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Surgical Hairline Advancement: Patient Candidacy and Best Techniques

The Trivellini System and Technique

## If hair is dead, when does it die? The Zombie Hypothesis

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### INTRODUCTION

In a recent manuscript in the *British Journal of Dermatology*, Jones et al. show that the hair shaft dies within the first 1mm of the proximal aspect of the dermal papilla and undergoes a predetermined cell death program that involves destruction of the cell nucleus within the first 0.5mm of this region.<sup>1</sup> Following the nuclear degradation, there is continued mitochondrial respiration and new protein translation even in this anucleated state. These brainless “zombie” cells continue to make and crosslink the final proteins for the structure of the hair shaft using a preprogrammed set of instructions up to the 1mm mark where the mitochondria are destroyed and cell death is unequivocal. With the average scalp follicle being ~4mm long, this leaves the remaining ~3mm of newly formed hair susceptible to damage and without active cellular defenses against oxidative damage from intra-scalp and extra-follicular influences.

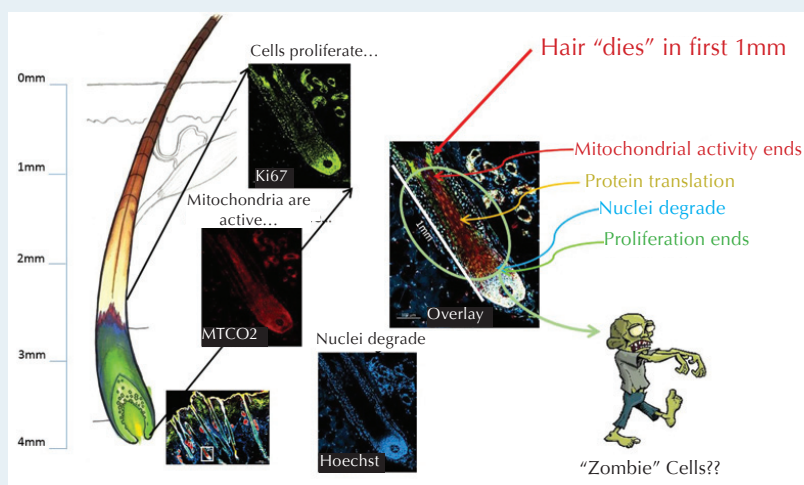
### BACKGROUND AND OBJECTIVE

The production of the hair fiber has been studied for hundreds of years with research spanning everything from natural fibers used in textiles (wool) to the hair we as humans have on our heads. Most of the work, however, is at the extremes, either on the “live” follicle or on the “dead” hair shaft, with little attention paid to the transition between these two very different states. In this work, we focused on that transition to better understand hair growth and formation. This effort was undertaken to understand when the hair can be a “cosmetic” substrate—a potentially new space where hair biology becomes hair chemistry—in order to understand pre-emergent hair damage.

### METHODS AND RESULTS

In this paper, human scalp biopsy samples and human follicular units (FUs) were sectioned and triple stained with Hoechst dye for nuclear staining, an antibody against Ki67 to mark cell proliferation, and an antibody against MTCO2, a mitochondrial enzyme indicative of metabolic activity. As shown in Figure 1, cellular proliferation (Ki67, green) is high in the matrix region of the follicle. This activity is required to provide the biomass needed to make the hair shaft as it is constantly formed from the bottom up. This is quickly followed by a loss of the cell nucleus (Hoechst, blue) once the cells are finished providing the fodder for the hair shaft. It’s at this point where the cells enter an anucleated state and maintain active processes of mitochondrial function (MTCO2, red), protein production, and

FIGURE 1.



NOV 13-16  
27TH WORLD CONGRESS  
ISHRS 2019 BANGKOK  
TRIPLE CROWN  
FUE FUT SMP  
WORLD LIVE SURGERY  
WORKSHOP NOV 16-17

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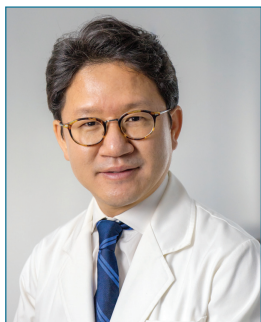
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## President's Message

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Dear Colleagues,  
I hope all of you are well!

This is my last message to you as president. It has been my honour to serve as president over the past year. As president, I have tried to be as democratic as possible and

to be open minded to all perspectives when issues arise. Furthermore, I have also tried to respect the recommendations from the Board of Governors, the Executive Committee, past presidents, and the Global Council to make unbiased and fair decisions. Looking back over the past year, I don't think I would have been able to have a good year without the help of many of the members. I would like to express thanks to you all and especially to the entire administrative staff of the ISHRS for their support.

