

Hair transplantation: Basic overview



Francisco Jimenez, MD,^a Majid Alam, PhD,^{b,c} James E. Vogel, MD,^d and Marc Avram, MD^{e,f}
Gran Canaria, Spain; Doha, Qatar; Baltimore, Maryland; and New York, New York

Learning objectives

After completing this learning objective, the reader will be able to recall the forgotten history of HT and its evolution down to the present day; to describe the anatomy of the follicular unit, the prime element in HT, as it is currently understood; to list hair disorders indicated or contraindicated for HT, and dermatological non-hair-related diseases that can be improved with HT (eg, vitiligo, ulcers); to describe key concepts for consideration when planning HT procedures; and to distinguish between good and bad HT candidates.

Disclosures

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Modern hair restoration surgery is based on a technique known as follicular unit transplantation, in which follicular units are the exclusive structures used as hair grafts. In Part 1 of this 2-part review, we describe how the techniques employed in hair transplantation have evolved into their present forms. Anatomic concepts of specific relevance for dermatologists are discussed, including the distribution and ex vivo morphology of scalp follicular units. Male androgenetic alopecia and female pattern hair loss are the most common reasons for hair loss consultations with dermatologists and will be the primary focus of this review. However, because not all hair disorders are suitable for transplantation, this review will also describe which scalp conditions are amenable to surgery and which are not. Guidelines are provided to help dermatologists better define good and bad candidates for hair transplantation. Other conditions for which hair transplantation surgery is indicated are reviewed. (J Am Acad Dermatol 2021;85:803-14.)

Key words: androgenetic alopecia; follicular unit excision; follicular unit; FUE; hair follicle; hair grafting; hair transplantation; scarring alopecia; strip harvesting.

INTRODUCTION

In 1931, Okuda¹ was the first physician to describe in detail the technique of autologous hair transplantation. He explained how circular punches were used to excise grafts from the scalp, which were

subsequently inserted into holes made with slightly smaller punches in areas affected by alopecia (Fig 1). Although he claimed a 100% success rate in over 200 reported cases, Okuda's paper was published in Japanese and received little attention

From the Mediteknia Dermatology and Hair Transplant Clinic, Universidad Fernando Pessoa Canarias, Gran Canaria,^a the Department of Dermatology and Venereology, Hamad Medical Corporation, Doha,^b the Translational Research Institute, Academic Health System, Hamad Medical Corporation, Doha,^c the Department of Plastic Surgery, The Johns Hopkins Hospital and School of Medicine, Baltimore,^d Weill Cornell Medical School, New York,^e and Private Practice, New York.^f

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Correspondence to: Francisco Jimenez, MD, Mediteknia Clinica, Av.

Alcalde Ramirez Bethencourt, 20, Las Palmas de, Gran Canaria 35004, Spain. E-mail: fjimenez@mediteknia.com.

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Abbreviations used:

AGA:	androgenetic alopecia
FDA:	Food and Drug Administration
FFA:	frontal fibrosing alopecia
FU:	follicular unit
LLLT:	low-level laser therapy
PRP:	platelet-rich plasma

internationally.²⁻⁴ It was not until 1959 that the concept of punch grafting re-emerged in a study by Orentreich,^{5,6} in which he coined the term “donor dominance.” This refers to the fact that grafts maintain their original characteristics after transplantation from a donor site to a new region.

Although the 4-mm punch grafts used in Orentreich’s time achieved good long-term growth, the resulting “pluggy” appearance was a cosmetic failure. Various refinements were developed to counter this effect, including subdividing the grafts into halves or quarters (minigrafts and micrografts).^{7,8}

The next important evolution took place in the mid-1990s with follicular unit transplantation, based on the idea of mimicking normal scalp growth.⁹⁻¹¹ The follicular unit transplantation (FUT) procedure, also known as strip harvesting FUT, involves excising a strip from the mid-occipital scalp followed by its stereomicroscopic dissection into follicular units. This results in long thin scars, which may be camouflaged by the remaining occipital hair, except in patients with very short hair.

In the early 2000s, follicular unit excision was developed, using 0.8-1.0 mm punches to directly remove individual follicular units from the donor hair.¹² As a result, there are no sutures and no linear scars. Follicular unit excision has now surpassed strip harvesting FUT to become the most commonly used donor harvesting technique.¹³

THE FOLLICULAR UNIT: ESSENTIAL KNOWLEDGE FOR SURGEONS

Key point

- Follicular units are the main structure used in hair transplantation.

