Response to Hair Repair Case #3

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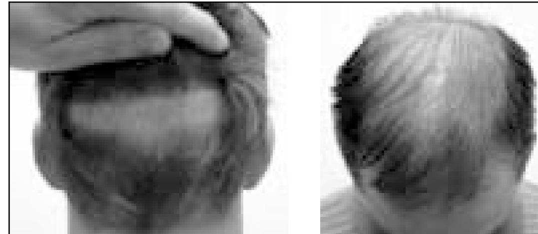
This patient (*Forum,* Vol. 13, No. 3, 2003; p. 355) has two main concerns: 1) the huge scar size of the donor site, 14cm × 2.5cm, and 2) the "grafty" appearance from his previous hair transplants.

From Dr. Elliott's information and pictures, we understand that the patient's occipital scalp has very little laxity and the temple and supra auricular area has excellent density and laxity. To treat this patient, let us treat the scar at the occipital area as if it were a scar at the top of the head. Then everything would be much less complicated because we do this type of procedure every day and we have a lot of experience in transplanting over the scar area, where we know the success rate is excellent. I do not see any reason why we should treat the occipital area different.

First, we should find out how much donor site is still available for us to use. From the picture, I estimate that the patient should have a donor site around the size of 10cm wide by 30cm long (the average person has about 30cm long donor length). The scar is 14cm long, so we still have 16cm available (30cm - 14cm = 16cm). Also, a 10cm wide donor site means we can use at least 5cm of this width for hair transplant purposes. It means the total area available for the donor site is at least $80cm^2$ (5cm × 16cm). In addition to that, 1- 2cm above or below the scar should have looser laxity than the scar area, which might be useful if more procedures are needed later in his life. The scar is 14cm long by 2.5cm wide; therefore, the area is $14 \times 2.5 = 35cm^2$.

Using 50% density as our goal for hair transplantation, we only need to use $17.5cm^2$. This is less than ¼ of $80cm^2$. There should be no problems in achieving this goal. For this patient, however, because hair overlap in the occipital area is better in the back than in the front top area, we do not even need 50% density to please the patient.

$35cm^2$ is actually a very small area for hair transplantation. My recommendation for treatment would be to perform two surgical procedures along with prescribing Propecia®. I would start to perform the hair transplant by first cutting 8cm × 1cm from each temple and supra-auricular area. The cut will line up to the bottom of the scar, and connect the scars together so that after the surgery it will look like one long scar instead of three small separate scars. The total donor area is $16cm^2$, while the coverage area is $35cm^2$. I would transplant 25% of the density and thus will need 25% of $35cm^2$, which is $8.75cm^2$. Scar tissue always has a limited circulation so I will use follicular units only. From the $8.75cm^2$ donor strip, I will cut that into about 875 grafts, and still have about $7.25cm^2$ left over.



Case 3. Scar pictured on left; top on right

Pattern of transplantation: Denser at the top of the scar, while toward the bottom, density is gradually reduced, thus treating the top of scar as one would the hairline.

Direction of hair: Very sharp angle, similar to the surrounding hair.

Position of transplant: The prone position would be acceptable; however, the table may take up too much space and be hard for storage, so we recommend using a *massage chair* instead (Figure 1). Both technicians can sit down and approach from each side (Figure 2).

Using my plan to treat this patient, we do not even need to do any scar revisions for these reasons:

1. The numbers of hairs is fixed. The size of the head never changes. Even if we do not consider the stretch back, the surrounding hair density will be reduced.
2. With scar revision, there is a possibility of damage to the micro circulator that will impact the new transplant area.
3. The coverage area is only $35cm^2$, a very small area in hair transplant standards.
4. Scar revision may also cause hyperplasia to the scar.

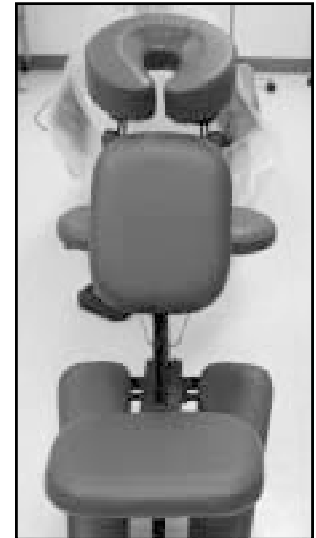


Figure 1.

Next, I would begin to correct the patient's second concern, the "grafty" appearance. The "grafty" look is produced from uneven density. If we were able to fill in all the empty spaces, to make the density even everywhere, then the "grafty" look will disappear. I do not believe in removing the big grafts. Instead, I believe the big grafts help us to achieve the patient's goal. How much density should we transplant to produce a more natural look? The answer is 50%, because at 50% density, it is hard for the

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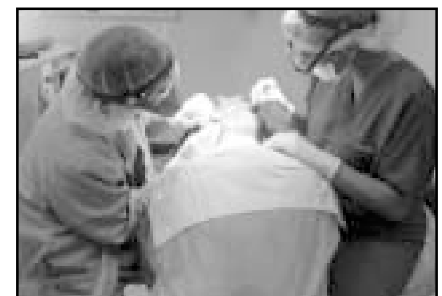

Figure 2.

