REVIEW PAPER



Follicular Unit Extraction (FUE) Hair Transplant: Curves Ahead

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Abstract The hair transplant has become widely popular aesthetic procedure. Follicular unit transplantation (FUT) and follicular unit extraction (FUE) are two commonly used and accepted techniques. FUT requires excision of strip of tissue from occipital donor area leading to linear scar. To overcome scarring and other complications of FUT, FUE technique has been attempted which involves harvesting of small individual follicular units. Hair transplantation has been successfully used in correction of alopecia, cleft lip scars, post-burn or surgical scars, vitiligo and as an adjuvant to other maxillofacial procedures. FUE demands greater skills and orientation but can vield excellent results in experienced hands. Several maxillofacial surgeons have incorporated hair transplantation procedure in their aesthetic practice successfully. Sound knowledge of surgical technique, armamentarium and proper surgical planning are essential for desired results. The aim of this article is to explain FUE technique, risk and complications, holding solutions and other associated factors in detail. A simple protocol has been put forth for reference and for better understanding of the technique.

Keywords Alopecia · Follicular unit extraction · FUE · Hair transplant · Holding solution · PRP

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Introduction

The history of hair transplant can be traced as early as 1822 when Dieffenbach experimented with hair transplant in birds [1]. The field of surgical hair restoration thereafter progressed in two different directions where one group started exploring role of autografts while other segment of surgeons attempted various flaps and serial excisions, the former technique by far dominated and was adopted globally with time [2, 3].

In early attempts, Japanese dermatologists Sasagawa [4], Okuda [5], Tamura [6] and Fujita [7] used small autografts containing hair follicles for the correction of scars and cicatricial alopecia, but they never reported the technique for androgenetic alopecia and their work went unappreciated for years. Later, Dr. Norman Orentreich who is also considered as father of modern hair transplantation performed hair transplant with 4-mm punch for "punch grafting" technique and discussed the idea of donor and recipient site dominance [8, 9]. But it was not until 2002 when Rassman et al. [10] described the FUE technique in detail and discussed various clinical and microscopic features of follicular grafts harvested from 1-mm punch. Since then, FUE technique which is also referred or modified as FOX procedure, FUSE (follicular unit separation extraction) method, Wood's technique, follicular isolation technique (FIT), individual follicular group harvesting (IFGH) [11, 12] is gaining constant popularity among hair restoration surgeons and their patients [3].

Hair loss is a worldwide problem affecting both sexes, males being more. At present, Hamilton–Norwood classification system for male pattern baldness and the Ludwig system for females are most commonly used classification systems [13]. In past few years, several maxillofacial surgeons have expanded their practice in cosmetic and hair

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restoration surgeries. Moreover, hair transplant techniques have been successfully used in camouflage correction of cleft lip scars, face lift scars, post-burn or traumatic scars, reconstruction of eyebrows, eyelashes, beard, mustache, vitiligo and as an adjunct to various maxillofacial procedures [14–19]. Despite worldwide interest, there is a general dearth of the literature in maxillofacial journals on this topic. The aim of this paper is to discuss the various aspects of novel FUE technique in detail, associated risks and complications, authors experience, graft holding solutions, recent advances and other key factors. Informed consent was obtained from the patients, and necessary ethical guidelines have been followed by the authors.

FUE v/s FUT

The two widely accepted techniques of hair transplant are follicular unit transplantation (FUT) also known as strip technique and follicular unit extraction (FUE). While FUT involves excision of hair-bearing strip from the donor area and dissecting into small follicular units, on the other hand in FUE, individual follicular grafts are harvested with the help of manual or motorized punches. Neither one technique is superior than other as both techniques have their own merits and demerits. The main advantages and disadvantages of FUE when comparing with FUT are enumerated in Table 1 [11, 20].

FUE does not leave a linear scar as compared to FUT. Several surgeons prefer trichophytic closure of the FUT wound or performing FUE for masking old conspicuous FUT scar in donor area. FUE is an ideal technique when

Table 1 Advantages anddisadvantages of FUE

hair from non-scalp areas (chest, beard, etc.) is harvested [12].

