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The Efficacy of a Novel Silver-Containing Bioresorbable Microfilm Matrix in At-Risk Surgical Wounds: A Clinical Case Series

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Abstract

Introduction. For persons with diabetes, surgery is fraught with complications; of primary concern is postoperative infection. A postoperative infection rate of up to 13% has been noted in patients with diabetes undergoing elective surgical procedures compared with less than 3% in nondiabetic populations. **Objective.** The objective of this study was to provide preliminary evaluation of the efficacy of a novel bioresorbable microfilm matrix (20 µm thick) containing very low amounts of silver (0.16 mg/in²) in preventing surgical site infections when placed at the level of subcutaneous tissue and dermis prior to primary closure in the patient with diabetes undergoing elective surgery. **Materials and Methods.** Twenty-two patients with diabetes undergoing nonemergent or elective foot or ankle surgery and who met at least 1 of the following 6 criteria were included in the study: neuropathy, infection, open wound, history of recurrent infection, nonhealing wound, or peripheral vascular disease. Patients underwent amputation, removal of exostosis, midfoot bone removal, Achilles tendon repair, bunionectomy, or an elevating osteotomy with primary closure of the wound. After hemostasis was obtained and subcutaneous closure achieved, if applicable, the bioresorbable microfilm matrix was applied just deep to the incision at the level of subcutaneous tissue and dermis, and the incision primarily closed. A nonadherent cover dressing was applied over the suture line, and routine follow-up was scheduled for 3 to 5 days later. **Results.** No patient exhibited signs of infection at initial follow-up, and all adherent patients achieved complete healing during the 3-month follow-up period. Eighteen patients healed at a rate typical for the respective procedure. In 2 patients, time to healing was delayed secondary to weight-bearing dehiscence. Two patients were not included in the results secondary to multiple infractions of nonadherence with the postoperative protocol. **Conclusions.** The application of microfilm matrix in surgical incisions at the level of subcutaneous tissue and dermis prior to primary closure is safe for and has the potential to prevent postoperative surgical site infections in at-risk patients with diabetes.

How Do I Cite This?

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Introduction

Diabetes is continuing to rise in the United States. Currently, it is estimated that more than 34 million people in the US have diabetes.[1] Surgical patients with diabetes present with several risk factors for infection, among them a compromised immune system owing to poor glucose control, peripheral neuropathy, and potential lack of perfusion at surgical sites, which can interfere with usual infection control methods such as systemic antibiotics.[2-4] These factors result in postoperative infection rates of up to approximately 13% in persons with diabetes, as opposed to 3% or less in persons without diabetes.[5] It is estimated that persons with diabetes are more than twice as likely as persons without diabetes to be hospitalized for infection management and that infection management among patients with diabetes in US hospitals cost $48 billion in 2011.[6]

Infection risk increases when an open wound is present, as is often the case in limb salvage; such risk is also linked to poor glycemic control, which can cause the first-response cells of the immune system to become increasingly inoperative.[2] Peripheral neuropathy, which often is present in persons with diabetes, has been recognized as an independent leading risk factor for postoperative infection.[7]

Because patients with diabetes present with perfusion difficulties,[4] systemic antibiotics tend to be less effective than they would be in other populations. Other challenges with systemic antibiotics include the rising tide of antibiotic-resistant infections and adverse effects such as allergic reactions, renal insufficiency, and the development of *Clostridium difficile* infection.[8] Although a topical silver bactericidal solution is unaffected by these downsides of systemic antibiotics, it remains ineffective against surgical site infections (SSIs) because of its short residence time and thus its reduced therapeutic potential. Furthermore, various silver-based antimicrobial dressings applied over sutured surgical incisions are ineffective in preventing SSIs[9-12] because superficial application of a conventional antimicrobial dressing over a sutured surgical site may not kill bacteria deep in the incision.

The objective of this clinical investigation was to preliminarily evaluate the efficacy of a new bioresorbable multilayered microfilm matrix (20 µm thick) impregnated with ionic and metallic silver in preventing SSIs when placed at the level of subcutaneous tissue and dermis prior to primary closure in patients with diabetes undergoing elective surgery. In contrast to conventional antimicrobial cover dressings, the ultrathin microfilm matrix is both antimicrobial and bioresorbable.[13] Therefore, the hypothesis of this study was that the application of microfilm matrix to the exposed subcutaneous tissue of a surgical incision prior to primary closure with sutures would provide localized, sustained antimicrobial activity while the matrix was absorbed gradually over 1 week and may thereby lower the risk of SSI significantly in patients with diabetes.

