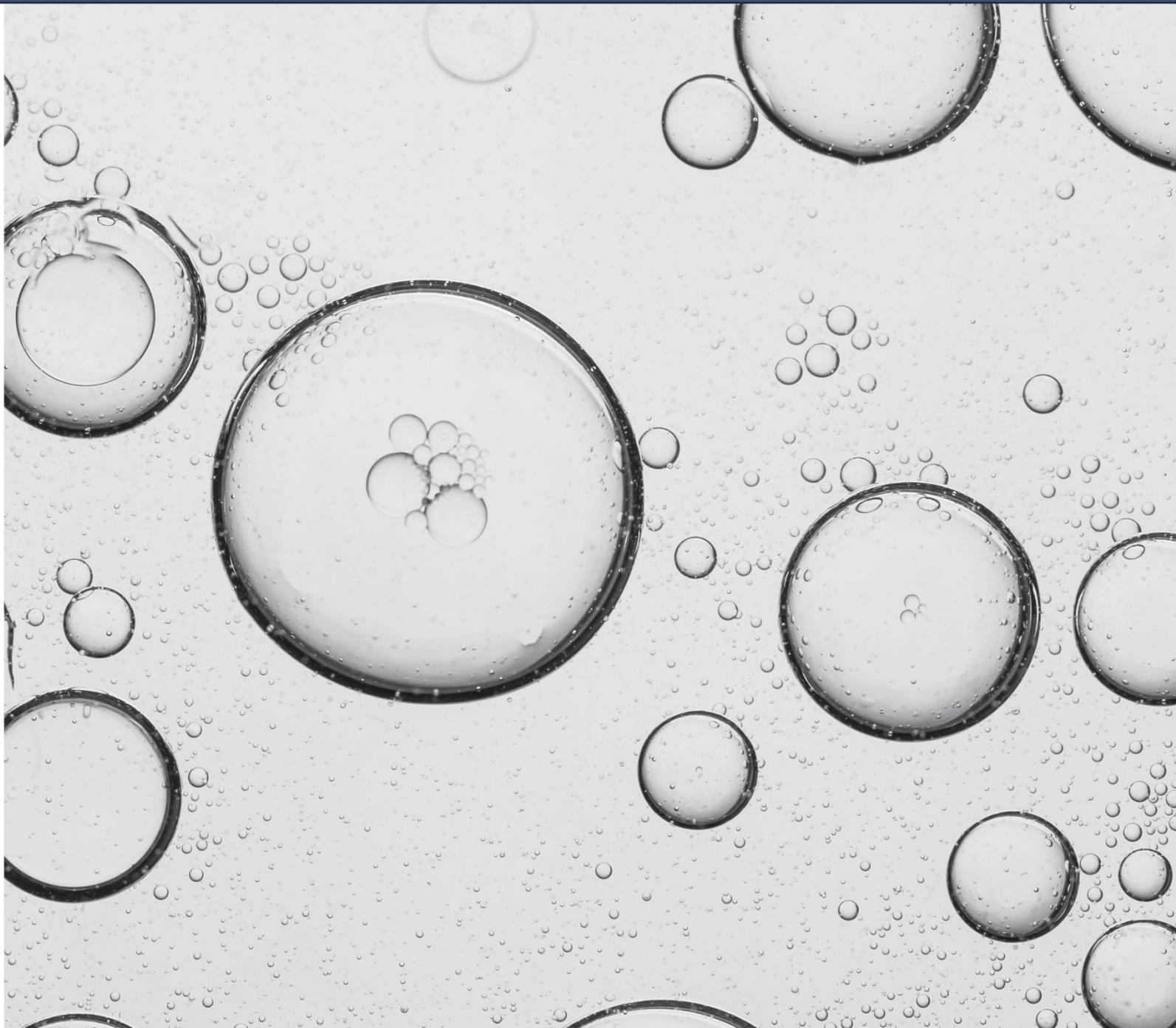
Easy-to-Use, Versatile Form Factor

Borate-Based Bioactive Glass Fiber Matrix is indicated for use with a variety of wound etiologies.¹

- Partial- and full-thickness wounds
- Diabetic ulcers
- Venous ulcers
- Chronic vascular ulcers
- Pressure ulcers
- Surgical wounds
Donor sites/grfts, post-Mohs surgery, post-debridement, post-laser, wound dehiscence
- Trauma wounds
Abrasions, lacerations, first- and second-degree burns, skin tears
- Tunneled/undermined wounds
- Draining wounds



What Is the Clinical Evidence?



