Abstract

Background: In case of large burn injuries, split-thickness skin graft (STSG) is limited by donor skin availability. It is not possible to achieve an expansion of more than 1:9 using conventional STSG. Here we introduce Xpansion® micrografting technique, which allows a substantially larger expansion ratio enabling adequate coverage of large wounds. Methods: Pre-clinical and clinical studies using the Xpansion® micrografting technique were reviewed in this study. In each pre-clinical study, the subject had a control wound and a substantially larger expansion ratio enabling adequate coverage of large wounds. Methods: Pre-clinical and clinical studies using expansion ratio and also in chronic ulcer wounds resistant to conventional therapies. Conclusions: This new technique has two main advantages: 1) In large wounds such as burn injuries, it provides an expansion ratio of 1:100, 2) In small wounds, it enables the wound care practitioner to graft the wound in an outpatient setting without the need for an operating room.

Keywords: Xpansion®, micrografting, split-thickness skin graft (STSG), wound healing

Background

Soon after Riverdin reported the first case of skin grafting in humans in 1869, Ollier reported in 1872 the advantages of carrying some dermis with the epidermis in a graft.1 Full-thickness skin grafts (FTSG) incorporating the full-thickness of the dermis and epidermis have the maximum advantages. They tend to resemble normal skin better than split-thickness grafts (STSG). They provide more padding, a better color match, a more nearly normal hair pattern, better elasticity and pliability, and they inhibit wound contraction in the recipient site. However, because they require ideal conditions for survival, full-thickness skin grafts (FTSG) must be placed in a vascular recipient site. Their thickness requires more nourishment prior to the establishment of vascular integrity. FTSG donor sites cannot heal spontaneously since no skin appendages are left behind. Therefore, the size of the graft is limited to dimensions which will allow primary closure of the donor site. For these reasons, when larger deficits of skin exist or the recipient areas have less than ideal vascularity, STSG have been the mainstays of treatment for traumatic injuries involving loss of skin secondary to burn injuries, trauma or chronic wounds.2 Use of STSG results in aesthetically and functionally improved wound healing since these wounds would have otherwise healed mainly through wound contraction and limited epithelialization from wound margins.3 In case of large burn injuries, STSG might be limited by availability of the donor skin. This limitation can be partially overcome by meshing the STSG to an expansion ratio of up to 1:10. However, expansion of STSG results in 'fish net' appearance with increased degree of meshing and therefore, the suitable expansion ratio is generally not more than 1:6.3,4 There have been multiple attempts to increase the limited expansion ratio of STSG. Meek’s technology was introduced in 1958, which achieved an expansion of 1:10 by mincing the skin grafts into small pieces.5 In this technology each minced skin graft serves as an island of regeneration and provides increased border for re-epithelialization [Figure 1]. However, the complicated instrumentation and the need to orient the minced skin grafts dermal side down resulted in limited adoption of the technique.6-8 Cultured epithelial autografts (CEA) have also been evaluated to possibly provide a significantly increased expansion ratios of up to 1:1000.9-13 However, this two staged procedure is extremely expensive, time consuming and requires good manufacturing practice (GMP) level laboratory facilities. Also, these cultured cell sheets are fragile, extremely susceptible to mechanical shear and lack a dermal compo-

Figure 1. Principle of increased expansion ratio of Skin micrografts. Adapted from Meek technique
Use of cultured allograft cell technology as biologic dressings has been studied in human subjects. It is also limited by aforementioned problems and requires multiple applications to achieve statistically significant efficacy as compared to the control wounds.

We have developed a new mincing methodology to address the limited expansion ratio of STSG. It is possible to achieve up to a 1:100 expansion ratio for skin grafts using this technique. It has been demonstrated in a previous study that the orientation of the skin graft is irrelevant in a wet or moist environment. We have also published several studies in a swine model evaluating the efficacy of wound healing using Xpansion® micrografting technique and comparing it to other conventional wound healing techniques. Multiple clinical reports have demonstrated optimal wound healing with this technique in human subjects.