Materials and Methods

Intervention

Microlyte Matrix (microfilm matrix; Imbed Biosciences, Inc) is an FDA-approved wound dressing indicated for the management of surgical wounds, burns, and chronic ulcers. It is a sterile, single-use absorbent ultrathin polymeric matrix that is only 20 µm thick. It is composed primarily of a hydrophilic, bioresorbable polymer (polyvinyl alcohol) that can rapidly absorb and maintain wound fluid within the wound bed and has an additional polymeric surface coating containing ionic and metallic silver. It has very low amounts of silver (0.16 mg/in^2, or 1 ppm when a 5 cm x 5 cm sheet of microfilm matrix is dissolved in 1 mL of fluid).[14] This is in stark contrast to conventional silver dressings, which contain 55 to 3000 ppm of silver.[15] When microfilm matrix is placed on a moist wound surface, it absorbs wound fluid and forms a soft gel that conforms intimately to the topography of the wound bed.[16] It is this unique property of hyperconformity to the wound bed that allows the silver in microfilm matrix to kill bacteria at a low dose of 1 ppm.

Furthermore, the matrix maintains a moist environment for wound healing, and it is well-known that moisture aids in the removal of nonviable tissue from the wound (autolytic debridement).[17] Other benefits of a moist wound environment include reduced pain, accelerated neovascularization, and prevention of tissue dehydration.[18,19] According to the published instructions for use of the microfilm matrix, biocompatibility of the matrix has been demonstrated through appropriate in vitro and in vivo ISO 10993 standard tests, including cytotoxicity, acute systemic toxicity, subacute/subchronic toxicity, acute intracutaneous reactivity, skin sensitization, and tissue implantation tests.[20] Sustained antimicrobial activity of the matrix has been documented for up to 3 days by relevant standard in vitro microbiological assays in simulated wound fluid, where it was reported to achieve a greater than 4 log^{10} reduction in colony-forming unit counts of microbes most frequently associated with wound infections, including *Staphylococcus aureus* (ATCC 6538), methicillin-resistant *Staphylococcus aureus* (ATCC 33591), vancomycin-resistant enterococci (ATCC 55175), *Pseudomonas aeruginosa* (ATCC 9027), *Escherichia coli* (ATCC 8739), *Klebsiella pneumoniae* (ATCC 4352), *Candida tropicalis* (ATCC 750), and *Candida albicans* (ATCC 10231). The matrix is reported to bioresorb within 7 days.[16] Other published studies have reported that components of microfilm matrix allow for growth and proliferation of fibroblasts[14] as well as migration of keratinocytes[21] on its surface and that they support normal vascularization and granulation tissue formation in the wound bed.[22]

Study design

Twenty-two patients with diabetes undergoing nonemergent or elective foot or ankle surgery and who were recognized as at-risk for SSIs were initially included in the study, which took place at an academic hospital in the southern United States. Patients identified as at-risk had 1 or more of the following criteria: neuropathy, infection (treated), open wound, history of recurrent infection, nonhealing wound, or peripheral vascular disease (treated). Patients with untreated peripheral vascular disease were excluded from the study. Fifty-five percent of the patients were male, and 45% were female. Mean patient age was 57.9 years. Patient demographics are summarized in **Table 1**.

Patients were educated about potential risks, benefits, and complications of enclosing the microfilm matrix in the surgical incision. After informed consent was obtained, patients underwent a foot or ankle surgical procedure specific to their pathology. These procedures included amputations (75%), removal of exostosis (5%), midfoot bone removal (5%), Achilles tendon repair (5%), bunionectomy (5%), and an elevating osteotomy (5%) (**Figure 1**). After meticulous hemostasis and subcutaneous closure (if applicable), the bioabsorbable microfilm matrix was applied just deep to the incision and the incision was primarily closed as shown in **Figure 2**. The matrix was tiled to cover the entire incision as needed (**Figure 3**). A nonadherent cover dressing was applied over the suture line, and initial follow-up was scheduled for 3 to 5 days following operation, with subsequent routine follow-up appointments until complete wound healing was achieved, as noted in **Table 2**. Microfilm matrix was placed at the time of surgery and was not reapplied unless revision surgery was required.

