Expedited infection control and wound healing by combining Matriderm®, a dermal matrix, and Stimulan® absorbable antibiotic beads: a case report

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Background: Since dermal matrices (DMs) were first described in surgery, they have become an integral part of the reconstructive ladder, providing plastic surgeons with new approaches to wound reconstruction. While they have been used in reconstruction of a wide range of wounds, there has been limited or no literature on their effects when used in conjunction with fully absorbable antibiotic beads. Therefore, the aim of this study was to analyze the effects of using Matriderm® dermal matrix concurrently with Stimulan® absorbable antibiotic beads on wound healing and readiness for skin grafting.

Case Description: In this manuscript, we report the case of an adult ethnic Chinese male patient with recalcitrant infected right lower limb fasciotomy wounds managed using Matriderm® dermal matrix in conjunction with Stimulan® absorbable antibiotic beads prior to split-thickness skin graft reconstruction. The patient was a non-smoker with no known comorbid medical conditions and had initially presented with right lower limb compartment syndrome and rhabdomyolysis following a fall with long lie. He subsequently underwent an emergency fasciotomy with resulting medial and lateral right lower limb fasciotomy wounds. In this case report, wound revascularization, granulation formation and readiness for skin grafting were observed after one week of concurrent application of Matriderm® and Stimulan®. The patient's post-operative recovery was uneventful and he was discharged eleven days post skin grafting. There was at least 97% graft uptake and the graft donor site had healed well and was left exposed.

Conclusions: The application of DMs in conjunction with absorbable antibiotic beads may shorten time to readiness for definitive wound coverage. Further randomized controlled trials are required to evaluate this potentially synergistic relationship.

Keywords: Enhanced antibiotic delivery; Matriderm®; Stimulan®; wound reconstruction; case report

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Introduction

A well-vascularized wound bed is essential for successful uptake of skin grafts, and remains a top priority for reconstructive surgeons during wound reconstruction. Conventional options for wound coverage include locoregional flaps, which are limited by the size of the defect, and free flaps, which are associated with considerable risk of flap loss and donor site morbidity (1,2). The advent of new technologies such as acellular dermal matrices (DMs) has opened new frontiers in wound reconstruction, demonstrating promising results for revascularization, subsequent graft uptake and eventual scar formation (3).

MatriDerm® (MedSkin Solutions Dr. Suwelack AG, Billerbeck, Germany) belongs to the first of three classes of DMs, which are biological, synthetic, and composite scaffold materials, used to strengthen and replace deficient or missing skin and soft tissues (4). MatriDerm® is a single-layer dermal substitute comprising a bovine collagen (type I, III, and V) and elastin hydrolysate. The collagen-elastin template creates a porous matrix facilitating guided fibroblast migration and formation of a neo-dermis. Enhanced neo-angiogenesis and formation of micro vessels promotes optimal split-thickness skin graft (STSG) uptake.

Stimulan® (Biocomposites Ltd., Keele, UK) is a synthetic hemihydrate form of calcium sulfate produced via a synthetic process resulting in 100% purity. It is biocompatible, composed of hydrophilic crystals, soft after hydration, and absorbable. It cures at a low temperature thus giving it the advantage of including a wider spectrum of heat-sensitive antibiotics in its delivery. The preparation of Stimulan® antibiotic beads involves mixing Stimulan® powder with surgeon-selected antibiotics, such as vancomycin and gentamicin, in the sterile field of the operating room intraoperatively. The resultant paste is pressed into a pelletizing mould (supplied with the product) and allowed to set. The resulting beads are then removed by flexing the mould over a sterile container and contained until their use.

Stimulan® has been used in orthopedic revision surgeries to manage periprosthetic joint infections, providing therapeutic antibiotic delivery locally above the minimum inhibitory concentration while avoiding toxic serum concentrations (5). However, there is limited literature on its concurrent use in reconstruction of skin defects.

Similarly, while DMs such as MatriDerm® have been used to treat a broad range of wounds, there is limited literature on its effects when used in conjunction with Stimulan®. In this manuscript, we report a case of an adult male patient with recalcitrant infected lower limb fasciotomy wounds managed using Matriderm® in conjunction with Stimulan® prior to STSG reconstruction. We present this case in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-24-44/rc).

Highlight box

Key findings

- The application of dermal matrices (DMs) in conjunction with absorbable antibiotic beads may shorten time to readiness for definitive wound coverage.

What is known and what is new?

- DMs have been used in reconstruction of a wide range of wounds, but there has been limited or no literature on their effects when used in conjunction with fully absorbable antibiotic beads.
- We report here a novel application of DMs in conjunction with absorbable antibiotic beads with observed favorable outcomes.

