Cyberspace Chat

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The following is a conversation between the co-columinsts of Cyberspace Chat, debriefing after the recent ISHRS Annual Scientific Meeting in Kuala Lumpur, October 8-11, 2014. The daily meeting write-ups will be included in the next issue of the Forum. *—RT*

John Cole began: I must say that the meeting in Kuala Lumpur exceeded my expectations. A tropical environment along with the friendly nature of the Malaysians made for the perfect setting to a wonderful meeting. Dr. Pathomvanich certainly did his work preparing for the meeting. We could tell this was not the first meeting he has organized. What would you say are your highlights, Brad?

Bradley Wolf offered: Well, John, overall it was a great meeting. As you are well aware, hair pilgrims are known to unite anywhere in the world. I anticipated a unique experience due to the location, Malaysia, as well as the demographics of the attendees. With the change in dates, location, and troubling geopolitical issues, there were concerns that attendance would be down, but attendance figures exceeded everyone's expectations. The hotel was spectacular, in the center of Kuala Lumpur, and a short, (and relatively inexpensive) cab ride to most tourist attractions. The meeting and hotel rooms were close, making for a cozy meeting, conducive for chance meetings as well as professional and casual interactions with colleagues. The hotel staff was extremely accommodating as were all Malaysians I encountered. Everywhere in the city, they were smiling and helpful.

Forty-one percent (41%) of attendees (214/526) had never attended an ISHRS meeting. The average percentage of first-time attendees the prior five years (2009-2013) was 26%. This is a significant change. I could feel the energy and excitement. The exhibitors' booths were buzzing with business and discussion. Many of the exhibitors' supplies were exhausted by Friday forcing them to take orders. I looked out over the crowd in the lecture hall on Friday, when in most meetings the attendees had thinned a bit, and the seats were as full as they were on Thursday, the first day.

The average number of total attendees over the last five meetings was 555. The last meeting not in North America, Amsterdam, had 476 attendees. So Kuala Lumpur at 526 was quite remarkable. Unlike most ISHRS meetings where North American members dominate attendance numbers, Asian attendees dominated in Kuala Lumpur. The averages by country the last five years show that the United States (236), Canada (35), Brazil (24), United Kingdom (24), and India (19) had the highest attendance. This year, the top five were India (58), United States (58), Thailand (39), South Korea (37), and Australia (29).

John Cole added: While it is impossible to single out any one highlight, I rank the lectures by Rodney Sinclair and Thomas Dawson equally at the top of my list. I thought Dr. Dawson's lecture was relevant to every hair loss practitioner, while Dr. Sinclair offered insights to the physiology of hair that I'd never considered. Dr. Sinclair revealed that there are primary follicles and secondary follicles for the follicular unit. The primary follicles form first in utero. The secondary follicles of a follicular unit form later also in utero. The secondary follicles are the first ones to depart in androgenic alopecia or, as he stated, "last in and first out." His talk centered on the arrector pili muscle. In androgenic alopecia, the arrector pili muscles separate from the secondary follicles first. In that the CK15+ stem cells are located in the arrector pili muscle, the capacity for follicle regeneration is lost when the arrector pili muscle disconnects from the secondary follicles. When the arrector pili muscle detaches from the hair follicle, the attachment is replaced with adipose. In alopecia areata, miniaturized follicles maintain their attachment with the arrector pili muscle. He also mentioned a niche of CK15+ cells at the junction of the arrector pili muscle and the epidermis. The arrector pili muscle does not form a single attachment to the follicle. Rather, muscle attaches at multiple points.

Paco Jimenez has noted that the insertion region of the arrector pili muscle to the hair follicle, which coincides with the lowest end of the isthmus, is located 1.6mm from the skin surface.[1] CK15+ cells are located an average depth of 1mm (0.9-1.35) below the skin surface and extend down to a depth of 1.8mm (1.6-2.25), just below the arrector pili muscle insertion. The average length of the bulge region as detected using anti-CK15 is 0.8mm, almost equivalent to the length of the isthmus.

While Dr. Sinclair suggests that regenerative capacity is lost when the arrector pili muscle detaches from the secondary follicles, Cotsarelis has found that follicle stem cells can migrate.[2] However, according to Dr. Sinclair, it seems imperative that we induce regeneration prior to a point of no return in the miniaturization process.

One thing that has always intrigued me is that the growth of single-hair grafts manufactured by reducing intact follicular units to single-hair grafts *in vitro* is less than 90% in many cases. It could be that stem cell niches are lost during the division process. Alternatively, the yield from secondary follicles of an individual follicular unit may be less than the yield of primary follicles when intact follicular units are fractionated.

