Post-Treatment Infection in Severe Burn Patient: A Comparative Review on Dermal Matrices

Zhiyu Zhang[1]

[1]Indiana University Bloomington, Bloomington, Indiana, USA

ABSTRACT

Artificial dermal regeneration templates have been widely used in burn reconstruction surgery, and this allows subsequent skin graft to be taken more successfully. However, many clinical studies have noted instances of infection when testing the effectiveness of a specific template. This review aims to compare two common dermal regeneration templates that are very different in nature -- Novosorb® Biodegradable Temporising Matrix (BTM) and Integra® Dermal Regeneration Template. Extensive literature search was conducted, and infection rates associated with each template were recorded. Based on the articles included, Integra has shown to be a more effective method and has resulted in lower infection rates. While current studies have begun to examine the use of dermal regeneration templates in additional settings, more long-term evaluations should be included in the future since wound contracture is a continuous process.

Introduction

Severe burns can often lead to adverse health and cosmetic consequences. A classic example of this involves infants and young children reaching up to stove or grills, creating burns on the palms and fingers that can scar and cause disabilities that would carry into their adult life.[1] Complications in the excision and skin grafting process for treating burns create significant challenges for surgeons. One of the most common complications is infection following severe thermal damage and permanent loss of dermal tissue.[2] In severe burns, autologous donor skin alone was found to be insufficient for debridement and grafting at an early stage, and patients are not capable of regenerating dermal tissue. Therefore, surgeons must choose a viable dermal regeneration template for wound coverage and tissue repair that will lead to larger percent take, less infection, and minimal scarring.[3,4]

For extensive burns, artificial dermal regenerative templates play a crucial role in primary dermal repair. This is followed by a split-thickness skin graft and post-surgery splinting and therapy. After the excision of the dead skin, a dermal graft would be applied and integrated to the skin via a three-step process. Imbibition occurs as the ischemic graft is maintained through the diffusion of nutrients from the underlying wound bed. Inosculation is accomplished by growth factors and leads to the development of blood vessels between the dermal graft and the capillary bed that is underneath. The final step is revascularization, or the ingrowth of the newly developed vessels into the dermal graft.[5] Based on manufacturer's recommendations, this process takes an average of 4 weeks until the patient is ready to receive a split thickness skin graft.[6,7] Burn wounds are prone to experience various degrees of infections, and some are characterized by lower graft take or even sepsis and shock.[2]

This paper focuses on two artificial dermal templates -- Novosorb® Biodegradable Temporising Matrix (BTM) and Integra® Dermal Regeneration Template. These templates are manufactured in two distinct ways and are associated with different risk levels and infection rates. Integra is a widely used dermal matrix derived from animals and contains crosslinked collagen that could be a target of bacterial infections.[4] Materials that are allogeneic in origin post some risks of infection. BTM is a fully synthetic alternative,[3] and bacterial colonization could occur in the porous structure of BTM matrices.

While many analyses have focused on the effectiveness of various dermal regeneration techniques, relatively few articles discuss the sources and solutions to many confounding variables. This study aims to compare the risks of infection associated with Novosorb® BTM and Integra®, which are both widely used and offer countless benefits.

Study Design

The outcome of interest being compared is the percent infection after applying the dermal regeneration template. The proportion of superficial versus invasive infections was included if noted in the article. The percentage of wound infection was recorded for each study to generate a data table for BTM vs. Integra. These data were obtained through a literature search on PubMed, Ovid, and Google Scholar. All results are from peer-reviewed publications that analyze the use of BTM or Integra following full-thickness thermal injuries. The articles selected were clinical trials or case series. All reviewed literature involved patients without preexisting injuries, health conditions, or infections.

Two additional case studies were compared. The two patients were treated with the two different dermal regeneration templates, and both patients experienced infections. The patients were chosen so that they are similar in age, percentage of total body surface area (TBSA), and sites receiving the graft. BTM or Integra was used on each of the patients, and their percent take, days it took to integrate, and infection conditions were assessed separately.

Results

From the articles that were included in this study, the percentage of infections was identified and recorded in the table below, and the percentage of superficial and invasive infections were recorded separately if applicable. In addition, the following data were obtained: the authors of the articles, the regeneration matrix used (Integra or BTM), the number of patients in the study, and the total number of sites that were grafted.

