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# Hair follicle—containing punch grafts accelerate chronic ulcer healing: A randomized controlled trial



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**Background:** A prominent role of hair follicle—derived cells in epidermal wound closure is now well established but clinical translation of basic research findings is scarce. Although skin punch grafts have been used as a therapeutic intervention to improve healing of chronic leg ulcers, they are normally harvested from nonhairy areas, thus not taking advantage of the reported role of the hair follicle as a wound-healing promoter.

**Objective:** We sought to substantiate the role of hair follicles in venous leg ulcer healing by transplanting hair follicle—containing versus nonhairy punch grafts.

**Methods:** This was a randomized controlled trial with intraindividual comparison of hair follicle scalp grafts and nonhairy skin grafts transplanted in parallel into 2 halves of the same ulcer.

**Results:** Ulcer healing measured as the average percentage reduction 18 weeks postintervention was significantly increased ( $P = .002$ ) in the hair follicle group with a 75.15% (SD 23.03) ulcer area reduction compared with 33.07% (SD 46.17) in the control group (nonhairy grafts).

**Limitations:** Sample size was small ( $n = 12$ ).

**Conclusion:** Autologous transplantation of terminal hair follicles by scalp punch grafts induces better healing than punch grafts harvested from nonhairy areas. Hair punch grafting is a minimally invasive surgical procedure that appears to be effective as a therapeutic tool for chronic venous leg ulcers. (*J Am Acad Dermatol* 2016;75:1007-14.)

**Key words:** follicular unit; hair follicle stem cells; hair transplantation; punch grafting; skin grafting; venous leg ulcer; wound healing.

Numerous studies emphasize the role of hair follicle—derived cells in promoting the wound-healing response.<sup>1-11</sup> Bishop<sup>12</sup> pioneer experiments demonstrated that re-epithelialization started around the remaining hair follicles, and that when the skin was destroyed down to the reticular dermis, the granulation

tissue originated from the connective tissue surrounding the follicles. However, despite decades of clinician awareness of the importance of hair follicles in wound healing, relatively few attempts have been made to use hair follicles or hair follicle—derived cells as a therapeutic tool in clinical practice.<sup>13-21</sup>

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A surgical procedure normally used to treat non-healing venous leg ulcers is the autologous skin transplantation (skin grafting) in all its variations, including pinch grafts, punch grafts, and split-thickness and full-thickness skin grafts.<sup>22-25</sup> However, none of these surgical methods were specifically aimed to include intact terminal hair follicles. In particular, punch graft harvesting has traditionally been performed using the thigh or buttocks<sup>26-28</sup> where the skin graft is preferentially composed of epidermal and dermal tissue with an absence of terminal hair follicles.

A pilot study showed that hair scalp punch grafts transplanted into the wound bed of chronic leg ulcers stimulated healing in the majority of patients.<sup>18</sup> Recently, a retrospective 14-case series supported those observations,<sup>21</sup> showing total re-epithelialization when nonhealing ulcers were covered by hair follicle units, although assessment was difficult because it was not randomized and lacked a control group.

Here, the results of a randomized controlled trial comparing the healing capacity of hair follicle scalp grafts and nonhairy skin grafts are reported. To compare whether a difference in healing capacity exists, both types of grafts were transplanted into the same ulcer, at the same density, and using the same punch size.

## METHODS

### Study design

This study was designed as an open, single-center, randomized controlled trial with intraindividual comparison. Each patient had 1 leg ulcer that was divided into 2 halves of as similar a size as possible. To avoid bias ulcers were divided vertically in 2 halves because the venous return flows upwards from bottom to top. The 2 halves were randomized for each wound into an experimental and control area by a methodologist blinded to study data (Fig 1). The random allocation sequence was concealed from the surgeon until intervention. The experimental half was transplanted with 2-mm punch grafts harvested from the scalp, and the control half with 2-mm punch grafts from abdominal skin with no visible hairs.

To fix the references for each half throughout the duration of the study, an ink dot was tattooed onto

the proximal and distal points of a line that divided the ulcer into 2 halves (Fig 2). The number of grafts to be transplanted per ulcer depended on its size. Because each ulcer was divided into 2 equal-sized halves, the same number of grafts was implanted in each half with a density of 5 grafts/cm<sup>2</sup>.

### Patient eligibility

In all, 17 patients with chronic leg ulcers of venous origin that had not responded to topical medications and standard ambulatory medical care (leg elevation, compression therapy, debridement of devitalized tissue, occlusive dressings) for a duration longer than 4 months were examined. Patients with ulcers of other, nonvenous causes; aged younger than 18 years or older than

95 years; with diagnosed coagulopathies; having hip or knee prosthesis on the same limb; having ulcers with signs of active infection; with contraindications for the hair transplant technique; who were incapacitated to participate in the study; or who did not sign the informed consent form were not considered for this study. Five patients were excluded and 12 patients were included in the study.

The diagnosis of venous insufficiency was based on clinical and physical examination (telangiectasia or reticular veins, varicose veins, edema, red-to-brown skin discoloration, lipodermatosclerosis). All patients had severe chronic venous disease according to the Venous Clinical Severity Score.<sup>29</sup> A Doppler study was performed to rule out associated arterial disease. Only patients in whom the arterial peripheral system was not affected were included in this study.

### Description of the intervention

All interventions were performed in an outpatient setting by the same dermatologic surgeon (F. J.) experienced in hair transplantation. After local anesthesia (lidocaine 1% and epinephrine 1/100,000; B. Braun, Melsungen, Germany), hairy and nonhairy grafts were harvested using 2.00-mm biopsy punches (GlaxoSmithKline, Bad Oldesloe, Germany). A slit was made in the wound bed with a needle and the grafts were completely inserted with a fine-tipped forceps leaving only the epidermis at the surface level of the ulcer. After the intervention,

### CAPSULE SUMMARY

- Hair follicles play a role in wound healing. Punch grafts induce healing of chronic venous leg ulcers.
- Hair follicle-containing punch grafts accelerate wound closure as compared with nonhairy grafts.
- Punch grafts from the scalp appear to accelerate wound healing and represent a therapeutic option for chronic venous leg ulcers.

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