What Do We Know About Hair Growth Induced by Wounding and Its Therapeutic Applications?

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BACKGROUND Many studies have reported the role of hair follicles (HFs) in the wound healing response, and vice versa, the creation of superficial injuries may stimulate hair growth, which has encouraged new treatments for hair loss.

OBJECTIVE To review the phenomenon of wound-induced hair growth and the usefulness of therapeutic procedures based on skin wounding in androgenetic alopecia (AGA).

METHODS A literature search was conducted to review cases of localized hypertrichosis induced by wounds and the role of microneedling, fractional laser, and scalp threading as monotherapy for AGA.

RESULTS Localized hypertrichosis has been extensively reported after bone fractures, burn injury, chronic venous ulcer, etc. Only 2 cases of wound-induced hair neogenesis in humans have been reported. As monotherapy for AGA, 1 of 3 studies of microneedling, 4 of 6 of fractional lasers, and 2 of 3 studies of scalp threading show good efficacy.

CONCLUSION Certain types of wounds seem to stimulate localized hair growth in humans, but the underlying mechanism is unclear. Reports on wound-induced HF neogenesis in humans are anecdotal and questions remain as to whether this is a true phenomenon in humans. Further clinical studies are needed before recommending wound-induced hair growth procedures as therapies for AGA.

A link between hair follicle (HF) growth and wound healing (WH) has been supported by basic research and clinical evidence.[1] This dual HF–WH connection has inspired the use of hair transplant grafts as an alternative novel therapy to accelerate chronic WH and the use of wound-induced procedures to stimulate hair growth. The mechanisms of both processes however (the role of HF as a WH promoter and the role of inflicting controlled wounds for hair growth induction) seem to be different. The role of HF as WH promoter has been explained by the migration of bulge epithelial stem cells to the wounded epidermis,[1,2] the migration of mesenchymal dermal sheath cells to the wounded dermis,[3] and by paracrine effects of the hair follicle during the hair cycle.[4] In contrast, the mechanism of hair growth after wounding in humans seems more likely because of the activation of existing HFs, through changes of the hair cycle (increasing the anagen phase or decreasing the telogen and/or kenogen phase) or activation of signaling pathways that result in increased HF proliferation and thickening of the hair shaft.[5,6] Although wound-induced HF neogenesis (WIHN) has been observed in certain mammals such as rabbits and mice, its occurrence in human skin is still an object of debate.[1] To our knowledge, only 2 cases have been reported as WIHN in humans[7,8]; 1 showed vellus hair regrowth after facial dermabrasion,[7] and the other the appearance of a single terminal hair at the center of a wound 6 months after excision of a basal cell carcinoma on the scalp.[8] We believe that these 2 reports do not provide sufficient and convincing evidence that WIHN actually takes place in humans because it is possible that hair regrowth might have occurred from hair remnants or stem cell activation from existing hairs.

In this article, we will review the clinical evidence of hair growth induced by wounding and the role of several wound-induced procedures such as microneedling, fractional laser, and scalp threading as hair growth therapies for patients with male androgenetic alopecia (AGA) and female pattern hair loss (FPHL).

Methods

A PubMed search and textbook review was performed to identify documentation regarding wound-induced hair follicle neogenesis, wound-induced hair growth, and procedures involving wound creations to treat androgenetic alopecia. The search terms used were: "wound-induced hair neogenesis," "hair regeneration," "Wnt," "WH," "androgenetic alopecia," "microneedling hair," "hypertrichosis," "laser hair growth," and "scalp thread hair." Any review articles, case reports, case series, and clinical trials were included for the literature review.

Results

Wound-Induced Hair Growth in Humans: Clinical Evidence

Fourteen clinical reports have described localized hypertrichosis induced by injuries (Table 1).[9–22] Most of these cases

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The authors have indicated no significant interest with commercial supporters.