Table 1. Articles that Discussed the Rates of Infection Using Integra vs. BTM

Author	Matrix Used	# of Patients	# of Sites	Infections (%)	Superficial (%)	Invasive (%)
Heimbach et al. [4]	Integra	216	758	16.3	13.2	3.1
Bargues et al. [9]	Integra	50	71	32.4	21.1	11.3
Dantzer et al. [10]	Integra	31	39	12.8	10.2	2.6
L Martínez et al. [11]	Integra	11	14	14.3	14.3	0
Lohana et al. [12]	Integra	23	37	13.5	13.5	0
Branski et al. [13]	Integra	20	20	20		
Lo et al. [3]	BTM	26	100	38.5		
Larson et al. [14]	BTM	3	3	66.7	33.3	33.3
Liu et al. [15]	BTM	36	36	19.4		
Greenwood et al. [16]	BTM	5	5	20	10	10

Table 1 involves a comprehensive literature search and summarizes the incidence of infection associated with the use of Integra vs. BTM. 351 patients with a total of 939 wound sites treated with Integra were included, and 70 patients with a total of 144 wound sites treated with BTM were included. Based on the available data, the rate of infection after Integra application is significantly lower than with the use of BTM (Table 1).

Based on the studies included in this review, using BTM in the treatment of burn wounds has shown an infection rate of above 20 percent. This is supported by the study conducted by Lo et al,[3] which is a multicenter, prospective study that included major adult burn centers in Australia and France. Following the application of BTM and in the period before split skin grafting, 10 patients (38.5%) experienced infection (One patient was excluded from the study prior to any analyses due to invasive *Staphylococcus aureus* infection).

Concerns about complications associated with infection were also addressed in a clinical trial of Integra conducted by Heimbach et al.[4], which is a prospective study involving 13 burn care facilities in the US. The total incidence of infection reported in the study was 16.3%, with most of the cases being superficial infections (13.2%), and 3.1% being invasive infections.

When examining specific cases, it was found that both templates have been used to treat patients with acute burns with TBSA greater than 40%. The study conducted by Lohana et al. in 2014 involved a 43-year-old patient who underwent burn reconstruction using Integra in her trunk and upper limbs.[12] The initial Integra application failed on the abdomen, and a second attempt resulted in 90% take. It took 22 days to integrate the Integra template before skin graft was applied. The patient developed infection in the process, but the final outcome was concluded as satisfactory.

A patient with similar demographic background was identified in a BTM study conducted by Greenwood et al in 2018[16]. This 47-year-old patient with 52% TBSA underwent BTM treatment in his limbs and the anterior trunk. It took 35 days for BTM to integrate. Infection was identified and prevented the adherence of BTM. Subsequently, the BTM on the anterior trunk was eventually lost and removed.

Discussion

Infection is one of the most common and serious adverse events after the application of dermal regeneration templates, especially in patients with severe burns. A growing number of researchers have aimed to evaluate the effectiveness and disadvantages of different brands of templates through clinical trials. This literature review helps to summarize the infection rates associated with two widely accepted matrices, and a direct comparison can be made based on the results.

The study conducted by Lo et al reported patient number and infection rates.[3] Since each patient could have multiple infected sites, this makes the potential incidence of infection greater than the reported number. Three months after the application of BTM, one patient experienced infection in one lesion, and no reported infections were identified at the 6- and 12-month follow-ups. This shows the effectiveness of BTM without long-term adverse effects.

Compared to BTM results, studies show that Integra is associated with a relatively lower infection rate. More data points were generated for Integra treatment based on the literature search, and the rate of infection is consistently lower when Integra is used. Heimbach et al. have concluded that infection rates were not affected by the patient's age or gender based on their study.[4] However, this result cannot be generalized to all instances, since an elevated risks could be associated with elders or patients with preexisting health conditions. In addition, the template used, the severity of the wound, and the surgeon's technique could still play a role in affecting the likelihood of infection.

It is noted that when compared to the items that discuss the infection rates associated with Integra, fewer present studies have focused on the cases of infections following the use of BTM, specifically in burn patients. Therefore, fewer data points were included. In addition, the year of the study could be a potential confounding variable. The study conducted by Heimbach et al was published in 2003, whereas the study conducted by Lo et al. was published in 2020. The reported rates could be different in the current year.

Although it has a few drawbacks, dermal regeneration templates have become widely accepted and continues to expand its usage in wound care treatment. While previous studies have used Integra in less than 20% TBSA, recent

studies have used Integra on severe burn patients with more than 50% TBSA.[13] In fact, these templates have been useful in additional areas, such as using BTM for the reconstruction of diabetic wounds in the foot.[17] More and more studies have used these matrices on pediatric patients, since these artificial dermis have offered many general usage in pediatric reconstruction surgery.[1]

Conclusion

Infection is by far one of the most common and most expected adverse events following severe burns, and Integra has been shown to be an effective method for treating burns while minimizing these risks. When compared to the outcomes using BTM, Integra has resulted in a lower rate of infection and a better outcome in general. Future studies could examine further changes and record the long-term outcomes of these dermal regeneration matrices.