Dr. Dawson gave a wonderful presentation on progressive loss of hair volume with age, styling habits that cause hair thinning, and biochemical options to improve hair. Curling, blow drying, shampooing, coloring, brushing, and teasing hair causes hair breakage predominantly in women. He suggested that shampooing three times a week was probably adequate and it is best to rinse in cold water. Dr. Dawson uses the same technology as sheep farmers to measure hair diameter. Wool that is 22 micrometers in diameter makes a pair of inexpensive socks, while wool 15 micrometers in diameter make an expensive garment. Using the methods he obtained from the wool industry, Dr. Dawson began to study hair diameter and calculate hair volume. Although hair is an elliptical structure, Dr. Dawson calculates hair volume using the formula for a cylinder. He included terminal hairs

ranging from 20 micrometers to determine the average diameter of hair is close to 60 micrometers. At age 45-46, women lose hair density from an average of 220 hairs/cm^2 to a density of 170 hairs/cm^2 by age 60. At age 40 to 45, both men and women begin to lose hair diameter and the loss is progressively worse over time. Hair volume decreases from 20,000 to nearly 12,000 by age 70. Thus, not only is the donor area impermanent as previously suggested, hair coverage becomes progressively worse over time due to a loss of hair volume.

In his measurement of hair volume, Dr. Dawson measures the long axis of the hair shaft. He noted that straight hair tends to lie on its minor axis, while curly hair lies on its long axis. Vellus hair is stated to have a diameter of less than 30 micrometers, therefore, I was surprised he included hair follicles lower than 30 micrometers to calculate the average hair diameter. Because a hair below 30 micrometers adds so little hair volume, I did not include follicles below 30 micrometers when I calculated the average hair diameter was approximately 68 micrometers.

Dr. Dawson reviewed a number of ingredients to improve hair quality and volume. Ultraviolet light is damaging to hair. He stated that deposition and coating was a problem with UV protectors for the hair. Caffeine up regulates the aquaporin gene. Aquaporin increases the absorption of water into the hair follicle. A combination of niacinamide and caffeine at the proper concentration, can improve hair diameter and hair coverage. Based on the progressive decrease in hair diameter in time, we certainly need to look at the biochemical solutions to improve hair diameter for our patients.

The workshop on micropigmentation given by William Rassman, Ryu, Jino Kim, and Milena Lardi was excellent. The epidermis varies in depth from 0.5 to 1.5 mm due to undulations. The procedure is angle, depth, and time sensitive. It is important to deposit the particles in the outer dermis. Dr. Rassman feels that it takes about 100,000 tries to get the feel. The ink that Dr. Rassman uses and sells is permanent. The ink Milena sells fades over the span of about one year. Milena uses particle sizes of 15 micrometers and coats them with silicone. She feels her silicone particles are absorbed. Because skin takes about 1 month to turn over and shed any pigment deposited in the epidermis, the result takes about 1 month before you can evaluate it. Dr. Rassman noted that the pigments are carcinogens and we must not promise anything to the patient. Dr. Rassman feels a full head takes about 25 hours to complete, while Milena can accomplish this is 2 hours. She does a second pass the next day that takes 1 hour and then a final touch up one month later that requires another hour.

Bradley Wolf continued: I was certainly surprised to hear Ms. Lardi can accomplish one pass on a patient with Class VI hair loss in two hours. That is fast! It seems that most who perform scalp micro pigmentation (SMP) develop their own technique and timing. Dr. Rassman emphasized that he thinks SMP will become an integral part of every practice that offers hair restoration surgery.

John Cole offered: Dr. Pathomvanich did a nice job organizing the meeting. I think you were our busiest speaker with the most presentations with five as I recall, Brad.

Bradley Wolf added: It takes so many people working a year in advance to pull off what appears to be a seamless event. Much credit goes to Victoria Ceh, our tireless Executive and CME Director, the staff of the ISHRS, and the CME Committee (Continuing Medical Education). I saw Victoria, Kimberly Miller, and Melanie Stancampiano everywhere. I thought they cloned themselves! Of course, Dr. Damkerng Pathomvanich, the program chair, also deserves much of the credit. Dr. Vincenzo Gambino, our president, and Damkerng, with Victoria, spend so many hours behind the scenes for a year working hard to make the five days of the meeting hum like clockwork. There are so many more who worked so hard, it's impossible to mention everyone.