Methods

DEVICE

The Xpansion® kit includes a hand-powered, pre-calibrated dermatome device for producing uniform STSGs, and an associated micro-autografting mincer device that consists of 24 parallel rotating cutting disks, which are 0.8 mm apart (Figure 2). The device is commercially available through SteadMed Inc, Fort Worth, Texas. Using this device, the skin graft is cut twice, with the second cut in a perpendicular direction to the first cut. This results in generation of multiple 0.8 x 0.8 mm micrografts (Figure 3).

METHODOLOGY

An extensive literature review was done using Pubmed, Medline and Google Scholar investigating the pre-clinical and clinical studies utilizing this new technique. All the available studies were included in our manuscript for discussion.

Results

PRE-CLINICAL STUDIES

In all pre-clinical studies, full-thickness wounds were created on the dorsum of female Yorkshire pigs. 0.8 x 0.8 mm micrografts were transplanted on the wounds without paying attention to the orientation of the grafts. In multiple studies, the wound healing was compared to non-transplanted wounds as well wounds covered with STSG and cultured keratinocytes. Different biopsy time points were studied to investigate the different wound healing techniques using histomorphometric analysis.

The purpose of the first study was to demonstrate the survivability of the micrografts in a wound bed and observe their ability to improve wound healing when compared to non-transplanted control wounds. The micrografts were transplanted on a full thickness wound bed with an expansion ratio of 1:100. Wound biopsies were taken on pre-determined days and wound healing was compared to control wounds. Histological analysis demonstrated that the micrografts were uniformly incorporated in the full-thickness wounds (Figure 4). The epithelial regeneration was significantly increased in the wounds transplanted with micrografts as compared to non-transplanted wounds (Figure 5). Conversely, the wound con-
traction was higher in the non-transplanted wounds. This study established that the transplanted micrografts survive in the wound and contribute towards faster re-epithelialization and decreased wound contraction.

Another study compared wound healing in full-thickness swine wounds treated with micrografts (1:100 expansion ratio), STSG, and cultured keratinocytes. The results demonstrated that both the STSG and the micrograft treated wounds had significantly decreased wound contraction and better Vancouver Scar Scale scoring when compared to non-transplanted group. Epidermal maturation determined by the thickness of neoeidermis and the strength of dermal-epidermal junction measured by rete ridges per linear mm were significantly increased in the STSG and micrografts groups when compared to non-transplanted control group. There was no significant difference in wound healing between STSG and micrograft group based on any of these parameters. The cultured keratinocyte group had decreased rate of re-epithelialization and increased wound contraction when compared to the STSG or micrografts groups.

We have used a polyurethane wound chamber containing keratinocyte culture media inducing a wet environment for these experiments. To facilitate the use of micrografts in a clinical setting, the wound chambers were replaced by a common moist dressing (hydrogel and foam). The re-epithelialization rate of the wounds treated with micrografts and moist dressing was significantly higher than the control moist dressing alone.

Clinical Reports

There have been several clinical reports of successful wound healing of chronic ulcers and large area burns with Xpansion micrografting technique. During Operation Iraqi Freedom (OIF), a 25 year old civilian suffered from 54% TBSA full-thickness burn from a propane tank explosion. Given the severity of the injury and scarcity of donor tissue, more than 1000 cm² of burned surface area over chest and right ankle was covered using Xpansion® micrografting technique. The micrografts were transplanted, without paying attention to the dermal orientation, at an expansion ratio of 1:100. Within 30 days, the patient achieved complete wound closure (Figure 6). When attempting to achieve as many of them as possible, some patients required repeated skin harvest from the donor site, which increases the risk of infection in a large burn injury. Even though this technique involves the principles of the Meek’s technique, it is different in multiple ways. The most important difference is that there is no need to orient the graft during transplantation, which makes this technique easily adaptable. Also, it enables 100 times expansion in comparison to 10-fold expansion achieved with Meek’s technique.