Technique

The fundamental technique of FUE followed by authors is explained here. The procedure is performed under local anesthesia, and sedation/general anesthesia is rarely indicated (usually in apprehensive patients or allergy with local anesthetic solution). Patient is asked to trim or shave head a day before surgery. (The donor area hair can be left around 1 mm for visualization and orientation.) Premedication protocol includes antibiotic (cephalosporins, azithromycin, etc.), steroid (methylprednisolone 8 mg) and an antiemetic orally 30 min before surgery. The recipient area is carefully marked keeping in mind the existing baldness, susceptible areas and patient expectations. Surface anesthesia with EMLA cream helps in reducing injection pain, but needs to be applied 1-2 h before surgery with occlusive dressing for optimal action. After surface asepsis with povidone iodine or chlorhexidine solution, ring block anesthesia of occipital and frontal region (frontal region anesthesia can be given just prior to recipient site preparation or once grafts are harvested) is given followed by tumescent infiltration of donor and recipient area with 30 ml 2% lignocaine mixed with 5 ml 0.5% bupivacaine, 30 ml normal saline, 0.5 ml adrenaline (1:1000) and 1 ml triamcinolone 40 mg/ml in a normal adult patient. Once desired anesthesia is achieved, the follicular units are harvested using adequate size punch (0.7-1 mm) and forceps [11, 21] (Fig. 1).

Pros
Less visible scar
Shorter postoperative recovery
Less armamentarium and staff
Minimum graft preparation
Body hair can be used (body hair transplantation)
Can be done in tight scalp cases
Minimal risk of nerve injury or excessive bleeding
Surgeon can selectively pick grafts from donor area
Cons
Time-consuming
Longer learning curve
Transection rate is higher/fragile grafts with loss of surrounding tissue
Higher chances of buried grafts or folliculitis
Wider donor area is required
Multiple sessions may be needed for extensive cases
Subsequent sessions may become difficult due to widespread tiny scars
Very fine trimming of hair is needed



Fig. 1 Follicular units harvesting with FUE technique

FOX test is done with first few grafts to evaluate ease of harvesting grafts and rate of transection. Then, the grafts are scored on the scale of 1–5 as explained in Table 2. The score of FOX 1 or 2 is ideal for FUE, while FOX 3 is known as neutral case, and surgeon should consider continuing with FUE technique on its own discretion, skills and indications. Transection rate will be high with significant loss of surrounding fat and damage to follicles in FOX 4 and 5, and hence, FUT is preferable in these patients [10, 11].

The grafts are preserved in cold 0.9% saline. Once the grafts are harvested (Fig. 2), the recipient slits are prepared using appropriate 18–20 gauge needles or blades. Each follicular graft is then carefully transplanted in the prepared slits. Utmost care should be practiced while handling of grafts and the grafts should be kept moist at all time during the procedure. Once the procedure is finished, the surgical area is thoroughly cleaned with saline. An antibiotic dressing is done on the donor area. Routine antibiotics, steroid, opioid analgesics and multivitamins are prescribed along with postoperative instructions.

The procedure is very well tolerated by most of the patients. Postoperative pain is often less which can be easily controlled by routine oral analgesics. Periorbital or facial edema occasionally occurs on third or fourth day after surgery and is aesthetically unpleasing to the patient. Cold packs, proper sleep posture, intraoperative and postoperative steroids are used to prevent or reduce facial edema [22, 23]. Scabs should be washed off with mild shampoo with very minimal pressure from second or third day onward. The grafts are secured to recipient site at sixth–ninth postoperative day [24]. Local application of aloe vera preparations has shown to be beneficial in folliculitis and healing of the surgical wounds [25]. Folliculitis or pustules at recipient site is another common complaint of patients after few weeks which mostly subside spontaneously without harming grafts, and oral antibiotics are rarely needed [26, 27].

The donor site heals, but hypopigmented scars of 1.5-1.6 mm diameter are often visible on donor area; hence, the term "scarless hair transplant" is a misnomer for FUE [28]. Inadvertent subluxation of follicular unit grafts below the dermis level intraoperatively may lead to cyst formation [29]. Necrosis leading to cicatricial alopecia of donor site has been reported as another rare complication of FUE [30]. Adverse drug reaction, surgical site hypopigmentation, bleaching of hair due to hydrogen peroxide irrigation, sensory disturbances of donor site, hiccups, etc., are other rare complications. Immediately after hair transplant, the grafted and surrounding hair may enter into postoperative effluvium or shock loss where sudden increased hair fall is frequently noticed by the patients. The common complications are enumerated in Table 3 [23, 26–31].

