

## Peer Review File

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### Reviewer A

This surgical case is regularly encountered in the practice of traumatic reconstructive surgery, and the use of Matriderm after negative pressure treatment has been widely presented.

It is inaccurate to claim:

- that systemic antibiotic therapy does not protect the dermal matrix: in fact, the vascularization of the matrix, which takes place between days 4 and 8, allows antibiotics to penetrate and nourishes the overlying epidermal graft. Since 2006, it has also been shown that skin grafting can be performed successfully in a single operation during Matriderm graft.

[Response: The manuscript has been modified as advised \(lines 151 – 152\).](#)

It is equally inaccurate to claim that only limited surfaces were grafted in a single operation, or that only lesions less than 2 cm in breadth were grafted.

[Response: The manuscript has been modified as advised \(lines 243 – 245\).](#)

I'm also puzzled by the authors' claim that Stimulan reduces the risk of hematoma.

[Response: The statement of concern has been removed.](#)

In conclusion:

Drawing conclusions about a case is not satisfactory. It is necessary to establish a cohort of a sufficient number of patients evaluated in a randomized fashion to present consolidated results. You also need to broaden research into Matriderm, which has been widely used since 2006 on large areas of substance loss, like burn patients, and traumatic or carcinological lesions. [Response: We agree that the need for further randomized controlled trials with a larger cohort of patients is required. This has been reiterated in the conclusion \(lines 252 – 253\).](#)

### Reviewer B

Grammar can be improved in several sections, please check entire manuscript. For example, "relook" on page 2.

[Response: "Relook" has been changed to "repeated" \(line 90\).](#)

Antibiotics: what were the conventional antibiotics (and concentrations) in the cement beads and what for systemic treatment?

[Response: The cement beads were formed from a cement pack impregnated with 2g Vancomycin \(lines 112 – 113\). Systemic antibiotics included Vancomycin, Imipenem and Cefepime \(lines 133 – 134\).](#)

It is not explained why treatment with Stimulan and Gentamycin/Vancomycin was started, when wound cultures were negative. This would also constitute a change in intervention (item 9c in CARE).

[Response: Upon transfer to our facility, the patient's wound cultures remained](#)

positive with moderate to light growth of multi resistant *Enterobacter cloacae* and *Klebsiella pneumoniae*. Systemic culture-directed antibiotics were continued after consultation with Infectious Diseases. This has been clarified in the manuscript (lines 91 – 111).

Only after debridement and insertion of Stimulan beads did the patient's intraoperative cultures return negative, allowing for single-stage reconstruction with Matriderm and STSG. This has also been clarified in the manuscript (lines 125 – 131).

The timeline for the different treatments is not always clear.

Response: The timeline of surgeries has been clarified as advised (lines 90, 113, 120).

Good vascularization of the tissue: related to Matriderm, antibiotics or other factor?

Response: We believe that it is likely a combination of both Matriderm and antibiotic delivery from Stimulan beads, as we observed that the patient's wounds became ready for grafting after 1 week under our care.

I'm surprised that patient has not given informed consent, yet his case is reported here.

Response: Written informed consent has been obtained, with the consent form submitted to the editorial office.

Statements regarding expediting wound closure and shortening time for definitive wound coverage cannot be made based on one case only.

Response: The conclusion has been edited to be more specific (lines 253 – 255).

### **Reviewer C**

The utilization of dermal matrices combined with antibiotic beads represents a promising strategy in the management of post-operative wounds. This was a well-presented case study. The need for further studies and RCT to determine the exact efficacy of the combination of products is paramount.

Response: We thank the reviewer for the encouraging comments. We agree that there is a need for further randomized controlled trials with a larger cohort of patients. This has been reiterated in the conclusion (lines 254 – 256).

### **Reviewer D**

In this article, authors report a case of an adult male patient with recalcitrant infected lower limb fasciotomy wounds managed using Matriderm® (a dermal matrix) in conjunction with Stimulan® absorbable antibiotic beads prior to split-thickness skin graft reconstruction.