Distribution of follicular units on the scalp

Human hair emerges from the scalp in groupings that are the visible portion of a histologic structure known as the follicular unit (FU; Fig 2).¹⁴ The FU contains terminal hair follicles (>40 microns in hair diameter), vellus follicles (<40 microns), sebaceous glands, arrector pili muscles,¹⁵ perifollicular dermis, adipose tissue, eccrine coils,¹⁶ and neural and vascular networks.¹⁷

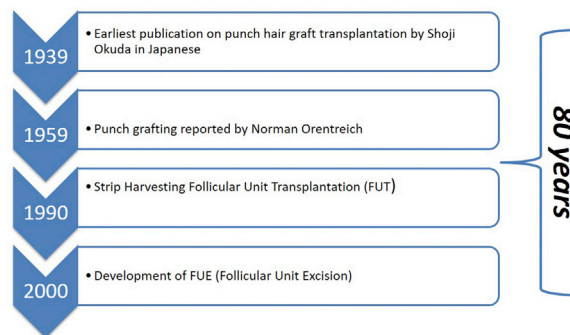


Fig 1. Schematic summary of the most relevant events in the history of hair transplantation. Although early work was reported by Okuda¹ and Orentreich,^{5,6} modern hair transplantation started in the early 1990s when follicular units became the main tissue structure used for hair grafting.

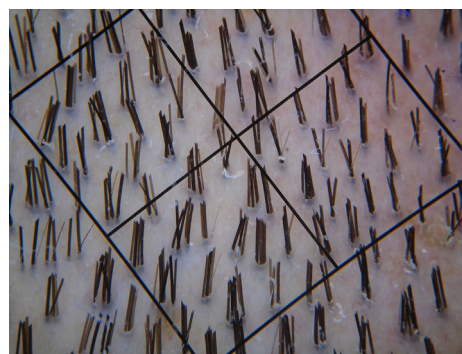


Fig 2. Macroscopic view of scalp FUs. This dermoscopic image shows the distribution of scalp hairs in groupings known as FUs. Note that this patient has a very high density of hair with many FUs of 4, 5, and even 6 terminal hairs. The FU density is around 70 FUs/cm². Each small square measures 0.5 cm × 0.5 cm. FU, Follicular unit.

Scalp FUs usually have 1, 2, 3, or 4 terminal hair follicles (Fig 3), the different proportions of which determine a patient’s hair density.^{18,19} In the mid-occipital scalp of Caucasians, FU density tends to range between 65-85 FU/cm² and most FUs consist of 2 hairs, followed by 3- and 4-hair FUs. Only 10% to 20% of FUs have 1 hair.²⁰ However, the FU density (FUs/cm²) and hair density (hairs/cm²) vary from patient to patient, from 1 scalp zone to another, and between different races. Asian and black skin have lower hair density than Caucasian skin (154-162 hairs/cm² in Asians, 148-160 hairs/cm² in blacks, and 214-230 hairs/cm² in Caucasians).^{18,19}

Measuring the hair and FU density using a high magnification device with quality optics, such as a dermoscope or a macro-video camera, is important to assess the amount of donor hair available for transplant and to estimate the size of the donor strip needed for harvesting. As a rule of thumb, hair

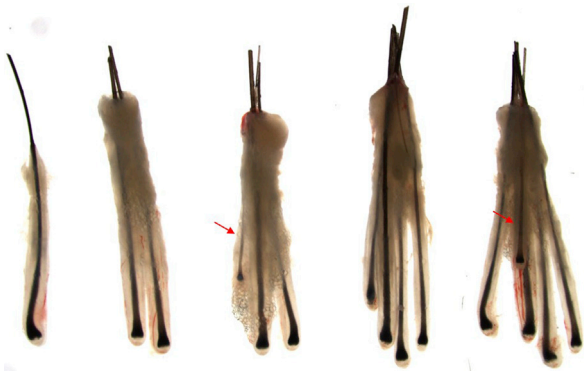


Fig 3. Diverse hair groupings in FU grafts. This image shows the diversity of FU grafts, which can be composed of 1, 2, 3, 4, and 5 hair follicles. The arrows indicate intermediate or miniaturized hair follicles. FU, Follicular unit.

density is about 2.5-3.0 times the FU density. Thus, if 2000 FUs are transplanted, the number of transplanted hairs will be around 5000-6000.

The terminal hair follicle

The terminal hair follicle produces the long, thick hair shaft that patients expect after a hair transplant and contains many cell types: epithelial cells, mesenchymal cells from the dermal papilla and dermal sheath, stem cells involved in self-renewal and pigmentation, and resident immunocytes (mast cells, macrophages, T cells, and Langerhans cells).²¹⁻²⁴ Terminal hair follicles cycle independently and can be at different stages of their hair cycle at any given time. Approximately 90% of scalp follicles are in anagen (the growing phase of the cycle) and the remaining 10% are in catagen or telogen.²⁵⁻²⁹ On average, anagen follicles are 4-5 mm long, although patients with thin hair may have follicles as short as 3 mm and those with thick hair, as long as 6 mm.³⁰ To facilitate graft implantation, the surgeon should match as closely as possible the depth of the slits made at the recipient site to the length of the terminal anagen follicles.