The micrografts help in re-epithelialization of the full-thickness wound by acting as an island of regeneration. Dividing the STSG into very small pieces increases the border length, which increases the regenerative capacity of the skin grafts (Figure 6). When attempting to achieve as many of them advantages of a FTSG while allowing the donor site to heal spontaneously with a STSG, the more dermis contained in a STSG the better. One advantage directly correlated to the amount of dermis in a STSG is the amount of wound contraction that occurs in the grafted wound. The amount of dermis present in the Xpansion minced micro-autograft determines the degree of contraction in the recipient bed. This is especially critical in the facial and extremities wounds where wound contraction can result in a limiting contracture.

In a clinical report, Smith et al. (2014) demonstrated complete closure of the wounds and healing with minimal scar at 6 weeks with micrografting technique. Mannella et al (2014) evaluated the utility of micrografting in three different patients with non-healing ulcers, which were non-responsive to conventional treatments such as negative pressure wound therapy, STSG, hyperbaric oxygen and compression therapy. Approximately 90% of the wounds completely re-epithelialized within 2 weeks in one patient and the ulcers completely healed in all the three patients using Xpansion® micrografting technique. Micrografting was performed in an outpatient clinic under local anesthesia in all the patients.

Discussion

The Xpansion® micrografting technique provides a solution to most commonly encountered limitation of STSG, which involves limited donor skin availability. It reduces the need for repeated skin harvest from the donor site, which increases the risk of infection in a large burn injury. Even though this technique involves the principles of the Meek’s technique, it is different in multiple ways. The most important difference is that there is no need to orient the graft during transplantation, which makes this technique easily adaptable. Also, it enables 100 times expansion in comparison to 10-fold expansion achieved with Meek’s technique.

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The fibroblasts in the mesenchymal mesodermal tissue of the dermis containing minced-autografts produce high levels of growth factors which facilitate the proliferative phase of wound healing. The presence of a supportive microenvironment surrounding the keratinocytes and fibroblasts of the skin grafts enhances the re-epithelialization process.

Figure 6. Complete re-epithelialization using Skin Micrograft technique in a patient with > 50% burn injury during Operation Iraqi Freedom.
micrografts might explain better wound healing parameters as compared to the cultured keratinocytes or epithelial grafts. The minced skin contains elevated levels of tumor necrosis factor alpha (TNFα), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF), all which favor re-epithelialization, neo-angiogenesis, and extracellular matrix deposition.\(^3\)\(^1\)\(^3\)\(^2\) This advantage is not present in epidermal grafts containing only keratinocytes.

Dermis containing minced micro-autografts also provides improved tensile strength to the repaired wound. Epidermal-only grafts are not stable and provide very limited strength. The long history of cultured epithelial autografts (CEA) demonstrated that they were fragile and susceptible to blistering and shearing.\(^3\)\(^2\) Epidermal grafts contain no rete pegs or ridges (Figure 7). The primary function of the dermis is to provide nourishment, mechanical support and tensile strength to the epidermis which has very limited mechanical strength.\(^3\)\(^6\)\(^3\)\(^5\) The tensile strength of the dermis (ultimate load divided by cross-section area) ranges from 5-30 Newtons/mm\(^2\).\(^3\)\(^6\)\(^3\)\(^7\) This is maximum at 21 N/mm\(^2\) at age 8 and decreases to 17 N/mm\(^2\) at age 95.

In order to realize the advantages of dermis in the intermediate thickness skin graft donor site: a prospective clinical trial for comparison of five different dressing materials. Burns. 2010; 36: 999 – 1005.


Conflict of interest: Dr. Eriksson is a member of a limited liability company that receives royalty payments on the sale of Xpansion micrografting device. All other author(s) declared no potential conflicts of interest with respect to research, authorship and/or publication of this article. They received no financial support for this research work.