Study objectives

The primary objective of this study was to decrease the SSI rate from 13% to 6.5% in 45 days. Fifteen days were added to the conventional 30-day time frame to account for delayed wound healing in patients with diabetes. Secondary outcomes included any foreign body response to microfilm matrix at the incision site as evidenced by visual erythema and general inflammation. An interim analysis of SSI incidence was performed at the first dressing change on day 3 or day 5.

Results

Two patients were removed from analysis owing to nonadherence to postoperative care. All remaining patients had at least forefoot loss of protective sensation as assessed by using a Semmes-Weinstein monofilament.[23] Seventy-five percent of these patients had open wounds, and 70% were treated for a previous infection that was eradicated at the time of surgery, denoting a significant increased risk of postoperative infection and necessitating prophylactic measures. Signs of infection at the first postoperative appointment (between 3 and 5 days) were absent in all 20 remaining patients, and all patients progressed to complete healing during the 3-month follow-up period without evidence of SSI. Eighteen of the 20 wounds healed at the typical rate specific to the respective procedure (between 10 and 34 days to full healing). Wound healing took longer than usual in 2 patients secondary to weight-bearing dehiscence (104 and 134 days from first intervention). The dehisced wounds were resolved with revision surgery, a second application of the microfilm matrix, and appropriate wound care. The details of each individual case and respective outcomes are summarized in **Table 2**; 3 representative cases are discussed below in detail.

Case 1 (patient 1)

A 38-year-old female patient with a history of MRSA infection and uncontrolled diabetes mellitus (although diabetes was controlled at the time of the procedure) presented after partial first ray amputation and subsequent dehiscence resulting in the development of osteomyelitis in the second toe and distal second metatarsal (**Figure 4**). Partial amputation of the second ray was subsequently performed, requiring percutaneous Achilles tendon lengthening to prevent excessive forefoot pressures and further wound development. Unfortunately, the patient experienced a fall resulting in an Achilles rupture in which conservative therapy was unsuccessful, and open repair was required. Achilles repair was performed under general anesthesia. After subcutaneous closure over the tendon, microfilm matrix was tiled over the area and primary closure was obtained. A Jones compression dressing and posterior splint were subsequently applied. During the recovery period, the patient followed a strict non–weight-bearing protocol with use of a posterior splint and was transitioned to a cast once edema allowed. The wound healed in 14 days (**Table 2**), as evidenced at a postoperative appointment with the surgeon. At the 10-week follow-up, the patient was placed in a diabetic shoe with ankle-foot orthosis to prevent hyperpronation. The patient did not experience any complications or recurrent wounding during the 3-month follow-up period.

Case 2 (patient 13)

A 63-year-old male cigarette smoker with poorly controlled diabetes presented with osteomyelitis of the left third digit and a chronic, nonhealing Wagner grade 3 diabetic foot ulcer. Intravenous antibiotics were started, and 4 days later the patient underwent amputation at the metatarsophalangeal joint level (**Figure 5**). Just prior to closure with 3-0 nylon sutures, microfilm matrix was applied at the level of subcutaneous tissue. Simple interrupted sutures were used to allow for

appropriate drainage from the site, and a gauze dressing was applied. At postoperative day 19, the wound was observed to be healed, with no incidence of infection. The patient was placed in a reduced weight-bearing postoperative shoe for 3 weeks and then transitioned to using diabetic shoes with accommodative inserts. No re-ulceration or complications were reported during the 3-month follow-up period.

Case 3 (patient 17)

A 62-year-old male cigarette smoker with a history of poorly controlled diabetes and neuropathy presented with gangrene limited to the great toe secondary to aggressive anaerobic infection. He was admitted to the hospital and placed on intravenous antibiotics, after which amputation of the toe was performed (**Figure 6**). Just prior to closure of the dorsal and plantar flaps, microfilm matrix was applied to the subcutaneous tissue surface and flaps were closed over the matrix by primary intention using 3-0 nylon sutures with a ¼-inch plain packing strip applied to allow for appropriate drainage. Gauze dressing was applied, and the patient was fitted with a postoperative shoe with reduced weight-bearing and elevation of the surgical site. Sutures were removed 3 weeks postoperatively, and the patient was transitioned to diabetic shoes with custom inserts, including a great toe filler. Wound healing was achieved in 29 days. The patient reported no complications in the 3-month follow-up period.