The grafted hair may usually take 6–12 months to grow, but may vary patient to patient. One of the most common complaint and complication of hair transplant is "unexpected results." The term "unexpected results" here may encompass visible results of the surgery. Generalized reduction of density of donor area or "moth eaten appearance" may appear when the harvested grafts are

Table 2 FOX test

Criteria	Significance		
All of the follicular units are extracted intact, least difficult harvesting (popping out of grafts)	Excellent. FOX positive		
Significant loss of surrounding fat around lower part of follicle or $< 20\%$ of amputation	Good. FOX positive, but may be difficult in subsequent sessions due to scarring		
Difficult emergent angle	Questionable; greater surgical skills, experience and orientation are needed. FOX neutral		
Significant amount of surrounding fat avulsed and amputation of significant number of distal follicles	Poor. FOX negative		
Significant damage to mostly all the grafts with upper portion of follicles avulsed from lower segment	Poor. FOX negative		
	Criteria All of the follicular units are extracted intact, least difficult harvesting (popping out of grafts) Significant loss of surrounding fat around lower part of follicle or < 20% of amputation		



Fig. 2 FUE grafts

Table 3 Common complications of FUE

Intraoperative Pain/inadequate anesthesia Bleeding Higher transection of grafts/FOX negative Instrument breakage Syncope Adverse drug reaction Loss of grafts (spillage, trauma, lost in swabs, dried grafts, etc.) Postoperative Pain Swelling Periorbital or facial edema Itching Shock loss Scabs Infection Delayed (> 1 month)Donor area scars (moth eaten appearance)/hypopigmented scars Folliculitis or ingrown hair Cysts Delayed or no growth Unaesthetic or below expectations results Loss of grafted hair (harvested outside of safe zone) Persistent pain or paresthesia

more. Two-sitting FUE is a preferable option in cases with large bald area where surgeon and patient can both assess the donor area, result, finances and then plan for second surgery of remaining bald area. Unnatural hairline, inadequate graft density, etc., are major concerns of patients which may be due to inexperienced hands or due to over expectations and over promise. FUE is a tiring and timeconsuming technique; hence, one should know his skills and limitations. FUT and FUE can both be done simultaneously or in separate sittings (FUT should be done first in such circumstances), and better results can be achieved. In cases without complete baldness of crown and vertex, the existing hair should be preserved with techniques like medications, platelet-rich plasma, laser, etc., to prevent further hair loss. Fall of grafted hair mostly occurs due to harvesting of grafts from hair-loss-prone zone, and hence, identification of safe donor area prior to surgery is crucial [31].

Technical Considerations

The two most important factors in success of FUE are accuracy and speed which come with time and practice. Unlike strip technique (FUT), graft harvesting in FUE is a blind procedure and hence, injury to the grafts during punching is common. Beehener [32] in his study found lower survival rates of FUE grafts as compared to FUT (53.9% vs 85.2%), while Tsilosani found survival of the FUE grafts equivalent to that of FUT grafts [33].

Transection or physical injury to the grafts is major drawback of FUE when compared to FUT which is one of the major reasons of failure of grafts [34]. The FUE punches are available in different sizes, sharpness, compositions and designs. Also the sharpness and other properties of the punches may differ from one manufacturer to other. All these properties affect tissue cutting capabilities of punches, quality of graft, fluid dynamics of the follicle, tissue distortion, etc. Inadequate size of punch, blunt or distorted surfaces of punch, inappropriate force, orientation and direction of insertion of punch will eventually lead to wider incision wounds and transection of grafts. The surgeon should be aware of his surgical armamentarium and the physics behind FUE well to achieve better results [35]. With motorized punches, the rate of harvesting graft has increased many folds, but it needs better control and dexterity as compared to manual punching [36].

Preservation and viability of grafts during the complete surgery is another important factor in FUE. Duration of hair grafts outside the human scalp affects viability of grafts. A study by Unger revealed graft survivability with 2 min, 30 min and 60 min out of body time to be 84%, 98% and 97%, respectively [37, 38]. Another study by Limmer revealed graft survivability for 2 h (95%), 4 h (90%), 6 h (86%), 8 h (88%), 24 h (79%) and 48 h (54%). Limmer also concluded that the approximate loss of graft viability was 1%/h outside the body. Both studies together indicate correlation between graft survivability and out of body (graft holding) time, and up to 2 h out of body time seems to yield satisfactory graft survival (95–98%) [39].