I remember back to 1999, when I participated in the ISHRS for the first time. Over the past 20 years, the ISHRS has changed significantly. During my time as president, my respect and passion for the ISHRS has grown. I learned that the ISHRS has flourished owing to the service of many members. Without their efforts, I don't think we would have been able to experience the immense growth of our society. We will be holding an event to honour some of these colleagues at the Hollywood World Congress. I hope you will join me in congratulating them and that we can all celebrate together.

This year, three members will retire and become Emeritus members. They are Bill Parsley, Richard Halford, and Walter Unger. On behalf of the society, I especially thank them for their dedication and service to our colleagues for the past several decades. Congratulations on becoming Emeritus members! I wish each of you good health and happiness. I am sure that our colleagues will not forget all your hard work.

In 2019, the World Congress will be held in Bangkok, Thailand, and in 2020 it will be held in Panama City, Panama. For the 2021 World Congress venue, we are considering Lisbon, Portugal, and Athens, Greece. If you would like to recommend a suitable city as a venue for the Congress, the Board of Governors will take all recommendations into consideration at the Hollywood meeting. Please express your interest and share your ideas for the most suitable place.

The 2019 World Congress in Bangkok, Thailand, was scheduled to host the Satellite Live Surgery Workshop one week prior to the General Session as we had done before. However, resulting from the positive feedback of our members, we adjusted the World Congress to November 13-16 and the Live Surgery Workshop to November 16-17 so that your leave period is not too long. I would like to ask for your active participation in this event.

Some good news! I am very glad to let you know that the nominating committee has nominated Ali Abbasi as the new

Board of Governor for the 3-year term, and Jean Devroye and Nilofer Farjo for the second 3-year term of the Board of Governors. In addition, Mel Mayer was nominated as the Secretary of the ISHRS after Francisco Jimenez, who was nominated as the Vice President of the ISHRS. In accordance with the ISHRS by-laws, alternate nomination petitions are available to voting members upon request. If the ISHRS does not receive a valid alternate nomination petition in accordance with the ISHRS by-laws before September 13, 2018, the above Slate will be elected by acclamation at the Hollywood World Congress of Voting Members on October 14, 2018, and the current Vice President, Arthur Tykocinski, will become the president of the ISHRS. They have been serving our society for a long time and have worked very hard over the past couple of years. I would like to congratulate all of them and express gratitude for their service. Also, I have no doubt that Arthur Tykocinski (the next president of the ISHRS) will do an excellent job as our new president, and will continue to develop our society over the next year.

Finally, there are many special events in Hollywood. I sincerely thank all those who have worked hard to prepare this Congress. I would like to invite all of you to participate actively and to enjoy your time in Hollywood.

Thank you again, and I look forward to seeing you all in Hollywood! ■

### ***Pardon my error...***

In Dr. Parsa Mohebi's, "A Novel Device to Insert FU Grafts into Premade Sites" (Vol. 28, No. 4; pp. 146-148), the photo in Figure 3 (p. 147) was inadvertently cropped. The photo on the right shows how grafts are arranged all in one direction.

My sincerest apologies for this oversight.

—Cheryl Duckler,  
Managing Editor





# Co-editors' Messages

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## **Everybody come to Hollywood!**

Our upcoming World Congress in Hollywood will provide another great opportunity for us to learn and exchange ideas and concepts.

Hollywood is the magical dream factory, the center of the international movie and entertainment business. Many film and music stars live and work here. And their hairstyle is one important way for them to express themselves and play their roles. In fact, many celebrities have had hair transplants and some even admit it, being role models for our patients.

Could you imagine all actors having the same hair in all their movies? Or no hair at all?

This illustrates the importance of hair loss prevention and hair restoration and how it can change a person's appearance and life quality. And we all know how rewarding it can be: just think of that happy smile on the patient's face as Dow Stough described in his speech in Prague.

But how do we get to that point? Hair loss patients come with high expectations. The question is, how to meet them. Basically, we should listen and examine carefully, and establish a clear diagnosis and a systematic long-term plan.

Hair loss may be a symptom of internal disease and the treatment may require special drugs and/or skilled surgery. The management of alopecia is certainly not just an aesthetic job but a complex medical task, a physician responsibility.

We have to communicate this to the public through all available channels. My Hollywood movie idea: the ISHRS produces a YouTube video on hair transplantation that all members can share on their websites. It may become a blockbuster.