Bibliography

1. Scott JR, Costa BA, Gibran NS, Engrav LH, Heimbach DH, Klein MB. Pediatric palm contact burns: a ten-year review. *J Burn Care Res*. 2008;29(4):614-618. doi:10.1097/BCR.0b013e31817db8f2

2. Gonzalez SR, Wolter KG, Yuen JC. Infectious Complications Associated with the Use of Integra: A Systematic Review of the Literature. Plast Reconstr Surg Glob Open. 2020 Jul; 8(7): e2869. Published online 2020 Jul 15. doi: 10.1097/GOX.0000000000002869

3. Lo CH, Brown JN, Dantzer EJG, et al. Wound healing and dermal regeneration in severe burn patients treated with NovoSorb® Biodegradable Temporising Matrix: A prospective clinical study. *Burns*. 2022;48(3):529-538. doi:10.1016/j.burns.2021.07.014

4. Heimbach DM, Warden GD, Luterman A, et al. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn treatment. *J Burn Care Rehabil*. 2003;24(1):42-48. doi:10.1097/00004630-200301000-00009

5. Chang DK, Louis MR, Gimenez A, Reece EM. The Basics of Integra Dermal Regeneration Template and its Expanding Clinical Applications. *Semin Plast Surg*. 2019;33(3):185-189. doi:10.1055/s-0039-1693401

6. Polynovo Pty Ltd. Novosorb BTM. https://usa.polynovo.com/ novosorb-btm/. [Accessed 12 Jan 2023].

7. *Integra LifeSciences Corporation. https://www.integralife.com/file/general/1453796564.pdf. [Accessed 12 Jan 2023].*

8. Cheshire PA, Herson MR, Cleland H, Akbarzadeh S. Artificial dermal templates: A comparative study of NovoSorb ™ Biodegradable Temporising Matrix (BTM) and Integra(®) Dermal Regeneration Template (DRT). *Burns*. 2016;42(5):1088-1096. doi:10.1016/j.burns.2016.01.028

9. Bargues L, Boyer S, Leclerc T, Duhamel P, Bey E. Incidence et microbiologie des complications infectieuses lors d'utilisation de la peau artificielle Integra chez le brûlé [Incidence and microbiology of infectious complications with the use of artificial skin Integra in burns]. *Ann Chir Plast Esthet*. 2009;54(6):533-539. doi:10.1016/j.anplas.2008.10.013

10. Dantzer E, Braye FM. Reconstructive surgery using an artificial dermis (Integra): results with 39 grafts. *Br J Plast Surg*. 2001;54(8):659-664. doi:10.1054/bjps.2001.3684

11. Martínez L, Ros Z, López-Gutiérrez JC, et al. La dermis artificial (Integra) en cirugía reconstructiva pediátrica [Integra Artificial dermis in pediatric reconstructive surgery]. *Cir Pediatr*. 2002;15(3):97-100.

12. Lohana P, Hassan S, Watson SB. Integra™ in burns reconstruction: Our experience and report of an unusual immunological reaction. *Ann Burns Fire Disasters*. 2014;27(1):17-21.

13. Branski LK, Herndon DN, Pereira C, et al. Longitudinal assessment of Integra in primary burn management: a randomized pediatric clinical trial. *Crit Care Med*. 2007;35(11):2615-2623. doi:10.1097/01.CCM.0000285991.36698.E2

14. Kenneth W Larson, MD, Cindy L Austin, MS, Simon J Thompson, PhD. Treatment of a Full-Thickness Burn Injury With NovoSorb Biodegradable Temporizing Matrix and RECELL Autologous Skin Cell Suspension: A Case Series, *Journal of Burn Care & Research*. 2020; 41(1): 215–219. doi.org/10.1093/jbcr/irz179

15. X Liu, MD, PhD, S Velamuri, MD, M Hassouba, MD, D Hill, PharmD, W Hickerson, MD. 473 The Application of Biodegradable Temporizing Matrix in Burn Reconstructive Surgery: Preliminary Results of 36 cases, *Journal of Burn Care & Research*. 2019; 40(1): S209–S210. doi.org/10.1093/jbcr/irz013.367

16. John E. Greenwood, Bradley J. Schmitt, Marcus J.D. Wagstaff. Experience with a synthetic bilayer Biodegradable Temporising Matrix in significant burn injury, *Burns*. 2018; 2(1): 17-34. doi.org/10.1016/j.burnso.2017.08.001.

17. Kuang B, Pena G, Cowled P, et al. Use of Biodegradable Temporising Matrix (BTM) in the reconstruction of diabetic foot wounds: A pilot study. *Scars, Burns & Healing*. 2022;8. doi:10.1177/20595131221122272