Another important debate is which holding solution and what temperature are ideal for storage of tender follicular grafts. The requisite properties of an ideal holding solution can be summarized as [40]:

- 1. Should be non-toxic, non-carcinogenic and nonallergenic
- 2. Should inhibit microbial growth
- 3. Prevent cell swelling, tissue destruction or injury
- 4. Should be able to maintain constant temperature and physical state during cooling or warming
- 5. Maintain viability of grafts for longer duration
- 6. Constantly maintain osmotic and ionic balance
- 7. Scavenge free radicals
- 8. Prevents acidosis
- 9. Nutritional/energy (ATP) support
- 10. Should facilitate restoration of metabolic activity on warming or reperfusion
- 11. Should be inexpensive or cost-effective

Extracellular solutions (isotonic) such as 0.9% saline, Ringer's lactate (both are widely used mainly because they are cheap and readily available), tissue culture media, PlasmaLyte-A have high Na⁺ and low K⁺ ionic concentrations and hence do not prevent cellular swelling at lower temperature. On the contrary, intracellular solutions (hypotonic) have low Na⁺ and high K⁺, maintaining osmotic support, and prevent cell swelling while chilling of grafts and are costly. Examples include Hypothermosol, Viaspan, Custodial, etc. [40–42].

A popular belief is that the temperature of storage media affects viability of grafts. This seems to be justified as lowering temperature will reduce metabolic activity, oxygen and nutritional demands of the tissues or grafts [40]. Studies have failed to demonstrate any significant improvement in graft survivability in cold environment for shorter duration (4-6 h); however, cold or chilled holding solutions are indicated for longer duration storage (> 24 h) and as already discussed above, intracellular holding solutions are ideal choice for chilling [38–44]. The authors prefer constant hypothermic extracellular storage media (saline/Ringer's at 4–10 °C) taking due care in manipulation and keeping the grafts moist during the whole surgery. Dehydration or drying of grafts is considered to have detrimental effect on graft survivability [38].

Also, one may prefer to prepare recipient site first before harvesting hair grafts to reduce holding time for grafts. Bernstein et al. have suggested the same technique and intentional delay of up to 24 h for graft harvesting and placement to allow recipient site healing [45]. Preparation of recipient site first seems to be a good choice, but intentional 24-h delay is more feasible in megasessions or where large number of grafts to be transplanted, and the procedure can run for two consecutive days.

A technique of direct hair transplant has been introduced obliterating the holding time of grafts to only few minutes, but the technique demands specialized and extra manpower and armamentarium; moreover, the study by Unger (84% survivability for 2-min holding time) seems to raise some doubts over the technique and hence, more controlled trials are needed to justify and compare the results [21, 37, 38, 46].

Few of the additives, antioxidants, micronutrients and supplements which have been reported with positive effects on grafts viability and hair shaft elongation are allopurinol, nitric oxide inhibitors, arachidonic acid inhibitors, vitamin B12, ATP-MgCl, deferoxamine, insulin, mannitol, amino acids and steroids, but further research is warranted [38, 47, 48].

According to some reports, the recipient site can influence hair growth and other characteristics and should be further explored for possible clinicopathologic classification of recipient sites for hair transplant [49, 50]. Androgenetic alopecia is a progressive disorder. Consideration should be made for possible areas of baldness which may appear in future. The surgeon can extend the grafts to these susceptible areas or may prefer to leave sufficient number of grafts for future hair transplant in young patients [51].

One major yet underrated advantage of FUE is freedom to selectively pick the grafts. A single follicular unit may contain 1–3 and rarely 4 or more hair, and selecting these units will definitely affect density at recipient site. Moreover, black hair as compared to white hair, thick and curly hair can also enhance the visible results without any need to increase number of grafts [27].
 Table 4
 Simple protocol for hair transplant (FUE)