CLINICAL EVIDENCE: Multicenter Randomized Controlled Trial¹

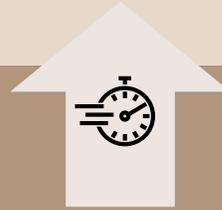
RCT compared diabetic ulcers treated with Borate-Based Bioactive Glass Fiber Matrix or standard of care (SOC). After 2 wks of screening, patients were randomized for 12-wk treatment.

0 infections



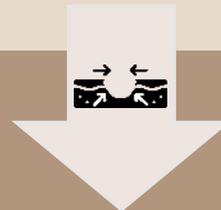
SOC had 25% of patients experience infection-related complications, Bioactive glass had 0 infections of the index ulcer

70% vs 25%



70% of wounds were closed at 12 wks with bioactive glass vs 25% closed with SOC

79% vs 37%



Mean wound percent area reduction (PAR) at 12 wks in the bioactive glass group was 79% vs 37% for SOC

Summary

Borate-Based Bioactive Glass Fiber Matrix

- Unique mechanisms of action with bioactive glass provide hope for closure, even with chronic and complex wounds where other tissue-based products have previously failed
- Demonstrated clinical efficacy with deeper wounds requiring quality granulation and shallower wounds requiring re-epithelialization
- Simple to adopt and use within your facility and your clinical/surgical processes – no pre-application (eg, product prep) or post-application (eg, tissue tracking) steps



Benefits of Integrating Synthetic Materials into Wound Care Armamentarium

Marcus Gitterle, MD, ABWM, FACCWS

Chief Medical Officer
WoundCentrics, LLC
Austin, TX

Other Advantages of Synthetic Materials

- Reduced infection risk compared with tissue-based products
- Reduced risk of disease transmission
- More effective scaffold effect
- No cultural or religious objections as with xenografts or donated tissue

Synthetic Glass Matrices Modulate Important Aspects Of Wound Physiology

- MMP reduction: Improving granulation velocity and quality
- Oxidative stress reduction: Facilitating proliferative conditions
- Anti-fibrotic activity: More favorable scarring and better remodeling

Inorganic Glass Matrix Pearls

- Borate-Based Bioactive Glass Fiber Matrix easily conform to wounds, regardless of shape
- Space-filling properties ideal for wounds with tunneling or undermining
- High porosity matrices have a much larger adhesion surface and better wettability

Example Case Illustrating Unique Properties of Inorganic Borate-Based Bioactive Glass Fiber Matrix

- 5th MTP joint capsulitis associated with DFU
 - Entire joint capsule was involved
 - Culture-directed abx therapy x6wks
 - Inorganic Glass Matrix Application x4



Pre-Application: Note void



**1 wk post 1st application:
Note deadspace reduction**



1 wk post 2nd application

Case 1: Illustrating Unique Properties of Inorganic Borate-Based Bioactive Glass Fiber Matrix (cont'd)

- 5th MTP joint capsulitis in 62y patient with diabetes



3 wks after 4th application: Note incorporation



2 months after 4th application: Note remodeling

Case 2: Borate-Based Bioactive Glass Fiber Matrix



- Type 2 DM with Wagner 4 DFU
- SFA stent placed
- Osteomyelitis of 4th MTP and proximal phalanx of 4th toe
- Bone C&S: MRSA > Abx therapy
- Tendon sparing serial debridement
- Nutritional supplementation
- DM optimization
- HBOT x40

Case 2: Borate-Based Bioactive Glass Fiber Matrix (cont'd)

- Osteomyelitis resolved based on inflammatory markers
- Good tendon coverage obtained
- Reduction in closure velocity was then noted, and a Bioactive Glass Fiber Matrix was elected to facilitate complete closure



Case 2: Borate-Based Bioactive Glass Fiber Matrix (cont'd)