Care must be taken throughout the transplantation process to preserve the anatomic integrity of the FUs because any damage could compromise graft survival.³¹ Although it is still uncertain which specific portion of the follicle, if damaged, directly affects growth, abundant evidence suggests that the bulge and the dermal papillae are the 2 main compartments involved in hair regeneration and the surgeon should be aware of their location. The dermal papillae contain specialized fibroblast-like cells easily identifiable in the deepest portion of the follicle.^{32,33} The bulge, which is the main niche of follicular epithelial stem cells,^{34,35} is located in the mid-portion of the

anagen follicle, 1-2 mm below the scalp surface (Fig 4, A and B).³⁰

HAIR TRANSPLANTATION FOR ANDROGENETIC ALOPECIA

Key points

- Androgenetic alopecia is the most common indication for hair transplantation.
- A combination of medical therapy and surgical intervention is key to maximize long-term density.

Male androgenetic alopecia

Androgenetic alopecia (AGA) is by far the most common indication for hair transplant surgery (Table 1).^{36,37} It is characterized by progressive, androgen-related hair thinning in a defined clinical pattern. Severity can be graded with the Hamilton-Norwood classification (Fig 5, A).^{38,39} A recent systematic review reported satisfaction rates of 90% to 97% and graft survival rates of 85% to 93% in transplanted patients with male AGA.⁴⁰ As well as contentment with their appearance, most patients report improved psychological well-being and self-esteem.^{41,42}

Hair transplantation does not involve a net increase of new hair, but rather a redistribution of the patient's existing hair from the donor zone to recipient zone. Because AGA is a lifelong process and hair transplantation does not alter its progression, the surgeon must plan the cosmetic distribution of transplanted hair so that it will always look natural. It is important to inform the patient that a long-term plan for future hair loss is required, usually involving medical treatment and 1 or more surgical procedures. Successful medical therapy will allow the greatest long-term density from a hair transplant.

Oral finasteride and topical minoxidil are the 2 first-line medications for male AGA that have been approved by the United States Food and Drug Administration (FDA).^{43,44} Finasteride stops hair loss in most men and results in partial regrowth in 66% of patients.⁴⁵ It should be continued for at least 6 months to assess its full effect. Dutasteride is normally used off label for patients who do not respond to finasteride.⁴⁶ Patients should be notified about its potential sexual side effects, including decreased libido, alterations to sperm, and erectile dysfunction.^{47,48} Topical finasteride is used off label in patients reluctant to take oral finasteride because of the side effects.⁴⁹ Combining oral finasteride and 5% topical minoxidil seems to achieve better results than monotherapy with either agent.^{50,51}

