INTEGRA™ IN BURNS RECONSTRUCTION: OUR EXPERIENCE AND REPORT OF AN UNUSUAL IMMUNOLOGICAL REACTION

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SUMMARY. Limited availability of autologous donor sites poses significant challenges for soft-tissue reconstruction in severe and complex burns. Integra™ is a bi-layered dermal regeneration template (DRT) which has played a significant role in soft tissue reconstruction since its initial use for full-thickness burn defects. The purpose of this study is to report our institutional experience of Integra™ in burns management over a 4-year period and highlight an unusual reaction to its second application. Twenty-four cases underwent Integra™ resurfacing for burn management from September 2007 to August 2011. Data on patient demographics, including co-morbidities, indications, operative data, complications, secondary reconstruction and outcomes were recorded. Integra™ was used in 24 patients on 37 anatomical sites. One patient died 3 weeks after injury and first stage of Integra™ application, and was therefore excluded from the study. Split-thickness skin grafting was performed within an average of 23 days (with a range of 7-55 days) and mean graft take was 87% (with a range of 75-100%). Five cases of local infection at the graft site were recorded. The average length of hospital stay was 47 days (with a range of 1-162 days). The mean follow-up time was 17 months (with a range of 9-34 months). Overall, our experience with DRT was mixed, that is to say we found it satisfactory with acute burns resurfacing but very good with secondary reconstruction. The main advantage of Integra™ is its immediate availability in unlimited quantities for soft-tissue reconstruction in major and complex burns. The main drawbacks are financial implications, two-stage procedure, complex wound care and risk of infection. We believe that Integra™ can be considered as a promising modality in burns management.

Keywords: burns, skin dressings, dermal substitute, reconstructive surgical procedures, contracture release

Introduction

The last few decades have seen a variety of advances in medical and surgical care of burn patients. This has significantly improved the overall outcome of burn patients. Early excision of a burn wound is one of the most important factors responsible for reducing mortality rates in major burns.[1] Adequate soft tissue coverage after excision is essential in preventing the physiological and metabolic consequences of a large open wound whilst inhibiting bacterial invasion.[2] In extensive burns there is often a scarcity of available donor sites for autologous skin grafting for wound closure following primary excision. Similarly, in secondary burn reconstruction for contractures or severe scars, there may be insufficient autologous tissue available due to donor site scarring.

Integra™ (Life Sciences Corp., Plainsboro, NJ) is a bilaminar dermal regeneration template (DTR). It was initially developed to improve functional results after the acute phase of a burn injury.[3] The dermal matrix layer is composed of bovine collagen and shark chondroitin-6-sulphate. The epidermal component is a thin layer of silicone. The deeper layer structure provides the "scaffold" for neodermis formation. The host fibroblasts migrate, proliferate and secrete a native collagen formation within the dermal template. The endothelial cells shortly follow the fibroblasts to form a vascular network within the neodermis.[4] Vascularisation becomes evident at approximately 2 to 4 weeks, following which the silicone layer can be removed and replaced with a thin split-thickness skin graft.

In our practice we gradually introduced Integra™ for major burns in both adult and paediatric populations, where inadequate autologous donor site was unavailable for wound resurfacing. Once the technique had been established for acute resurfacing we were able to apply it to secondary late burns reconstruction. This paper reports our recent experience of the use of Integra™ as a reconstructive tool in burns surgery and reports of an unusual immunological reaction to second application of Integra™.

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Table I - Summary of use of Integra™ for primary burns reconstruction