Status Post BBGFM application #1



2 wks after BBGFM #4



6 wks after application 4

Case 2: BBGFM (cont'd)



**Initial vs final result:
Note excellent remodeling**

Case 3: BBGFM

- 95y Male s/p TMA with dehiscence
- 7cm tunnel
- Conforming and space-filling properties are well illustrated
- Tunnel closed with 2 applications
- Complete closure after 5 total applications



Clinical Pearls

- Synthetic materials are likely to play an increasing role in the care of complex wounds due to a multitude of factors, including
 - Antimicrobial properties
 - Diversity of form factors
 - Space-filling characteristics and wound closing
 - Fiber characteristics that mimic biologic fibrin scaffolds
 - Favorable effects on wound physiology, including MMPs and oxidative stress reduction
 - Anti-fibrotic actions that diminish scarring

Clinical Cases Using BBGFM

Ralph J. Napolitano Jr, DPM, CWSP, FACFAS

Director, Wound Care and Healing, OrthoNeuro
Adjunct Clinical Assistant Professor,
Ohio University Heritage College of Osteopathic Medicine
Columbus, OH

So Why Do Wounds NOT Heal?

Intrinsic patient factors — focal/wound:

Infection, growth factors, scar tissue, necrosis, pressure, etc.

Intrinsic patient factors — systemic/host:

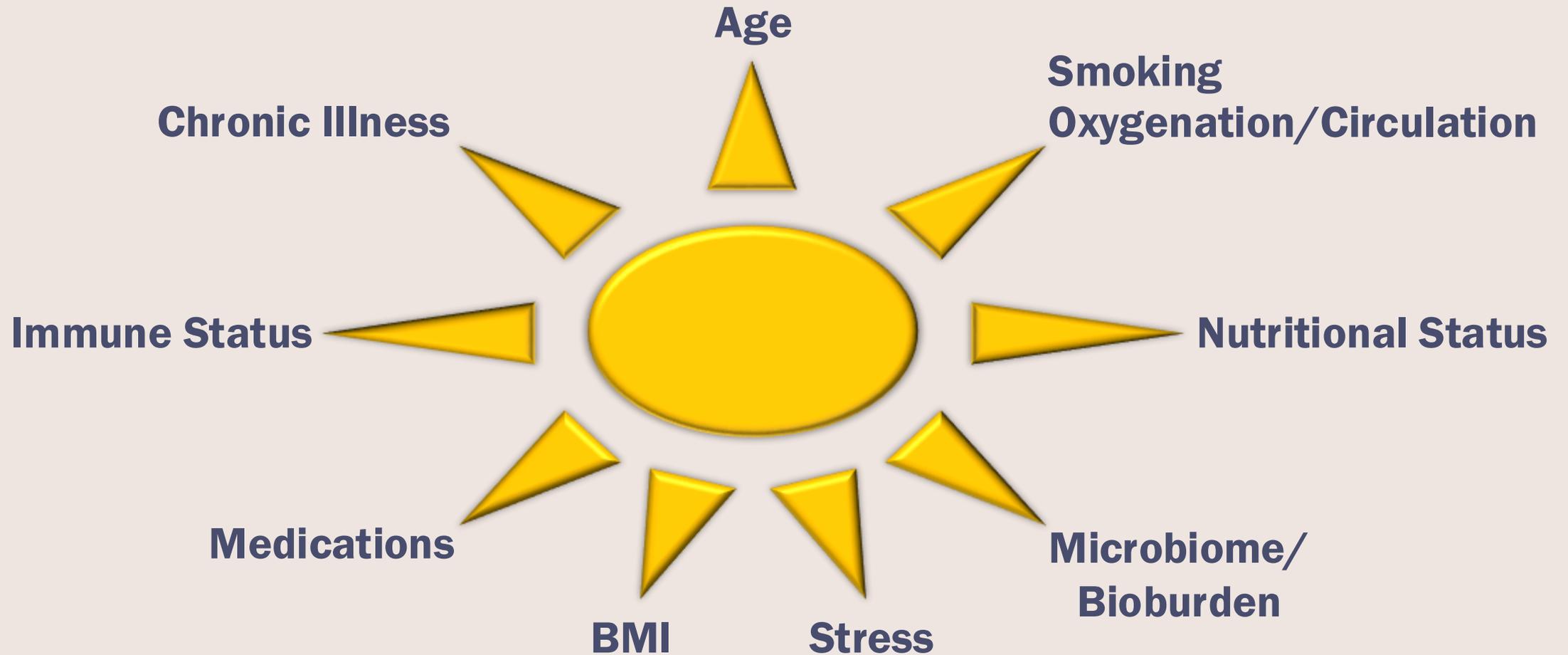
Circulation (PVD) immunity (Diabetes), metabolism, nutrition, and so on...