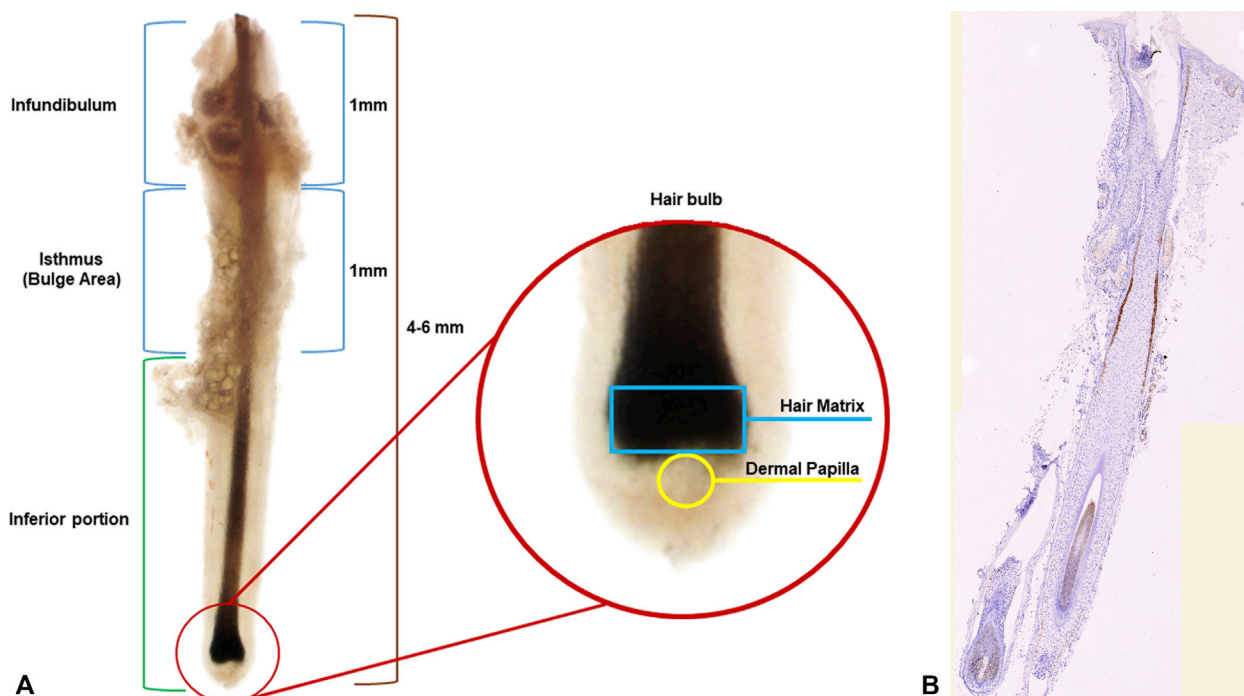


Fig 4. The macroscopic and microscopic anatomy of the anagen hair follicle. **A**, Stereomicroscopic view of a terminal anagen hair follicle removed from the scalp. The surgeon should take care to preserve 2 important anatomic landmarks: the isthmus/bulge stem cell region located at a depth of 1-2 mm beneath the epidermis and the dermal papilla at the deepest part of the follicle. **B**, The bulge can be delineated immunohistochemically with cytokeratin 15 antibodies (brown staining).

Table I. Different types of alopecia and their suitability or otherwise for hair transplantation

Suitable	Not suitable	Miscellaneous uses
<ul style="list-style-type: none"> • Male androgenetic alopecia • Female pattern hair loss • Secondary scarring alopecias (post-trauma, burns, post-radiotherapy, and postsurgery) • Temporal triangular alopecia • Advancement of frontal hairline in congenital high hairlines and traction alopecia • Eyebrow hair loss (excessive plucking, trauma, and postsurgery) • Eyelashes, beard, and pubic hair loss 	<ul style="list-style-type: none"> • Primary scarring alopecias (lichen planopilaris, frontal fibrosing alopecia, folliculitis decalvans, and discoid lupus) • Alopecia areata 	<ul style="list-style-type: none"> • Vitiligo • Wounds (chronic)

Other therapeutic options include platelet-rich plasma (PRP) injections and low-level laser therapy (LLLT). Clinical trials with PRP have generally reported more positive results than negative.⁵²⁻⁵⁴ Further research is needed to determine the optimal PRP regimen, but most patients are treated 3 times in 4- to 6-week intervals.^{55,56} Studies have shown that LLLT, based on the use of red light (wavelengths

from 635-678 nm), improves hair density and is safe and effective.⁵⁷ LLLT can be delivered with a helmet, cap, band, or comb.⁵⁸ The protocols range from 10-30 minutes per session and 2-7 sessions per week.⁵⁷ Combinations of the above medical therapies are likely to be synergistic, but further clinical trials are needed to confirm the efficacy of combination medical therapy.