Discussion

Patients with diabetes present with perfusion difficulties[4] and thus, systemic antibiotics tend to be less effective than they would be in other patient populations. Other challenges with systemic antibiotics include increasing antibiotic-resistant infections, adverse effects such as allergic reactions, renal insufficiency, and the development of *C difficile*.[8] This prospective single-center study demonstrated the efficacy of a bioresorbable antimicrobial microfilm matrix in preventing SSIs in at-risk patients with diabetes. The results of this preliminary trial surpassed the primary endpoint of a 50% reduction in SSI rates at day 45, with a 0% infection rate in all patients at the first dressing change on day 5. At the end of the study, the SSI rate of the intention-to-treat population was 0%, as opposed to the historical 13% rate of SSI expected in similar populations of patients with diabetes.[5] Even more significant is that a majority of the patients in the present study (70%) presented with infected wounds, which further increased the risk of SSIs. These results are especially remarkable given the 100% heal rate of the per-protocol population. Of note, all patients without a weight-bearing surgical dehiscence event (18/22 or 82%) experienced complete healing in an average of 21 days.

Absence of SSIs associated with the use of microfilm matrix may be attributed to the sustained localized antimicrobial activity of the matrix in the tissue microenvironment.[16] This was especially significant in patients 1 and 18, who underwent Achilles tendon repair and a bunionectomy, respectively. These procedures are associated with an increased risk of SSIs. The 100% healing rate may be due to the ultrathin (20 µm) form factor and bioresorbability of the microfilm matrix, as it does not act as a physical barrier to wound healing and may even support normal vascularization and granulation tissue formation in the wound bed.[22] Another notable outcome of this investigation is that the patients in the current study showed no adverse effects, including an absence of localized foreign body response to enclosing the microfilm matrix in the surgical incisions. This is consistent with published preclinical studies on the microfilm matrix that report it to be nontoxic, biocompatible, and bioresorbable.[16]

Limitations

The primary limitation of this evaluation is the noncomparative and small design; as a result, statistical significance is weak. The use of historical controls, although helpful, is not ideal, and a larger study with a cohort match is warranted to definitively establish the efficacy of the microfilm matrix in preventing SSIs relative to controls undergoing standard of care treatment. Finally, the time frame for a formal randomized controlled trial study design would be within 30 days of surgery as mandated by the US Centers for Disease Control and Prevention definition of an SSI.[24]

Conclusions

This prospective clinical study suggests that application of this antimicrobial microfilm matrix at the level of subcutaneous tissue and dermis in surgical incisions prior to primary closure is safe and has potential for prevention of postoperative SSIs in at-risk patients with diabetes,

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References

1. National Center for Chronic Disease Prevention and Health Promotion. Diabetes and prediabetes. Updated November 3, 2020. Accessed December 1, 2020. https://www.cdc.gov/chronicdisease/resources/publications/factsheets/diabetes-prediabetes.htm

2. Martin ET, Kaye KS, Knott C, et al. Diabetes and risk of surgical site infection: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol*. 2016;37(1):88–99. doi:10.1017/ice.2015.249

3. Wukich DK, Crim BE, Frykberg RG, Rosario BL. Neuropathy and poorly controlled diabetes increase the rate of surgical site infection after foot and ankle surgery. *J Bone Joint Surg Am*. 2014;96(10):832–839. doi:10.2106/JBJS.L.01302

4. Levy BI, Schiffrin EL, Mourad JJ, et al. Impaired tissue perfusion: a pathology common to hypertension, obesity, and diabetes mellitus. *Circulation*. 2008;118(9):968–976. doi:10.1161/circulationaha.107.763730

5. Wukich DK, Lowery NJ, McMillen RL, Frykberg RG. Postoperative infection rates in foot and ankle surgery: a comparison of patients with and without diabetes mellitus. *J Bone Joint Surg Am*. 2010;92(2):287–295. doi:10.2106/JBJS.I.00080

6. Korbel L, Spencer JD. Diabetes mellitus and infection: an evaluation of hospital utilization and management costs in the United States. *J Diabetes Complications*. 2015;29(2):192–195. doi:10.1016/j.jdiacomp.2014.11.005

7. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS Jr. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol*. 2001;22(10):607–612. doi:10.1086/501830

8. Selva Olid A, Solà I, Barajas-Nava LA, Gianneo OD, Cosp XB, Lipsky BA. Systemic antibiotics for treating diabetic foot infections. *Cochrane Database Syst Rev*. 2015;(9):CD009061. doi:10.1002/14651858.CD009061.pub2

