A Multi-Center, Single-Blinded Randomized Controlled Clinical Trial Evaluating the Effect of Resorbable Glass Fiber Matrix in the Treatment of Diabetic Foot Ulcers

David G. Armstrong, DPM, MD, PhD[1], Dennis P. Orgill, MD, PhD[2], Robert D. Galiano, MD[3], Paul M. Glat, MD[4], Lawrence A. DiDomenico, DPM[5], Marissa J. Carter, PhD, MA[6], Charles M. Zelen, DPM[6]

[1]Division of Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA; [2]Division of Plastic Surgery; Brigham and Woman's Hospital, Boston, MA ; [3]Division of Plastic Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL; [4]Department of Surgery, Drexel University School of Medicine, Philadelphia, PA; [5]Lower Extremity Institute for Research and Therapy, Youngstown, OH; [6]Strategic Solutions, Inc., Bozeman, MT; [6]Professional Education and Research Institute; Roanoke, VA

Introduction: Diabetic foot complications continue to plague patients, providers and health systems around the world. In particular, the lifetime incidence of developing a diabetic foot ulcer (DFU) is 34%, and between 9.1-26.1 million people with diabetes develop a foot ulcer every year.[1] Thus, there is a significant need to explore advanced wound care modalities that can enhance wound healing in this complex population and potentially save limbs and lives.

Bioactive glass materials are biocompatible water-soluble materials that release their constituent ions when immersed in body fluids. Although the focus of these products has been the development of a scaffold material for bone tissue engineering, researchers have been intrigued by their potential to heal wounds through improving angiogenesis,[2] increasing metabolic activity and cell proliferation,[3] and serving as antimicrobial agents.[4,5] All of these processes are essential components in the healing of chronic wounds.
Mirragen Advanced Wound Matrix (BBGFM) is a novel, borate-based, bioactive glass nanofiber (ETS Wound Care; Rolla, Missouri) with a target composition of $53B_2O_3$–$6Na_2O$–$12K_2O$–$5MgO$–$20CaO$–$4P_2O_5$ wt%. Borate-based bioactive glasses have been formulated to degrade in the wound over a period of days or weeks. The rate of degradation depends in part on the wound exudate and thus can be washed out or degraded as the wound heals.

Methods: In this parallel, two-group, single-blind randomized controlled trial, forty patients with chronic, full-thickness, non-infected, non-ischemic DFUs (Wagner 1) were randomized to either standard of care (SOC) alone or BBGFM + SOC and treated for a period of 12 weeks. Both groups received SOC, including glucose monitoring, weekly debridements (when needed) and application of a collagen alginate primary dressing (Fibracol; 3M corporation Minneapolis, MN) topped with a padded three-layer dressing (Dynaflex, 3M Corporation, Minneapolis, MN) or equivalent, and an offloading device. In addition, patients in the active treatment group received weekly application of the BBGFM dressing. Because BBGFM is completely bioabsorbable and is eventually absorbed at the wound site, only loose sections from prior applications were removed at subsequent visits during debridement.

Primary objective: To compare a unique resorbable glass microfiber matrix (Mirragen Advanced Wound Matrix [BBGFM])with a standard of care group at 12 weeks.

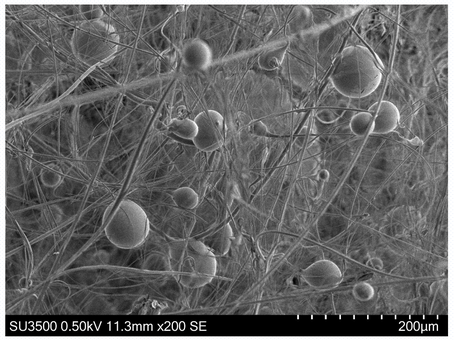
Primary endpoint: Proportion of full-thickness, non-infected, non-ischemic wounds healed at 12 weeks.

