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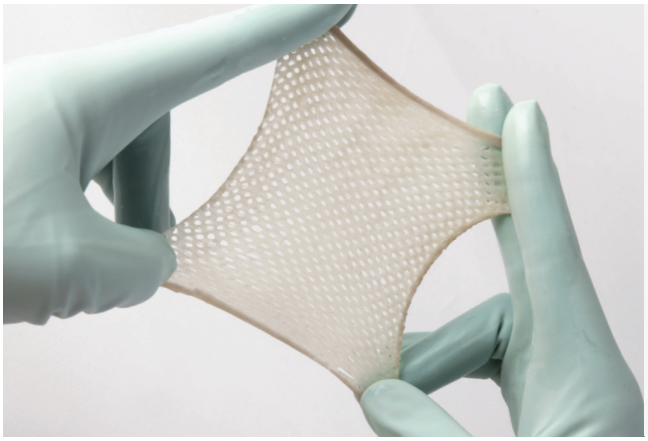
TREATMENT OF RECALCITRANT DIABETIC FOOT ULCERS WITH DERMAL ALLOGRAFT (ALLOSKIN™ RT) IN A CLINICAL OFFICE SETTING

Pam Sabet, DPM, Donald Green, DPM
Scripps Mercy Hospital, San Diego, CA

ABSTRACT

A new, sterile, room temperature storage skin allograft is available, eliminating the necessity for special storage conditions. This case series describes 10 patients suffering from diabetic foot ulcers, all of which had not previously responded to other treatments. All wounds achieved closure with the use of AlloSkin™ RT.



Introduction

An extensive bibliography exists detailing the efficacy of allograft skin as an adjuvant to jumpstart wound healing in stalled wounds.[7,9,10,11] While the vast body of clinical reports support the use of *cryopreserved* allograft skin, a proportion of wound treatment has moved into the out-patient clinical setting, where many clinicians do not have access to a cryo-rated (–80˚ C) freezer. Now a room temperature storage skin allograft is available eliminating the necessity for a cryo freezer. Previous studies have looked at the general efficacy of such skin grafts in wound care, but no case study has been published charting wound healing in recalcitrant lower extremity wounds treated with dermal skin allografts stored at room temperature.

Allograft skin is commonly used on a broad spectrum of complex wounds including lower extremity wounds and foot ulcers caused by diabetes, trauma, arterial and venous disease.[3,4,5,6,8,9] Once adhered to the wound, allograft skin not only serves as a prophylactic to bacterial invasion,[7,8] but also recruits immune cells to the wound site to manage bacteria and other contamination.[1,2,5,7,8,9,11,13] Biologic closure for the wound is critical to keep bacterial levels sufficiently low to effect healing. Agents that act as biologic dressings are reported to allow inflammatory tissue to function optimally, allowing phagocytosis to occur efficiently.[13] Allograft skin acts as a mechanical barrier to help the wound bed preserve electrolytes, proteins and heat—all critical elements in the healing process and cellular regeneration.[7] These factors make allograft skin an ideal treatment option for use in recalcitrant wounds like diabetic foot ulcers that have stalled in the healing process.

AlloSkin™ RT Dermal Allograft (AlloSource®, Centennial, CO) is a sterile, skin allograft that is meshed in 1:1 ratio and processed such that it can be stored at room temperature. Because the patient does not need to be taken to the OR for application of this allograft, it may prove to be an effective and readily accessible treatment modality in the clinical and private office settings for non-healing diabetic foot ulcers. Furthermore, unlike bioengineered skin substitutes requiring cold storage and timely use once received from the manufacturer, AlloSkin RT can be stored at ambient room temperature and has a shelf life of two years. Regulated by the FDA's Center for Biologics Evaluation and Research as a minimally manipulated, transplantable allograft tissue (21 CFR 1270 and 1271)[12], AlloSkin RT is available for homologous use in treating integumental defects.

In this article, data is presented regarding the effectiveness of AlloSkin RT gathered from 10 clinic patients with refractory lower extremity ulcers that have failed other treatment modalities.