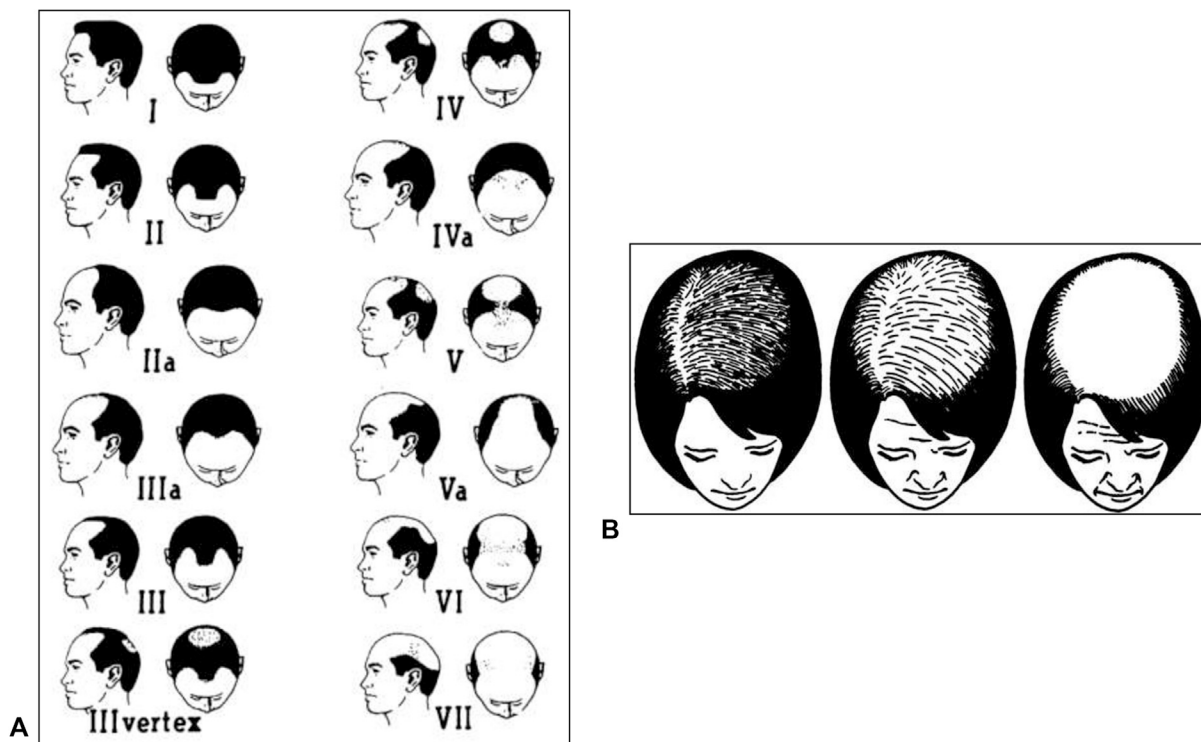


Fig 5. The Norwood and Ludwig scales of hair loss. **A**, Male androgenetic alopecia according to the Norwood scale. I, no hair loss; II, mild recession of the frontotemporal hairline; III further frontal hair loss; IV, further frontal hair loss coupled with formation of a bald vertex area; V-VII, confluence of the affected areas until only the occipital area maintains significant amounts of hair. **B**, Female pattern hair loss according to the Ludwig scale. Grade I (*left*) begins with slight thinning of hair. In grade II (*middle*), the scalp becomes increasingly visible. In grade III (*right*), most of the hair on mid-scalp is lost.

Female pattern hair loss

Women can present with 3 different hair loss patterns: the Ludwig pattern,⁵⁹ characterized by diffuse central thinning over the mid-frontal scalp with maintenance of the anterior hairline (Fig 5, B); the androgenic pattern, which is similar to male pattern hair loss; and diffuse unpatterned alopecia, which involves generalized hair miniaturization.

Patients with diffuse unpatterned alopecia are not good transplant candidates, especially because the diffuse nature of hair loss in diffuse unpatterned alopecia limits the amount of available donor hair. Additionally, the diffuse thinning of the whole recipient scalp makes cosmetic improvement much more difficult to achieve. In contrast, women with androgenic or Ludwig patterns are, in principle, good candidates for hair transplantation, although careful assessment is needed of the donor area.⁶⁰

As in male AGA, hair transplantation in female pattern hair loss should be combined with medical therapy to slow the ongoing loss and potentially reverse hair miniaturization. The first-line therapy, and the only FDA-approved medical therapy for female pattern hair loss, is topical minoxidil (1 ml of

2% twice daily, or 1 ml of 5% solution or foam once daily).⁶¹ Other off-label oral antiandrogen options include finasteride, spironolactone, cyproterone acetate, and flutamide. However, no study has offered good evidence of their efficacy, and sexually active premenopausal patients require contraception.^{44,61,62} Low-dose oral minoxidil (0.25 to 1.25 mg/day) has shown good results, but randomized studies are needed.⁶³ PRP and LLLT have shown positive results in clinical trials in both AGA and female pattern hair loss.^{55,56}

Choosing good candidates for hair transplantation

A consultation is mandatory prior to hair transplantation.⁶⁴ The following 5 factors assess whether a patient is a good or bad candidate.

Age and personal and family AGA history. Due to the polygenic inheritance of AGA,⁶⁵ patients with a family history of hair loss will be more prone to developing severe AGA. The patient's personal history, including duration and rate of hair loss, serves to gauge the extent of expected hair loss. In principle, hair surgeons should



Fig 6. An old school hair transplantation in a young patient. Long-term planning is very important when performing hair transplantation in young patients with male androgenetic alopecia. This patient had a hair transplant procedure in the frontal hairline, which was performed with the typical 1970s technique of large 3-4 mm punch grafting. As the androgenetic alopecia advanced, he presented with a balding area behind the grafts 30 years later, which made the transplanted hairs more visible and unaesthetic.

be wary of undertaking hair transplants in men in their early 20s because hair loss is likely to be progressive and may lead to an unsightly hair appearance pattern with further balding (Fig 6). Moreover, patients of this age may not fully understand the need to commit to future sessions and it may be wiser to prescribe solely medical therapy, postpone the transplant, and evaluate the response to the medication.

Response to medical therapy. A successful medical treatment is key to stopping hair loss progression and offering a better guarantee of a sustained long-term transplant outcome. The net perceived density of transplanted hair is equivalent to the amount of transplanted hair minus the rate of ongoing hair loss.

