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# Topical negative pressure improves autograft take by altering nutrient diffusion: A hypothesis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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The one-step surgical procedure for dermal substitutes combined with topical negative pressure (TNP) has proven effective for treating deep skin defects with improved graft take. The primary mechanism by which TNP improves autograft take is unknown. Some studies suggest that TNP promotes the rapid angiogenesis of dermal substitutes, improving graft take. However, at the early stage of one-step transplantation, the vascular system has not formed and imbibition is the main mode of nutrient supply. TNP can shorten the diffusion distance from the wound bed to the graft, leading to the timely renewal of the wound exudate via suction, removing any surplus exudate, and reducing tissue edema. In addition, TNP can regulate the local blood flow and inhibit bacterial colonization. Therefore, we hypothesized that TNP establishes a rapid balance between the nutrient supply to the wound bed and nutritional requirement of the graft via these pathways in the relatively closed, moist environment, improving autograft take. However, this balance could be affected by any negative pressure, intermittent or continuous. It is necessary to test this hypothesis in laboratory and clinical studies of the mode of nutrient supply in the imbibition phase and the change in exudate content.

**MeSH Keywords:** topical negative pressure • wound healing • autograft

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## Background

Dermal substitutes that serve as scaffolds for neotissue ingrowth and deposition have been introduced to the treatment of full-thickness skin defects [1]. For wounds, burns, and orthopedics, commercial substitutes such as Integra®, Pelnac®, MatriDerm®, and AlloDerm® have been used widely with one- or two-step surgical procedures [2–4].

The two-step surgical procedure is used most frequently. For example, Integra®, a bilayer dermal substitute developed by Yannas et al. [5,6], is a commercial collagen-based dermal substitute combined with a silicone top layer that functions as a temporary epidermis to keep the wound moist and to resist infection. The top layer is removed and replaced by a split-thickness autograft when the artificial dermis appears to be vascularized. This two-step procedure seems to be essential for vascularization of the scaffold to ensure that the split-thickness autograft takes. However, these dermal substitutes can take more than 3 weeks to become fully vascularized [7,8]. During this period, the risk of wound infection is high. With this approach, patients require at least 2 operations before complete wound closure.

Recently, the one-step procedure has become increasingly popular. One-step grafting involves the simultaneous application of the dermal substitute and a split-thickness skin graft to close the wound in a single operation. This approach enables earlier wound closure and avoids a second operation, but the presence of a non-vascularized dermal substitute acts as a barrier to nutrient diffusion to the autograft. Hence, graft loss is frequent. In the early stage, before complete vascularization of the dermal substitute, the graft survives only by the diffusion of nutrients from the wound bed. Any barrier between the graft and wound bed can inhibit this process and result in graft loss. The application of topical negative pressure (TNP) in the one-step procedure has been shown to improve graft take [9,10]. Some researchers stated that TNP reduces the time necessary for vascular ingrowth into the dermal substitute and improves graft take [9], although the exact mechanism and effect of TNP on graft take are not yet fully understood.

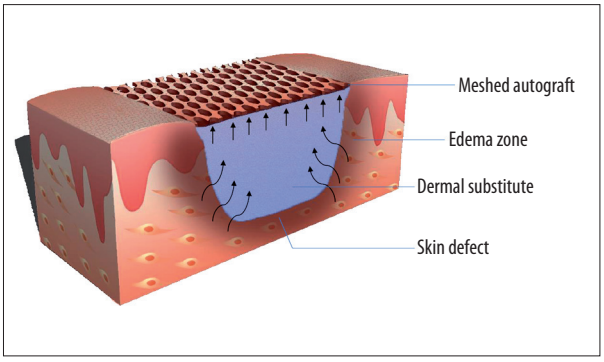


**Figure 1.** Illustration of the traditional one-step surgical procedure used to repair partially deep skin defects with a dermal substitute and meshed autograft. The black arrows indicate possible routes of nutrient diffusion in the imbibition phase. The edema zone around the wound is evident. A compression dressing is usually used in such cases.