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Dermatol Surg 2023;00:1–6
http://dx.doi.org/10.1097/DSS.0000000000003901

occurred after bone fractures,[13,14] orthopedic surgeries,[15,21] or by chronic self-biting,[9] whereas anecdotal cases have been described after burn injury,[11] chronic venous ulcers,[10] inguinal lymphadenectomy,[12] parotidectomy,[16] BCG vaccination,[19] traumatic panniculitis,[17,18] and laceration.[22] The largest prospective study, which involved 117 patients with a history of bone fractures treated with cast application, reported localized hypertrichosis in 40 patients (34.2%).[14] Another case series reported 19 cases of localized hypertrichosis in patients with knee replacement surgery.[15] According to these studies, the hypertrichosis appeared 2 to 6 months after the injuries. In 5 studies, reported spontaneous resolution of acquired hypertrichosis occurred within 3 to 18 months, whereas 9 of 14 studies did not document the duration of hypertrichosis because of lack of follow-ups.[9,11–15,19,20,22] Another limitation of these studies was the lack of histologic and molecular studies.[10–22] The explanation for the spontaneous resolution of hypertrichosis may be the temporary increase of inflammatory molecules, growth factors, and transient angiogenesis during WH.

Therapeutic Procedures Used for Androgenetic Alopecia Based on the Concept of Wound-Induced Hair Growth

Scalp Microneedling

Microneedling is a minimally-invasive procedure using multiple tiny needles that create microscopic wounds on

TABLE 1. Studies Addressing Wound-Induced Localized Hypertrichosis

Author	Cause of Hypertrichosis	*N*	Study Type	Anatomical Site	Duration to Hypertrichosis (mo)	Clinical Course of Hypertrichosis
Ressmann and Butterworth[9]	Chronic self-biting in psychiatric patients	13	Case series	Forearm Wrist Dorsum of hand	NR	NR
Schraibman[10]	Chronic venous ulcer	2	Case report	Leg	2	SR in 18 mo
Shafir and Tsur[11]	Deep second degree burn	1	Case report	Thigh (surrounding the wound)	1/2	Persisted more than 6 mo
Finck et al.[12]	Radical inguinal lymphadenectomy	1	Case report	Leg	5	NR
Bergen[13]	Colles' fracture treated by closed reduction with cast	1	Case report	Forearm	2	Persisted more than 1 mo
Akoglu et al.[14]	Cast application after bone fracture	117	Prospective observational cross-sectional study	Forearm, leg, thigh	NR	34.2% of 117 patients had postfracture hypertrichosis
Gupta et al.[15]	Knee replacement surgery	19	Case series	Knee	8.4	100% of 19 patients had postsurgical hypertrichosis
Syme-Grant and Naasan[16]	Parotidectomy and temporoparietal flap	1	Case report	Face	4	SR within 3 mo
Lee et al.[17] Ploydaeng et al.[18]	Traumatic panniculitis	3	Case reports	Leg	1–2	SR within 5–15 mo
Poonia et al.[19]	BCG vaccination	1	Case report	Thigh	4	NR
Ramot et al.[20]	Facial fat grafting and facelift	1	Case report	Face	1	Persisted more than 4 mo
Al Dhafiri and Boeisa[21]	Surgical tibial lengthening with external fixation	1	Case report	Leg	2	SR within 3 mo
Jassi et al.[22]	Laceration wound treated by suturing	1	Case report	Chin	2	NR

BCG, Bacillus Calmette-Guerin; NR, not reported; SR, spontaneous resolution.

the skin.[23] Only 1 of the 3 randomized clinical studies using 1.5 to 2.5 mm depth microneedles reported a significantly increased hair density, although not hair thickness.[24] The other 2 studies did not reveal any significant improvement.[25,26] (Table 2) It was also reported that microneedling may stimulate hair growth via the Wnt signaling pathway and vascular endothelial growth factor (VEGF).[36]

Fractional Laser

One study using ablative CO_2 laser reported a significant increase in the mean number of hairs and hair diameter in male AGA patients treated with 6 sessions of ablative CO_2 laser alone.[27] Another 2 studies using the nonablative fractional 1,550-nm Erbium glass laser[28,29] and 1 study using nonablative fractional 1,927-nm Thulium laser[31] reported significantly increased hair density and hair shaft diameters in AGA after 12 sessions of laser irradiation (Table 2). In addition, a study of nonablative fractional 1,550-nm Er glass laser[30] also reported significant improvement in hair count after 5 sessions, but hair diameter was not evaluated. Only 1 retrospective study of nonablative 2,940-nm Er:YAG laser claimed good effectiveness.[32] However, because the results were obtained through patient self-evaluation and no hair count or hair diameter measurements were performed, they should be interpreted with caution.[32]