Detailed examination	History (general, systemic, family, medical, previous treatment)		
	Clinical examination (grading/staging)		
	Pull test		
	Dermoscopy (trichoscopy)/folliscopy		
	Scalp/skin assessment		
	Biopsy (if needed)		
Counseling	Patient expectations		
	Discuss problem, cause, technique, pros and cons, risk and complications, alternative approaches		
	Recipient site, hairline marking		
	Expected results		
	Possible need for further therapy/surgery		
	Cost		
Presurgical evaluation	Density test (donor area)		
	Blood test (complete blood counts, blood sugar, bleeding time, clotting time, HIV, HbsAg, etc.)		
	Physician/anesthetic evaluation		
	Drug allergy test (local anesthesia, etc.)		
	Preoperative photographs		
Informed Consent	Technique, common risk and complications, prognosis, further treatment required, etc.		
Surgery	Premedication, fine trimming of hair, surface anesthesia, marking of planned recipient site, standard painting and draping		
	Ring block, tumescent anesthesia of donor site		
	FOX test: continue if score 1, 2, ?(3)		
	Donor graft harvesting		
	Storage of grafts in holding media at hypothermic solution (Ringer's/saline/others at 4-10 °C)		
	Anesthesia and preparation of recipient site		
	Transplantation of follicular grafts		
	Saline/Ringer's irrigation on transplanted grafts intraoperatively (every 5-10 min). Keep grafts wet.		
	Hemostasis, donor site dressing		
Postoperative instructions	Medications (antibiotics, opioid analgesics, steroid)		
	Sleep posture with head elevation		
	Avoid strenuous activity, head down or bending, exercise, swimming, physical trauma, harsh chemicals, alcohol, etc		
	Saline irrigation on recipient site, ice compress on forehead and periorbital area		
Follow-up	3rd day: check graft area, swelling, crusting, remove donor site dressing. Advise mild shampoo		
	10th day: surgical site healing, crusting		
	1-6 months: healing and growth, folliculitis, consider starting minoxidil, PRP, other therapies.		
	> 6 months: healing, hair growth, alternative therapies, second surgery		

Recent Developments and Future Trends

Hair transplant is a developing technique, and no standard recommendations have been put forth yet. A very simple, easy to understand protocol for planning and performing hair transplant is proposed here (Table 4), which may be adopted or modified by surgeons as per their experience with the procedure. Standardization of punches, forceps, motorized devices, holding solutions, etc., is the need of time [11, 20, 27].

At present, dental micromotors and handpieces are serving the hair transplant industry in economical and efficient way, but several advancements in motorized punching techniques and devices have been introduced in market like surgically advanced follicular extraction (SAFE) [52], FUExtractor system [53], Cole Isolation Device, True Device, Alphagraft, Devroye, Feller, Neograft suction-assisted motorized device, etc. [54].

Robotic hair transplantation is the leading technological advancement in hair transplant surgery recently. The use of robotic devices makes grafts harvesting and preparation of recipient site more precise and fast as compared to manual hair transplant [55].

Recently, Wesley has introduced a technique termed "piloscopy," a below the surface graft harvesting approach, and has designed an innovative endoscopic device "piloscope." The technique offers several advantages over conventional FUE including less scarring and graft transaction [56].

In vivo hair follicle multiplication, partial follicular extraction or techniques to divide single hair follicular unit into two has been reported in the literature. The technique may be useful for cases with compromised donor area, but the preliminary results are mixed and long-term evaluation and larger trials are needed [57–61].

Recently, autologous plasma has been tried as extracellular holding media for hair follicles which exhibited prevention of postoperative anagen effluvium and better results [62]. Intraoperative and postoperative injections of platelet-rich plasma (PRP), extracellular matrix (ECM) and platelet-rich fibrin matrix which is the rich source of various growth factors have also shown beneficial and promising results [63–65]. The authors prefer PRP injections usually 1–2 months after hair transplant on donor and recipient area and have noticed better and early results. The role and correct time for the use of topical minoxidil, PRP, low-level laser therapy and other adjuvant therapies should be explored more to achieve early and better results [66].

According to a survey report by International Society for Hair Restoration Surgery (ISHRS), hair cloning or stem cell can be the next big "technological leap" in the field of hair restoration followed by mechanization/FUE/robotic surgery/automation and therefore, bioengineering of hair follicle can prove penultimate solution to the hair gain therapy; till then, hair transplant offers predictable and long-term results to the balding population [3, 67, 68].

Conclusion

Hair transplant has seen several developments, but still is in its inception stage. With gaining interest worldwide and more and more doctors learning the techniques, the science and art of hair transplant surgery is expected to see major advancements in coming years. FUE has longer learning curve and is more tiring and time-consuming technique as compared to FUT, but can yield exceptional results in skilled hands. Hair transplant is proving to be more than just a cure for baldness, and the possible application of the technique in maxillofacial region is yet to be fully explored.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical Approval The manuscript has been read and approved by all the authors, the requirements for authorship as stated earlier in this document have been met, and each author believes that the manuscript represents honest work.

Informed consent Informed consent was obtained from all individual participants included in the study.

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