Donor characteristics. The rate-limiting step for hair transplantation is the amount of available donor hair. The key is to harvest enough follicles to solve the balding problem without depleting the donor area.⁶⁶ The main parameters to evaluate in the donor area are FU density, hair density, and hair thickness (estimated using a micrometer). Patients with normal-to-high FU density (≥ 65 FU/cm²) and thick hair (>50 - 60 microns) are good candidates. In contrast, patients with diffuse hair loss, low FU density (≤ 40 - 50 FUs/cm²), and donor hair miniaturization ($>20\%$ miniaturized) are poor candidates (Fig 7). Coarse hair will cover better than fine hair, and curly hair better than straight hair of comparable thickness.

Artificial hair implantation (synthetic fibers) is an alternative treatment when the donor area is depleted or unsuitable for hair transplantation.^{67,68}

However, its use remains controversial and has been banned by the FDA. Adverse reactions, such as recurrent folliculitis, scarring, and foreign body reactions, limit the benefits of artificial hair implantation.⁶⁹

Degree of baldness. Patients with moderate to advanced baldness (Norwood III-V and Ludwig II) are the best candidates. Men and women with mild AGA (Norwood II and Ludwig I) should probably be put on medication first to avoid hair loss progression. Patients with advanced baldness (Norwood VI-VII and Ludwig III) should be considered on an individual basis. They may be acceptable candidates, provided the donor area has sufficient density and they understand that several sessions are needed and the goal is not to obtain a full head of hair but rather to frame the face. Fortunately, a return to the original recipient area density is not needed for a successful outcome. Marrit⁷⁰ and Limmer⁷¹ have described how the visual appearance of hair fullness can be obtained with just 50% of the original density.

Patient's expectations. Surgeons should clearly inform patients about what to expect from the surgery, the limited nature of donor hair, the impact of ongoing hair loss, and the importance of adjuvant medical therapies. The surgeon should be aware of the patient's expectations and moderate them, if necessary. As in any cosmetic surgical procedure, patients with unrealistic expectations are not good candidates for hair transplantation.

The patient's psychological status should also be considered in candidate selection. Body dysmorphic disorders are common among patients complaining of hair loss.⁷² Such patients are more likely to be unsatisfied with cosmetic surgery outcomes regardless of how well the final transplant result objectively looks.

HAIR TRANSPLANTATION IN SCARRING ALOPECIAS

Key points

- Noninflammatory secondary scarring alopecia can be successfully treated with hair transplantation.
- Primary scarring alopecias, including lichen planopilaris and frontal fibrosing alopecia, are generally unsuitable for hair transplantation, although assessment should be made on a case-by-case basis.

The outcome of hair transplantation in scarring alopecias varies, depending on their type (primary or secondary). Secondary (noninflammatory) types are the result of post-traumatic wounds, surgical scars (eg, linear scars of previous hair transplants, facelifts,