Regarding the duration of the hair growth after laser therapy, 1 study[31] demonstrated decreasing hair count and diameter back to baseline level within 4 weeks after the last laser treatment, whereas the other studies did not mention any follow-ups after the last session of laser irradiation.[27–30,32]

Scalp Thread Embedding

Scalp thread embedding is a procedure in which threads are inserted into the dermal layer of the scalp resulting in intradermal wounds and foreign body reaction. Three studies have been published that used intradermal threading to stimulate hair growth. One pilot study[34] that included 5 patients with male AGA used intradermal monofilament polydioxanone (PDO) threads, whereas another pilot study in a woman with receding temporal hairline received gold thread embedding for facial rejuvenation.[33] The third study was a double-blinded, placebo-controlled trial ($n = 28$)[35] that compared the results between a group of women patients with FPHL treated with monofilament poly-L-lactic acid (PLLA) thread and a group treated with saline. All studies demonstrated significant clinical improvement in hair density and hair thickness.[33–35] However, it should be taken into account that none of these 3 studies gave information about the duration of hair growth or if the spontaneous resolution of hair growth had occurred.[33,34,35] Two studies only provided the hair count and hair mass at the 12th week[34] and the 26th week[35] after the procedure. The other study only provided before and after photos 24 months after the procedure.[33] Short-term complications included mild pain, transient swelling, and bruising. Furthermore, the thread can induce chronic inflammation along with foreign body reaction that could last up to 16 weeks.[39,40]

Discussion

According to our literature search, there is sufficient clinical evidence to support that certain wounds can stimulate localized hair growth, but the specific optimal wound conditions for such stimulation are yet to be discovered. Interestingly, rupture/breakage of the cutaneous surface is not always mandatory to stimulate hair growth. In fact, most reported cases occur in cases of deep traumatic wounds.[14,15] When hypertrichosis occurs after cutaneous injuries, it seems to be more common in chronic injuries (chronic self-biting)[9] than in acute injuries. We speculate 3 possible pathways explaining the phenomenon of wound-induced hair growth (Figure 1). First, chronic inflammation after wounding, which triggers activation of the Wnt signaling pathway[41] in bone healing,[13–15] chronic venous ulcers,[10] panniculitis,[17,18] vaccination sites,[19] and fat grafting.[20] Second, macroenvironment changes (moisture, warmth, and friction), which could explain the localized hypertrichosis observed on the forearms of psychiatric patients with chronic self-biting.[9] And third, increased angiogenesis that could stimulate hair growth by transferring oxygen and nutrients to the healing site[42] that occurred in the hypertrichosis after bone fractures. In this regard, a bone fracture induces a significant amount of bleeding, which leads to a transient hypoxia,[43] causing increased levels of hypoxia-inducible factor 1 alpha. This in turn stimulates VEGF production, resulting in neovascularization.[44,45]

Regarding the clinical application of wound-induced procedures to stimulate hair growth, although microneedling and laser resurfacing modalities have been demonstrated to be generally effective in particular as drug delivery enhancers, an insufficient number of studies have been performed assessing the efficacy of these procedures as monotherapy for AGA. Given that only 1 of 3 studies using microneedling showed a significant improvement in hair count, there is insufficient evidence to support its use for AGA. Although multiple microneedling or laser irradiation sessions are necessary to establish hair growth stimulation, scalp threading seems to be able to provide significant improvement of hair density and hair thickness with just 1 session. The reason may be that the thread can induce longer duration of chronic inflammation along with foreign body reaction compared with a single session of laser irradiation. However, further studies on scalp threading with a larger number of subjects are required to properly evaluate its effectiveness, safety, and complications.