9. Staveski S, Abrajano C, Casazza M, et al. Silver-impregnated dressings for sternotomy incisions to prevent surgical site infections in children. *Am J Crit Care*. 2016;25(5):402–408. doi:10.4037/ajcc2016843

10. Dickinson Jennings C, Culver CR, Baker JW. A prospective, randomized controlled trial comparing 3 dressing types following sternotomy. *Ostomy Wound Manage*. 2015;61(5):42–49. Accessed December 1, 2020. https://www.hmp

globallearningnetwork.com/site/wmp/article/prospective-randomized-controlled-trial-comparing-3-dressing-types-following-sternotomy

11. Ozaki CK, Hamdan AD, Barshes NR, et al. Prospective, randomized, multi-institutional clinical trial of a silver alginate dressing to reduce lower extremity vascular surgery wound complications. *J Vasc Surg*. 2015;61(2):419–427.e1. doi:10.1016/j.jvs.2014.07.034

12. Biffi R, Fattori L, Bertani E, et al. Surgical site infections following colorectal cancer surgery: a randomized prospective trial comparing common and advanced antimicrobial dressing containing ionic silver. *World J Surg Oncol*. 2012;10(1):94. doi:10.1186/1477-7819-10-94

13. Manning SW, Humphrey DA, Shillinglaw WR, et al. Efficacy of a bioresorbable matrix in healing complex chronic wounds: an open-label prospective pilot study. *Wounds*. 2020;32(11):309–318. Accessed December 1, 2020. https://www.hmpgloballearningnetwork.com/node/5365

14. Agarwal A, Weis TL, Schurr MJ, et al. Surfaces modified with nanometer-thick silver-impregnated polymeric films that kill bacteria but support growth of mammalian cells. *Biomaterials*. 2010;31(4):680–690. doi:10.1016/j.biomaterials.2009.09.092

15. Lee Y, Atchley DH, Proctor CA, Smith FL, Yi S, Loftis CM, Yates KM. Time-kill kinetics of a novel antimicrobial silver wound gel against select wound pathogens. *Wounds*. 2015;27(12):336–346. Accessed December 1, 2020. https://www.hmpgloballearningnetwork.com/node/5850

16. Herron M, Agarwal A, Kierski PR, et al. Reduction in wound bioburden using a silver-loaded dissolvable microfilm construct. *Adv Healthc Mater*. 2014;3(6):916–928. doi:10.1002/adhm.201300537

17. Agarwal A, McAnulty JF, Schurr MJ, Murphy CJ, Abbott NL. Polymeric materials for chronic wound and burn dressings. In: Farrar D, ed. *Advanced Wound Repair Therapies*. Elsevier; 2011:186–208. doi:10.1533/9780857093301.2.186

18. Mankowitz SL. Laceration management. *J Emerg Med*. 2017;53(3):369–382. doi:10.1016/j.jemermed.2017.05.026

19. Svensjö T, Pomahac B, Yao F, Slama J, Eriksson E. Accelerated healing of full-thickness skin wounds in a wet environment. *Plast Reconstr Surg*. 2000;106(3):602–612. Accessed December 1, 2020. https://journals.lww.com/plasreconsurg/Fulltext/2000/09030/Accelerated_Healing_of_Full_Thickness_Skin_Wounds.12.aspx

20. Microlyte Matrix. Package insert. Imbed Biosciences, Inc; 2020.

21. Gorouhi F, Shah NM, Krishna RV, et al. Epidermal growth factor-functionalized polymeric multilayer films: interplay between spatial location and bioavailability of EGF. *J Invest Dermatol*. 2014;134(6):1757–1760. doi:10.1038/jid.2014.7

22. Guthrie KM, Agarwal A, Teixeira LB, et al. Integration of silver nanoparticle-impregnated polyelectrolyte multilayers into murine-splinted cutaneous wound beds. *J Burn Care Res*. 2013;34(6):e359–e67. doi:10.1097/BCR.0b013e31827e7ef9

23. Assessing protective sensation with a monofilament. *Adv Wound Care* (New Rochelle). 2004;17(7):346. Accessed December 1, 2020. https://journals.lww.com/aswcjournal/Fulltext/2004/09000/Assessing_Protective_Sensation_with_a_Monofilament.12.aspx.

24. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al; Healthcare Infection Control Practices Advisory Committee. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017;152(8):784–791. doi:10.1001/jamasurg.2017.0904