What is the implication, and what should change now?

- MatriDerm® used in conjunction with Stimulan® can be considered in high volume centers providing lower limb reconstructive services.
- Further studies to ascertain the synergistic effect of using MatriDerm® and Stimulan® in conjunction are recommended.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 29-year-old ethnic Chinese male patient, a non-smoker with no known comorbid medical conditions, was initially admitted to another hospital with right lower limb compartment syndrome and rhabdomyolysis following a fall with long lie. He underwent emergency fasciotomy with resulting medial and lateral leg fasciotomy wounds. Over the course of 7 weeks, he underwent five repeated wound debridements before being transferred to Ng Teng Fong General Hospital for continuation of wound care. Upon transfer, he was still septic and his wound cultures remained positive with moderate to light growth of multi resistant *Enterobacter cloacae* and *Klebsiella pneumoniae*.

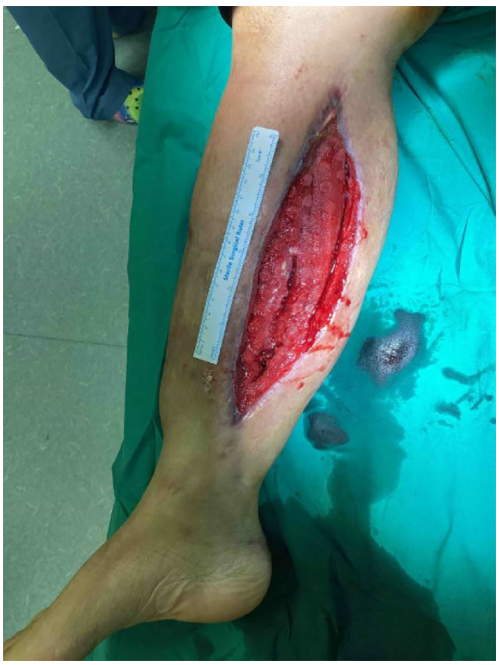

Figure 1 Medial fasciotomy wound with deep cavities.

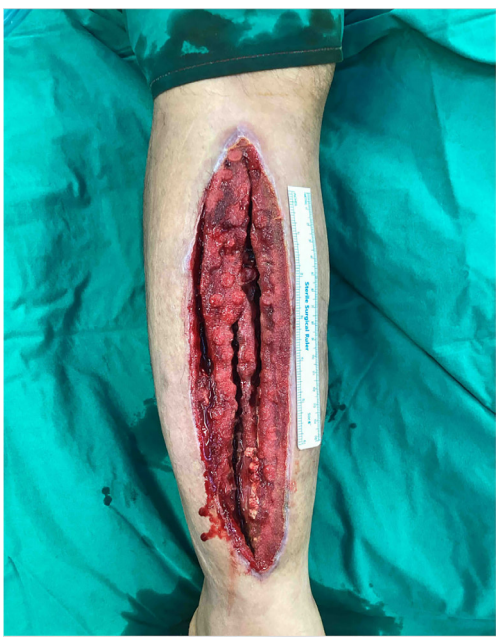

Figure 2 Lateral fasciotomy wound with deep cavities.

After consultation with our Infectious Diseases service, he was continued on courses of systemic culture-directed antibiotics. He underwent two further wound debridements with insertion of conventional antibiotic cement beads

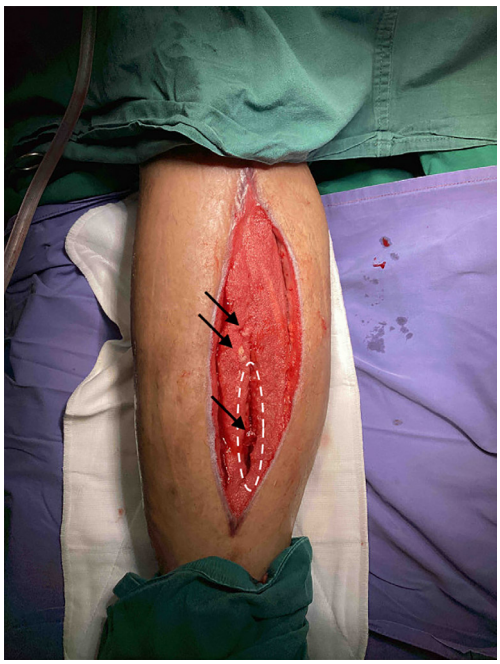

Figure 3 Medial fasciotomy wound, post index debridement and Stimulan® bead insertion (black arrows), with Matriderm® used to bridge areas of depression (outlined in white).