TABLE 2. Studies Addressing Microneedling, Fractional Laser, or Scalp Threading as Monotherapy for AGA in Humans

Author	Procedures	Interval (wk)	No. of Sessions	*N*	Study Type	Result	
						Increased Hair Count (Hairs/cm^2)	Increased Hair Diameter (μm)
Bao et al.[24]	Microneedling (depth 1.5–2.5 mm) for 3–4 passes	2	12	18	Randomized clinical trial (humans)	23.4 ± 5 at week 24 ($p < .001$)	3.2 ± 6.2 (week 24) ($p = .09$)
Bao et al.[25]	Microneedling (depth 1–2 mm) for 3–4 passes	2	12	23		21.53 ± 6.19 at week 24 ($p = .074$)	10.41 ± 4.83 at week 24 ($p = .058$)
Yu et al.[26]	Microneedling (unknown depth) followed by normal saline spray	1	16	10		0.14 ($p = .951$) at week 16	1.0 ± 3.39 ($p = .678$) at week 16
Salah et al.[27]	Ablative fractional CO_2 laser (scanning mode, 1 pulse, spot size 15 mm, power 5 W, dwell time 500 μs, stack 3 then with emission mode spacing 700 μm, density 8.7%, fluence 4.68 J/cm^2, pulse energy 51.6 mJ)	2	6	15	Randomized clinical study	21.2 at week 12 ($p = .005$)	21 at week 12 ($p = .008$)
Meephansan et al.[28]	Nonablative fractional 1,550-nm Erbium glass laser 2 × 12 mm tip, power 6 mJ, 300 spots/cm^2 (static mode) for 2 passes	2	12	23	Uncontrolled clinical trial (humans)	23.48 ± 3.08 at week 16, $p = .001$)	8.22 ± 0.87 ($p = .027$) at week 16
Lee et al.[29]	Nonablative fractional 1,550-nm Erbium glass laser 5–10 mm tip, power 6 mJ, 800 spots/cm^2 (static mode) for 1 pass	2	12	26		57 ± 14 at week 20, $p < .001$)	17 ± 1 ($p < .001$) at week 20
Kim et al.[30]	Nonablative fractional 1550-nm Erbium glass laser with unknown spot size, power 5 mJ, 300 spots/cm2 (static mode) unknown amount of passes	2	5	20	Split scalp study (controlled trial)	20 at week 12 (no *p* value)	NR
Cho et al.[31]	Nonablative fractional 1927-nm Thulium laser with unknown spot size, power 5 w with energy of 4 or 6 mJ in static mode, 100–140 pulses	1	12	10	Split scalp study (uncontrolled trial)	31.4 at week 12 ($p < .001$)	12 at week 12 ($p = .001$)
Day et al.[32]	Nonablative fractional 2940-nm Er:YAG laser (7-mm spot size, 7.00 J/cm^2, 3.3 Hz) for 4 passes	2	8	6	Retrospective cohort clinical study	4 out of 6 patients were satisfied. (No measurement of hair count or hair diameter)	
Kim et al.[33]	Facial rejuvenation with thread and gold thread braided with a strand of absorbable PGA	—	1	1	Case report	Photograph at 24 months after the procedure shows increased hair density	

TABLE 2. Studies Addressing Microneedling, Fractional Laser, or Scalp Threading as Monotherapy for AGA in Humans *(Continued)*

Author	Procedures	Interval (wk)	No. of Sessions	*N*	Study Type	Result	
						Increased Hair Count (Hairs/cm^2)	Increased Hair Diameter (μm)
Bharti et al.[34]	Intradermal insertion of monofilament PDO thread (30 mm long) in a radial orientation with 1 cm spacing between each insertion on balding area of male AGA	—	1	5	Uncontrolled clinical trial	67/cm^2 at week 12	NR
Metwalli et al.[35]	Intradermal insertion of thread monofilament PLLA in a radial orientation with 1-cm spacing between each insertion in FPHL	—	1	28	Double-blinded, placebo-controlled clinical trial	17.77/cm^2 ($p <$ .001) at week 26	Increase hair mass index (Cohen hair check system) 5.55 ($p <$ .001) at week 26

$p \leq .05$ means significant result.
AGA, androgenetic alopecia; FPHL, female pattern hair loss; PDO, polydioxanone; PGA, polyglycolic acid; PLLA, poly-L-lactic acid; NR, not reported.