Patients and Methods

This prospective 10 patient case series on recalcitrant (greater than four weeks in duration) lower limb diabetic ulcers that were unresponsive to other treatment modalities was created to define (1) the effectiveness of AlloSkin RT as an adjunct to wound closure in lower extremity diabetic ulcers, (2) the number of AlloSkin RT grafts required to achieve wound closure and (3) what healing rate associated with use of AlloSkin RT might be expected when treating ulcers with dermal skin allograft. Exclusion criterion is the presence of gross infection at the wound site. The study was conducted according to the principles of Good Clinical Practices proposed by the Office for Human Research Protections (OHRP) and the Scripps Institutional Review Board (Scripps Office for the Protection of Research Subjects) provided oversight for the conduct of our case study series.

The patient population age ranged from 42–62 years with six males and four females. All skin ulcers were classified as full thickness ulcers, either Grade 1 or Grade 2, using the Wagner Classification of Diabetic Foot Ulcers:

Wagner Classification of Diabetic Foot Ulcers

Grade 0: No ulcer in a high risk foot.

Grade 1: Superficial ulcer involving the full skin thickness but not underlying tissues.

Grade 2: Deep ulcer, penetrating down to ligaments and muscle, but no bone involvement or abscess formation.

Grade 3: Deep ulcer with cellulitis or abscess formation, often with osteomyelitis.

Grade 4: Localized gangrene.

Grade 5: Extensive gangrene involving the whole foot.

All patients selected for this study were patients of the Scripps Mercy Hospital Clinic. Once the patient was selected to participate in the study, the ulcer description and measurement were recorded. Each ulcer was debrided to healthy granular tissue. During the same visit, AlloSkin RT Dermal Allograft was placed on the wound and secured either using 3-0 nylon sutures with a single stitch in graft corners or utilizing sterile adhesive strips. The product comes from the processor as a sterile packaged allograft, which is applied to the wound in a sterile fashion with the reticular side of the cadaveric dermis down and in contact with

the entire wound topography. The wounds were dressed with Adaptic® and Silvercel® (both from Systagenix, Gargrave, U.K.), Kerlix™ 4x4 gauze (Covidien, Mansfield, MA), and wrapped with an Ace™ Bandage (3M, St. Paul, MN). The patients were instructed to follow up on a weekly basis. If the wound was on a weightbearing surface, the patient would require non-weightbearing status, e.g., through the use of crutches or a Roll-A-Bout™ walker (Roll-A-Bout, Frederica, DE).

During each visit, the dressings were removed and the wound was re-measured. The investigator would determine if a new graft was necessary depending on uptake of the skin graft during each visit. A new graft was applied when the surrounding would bed edges exhibited epithelialization, and the would decreased in area with resulting granulation tissue formation under the existing graft.

Regardless of whether or not the wound required a new skin graft, the wound would be re-dressed in the same manner as described above.

Results

The number of patient clinic visits ranged from 7 to 20.* Wound size for the patient population ranged from 5.52 cm^2 to 90.72 cm^2 (Table 1). All patients in this study achieved wound closure. Each patient required at least two skin grafts and some patients required up to five total skin grafts to achieve full wound closure.

* There was hypergranulation reported in Patient 2 which we believe delayed time to wound closure. We did not apply the skin graft on the hypergranulated tissue until it resolved. On that specific case, we applied a silver nitrate stick to the hypergranulated tissue, week after week, until a healthy smooth wound base was achieved for placement of a new skingraft.

PATIENT	1	2	3	4	5	6	7	8	9	10
WOUND AREA AT INITIAL GRAFT (cm^2)	24.5	68.88	43.2	44.5	16.5	90.72	26.0	48.98	22.4	5.52
TOTAL NUMBER OF GRAFTS TO CLOSURE	3	4	5	3	3	5	3	4	3	2

Table 1. Wound size (cm^2) at initiation of study and total number of AlloSkin™ RT allografts used to achieve wound closure.

Discussion

Using a paired sample test, the wound closure rate was significant in our patient population between the first and seventh clinic visit versus measured total wound area, with a P value of 0.002. The reason we compared the first to the seventh clinic visit was because all of our patients required at least seven visits (with a maximum of 20 visits for one individual). No complications occurred with the AlloSkin RT graft in the study population.

Based on our study, it appears AlloSkin RT is a satisfactory graft to have available in clinic. The fact that it does not require freezing makes it easily accessible. All of our patients were enrolled in the study until complete wound closure was achieved. Patients were able to progress to wound healing with the graft despite using other treatment modalities in the past and not progressing to wound closure.

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