This issue again contains some interesting articles. I especially would like to thank the authors of the FUT vs. FUE survival study. The methodology is excellent. While a larger study would provide even more statistical evidence, it could be shown that FUT and FUE may produce a high yield in skilled hands. I think both harvesting methods have their own advantages and indications. While some patients may be more suitable for one method only, others may profit from a combination.

Some topics are controversial, so we expect to read your opinions in letters and articles. Send them to [forumeditors@ishrs.org](mailto:forumeditors@ishrs.org). ■



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Thanks to Mike Davis for presenting the synopsis of a study on the living-dead transition seen in hair follicles, which he performed with Dr. Jones et al. Mike presented this paper at Tri-Princeton's 8th International Conference on Applied Hair Science in Red Bank, New Jersey, where I

gave a keynote presentation, "Modern Techniques in Hair Restoration Surgery." The main theme at this meeting of scientists and hair product manufacturers was the live vs. dead dichotomy of hair. The activity of the live follicle (first 1mm) is considered biology (treated medically) whereas the study of the dead hair shaft is considered chemistry (influenced by cosmetic hair care products). It also has implications for us as manipulation or injury in this crucial area during hair transplantation may cause pre-emergent damage.

The above study and the studies reviewed by Vlad Ratushny (Hair Sciences) on the WNT/  $\beta$ -catenin pathway and Nicole Rogers (Literature Review) on PRP are well-constructed scientific studies that are lacking in our field.

Speaking of well-constructed studies, congratulations to David Josephitis and Ron Shapiro on their article comparing FUE and FUT results. It's not surprising to learn FUE and FUT grafts grow equally (when transplanted properly) but it's necessary to see evidence. We hear reports of 1,000 FUE grafts harvested per hour, transplanting 7,000 grafts in one day, and the advantages of implanters for placing grafts. But few are the studies that document results including yields/counts of grafts and follicles. I believe reports and claims made should not be published or reported at meetings until 6-12 months of growth and the type of survival analysis performed in this article. We are headed towards this standard for claims to be taken seriously.

Articles by Jeffrey Epstein and Gorana Kuka Epstein as well as Roberto Trivellini contain updates to similar published past *Forum* articles. While the ISHRS does not endorse either surgical technique or surgical device/instrument, their descriptions of the mechanics of their procedures/device are insightful and instructive as knowledge of the scalp and its follicles advances.

I was neither familiar with the work of nor ever met Felipe Coiffman, but I was stuck by David Perez-Meza's heartfelt eulogy. I was also struck by the quote concerning the harvesting of 4mm punches in the donor in the 1960s: "He [Dr. Coiffman] pointed out that donor strip removal and suturing leave a linear scar, which results in less scarring than the circular punch (4mm dia.) in the donor." Walter Unger stated: "I guess we had all forgotten Dr. Coiffman's ingenuity and its intrinsic long-term advantages over punch harvesting for decades." Now, the size of the punch and the scar are much smaller with FUE, strip scars have gotten thinner, the calculations have been made, and it appears history does repeat itself.

Finally, all roads lead to Hollywood—hair pilgrims unite. If you have any ideas, articles, or comments for the *Forum*, don't hesitate to talk with Andreas or me during the conference. I look forward to seeing all in LA. Safe travels! ■

and protein crosslinking; activities normally only seen in complete nucleated cells. This suggests that a preordained program was established prior to enucleation and the cells act like “zombies,” carrying out activity without an active internal nucleus as the command and control center.

To further investigate the process of hair cell death, we characterized the way in which the organelles are prescriptively destroyed and have shown that the nucleus is degraded via canonical apoptotic and non-apoptotic processes and within the first 0.5mm of the proximal dermal papillae. Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) is a nonspecific measure of nuclear destruction. Caspase-dependent and -independent processes were mapped using antibodies against caspase-activated deoxyribonuclease/DNA fragmentation factor subunit B (DFFB), a marker for apoptosis, and cell-autonomous nuclear degradation (DNase1L2), a marker for cell-autonomous nuclear degradation.

After destruction of the nucleus, the cells in the follicle maintain mitochondrial activity to the 1mm mark where staining with ubiquitin-like protein LC3B and Bnip3L showed that the mitochondria then undergo a specialized form of autophagy specific to mitochondria called mitophagy. It is at this point when the cells that make up the hair shaft are considered dead as they continue their one-way journey upward and continue the cornification process that forms the hair shaft. This autophagic process has been recently shown to be critical to hair follicle function in a cultured hair follicle model.<sup>2</sup>

## DISCUSSION

Proper hair architecture at the molecular level is an important characteristic of hair that has a healthy look, shine, and feel. Ironically, this lively, healthy hair is actually dead and is not regenerative after it exits the scalp. However, the origin of hair begins as a very active follicle that is full of specialized cells that ultimately make up the cosmetic hair fiber. The questions raised in the manuscript by Jones et al. include: Where does the transition of living-to-dead happen? and What are the molecular processes that happen during this transition?