S.No	Sex	Age (Yr)	Site	Integra take	Skin graft		Complication	Outcome	Follow-up
					Days	Take			
1	M	4	R Leg	100%	22	90%	HTS	Satisfactory	12 months
2	F	5	Back, Arm	100%	7	98%	Infection	Satisfactory	11 months
3	F	5	Both hands	95% (L) Failed(R)	20	90%	Contracture – Left hand	Satisfactory	11 months
3	M	14	Chest	100%	13	100%	None	Satisfactory	18 months
4	M	19	Both Arms	100%	34/38*	90/95%	Infection	Satisfactory	17 months
5	M	19	Chest/ Abdomen & both Arms	95%	23	100%	MRSA	Satisfactory	9 months
6	F	19	L Hand	100%	13	80%	Infection	Satisfactory	27 months
7	M	40	Both Arms	100%	15	95%	MRSA	Satisfactory	15 months
8	F	41	Upper Back	100%	23	100%	None	Satisfactory	9 months
9	F	51	Both Legs	100%	30/55*	80/85%	Infection	Satisfactory	34 months
10	F	70	Scalp	100%	16	75%	MRSA – graft fragile	Satisfactory	18 months
11	F	73	L Arm	100%	7	100%	None	Satisfactory	11 months
12	M	17	L Arm, Chest/ Abdomen	90%	21	100%	None	Satisfactory	24 months
13	F	41	Both Lower limbs, Chest	85%	21	95%	None	Satisfactory	22 months
14	M	23	R. Upper limb, Chest	100%	21	100%	1% area delayed healing	Satisfactory	24 months
15	F	43	Chest/ Abdomen, both upper limbs	Failed – 100% Reapplied after 1 wk	22	95%	Infection	Satisfactory	2 months

*Sites where skin graft was applied at different time MRSA – Methicillin Resistant *Staphlococcus aureus*; HTS – Hypertrophic scar

Patients and methods

Medical records of patients who underwent Integra™ reconstruction for burns from September 2007 to August 2011 were reviewed. A total of 24 patients underwent Integra™ reconstruction for acute and secondary burns reconstruction during this period. One patient died due to multisystem organ failure three weeks after first stage resurfacing using Integra™ and was therefore excluded from the study - 80% Integra™ take was recorded in this patient. Data on patient demographics, including co-morbidities, indications, operative data, complications, secondary reconstruction and outcomes were recorded.

Surgical Technique

All acute burn wounds were treated with the same approach by the senior author. The wounds were cleaned with betadine solution. The eschar was tangentially excised to remove dead necrotic tissue down to healthy bleeding and viable tissue. The Integra™ was meshed in order to reduce the overall quantity used and prevent formation of haematoma. Once cut to fit the dimension of the wound, the Integra™ was stapled into position and covered with 0.25% silver nitrate soaked gauze, before being wrapped in dry absorbant guaze/Gamjee and crepe bandage. In delayed burn reconstruction we used betadine soaked guaze instead of 0.25% silver nitrate, together with dry absorbant gauze and crepe bandage. In both acute wound resurfacing and burn reconstruction, the Integra™ was inspected every 3-5 days depending on clinical indication. Once the Integra™ became fully vascularised (on average after 3 weeks) the patient underwent removal of the silicone sheet and application of a thin split-thickness skin graft. The skin graft was secured with staples, jelonet, absorbant guaze and crepe bandage.

Results

Of the 23 patients, 14 were female and 9 male, with ages ranging from 4-73 years (giving a mean of 28 years). Integra™ was used in acute burns in 15 (66%) and secondary burn reconstruction in 8 (34%) cases (*Tables I and II*). Integra™ was used on 37 anatomical sites. Common sites of application were the upper limb 17 cases (45%),

Table II - Summary of outcome of Integra™ for secondary burn reconstruction

S.No	Sex	Age	Site	Integra take	Skin graft		Complication	Outcome	Follow-up
					Days	Take			
1	M	9	R Foot	98%	13	95%	Infection, HTS	Satisfactory	22 months
2	F	10	R Foot	100%	21	100%	None	Satisfactory	18 months
3	M	18	L Hand	100%	21	100%	None	Satisfactory	26 months
4	F	21	Abdomen	98%	15	100%	HTS	Satisfactory	13 months
5	F	22	L Hand	100%	30	100%	None	Satisfactory	12 months
6	F	37	Abdomen	100%	21	100%	None	Satisfactory	24 months
7	F	16	L Chest/ Abdomen	100%	22	100%	None	Satisfactory	9 months
8	F	15	Ant Chest	100%	22	100%	Few over-granulation areas*	Satisfactory	2 ½ months

HTS – Hypertrophic scar; * *Staphlococcus* infection at graft stage

torso 13 (36%), lower limb 6 (16%) and head and neck 1 (3%). The largest total body surface area (TBSA) covered with Integra™ in acute burns was 64 percent. Twenty-three patients underwent second-stage skin grafting. The mean time from Integra™ to grafting was 23 days (with a range of 7- 55 days) and mean graft take was 87% (with a range of 75-100%).