(impregnated with 2 g vancomycin in each pack of cement) on the first- and sixth-day post-transfer to our facility (49th and 54th day after the initial fasciotomy).

He eventually had 3 cavities on the medial wound and 3 cavities on the lateral wound. These cavities either had tendons or bone exposed, or both. The wound on the medial side measured 25 cm × 7 cm while the wound on the lateral side measured 20 cm × 5 cm (*Figures 1*,*2*). As a result of his long hospitalization, the patient was understandably undergoing an acute adjustment disorder, and he was very keen for a timely resolution of his infection and wounds.

Eleven days post-transfer, the patient underwent another wound debridement, with the insertion of Stimulan® beads in the cavities and wound bed (*Figures 3*,*4*). This was done to fill the wound cavities in a single stage, allow local antibiotic delivery to continue, and prepare the entire wound bed to be filled, flushed and ready for skin grafting. Intraoperatively, Stimulan® beads impregnated with culture directed gentamicin and vancomycin were buried into each soft tissue cavity in both the medial and lateral fasciotomy wounds. Negative pressure wound therapy was applied with a contact layer of Mepitel One®. The post debridement cultures were negative. Seven days after this

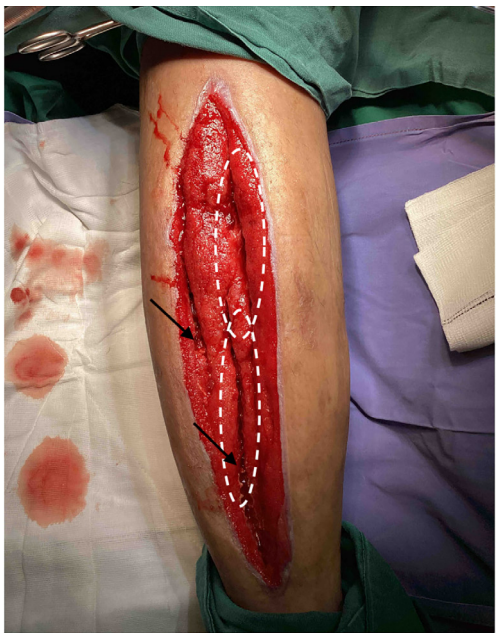

Figure 4 Lateral fasciotomy wound, post index debridement and Stimulan® bead insertion (black arrows), with Matriderm® used to bridge areas of mild depression (outlined in white).

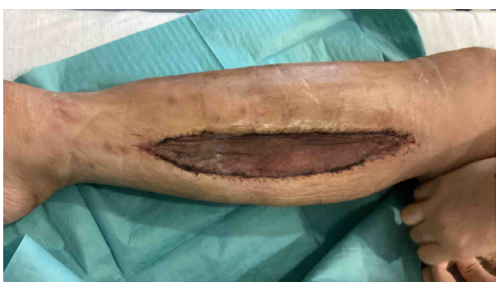

Figure 5 Medial fasciotomy wound, 11 days post-split-thickness skin graft.

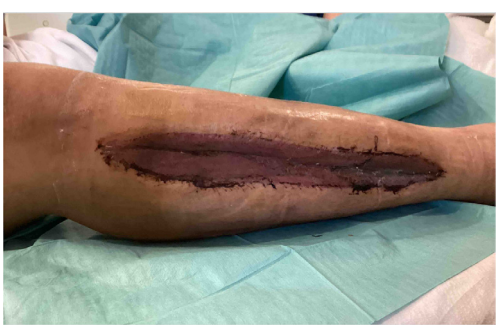

Figure 6 Lateral fasciotomy wound, 11 days post-split-thickness skin graft.

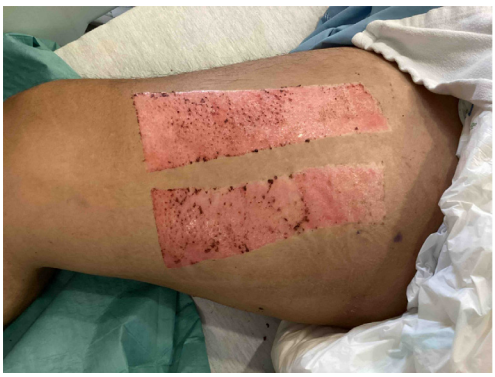

Figure 7 Split-thickness skin graft donor site.

debridement, the patient's wound cavities were observed to be filled and flush to the surrounding tissues, and ready for grafting. He then underwent a single-stage reconstruction with MatriDerm® 1 mm thickness (to areas of exposed Stimulan® beads, areas of contour irregularities and areas of mild trough depression in between compartments or filled cavities (*Figures 3*,*4*), and STSG. We used a STSG of nine-a thousandths' inch thickness, meshed to a 1:1.5 ratio, which was inset with Artiss® and 4/0 Vicryl Rapide sutures. Negative pressure wound therapy was continued immediately post-operatively for 1 week with immobilization.