In conclusion, despite the rise in popularity of the aforementioned minimally-invasive procedures because of their simplicity and short recovery time, there remains a lack of high-quality evidence demonstrating their good efficacy and safety as AGA treatment. Taken together, one implication of these findings is that physicians should be aware of the limited available evidence when considering these procedures. Further randomized controlled studies with larger patient numbers and more appropriate objective outcome measurements are needed to evaluate their true effectiveness and generate standard protocols for each procedure.

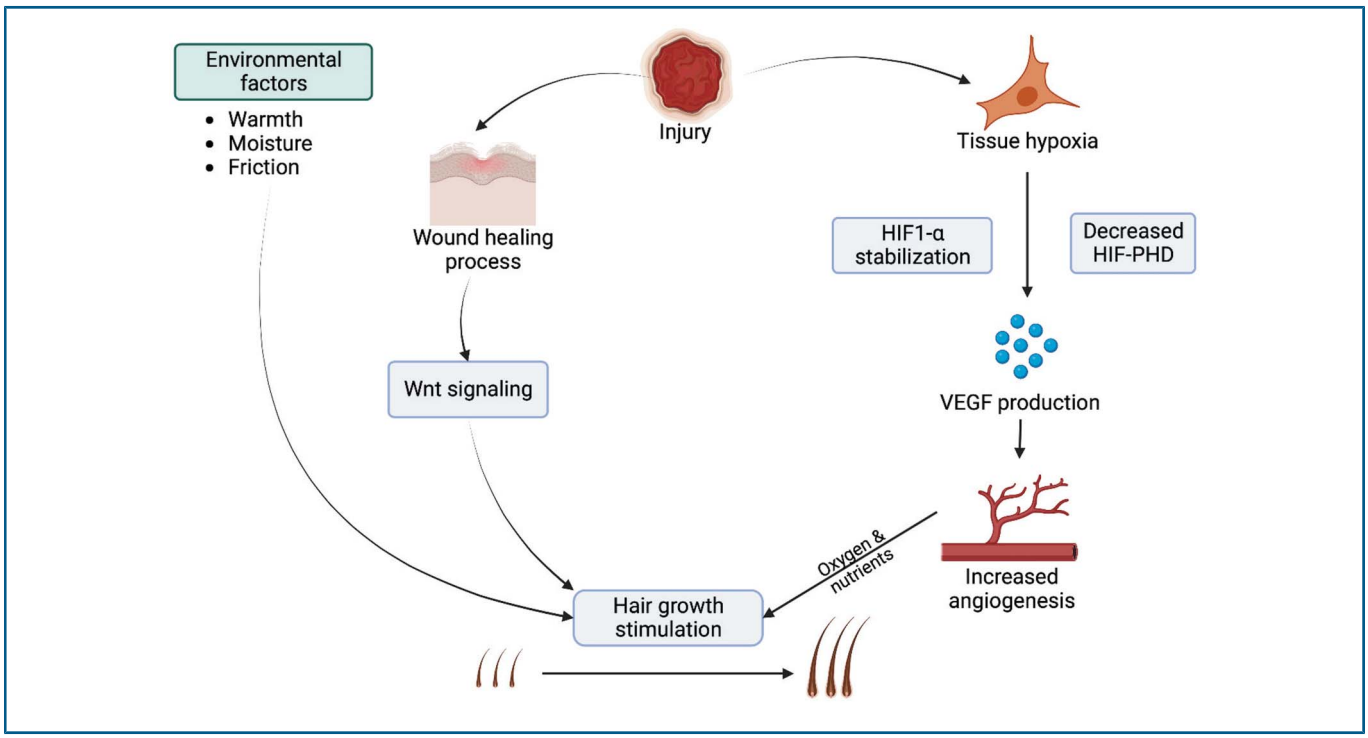

Figure 1. Possible mechanism of wound-induced localized hypertrichosis.

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