Integra™ failed to take in two patients. Of these, one had complete failure (excision 20% TBSA trunk) and required further Integra™ resurfacing one week later, achieving 90% take, whilst the second patient had 100% take on one limb but complete failure on the other limb. We recorded five local infections at the graft site. Four patients grew MRSA, whilst *Pseudomonas*, coliforms and *Staphylococcus* aureus were other common species.

Average length of stay in hospital was 47 days (with a range of 1-162 days). Three patients who underwent Integra™ resurfacing for acute burns required secondary surgery for scar contracture release. The mean follow-up time was 17 months. Overall, we achieved adequate wound coverage in our cohort.

Case of Interest

A 40-year-old female sustained major burns during her childhood and required multiple procedures for burns management. In her third decade, she underwent release of a burn contracture and resurfacing with Integra™ to both thighs. Seven years later, further Integra™ resurfacing for scar contracture release to the upper abdomen was required. The graft take was excellent with a satisfactory final outcome. Unfortunately, the patient was readmitted within 6 weeks with swollen papulonodular erythematous areas to both thighs, corresponding to the previous Integra™ site (*Fig. 1*). Interestingly, the recent graft sites on the upper abdomen were entirely normal.

The majority of investigations were unremarkable, except elevated C reactive protein and eosinophils with normal white blood cells on peripheral blood film. Wound swabs taken from her thighs and sent for culture failed to identify a causative microbial pathogen and no response was achieved with antibiotic usage. Incision biopsies showed inflammatory process at mid-deep dermal layers. The patch test and immunological studies were negative for hypersensitivity reaction, although the patient responded

Fig. 1 - Left Thigh - Immunological reaction to Integra site, seven years after first application.

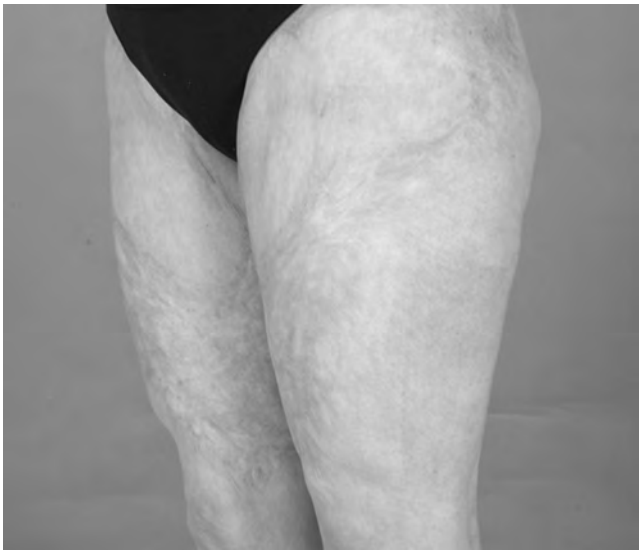

Fig. 2 - Left Thigh - Immunological reaction settled.

to topical steroids. She had a slow but protracted recovery (*Fig. 2*). To the best of our knowledge, this finding is not previously reported in the literature.

Discussion

Advances in medical and surgical care have improved the overall outcome and reduced mortality from major and complex burns.[1,5] This is largely due to better patient and wound care, but also to a greater understanding of physiologic and metabolic consequences of burn injuries.[1] The last decade has also witnessed rapid expansion in the number of bioengineered skin replacements, ranging from temporary epidermal to permanent dermal replacement systems to secure better aesthetic and functional outcomes.[6] In order to achieve favourable outcomes, early excision of burn wounds and closure of defect are fundamental. This can be challenging in burns over 40% TBSA due to limited availability of donor sites.[7] In 1981 Burke reported on his experience of using Integra™ in 10 patients to provide wound cover of up to 60% of the total TBSA. Since then, Integra™ has been established as an important treatment option in the management of acute burns and reconstructive surgery such as scar contracture release, lower limb defects and cancer surgery.[8-10]

Histological analysis of Integra™ shows complete replacement of the artificial skin with the host dermis. Microscopically, both papillary and reticular dermis show remarkable differentiation and are structurally comparable to normal skin.[11] Four distinct phases of dermal regeneration - imbibition, fibroblast migration, neovascularisation, remodelling and maturation - have been reported. The new collagen is histologically indistinguishable from normal dermal collagen.[5] Full vascularisation is achieved within 2-4 weeks.[4,11]