I agree that this report is interesting and might be useful. However, authors should review some points:

1. In Introduction, authors should better explain the role of Stimulan as an absorbable antibiotic bead, such as what are the antibiotics included in the product.

Response: Antibiotics are selected by surgeons and mixed intraoperatively before leaving to set. The manuscript has been modified for clarification (lines 70 – 73).

2. I do not understand the real need to use MatriDerm 1mm thickness instead of directly skin grafting without Matriderm in this patient because the wound bed seems to be very well prepared, without bone or tendon exposure. Could you please explain?

Response: MatriDerm was targeted at areas of exposed Stimulan beads, areas of contour irregularities and areas of mild trough depression in between compartments or filled cavities. This has been clarified in the manuscript (lines 127 – 129), and labelled in Figs 3 and 4.

3. In figures 3 and 4, where are the exposed Stimulan® beads? Authors should indicate using arrows.

Response: The exposed Stimulan® beads have been labelled with arrows in Figs 3 and 4.

4. Why should the MatriDerm® cover areas of exposed Stimulan® beads?

Response: Stimulan® beads are avascular and we believe that the by applying Matriderm over, its subsequent vascularization will provide an optimal wound bed for skin graft take.

### **Reviewer E**

Let me first say that I appreciate the work of the physicians on this case. It appears to be a successful management of the injury which is good news. However, there are some issues with this manuscript.

First of all. In my opinion, there is little to conclude from a case study and the authors should therefore be careful with their claims. At the end of the abstract, the authors write: “We conclude that the application of dermal matrices in conjunction with absorbable antibiotic beads can expedite time taken for wound cavities to be filled with granulation, cavity closure and integration with other compartments, therefore shortening time to readiness for definitive wound coverage.” It is impossible to conclude this based on one single patient. This should be tested in a randomized-controlled trial, or at least a series of patients. I therefore suggest to remove this conclusion. The same goes for their first 2 key findings.

Response: The abstract and key findings section has been modified as advised.

There is little information of the use/effect of Stimulan in the Introduction. The authors should describe the studies done previously that show the effect of Stimulan.

Response: The use and effect of Stimulan® in orthopedic revision surgeries to manage periprosthetic joint infections has been included (lines 75 – 77).

Timeline could be presented clearer, how many days after the onset of the injury was each treatment applied?

Response: The timeline of surgeries has been clarified as advised (lines 90, 113, 120).

Information about the patient is lacking: were there underlying conditions? What is the exact cause of the injury?

Response: The patient did not have any known medical comorbid conditions previously. The cause of compartment syndrome was a fall with long lie. This has been clarified in the manuscript (lines 87 – 89).

“A decision was made to use...” is not informative. It should be clear to reader why certain decisions were made.

Response: The statement of concern has been rephrased, and the reason for Stimulan use has been clarified as advised (lines 117 – 118, 121 – 122).

Is the use of Stimulan common in this hospital or is the use of Stimulan a deviation from standard procedures?

Response: The use of Stimulan is becoming increasingly common in our hospital, and is not considered a deviation from standard practice.

In the checklist at the end of the manuscript, the document states that the patient did not give informed consent. Writing results in a manuscript without patient/representative consent is unethical and possibly illegal depending on the country regulations. I find this concerning.

Response: Written informed consent has been obtained, with the consent form submitted to the editorial office

Patient information is provided in the Discussion but should be provided in the case description.

Response: The manuscript has been modified as advised (lines 87 – 88).

How can it be that Stimulan does not promote tissue growth, but proposedly have a synergistic effect on graft take in combination with Matriderm?

Response: We have removed the statement of concern, and have rephrased the possible synergistic effect of Stimulan due to its continuous antibiotic delivery and slow resorption rates (lines 242 – 243).

Matriderm is more widely used than the authors describe in the Discussion. Also for the use of large skin defects. Therefore their claim seems incorrect.

Response: The manuscript has been modified as advised.

I highly encourage the authors to test their hypothesis in a series of patients, with the right informed consent protocols.

Response: The need for further randomized controlled trials with a larger cohort of patients has been reiterated in the conclusion (lines 247 – 249).