John Cole noted: The first argument of the meeting occurred between Dr. Puig and me. Dr. Puig feels that he is seeing much mature results much faster with liposomal ATP while I disputed this contention. We have some work to go in establishing a protocol for platelet rich plasma (PRP). In presenting a response to PRP it is important to discuss the protocol used so that we can better evaluate the result. We need to disclose the needle size for injection, the concentration of PRP, the depth of the injection, how the PRP is activated, the hematocrit of the PRP, and any ancillary treatments such as microneedling. Dr. Puig gave a wonderful paper that suggests that a 1× concentration of PRP and a hematocrit less than 3% without activation of the PRP produces no improvement in the Hair Mass Index in women with Ludwig II female pattern hair loss (FPHL). Dr. Kumar found no hair transplant surgical result benefit (hair count or hair diameter) in a small sample size of patients with a concentration of 1 million platelets/µl and activation with calcium chloride or thrombin. Dr. Kumar stated that he used to trichoscan to document his results, but he did not present results demonstrated the use of a trichoscan. I have definitely seen an improvement in hair mass in women using a 5× concentration, a 2% hematocrit, injected in all layers from upper adipose to upper dermis using a 25 gauge needle, and activation with Calcium gluconate. I have seen the cross-sectional trichometry improve from 60 to 98 after one year in one woman. Clearly, we need more data with the specific protocol noted. We are lucky to now have some studies that demonstrate protocols that seem to offer no benefit from PRP.

Bradley Wolf added: As with most new medications, surgical modalities, or ancillary treatments, it takes time and studies to determine efficacy. From the lectures in Kuala Lumpur, it appears there is much work to be done on determining optimal concentrations of PRP, which activator, and the needle size that maximize the effects of PRP. It's interesting that there were no studies or lectures on ACell presented in Kuala Lumpur.

John Cole followed: I generally don't care for talks on scarring alopecias, but Dr. Paul McAndrews gave a wonderful talk on hair transplantation in Non-AGA & Scarring Alopecia. I tried grafting into incision scars with slightly larger grafts in the early 1990s. But I did not like the results. I was happy to see some nice results from Ryu using smaller grafts. This clearly gives us one more option in addition to trichophytic closure to improve the appearance of strip scars. In addition to an award for presentation skills, Sarah Wasserbauer gave a wonderful talk on grafting eyebrows. She worked the audience magically. I loved your high speed video, Brad. What camera did you use?

Bradley Wolf responded: I used a GoPro camera on a stationary mount just behind me. It was a challenge to dodge the camera while doing the strip excision surgery. I tried mounting it on my head but there was just too much movement in the video. The GoPro Studio editing software was quite a challenge.

John Cole continued: I think Dr. True presented a very nice study documenting the benefits of human recombinant hyal-

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uronidase in strip surgery. I can't imagine doing a strip without it. One of your scars where you closed with metal sutures was pink. I wonder if you see an increase in pink scars with metal sutures. We perform hair transplants rather than fat transplants so I always wondered what the benefit was from chubby grafts and why so many were worried that FUE grafts lack adipose. I think you clearly demonstrated that we are transplanting the essential structures with FUE in your genomics study comparing hair follicles from FUT, FUE, and plucks, Brad.

Bradley Wolf followed: Thanks to P&G (Proctor & Gamble Co.) who did the genetic analysis. They studied 55,000 transcripts of 18,000 genes and looked closer at 132 genes of hair relevant keratin and keratin associated proteins. I think it's the best evidence to date that shows FUT and FUE grafts are pretty much the same down to the stem cells present in both.

John Cole replied: I'm not sure what to make of the hidden transection rate talk given by Dr. Kim. However, I just received a communication from Dr. Kyuhu Lee discussing the same thing. I believe we have to consider this. Dr. von Albertini gave a nice presentation on the benefits of limiting the incision depth. The volume of the contiguous wound is important in my opinion. A 1cm-wide strip cut 30cm long and 1cm deep removes 30,000 mm^3 of tissue and might yield 2,400 follicular units. A 1mm punch incision 2mm deep removes about 1.56mm^3 of tissue and each incision is separate from the next wound. In total, this would result in the removal of less than 3769.8mm^3 of tissue when 2,400 grafts are removed. I can only approximate with FUE simply because with FUE the lower incision is always deeper than the upper part of the incision, so the excision is always less than a complete cylinder. However, because the punch enters the skin at an angle based on the angle of hair growth, the incision is always an ellipse and the volume of tissue removed is greater than the volume of a cylinder. Regardless, the volume of contiguous wounding with FUE is significantly less than the contiguous excision volume with strip excision.