There is a great deal of literature available outlining the successful use of Integra™ in various reconstructive procedures. Lee et al. presented seven cases with Integra™ resurfacing for complex lower limb burn injuries with tendons, open joints and exposed bones. All patients had stable wound coverage with Integra™ and split-thickness skin graft, and none required further surgical procedure for wound closure.[6] Integra™ has been successfully used on bony scalp after burn injury and cancer resection.[3,10] Tufaro et al.[12] presented 100% graft take on four patients with Integra™ resurfacing on bony and burned scalp. Komorowska et al.[13] also reported their experience of Integra™ reconstruction on complex scalp wounds: among the seven patients treated, graft take was successful bar one case of recurrence requiring further treatment. Fullhaber et al.[14] presented successful long-term results of 19 patients who underwent Integra™ reconstruction on scalp following cancer resection. They observed no local recurrence after 72 months follow-up. They reported multiple small, regular, round-shaped ulcerations and partial necrosis in one case, when the patient developed renal failure 29 months after the initial operation.[14] We also noted an unusual hypersensitivity at Integra™ site seven years post reconstruction. Although patch test and immunological studies were negative, the patient responded to topical steroids.

Infection still remains the most commonly reported complication of Integra™ use.[3,10] We experienced five local infections at the graft site. We believe careful wound bed excision and meticulous haemostasis are important. In addition, we also prescribe flucloxacillin to all our patients.

Conclusion

Integra™ is a safe, reliable and valid alternative option for closure of large burn wounds when inadequate healthy donor site is available. Integra™ reduces long-term formation of postoperative contracture in a similar way to full-thickness skin grafting; but unlike full-thickness skin grafts Integra™ has unlimited availability.[4] The main difficulties with Integra™ are its two stage procedure, expert application, risk of infection, frequent dressing changes, wound assessment, cost of purchase and storage.

Our experience of the use of Integra™ has been mixed. We noticed from our results that Integra™ take was very good initially but because of shear stress, movement and rehabilitation the overall outcome was decreased slightly at the shoulder. Nonetheless, we observed that the pliability, final functional and cosmetic appearance with Integra™ dermal regeneration template were satisfactory to both patient and surgeon. We believe that Integra™ can be considered as a promising modality for the treatment of both acute burns and in reconstructive surgery.

RÉSUMÉ. La disponibilité limitée des sites donneurs autologues pose des défis importants pour la reconstruction des tissus mous des brûlures graves et complexes. Integra™ est un modèle de régénération dermique à double-couche qui a joué un rôle important dans la reconstruction des tissus mous depuis sa première utilisation pour des défauts des brûlures de pleine épaisseur. L'objectif de cette étude est de rapporter notre expérience institutionnelle d'Integra™ dans la gestion des brûlures, pendant une période de 4 ans et mettre en évidence une réaction inhabituelle à sa deuxième application. De Septembre 2007 à Août 2011 l'Integra™ a été utilisé dans la gestion des brûlures dans vingt-quatre cas. Les données sur les caractéristiques démographiques des patients, y compris les co-morbidités, les données opératoires, les complications, la reconstruction secondaire et les résultats ont été enregistrés. Integra™ a été utilisée chez 24 patients dans 37 sites anatomiques. Un patient qui est décédé 3 semaines après la blessure et le premier stade de l'application Integra™ a été exclus de l'étude. La greffe de peau mince a été réalisée dans un délai moyen de 23 jours (avec une gamme de 7-55 jours) et la moyenne prise de greffon était de 87 % (avec une gamme de 75-100%) Cinq cas d'infection locale au site de la greffe ont été enregistrées. La durée moyenne d'hospitalisation était de 47 jours (extrêmes: 1-162 jours). Le temps moyen de suivi était de 17 mois (extrêmes: 9-34 mois). Dans l'ensemble, notre expérience avec Integra™ a été mélangé : c'est satisfaisant avec le resurfaçage des brûlures graves mais très bon avec la reconstruction secondaire. Le principal avantage d'Integra™ est sa disponibilité immédiate en quantités illimitées pour la reconstruction des tissus mous des brûlures importantes et complexes. Les principaux inconvénients sont les incidences financières, la procédure en deux étapes, les soins de plaies complexes et les risques d'infection. Nous croyons qu'Integra™ peut être considéré comme une modalité prometteuse pour la gestion des brûlures.

Mots-clés: brûlures, pansements cutanés, substitut dermique, procédures chirurgicales de reconstruction, libération contracture

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