THE BIOLOGICALLY BANKRUPT PATIENT

Extrinsic factors:

Compliance, socioeconomic, etc.

Patient Factors Which Impede Healing



So Why Do Wounds NOT Heal?

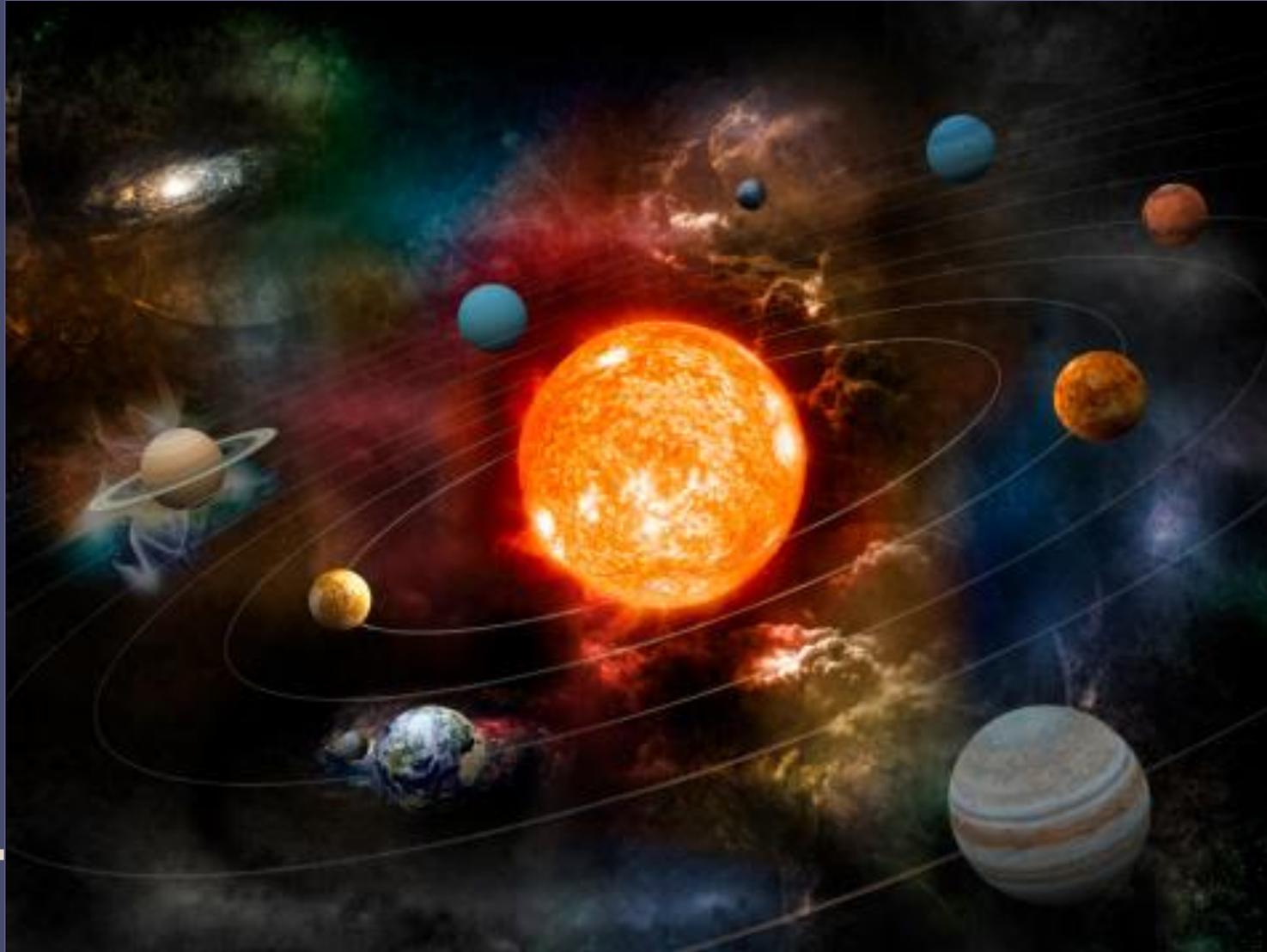
- In other words...