Throughout the patient's hospitalization, systemic culture-directed antibiotics, namely vancomycin, imipenem and cefepime, were continued sequentially under guidance of the Infectious Diseases service.

His post-operative recovery was uneventful and he was discharged eleven days post skin grafting. There was at least 97% graft uptake with only a small area on the lateral wound with graft loss which was left to fully epithelialize spontaneously (*Figures 5*,*6*). Graft donor site had healed well and was left exposed (*Figure 7*).

Discussion

We report a technique of expedient wound bed preparation using MatriDerm® in conjunction with Stimulan®, allowing for a single-stage STSG procedure to be performed in an expedited interval of one week. The patient was a non-smoker with no known cardiovascular comorbidities, which were favorable factors contributing to accelerated wound healing and readiness for grafting. Mean time to STSG following the use of various DMs alone has been found to

range from 14 to 31.9 days, depending on type used (6). In these studies, time to STSG was used as a marker of time to integration. We report the case of a shorter time to STSG when MatriDerm® was used in conjunction with Stimulan® which may be of benefit to high volume centers providing lower limb reconstructive services.

Dermal matrix infections have been identified as the "Achilles Heel" of all dermal regenerative strategies (7), and many centres have developed protocols to aggressively detect and eradicate infections before invasion into the underlying wound bed and systemic spread. While these protocols invariably include systemic antimicrobial therapy, the addition of a local antimicrobial delivery system may also be beneficial.

The most prevalent local antimicrobial delivery tool which has been used for decades is polymethyl methacrylate (PMMA) cement beads. Antibiotic release from these beads is divided into two different phases—initial release, which occurs minutes to hours after implantation, and sustained release, which follows after several days and results in a prolonged local antibiotic concentration (8). The main drawbacks to their use include the need for removal at a second procedure to eradicate potential foci of bacterial colonization and infection, and the limitation to only heat-resistant antibiotics due to their highly exothermic setting reaction (9,10). Cefazolin, vancomycin, ceftriaxone and gentamicin are commonly used in the cement beads.

The use of biodegradable alternatives such as calcium sulfate, of which Stimulan® is an example, has been shown to overcome these issues. In addition, *in vitro* studies have reported higher antibiotic elution and greater inhibition of bacterial growth with calcium sulfate beads (10), with smaller sized beads eluting faster (11) as a result of increased surface area.

Comparing between conventional calcium sulfate beads and Stimulan®, the latter has demonstrated a predictable, supra-therapeutic antibiotic elution profile for over 40 days (12). In addition, studies have also reported increased wound complication and discharge with calcium sulfate beads (13,14), possibly due to impurity of the calcium sulfate (15). Fortunately, this was not encountered in our reported patient, possibly because Stimulan® beads are made with higher purity and less reactive materials that may result in lower drainage rates (16).

Our hypothesis is two pronged. First, by using Matriderm® over the exposed Stimulan® beads and the cavities, it provides good vascularised tissue which seals off the cavities and non-vascularised Stimulan® beads. Second, the continuous antibiotic delivery provided by Stimulan® beads, together with their slow resorption, may expedite wound bed preparation, facilitate graft take and prevent infections causing graft loss. As we report above, this may be achieved within one week from Stimulan® bead insertion into the cavities. Further studies to ascertain the synergistic effect of using MatriDerm® and Stimulan® in conjunction are recommended.

Finally, this case report adds to existing literature demonstrating that the use of MatriDerm® as single-stage defect coverage is suitable for larger defects (17). In the case we reported, defects of up to 25 by 7 cm were successfully grafted with the use of MatriDerm®, avoiding local or free flap surgery and with no occurrence of donor deformity.

Conclusions

DMs are an integral part of the reconstructive ladder. Time to STSG following application of DMs varies, and may be delayed by dermal matrix infections. A local antimicrobial delivery system such as Stimulan® may be beneficial in preserving the integrity of implanted DMs, which are at risk of infection or persistent discharge. We report a case in which the combined use of Matriderm® and Stimulan® facilitated a single-stage STSG procedure to be performed in an expedited interval of one week. Further randomized controlled trials with a large cohort of patients are required to evaluate the presence of a synergistic relationship between the two, which if proven, would lead to an exponential increase in their respective uses.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-24-44/rc

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-24-44/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-24-44/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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