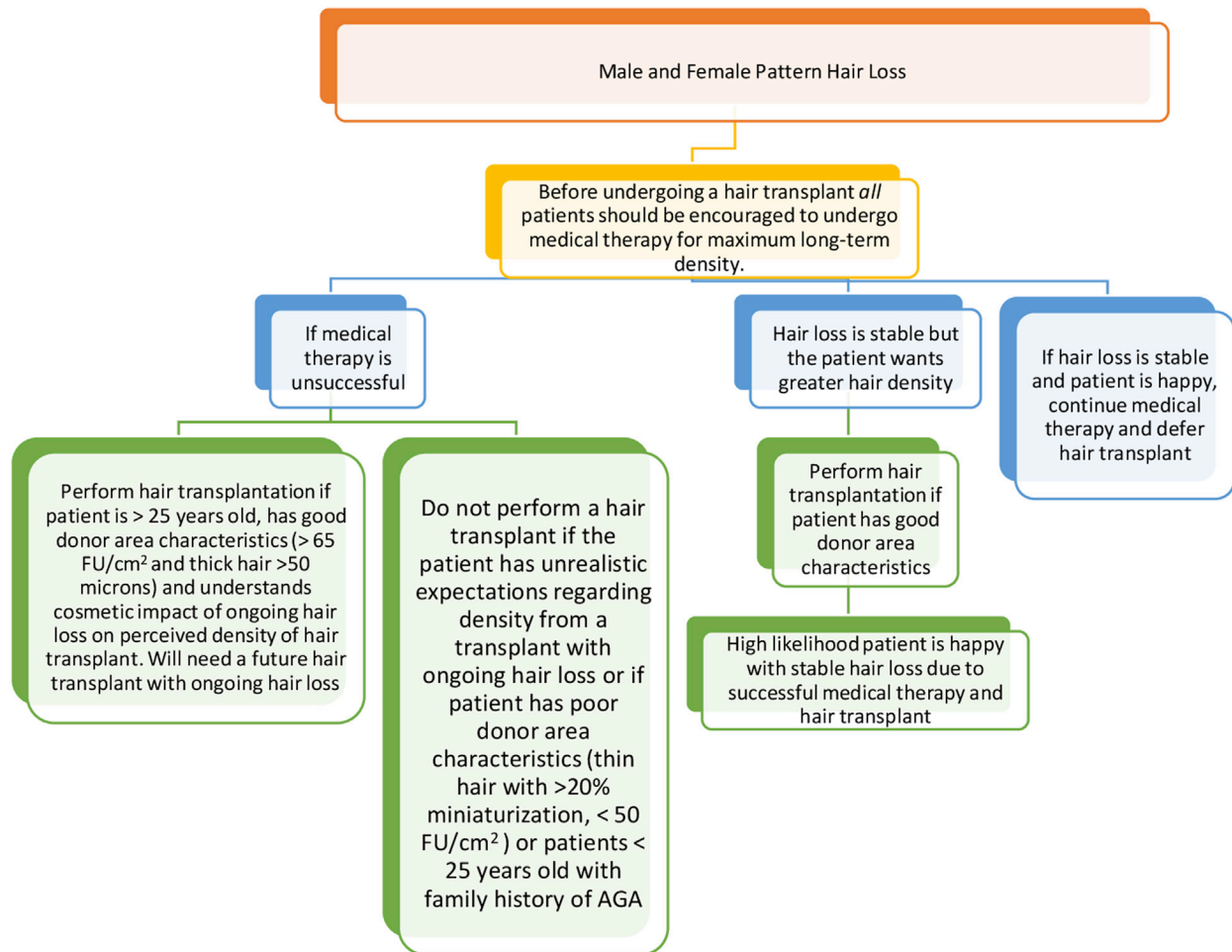


Fig 7. Decision tree diagram for choosing an ideal candidate for hair transplantation in patients with male AGA and female pattern hair loss. *AGA*, Androgenetic alopecia; *FU*, follicular unit.



Fig 8. Hair transplantation in a secondary (noninflammatory) scarring alopecia. This patient suffered scalp necrosis due to an electrical burn in his infancy that required multiple reconstructive procedures with skin grafts and flaps. Before (**A**) and after (**B**) hair transplantation. Secondary scarring alopecias are good indications for hair transplant surgery, provided patients have enough hair in the donor area.

neurosurgery), radiotherapy, or burn scars (**Fig 8**). In such cases, hair transplantation is very rewarding and its success depends on whether the patient has sufficient hair in the donor area to harvest enough grafts to cover the scarring area.^{73,74} Graft survival and patient satisfaction rates of up to 86% to 88% have been reported.^{42,74} Postburn scars (including

skin grafts) generally achieve better results than traumatic or incisional scars, probably due to the deeper scarring damage in the latter.⁷⁵

The implantation process in scarring areas might be technically more challenging than in normal skin due to scar stiffness. Most surgeons recommend avoiding dense packing and maintaining a graft



Fig 9. Lowering of the frontal hairline in a female patient. Many young women seek hair transplantation to lower a congenitally high frontal hairline. This 21-year-old woman underwent a follicular unit hair transplant procedure to lower her frontal hairline by approximately 2 cm. Before (A), 24 hours after transplant (B), and outcome 8 months after transplant (C).

density of ≤ 30 FU grafts/cm² due to poor blood circulation. As a result, patients may need more than 1 operation for an aesthetically successful result.⁷⁵

Hair transplantation in primary scarring alopecias is controversial. A systematic review revealed a positive outcome rate of 76%, mainly in patients with centrifugal cicatricial alopecia, en coup de sabre, discoid lupus, pseudopelade de Brocq, and folliculitis decalvans. Positive and negative results have been reported in lichen planopilaris and frontal fibrosing alopecia (FFA).⁷⁴ The data, however, must be interpreted with caution, because it is suspected that the incidence of negative transplant outcomes is actually higher than published and that there is a reporting bias in the literature in which mainly cases with a positive outcome are reported.⁷⁴ The general consensus is that hair transplantation should not be performed on patients with primary scarring alopecias and active inflammation. In nonactive cases, stable hair loss for a minimum of 24 months, and up to 5 years if possible, may be advisable before considering hair transplantation.⁷⁶

Regarding hair transplantation in nonactive cases of FFA, although initial hair growth appears to be satisfactory, recurrence of FFA at graft sites after 3 to 4 years post-transplant has been reported in multiple cases.⁷⁷⁻⁷⁹ It is unclear why this occurs, but recent evidence indicates that follicles with an apparently normal appearance in patients with lichen planopilaris and FFA may have subclinical perifollicular inflammation.⁸⁰ Some surgeons advise

a preliminary test, transplanting 30-50 FU grafts in a small area and monitoring the outcome.^{78,79}

HAIR TRANSPLANTATION IN OTHER SCALP AND NONSCALP CONDITIONS

Key points

- Temporal triangular alopecia can be treated with hair transplantation.
- Lowering a congenital high hairline is a common indication for hair transplantation in young women.
- Hair grafts transplanted into chronic wounds appear to stimulate their healing.