Something is wrong with the wound,
or something is wrong with the patient

If neither, look in the mirror...



“The Goldilocks Zone”



Case 1

- 69y Female; sustained left lower leg and ankle fracture
- Underwent ORIF at the hands of her orthopedic surgeon
- Bone healing progressed uneventfully but developed some delayed surgical wound healing involving the medial lower leg incision
- Was referred over for advanced wound care
- Initial debridement was carried out, and BBGFM applied

Initial presentation



Initial BBGFM application



**1 wk after BBGFM
application**



**3 wks after BBGFM
application**



**Complete closure
at \approx 6 wks**



Case 2

- 59y Male; sustained crush injury of right foot while operating heavy printing machinery at work
- Although he did not sustain any fractures, he did suffer partial lateral collateral ankle ligament sprains, partial tears, and a full-thickness, deep lateral rearfoot wound
- Initial care consisted of walking boot immobilization and serial debridement with supportive advanced wound dressings

Initial presentation



Initial BBFGM application



**1 month after BBGFM
application**



**After 2nd BBGFM application;
≈2 wks after 1st application**



Complete closure 2 months after initial BBGFM application



Case 3

- 57y Male; presented with limb and life-threatening deep space infection of the right foot in the setting of long withstanding poorly controlled diabetes
- He underwent prompt surgical debridement with application of negative pressure wound therapy with instillation and dwell (NPWTi-d) utilizing normal saline (NS) as the irrigant

Initial presentation

- Note significant purulent bullous, dorsal foot



Initial presentation

- Note significant swelling and erythema



Initial presentation

- Note multiple plantar foot wounds — likely infection portal of entry



Case 3, cont.

- He was admitted and underwent prompt surgical debridement with application of NPWTi-d utilizing NS as the irrigant
- His infection cleared, but recalcitrant soft tissue necrosis persisted

Intra-op Photos



After 3 days of NPWTi-d



After 3 days of NPWTi-d



1 wk after NPWTi-d



Case 3, cont.

- Ultimate limb salvage prognosis was grim, and he was offered below-the-knee (BTK) amputation on at least 3 separate occasions
- He declined and opted for serial debridements coupled with standard NPWT
- As wound healing trajectory progressed, he was offered bioactive fiber wound matrix and received 2 applications spaced ≈ 2 wks apart

Presentation after multiple debridements and traditional NPWT just before 1st BBGFM application



Initial Borate-Based Bioactive Glass Fiber Matrix Application



**Presentation ≈1 wk after
1st BBGFM application**

**Note areas of intact
BBGFM and new
granulation**



**Presentation \approx 1 wk
after 1st BBGFM
application**

**Note areas of
intact BBGFM and
new granulation**



**After 2nd BBGFM
application \approx 1 wk
after application**



**Continued wound
healing progress
after 2 applications
of BBGFM**



**Ultimate closure less than
4 months after 1st BBGFM
application**





Bioactive Glass Effectively Heals Complex Lower Extremity Wounds: A Case Series



Ralph J. Napolitano, Jr., DPM, CWSP, FACFAS^{1,2}, James Wischmeier, OMS II², Samir Balraj, BS¹

¹OrthoNeuro, Columbus, Ohio
²Heritage College of Osteopathic Medicine, Ohio University, Athens, Ohio

INTRODUCTION

Lower extremity wounds often pose unique treatment challenges to both clinicians and patients. Because of such challenges, it is often necessary to utilize a combination of different techniques, modalities, and products to successfully treat lower extremity wounds. Skin substitutes belong to a family of advanced wound care products used in challenging wounds. Bioactive glass wound matrix (BGWM[®]) is a new category of skin substitutes that is composed of a water-soluble matrix of fibers and microspheres that readily adheres to wound surfaces. The porous BGWM absorbs wound exudate to maintain moisture balance and serves as a scaffold to support wound healing. The objective of this case series is to describe our experience with BGWM after application on six patients with complex lower extremity wounds.