It was interesting to discover that 47% of FUE physicians use motorized extraction. Only 21% of physicians use a dull punch. In five years, 32% of physicians expect to perform FUE 76-100% of the time and nearly 75% expect to perform FUE at least 26% of the time. Emre Karadeniz found that his grafts from FUE average only 2.03 hairs while his FUT grafts average 2.25 hairs. Clearly, this is a function of punch size and technique. Dr. Lorenzo averages 2.25 hairs per grafts from FUE. In the Farjo clinic, the ARTAS averaged 2.12 hairs per graft, while FUT averaged 1.98 hairs per graft. Quite frankly, I've never seen a clinic consistently average more than 2.05 hairs per graft from FUT though Bernstein's microscope vs. Loop study showed an average of 2.28 hairs per graft from microscopically dissected grafts compared to 2.14 hairs per graft from loop dissection.[3] Sharon Keene gave a nice review of low level laser therapy (LLLT). She clearly did her homework. I appreciate the idea from Dr. Hwang to control the depth of graft placement based on the graft length. Pitting can produce low yields. This is a step in the right direction as variation in graft length can produce pitting when a single depth of insertion is followed.

Yun Joo Lee presented some fascinating data on patient satisfaction in Korean patients from hair transplantation. He found 75% of men were satisfied (3% dissatisfied) and 60% of females were satisfied (13% dissatisfied). I think it is always harder to please a woman. Dr. Dua avoids the mid-sternal area when harvesting chest hair grafts due to a concern about hypertrophic scarring. In hundreds of cases using punches up to 1mm in diameter, I have not seen hypertrophic scarring on the chest regardless of anatomical location. I have seen hypertrophic scarring on the chest in multiple locations by another physician, so clearly there is a way to cause hypertrophic scarring. Fortunately, this patient responded well to injections of 10mg of kenalog/cc with a loss of elevation. The discoloration from the scarring remained on his chest. Drs. Bernstein and Harris were the "caboose" of our meeting. It is exciting to see the advances in robotic recipient site creation as demonstrated by Dr. Bernstein. Dr. Harris presented some retrospective data average hairs per graft by robotic harvest (12.2% one hair, 41.85 two hair, 30.8% three hair, 15.2% four hair). In my regional variation study, I found that in the entire donor area from the mid-occiput to the supra-auricular region the average was number of hairs per follicular group was 12.32% one hair, 36.3% two hair, 31% three hair, 14.9% four hair, 4.24% five hair, and 1.24% six hair.[4] However, if we looked only at the mid-occipital area and the mid-mastoid area, the average number of hairs per group was 9.15% one hair, 37.6% two hair, 28.54% three hair, 17.35% four hair, 5.48% five hair, and 1.86% six hair. The robot harvests most of the grafts from the central part of the donor area and progressively less laterally. The robot is unable to harvest the larger groups containing more than 5 hairs and selectively chooses the smaller grafts. In general, the data is similar in both studies; however, we must also consider that a small amount of fractionation of follicular groups is occurring. Furthermore, when I harvest grafts by FUE using a punch size similar to that of the ARTAS I find it difficult to locate single hair grafts and my mean calculated density is 2.93.[5] Still, we must be impressed with the progress the robot is making. Or should we?

If we look at a photograph comparing the ARTAS to a 0.8mm punch, we note the wounding is much larger with the ARTAS (Figure 1). In fact, the wounding with the ARTAS is much larger than 1mm. The reason we find 12.32% natural single-hair grafts in my regional variation study is that on the surface of the skin we can arbitrarily define natural single hair follicular units (Figure 2). What we cannot do is isolate these single-hair follicular units from the larger adjacent cluster using a punch that cuts holes the size employed by the ARTAS. If we use a punch that cuts holes similar to that of the ARTAS as depicted in Figure 1, we will find it almost impossible to isolate single hair grafts. In order to isolate single-hair grafts in FUE, we must use a punch similar in size or smaller than the 0.8mm punch depicted in Figure 1. We isolate single-hair grafts by taking small bites from larger clusters (Figure 3). In fact, natural single-hair follicular units are uncommon especially in the middle of the donor area where the ARTAS is most efficient. Only patients with a low calculated density and poor candidates for hair restoration surgery will have a large number of natural single-hair follicular units in donor boxes 1,2, 5, and 6.[6] Due to efficiency, the ARTAS often harvests predominately in the middle of the donor area and progressively less laterally (Figure 4). The ARTAS is known to over harvest isolated portions of the middle of the donor area where the resulting follicular unit density in this 0.1cm^2 area following a single pass with the ARTAS was equivalent to only 20 follicular units/cm^2 (Figure 5). The high percentage of single-hair grafts given a wound this size, the predilection to harvest predominately