Temporal (congenital) triangular alopecia presents at birth or in childhood with a nonscarring patch of hair loss in the frontotemporal scalp. Temporal triangular alopecia is not progressive, its etiology is unknown, and it affects most patients unilaterally. Although relatively few cases of Temporal triangular alopecia treated with hair transplantation have been reported, all have shown satisfactory outcomes.⁸¹⁻⁸⁶

Advancement of the frontotemporal hairline is a common indication for hair surgery in women with congenital high hairlines (Fig 9) or traction alopecia due to hair styling practices. Most patients consider the results satisfactory but a successful outcome depends largely on the surgeon's expertise. Lowering a congenital high hairline can be performed with hair transplantation⁸⁷ or with flap

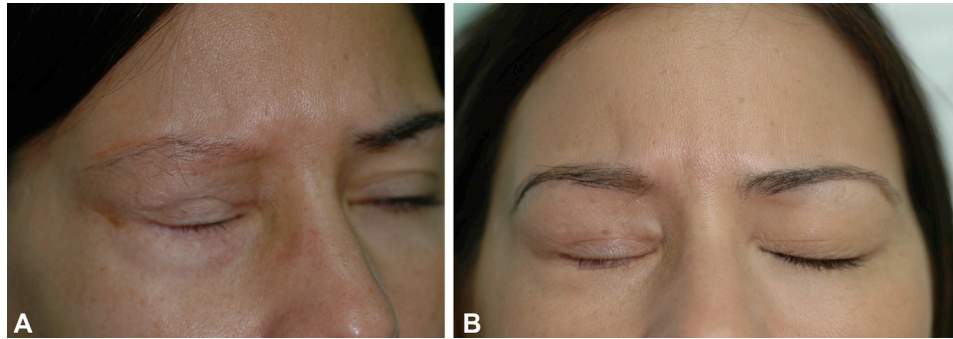


Fig 10. Hair transplantation of the eyebrows. Hair transplantation using single hair grafts for aesthetic reconstruction of the eyebrows is an excellent option. This patient lost her right eyebrows due to radiation therapy for an ocular tumor. Before (A) and after (B) hair transplantation.

advancement.^{88,89} Hairline-lowering with flap advancement, however, should not be performed in patients with active FFA because the progression of frontal hair loss may lead to exposure of the hairline scar.⁸⁹

Hair transplantation has been used in patches of stable vitiligo that have shown no response to medical therapies.^{90,91} Results appear to show that it is particularly effective in hair-bearing areas associated with leukotrichia.⁹² Repigmentation rates of around 68% have been reported for follicular transplantation in stable vitiligo, similar to those obtained with the mini punch grafting technique (73%) using the 1-mm punch.⁹⁰

Hair transplantation is not considered an acceptable treatment for alopecia areata. No studies since have contradicted Orentreich's report of either complete failure or only sparse and weak hair growth in 9 patients with alopecia areata.⁵

The hair follicle plays an important role in the cutaneous wound healing response.⁹³ Transplanting hair grafts into a wound to promote its healing is considered a viable therapeutic alternative.⁹⁴⁻⁹⁸ The technique is similar to the punch grafting technique used for many years in chronic ulcers,⁹⁹ with the difference that the punch graft source is the hairy scalp. A study comparing transplantation in chronic leg ulcers of grafts harvested from hairy scalp versus nonhairy areas showed a greater healing response with hair grafts.⁹⁵ Another study showed that hair transplantation into chronic wounds achieved better skin/scar quality than split-thickness skin grafts,¹⁰⁰ suggesting a scar remodeling effect induced by the transplanted follicles that needs further investigation.

Hair transplantation can also be used to treat eyebrow loss due to continuous plucking, postsurgical scars, trauma, radiation therapy (Fig 10), or burn scars.¹⁰¹⁻¹⁰³ Scalp hair is generally used in eyebrow transplantation. The follicular survival rate is above

75%, although survival rates tend to be lower in patients with burn injuries and significant scarring.¹⁰¹ The results of eyebrow transplantation in FFA patients are variable; while short-term outcomes appear to be satisfactory, most patients suffer progressive loss of the transplanted hairs after 3 to 4 years.¹⁰⁴

Conflicts of interest

None disclosed.

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