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human eye to tell the difference between 50% and 100% density of hair. The leftover donor strip of 7.25cm^2 will be used for this purpose. The size of the grafts will be 1mm × 2mm. So we will be able to cut the donor strip into about 360 grafts, covering up to 30cm^2.

In addition to the hair transplant procedures, I would encourage the patient to take Propecia®, because it may grow some hair to reduce the "grafty" look. Further treatment for the "grafty" look needs to be reevaluated 6 months later after examining the results of transplanting the recipient area and looking at the effects of Propecia.✧

Update in Research

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known to direct growth and patterning during embryonic development, and recent evidence implicates them in postembryonic regulation of stem cell number and development in tissues such as epithelium that undergo constant renewal.

Potential therapeutic applications for hair growth genes have yet to be realized, Dr. Christiano said. Genes involved in diseases affecting millions of people, such as alopecia areata, have yet to be identified. In the case of alopecia areata, it is generally accepted that a complex combination of genetic and environmental factors results in a typical phenotype. Studies that seek to identify the relevant genes are under way.

However, the genes involved in the *hairless* and *nude* models, and in DSG4, could be excellent targets for development of hair removal and hair inhibition agents.

Cellular Approaches and Stem Cell Plasticity

Recent work, Dr. Christiano said, has shown remarkable plasticity in neural, hemotopoietic and muscle stem cells, depending on environmental stimuli. Much less is known about the potential for epithelial cell reprogramming.

Epithelial cell reprogramming has shown promise as a cellular approach to tissue engineering. The first evidence that a distinct (and presumably irreversibly committed) population of transient amplifying (TA) cells can be reprogrammed was provided by Ferraris et al [*Ferraris C, Chevalier G, Favier B, Jahoda CA, Dhuoailly D. Adult corneal epithelium basal cells possess the capacity to activate epidermal, pilosebaceous and sweat gland genetic programs in response to embryonic dermal stimuli. Development 2000; 127:5487-5495.*]. The investigators showed that adult rabbit central corneal epithelial cells can be reprogrammed into skin with sebaceous glands and hair follicles. The rabbit corneal epithelium was associated with mouse embryonic tissue, then grafted onto nude mice. The corneal cells responded to signaling from embryonic dermis, and gave rise to a new basal stratum, then to pilosebacous units or sweat glands, and to upper layers expressing epidermal-type keratins.

More recent work summarized by Dr. Christiano showed that both cornea and amnion can be reprogrammed by methods similar to those used by Ferraris et al. Potential therapeutic applications for epithelial reprogramming include providing epidermis for patients with inherited skin diseases such as ichthyoses where the epidermal compartment is defective.

Also, Dr. Christiano pointed out, the plasticity of epithelial and dermal cells of the skin to become osteoblast, adipose, neural and muscle cells suggests that hair follicles could become an easily obtainable source for adult multipotent stem cells for cell-based therapies. The presence of stem cells in the bulge area of the follicle has been a subject of intense investigation.

Hair Follicle Induction: Combined Genetic and Cellular Approaches

The plasticity of dermal papilla cells has been recognized for two decades, since Colin Jahoda and colleagues reported induction of hair growth by implantation of dermal papilla cells. The dermal papilla is known to be critical to hair growth. While it is related biologically and anatomically to the dermal sheath of the hair follicle, investigation has shown a critical difference in regard to inductivity: the dermal papilla is in direct contact with overlying epithelial cells while the dermal sheath is not.

Ear skin wound assay of dermal papilla and dermal sheath cells has shown that 1) both are inductive when freshly dissected and in early passage, 2) both lose inductivity in late passage, and 3) inductivity can be restored by co-culture with epithelial cells.

Dr. Christiano described the hypothesis that was developed to pursue further investigation:

- Gene expression comparison of dermal papilla versus dermal sheath wound identify genes where expression is interaction-dependent or inductive, and is lost upon explant culture.

Emerging from the subsequent microarray analysis of sample populations of freshly dissected mouse dermal papilla and dermal sheath was discovery of interaction-dependent expression of a novel gene, uterine sensitization-associated gene-1 (USAG-1) in dermal papilla. USAG-1 has been identified as a gene associated with successful implantation of the blastocyst stage of the embryo. It belongs to a small cysteine-knot containing gene family that to date has only one other member— a gene called SOST that appears to encode a regulator of bone homeostasis.

USAG-1 has a novel WNT signaling fuction that is mediated by the binding of a secreted frizzled-related protein (sFRP2). The Wnt4/USAG-1/sFRP2 axis has potentially an important role in many epithelial-mesenchymal (ectodermal-mesodermal) interactions during vertebrate development and organogenesis. USAG-1 has been found to be highly conserved in vertebrates.

The findings regarding USAG-1 have implications for understanding the underlying basis for hair multiplication, and for therapeutic applications of hair multiplication. The implications are even more broad for understanding and treating human genetic disorders of hair growth and loss, for developing more elegant mouse models, and for conducting functional studies.✧