Secondary endpoints:

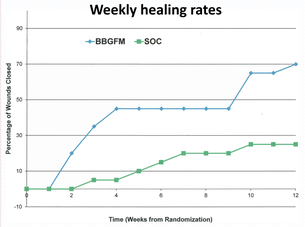
- Percent area reduction (PAR) at 12 weeks
- Changes in Semmes-Weinstein monofilament testing
- Safety and Adverse Events

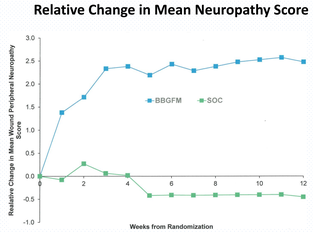
Mirragen Advanced Wound Matrix (ETS Wound Care)

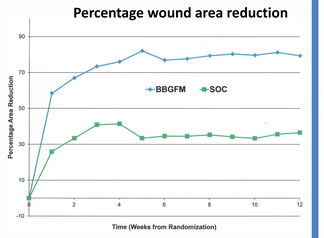
Gross illustration of BBGFM (Mirragen)



EM image of BBGFM at x200 magnification demonstrating its intricate bioabsorbable glass fiber and sphere structure







Results

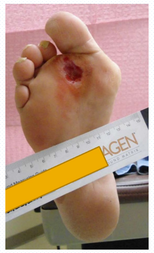
- **70% (14/20) of the BBGFM-treated DFUs healed compared with 25% (5/20) treated with SOC alone**
- **Mean PAR at 12 weeks was 79% in the BBGFM group compared with 37% in the SOC group**
- **Mean change in neuropathic score between baseline and up to 12 weeks of treatment was 2.0 in the BBGFM group compared with -0.6 in the SOC group**
- **The mean number of BBGFM applications was 6.0**
- **No adverse events (AE) with BBGMF treatment vs. 5 AE with SOC**

Case example 1

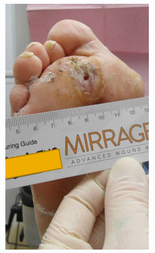
Chronic plantar forefoot DFU

Ulcer history: 24 weeks

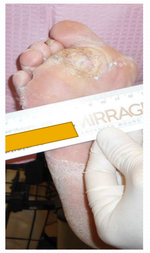
Baseline:
Area: 4.00 cm^2
HbA1c: 10.1
Serum creatinine: 0.87



Screening visit



Treatment visit 2



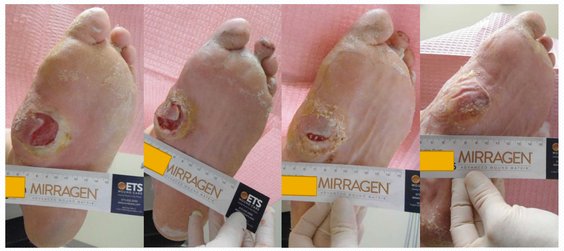
Healed at 3 weeks

Case example 2

Chronic plantar midfoot DFU

Ulcer history: 50 weeks

Baseline:
Area: 6.00 cm^2
HbA1c: 7.2
Serum creatinine: 0.91



Screening visit | Treatment visit 4 | Treatment visit 8 | Healed at 11 weeks

Conclusions: The results of this trial demonstrate that the addition of a bioactive glass microfiber matrix containing boron (BBGFM) to SOC led to significantly improved wound healing in DFUs compared with SOC alone.

In addition, encouraging results were observed regarding infection and neuropathy. Notably, patients treated with BBGFM had a significant improvement in Semmes-Weinstein sensory testing

Furthermore, no adverse events related to infection of the index ulcer were observed in the BBGFM group whereas five infection occurred in the SOC group. This may be due to the ability of boron ions to inhibit the growth of both gram-positive and gram-negative bacteria and disrupt biofilm in chronic wounds. Further studies are needed to confirm these findings and support the role of BBGFM for the treatment of chronic DFUs.

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