## The Hypothesis

Topical negative pressure leads to a rapid balance between the nutrient supply from the wound bed and the nutritional requirements of the graft in the relatively closed, moist environment, and further improves the take of autografts.

## Evaluation of the Hypothesis

Dermal substitutes, which lack a vascular structure, can be applied in a one-step surgical procedure to repair full-thickness skin defects. In the early stage of transplantation, the main nutrient supply is via simple diffusion from the wound bed and surrounding tissues (Figure 1). Then, angiogenesis begins and takes at least 3 weeks to finish [8]. Simple diffusion is an inefficient mode of nutrient supply and is affected by hematomas, seromas, infection, and dermal substitutes [11,12], as is the removal of metabolic products.

Topical negative pressure can shorten the diffusion distance from the wound bed to the graft and the suction ensures the timely renewal of the wound exudate. Since local tissue edema increases the after-load on capillaries and decreases the supply of oxygen, nutrients, and bioactive factors to the wound, TNP can remove the surplus wound exudate and reduce the tissue edema [13,14]. In addition, TNP can regulate the local blood flow and inhibit bacterial colonization. Therefore, TNP has the potential to improve the nutrient supply to wounds and promote wound healing (Figure 2).

The rapid angiogenesis of dermal substitutes is also very important for graft take. TNP promotes cell proliferation and penetration, and angiogenesis [15]. Molnar et al. used TNP to manage Integra®-treated complex tissue defects and observed an Integra® take rate of 96%, while split-thickness skin grafting performed at 4–11 days had a 93% take rate [16]. A prospective study by Moiemen et al. indicated that the application of TNP dressings to dermal templates reduced the shearing force, limited seroma and hematoma formation, simplified wound care, and improved patient comfort, but did not demonstrate that TNP accelerates neovascularisation as verified by the presence of histologically patent vascular channels [17]. Hence, the level of angiogenesis is not related to the improved autograft





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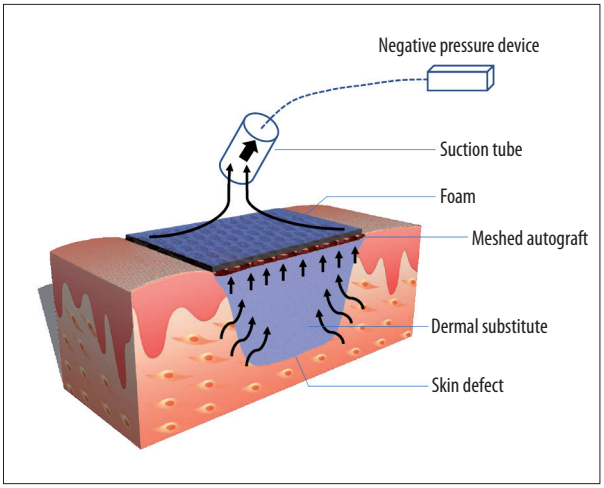


**Figure 2.** Illustration of the novel one-step surgical procedure that includes topical negative pressure (TNP). The black arrows indicate the possible routes of the wound exudate during the early transplantation stage. TNP removes the surplus wound exudate, reduces the tissue edema, and improves the local nutrient exchange.

take in the one-step procedure. It appears that nutrient diffusion is critical for graft take before complete vascularization of the dermal substitute. In the early stage of transplantation, TNP affects the barrier resulting from the dermal substitute, and alters the mode of nutrient supply in the one-step surgical procedure. Moreover, TNP improves autograft take by establishing a rapid balance between the nutrient supply from the wound bed and nutritional requirements of the graft in the relatively closed, moist environment.

## Conclusions and Future Perspectives

We hypothesized that TNP would result in a rapid balance between the nutrient supply from the wound bed and the nutritional requirements of the graft in the relatively closed, moist environment, improving the autograft take. However, this balance can be affected by the negative pressure and whether it is intermittent or continuous. One study showed that intermittent negative pressure has greater benefits in terms of cell ingress and local nutrient exchange [18]. Laboratory and clinical studies should test our hypothesis, especially the effects of TNP during the imbibition phase.

### Conflicts of interest statement

The authors declare that they have no conflict of interest in any matter related to this work.

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