METHODS

A total of six patients had foot, ankle or lower leg wounds and received BGWM applications as determined by medical necessity. Each patient received between one and three applications of BGWM during the course of wound therapy. The patients were four males and two females, aged 49 to 71 years old. Wound etiologies included delayed surgical wound healing, a crush injury, diabetic foot wounds, a decubitus ulceration, and a chronic venous leg ulceration. Wound debridement was performed as needed prior to each BGWM application. No additional dressings or therapies were utilized after initiation of BGWM other than basic cover dressings and debridement when warranted. Deidentified data was collected after obtaining informed patient consent and stored in accordance with federal regulations.

RESULTS

BGWM was utilized to effectively treat lower extremity wounds, resulting in positive healing outcomes in all six wounds. All patients healed or demonstrated marked improvement in wound size and disposition during the study period. None of the patients acquired an infection once the BGWM was applied.

DISCUSSION

Wounds from a variety of etiologies saw successful outcomes after the application of the BGWM. These complex wounds were consistent with chronic and refractory wounds treated with BGWM by other investigators¹⁻⁴. BGWM has been shown effective in DFUs in a 40 patient RCT while other wounds that have been refractory for years were found to close after applications of BGWM¹⁻⁴. A common outcome reported in the literature has been a significant reduction in complications associated with wound infection once BGWM was applied to wounds¹⁻⁴. This outcome continues to hold true in this case series.

Diabetic Foot Infection



Delayed Surgical Healing, Lower Leg



Foot Crush Injury



References:

1. Armstrong D, Orgill D, Gallano R, et al. A multi-centre, single-blinded randomized controlled clinical trial evaluating the effect of a resorbable glass fibre matrix in the treatment of diabetic foot ulcers; *Int Wound J*. 2021;1:1-11.
2. Johnson M, Ortega E, Armstrong D; How can novel bioactive glass wound matrix optimize hard-to-heal venous leg ulcers in geriatric patients with multiple comorbidities? *Wound Masterclass March 2024*;3:1-7.
3. Castillo-Garcia E, Thuy Nguyen P; Complex refractory wounds: How to overcome treatment recalcitrance and restore the healing trajectory using innovative bioactive glass; *Wound Masterclass March 2024*;3:1-12.
4. Beckford J, Rathinasamy P; How to reduce treatment costs for hard-to-heal wounds: The bioactive glass wound matrix option; *Wound Masterclass March 2024*;3:1-5.

Acknowledgements: *Mirragen Advanced Wound Matrix, ETS Wound Care, LLC. This poster was prepared in collaboration with ETS Wound Care, LLC. All protocols and clinical assessments were conducted and reported independently by OrthoNeuro without any financial compensation from the manufacturer. For application instructions and risks of this device, please refer to the Mirragen Instructions for Use.

Summary

Of the tools in one's tool belt, where does BBGFM play a role?

- Granulation and or re-epithelialization
- Can be used in different care settings from OR to the clinic
- Head to toe indications
- Can be initiated early on in wound healing or later as wound moves through healing cascade
- Impressive changes with less applications



Polling Question

Boron containing synthetic dressings have demonstrated both anti-fibrotic and pro-angiogenic effects.

1. True
2. False

Polling Question



Synthetic dressing materials offer, among other advantages, a reduced risk of disease transmission.

1. True
2. False



Polling Question

Synthetic dressing matrices with high-porosity favorably affect wettability and wound bed adhesion.

1. True
2. False

Polling Question



Synthetic dressings have the disadvantage of limited form factor and sizing options

1. True
2. False

Polling Question



Main reagent in the bioactive glass fiber matrix is:

1. Collagen
2. Silicone
3. Borate
4. Carbon

Polling Question



BBGFM is contraindicated for full thickness wounds with exposed structures?

1. True
2. False

Polling Question



Tissue-based products may be prone to microbial colonization

1. True
2. False

Thank You!

**Please submit your questions
via the question box!**