The article states: “Transition of keratinocytes from actively respiring nucleated cells to anucleated structural cells within the hair follicle is key to the creation of a strong, healthy hair fiber. This specialized form of cell death, or cornification, requires cellular organelle removal to allow the cytoplasm to become packed with keratin bundles that are further strengthened by a carefully orchestrated, reactive oxygen species dependent cross-linking.” This research demonstrates a programmed stepwise progression from the live to the dead state within the first 1mm of hair formation seemingly to make space for keratin proteins that make up the hair shaft and provide a healthy hair deep within the scalp.

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## Notes from the Editor Emeritus, 1999–2001

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### The Boys and Girls from Brazil

I have just had the privilege of attending the 7th Congress of the Brazilian Association of Hair Restoration Surgery. This was an

excellent program consisting of high-quality presentations by speakers who were predominantly Brazilian but who were supplemented by speakers from many other countries.

Brazil occupies a special place in the field of cosmetic surgery in general, and hair restoration surgery in particular. Historically, we know of the special contributions of plastic surgeons such as Carlos Uebel, who published on micro-grafts in 1986 and won the Platinum Follicle in 2000. Other prominent contributors have been Fernando Basto (published on irregular hairline design in 1993), Marcelo Gandelman (Manfred Lucas award and Platinum Follicle winner), and Marcelo Pitchon, who described “preview long hair” FUT transplants in 2006.

In recent years, the field has also expanded to dermatologists, enlarging the talent pool. I can say with complete confidence that Brazil is currently enjoying a “golden age” with a whole generation of innovative, world-class surgeons becoming prominent in our field. The incoming president of the ISHRS, Arthur Tykocinski, is one. The current president of the Brazilian Association of Hair Restoration Surgery, Mauro Speranzini, is another. Then also consider Tony Ruston, Márcio Crisóstomo, Henrique Radwanski, and Maria Angelica Muricy.

Many Brazilian surgeons embrace the concept of “preview long hair” FUT transplantation pioneered by Marcelo Pitchon. I have always wondered about the wisdom of giving instant temporary gratification to patients with long hair grafting as I felt the resulting disappointment 2 weeks later, as the grafted hair shed, negated the early euphoria of the patient. However, every Brazilian surgeon who performs this told me that there was 100% patient satisfaction with this technique. Interestingly, it may be that the “preview long hair” technique “saves” grafts by allowing the surgeon and patient to decide when sufficient density has been obtained intra-operatively. It will not surprise you to know that “preview long hair” FUE is being trialed in Brazil and that modern punch technology has allowed impressive results to be demonstrated by this example from Dr. Muricy, who harvested 200 long-hair FUE grafts in 15 minutes! (Figure 1.)

Other surgeons to whom I spoke insisted that they could harvest more FUE grafts in a session if the donor area was shaved. As we have come to expect, there was much discussion about donor area harvesting with FUE and the definition of the “safe” donor area. I am inclined to think that we should talk about the “safer” donor area and the “less safe” donor areas. It is clear from the presentations there is wide

variation in what different surgeons declare as safe...

Another big topic at the meeting was the “homogenous” depletion of density in the donor area using FUE. The reality of this philosophy is that the “less safe” donor areas will be depleted at the same rate as the “safer” areas. I fear history will not be kind to us in this regard as the progression of balding exposes some donor areas. With this in mind, there was further discussion of the selective use of “less safe” donor hairs strategically placed in the recipient area to allow a future natural balding pattern to develop if the grafts were lost. I remain skeptical of the wisdom of this approach but time will tell.

I was very pleased that the theme of the conference was “FUT and FUE: Staying Together,” and that equal time was given to both techniques with high-quality presentations discussing the strengths of both approaches. This does not surprise me given the predominance of plastic surgeons practicing hair restoration in Brazil.

After the conference, Bob Haber and I had the privilege of visiting the offices of Tony Ruston, Mauro Speranzini, and Arthur Tykocinski. It was clear to us that cutting-edge work was being performed in these clinics. They all exclusively place grafts with various implanters (dull for Ruston and Speranzini, sharp for Tykocinski), and the skill sets of their staffs was something to behold.

As well respected as the Brazilian surgeons are in our field, I can’t help but think that their innovations would be more widely known if their published contributions had been in English rather than Portuguese.

Muito obrigado to our learned Brazilian colleagues! ■

FIGURE 1. Long hair FUE grafts harvested by Dr. Muricy.