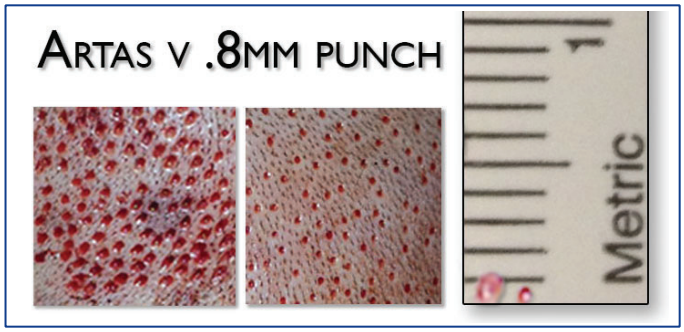

Figure 1. Side-by-side comparison of the ARTAS *(left)* vs. .8mm *(right)* wound size.

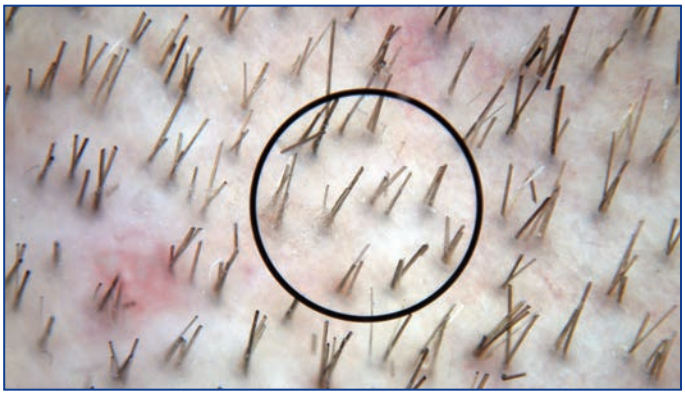

Figure 2. True single-hair follicular units are uncommon in an average donor area. In FUE, single-hair grafts are generally obtained by fractionating the larger follicular units using a punch 0.85mm in diameter or smaller. Isolating single hairs is far more difficult if not impossible with punches 1.1-1.2mm in diameter.

Figure 3. Single-hair grafts in FUE may be isolated *in vivo* using a punch 0.85mm in diameter or smaller.

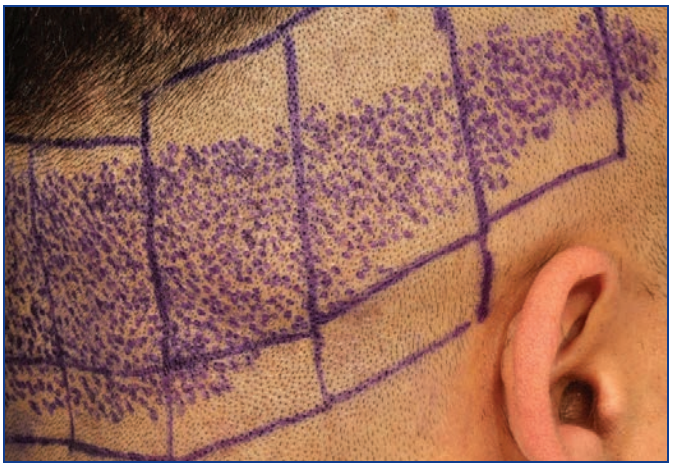

Figure 4. Due to efficiency, the ARTAS often harvests predominately in the middle of the donor area and progressively less laterally.

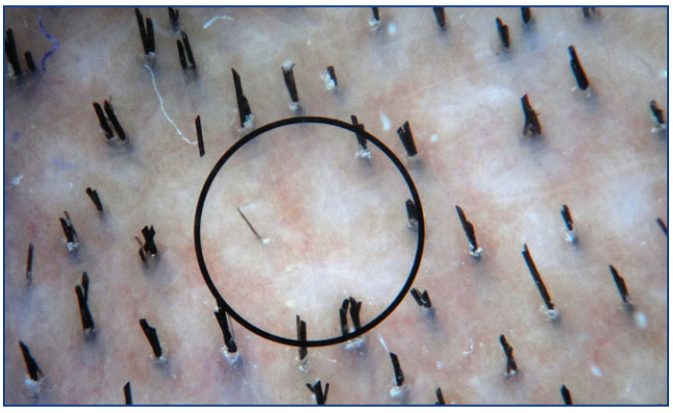

Figure 5. The ARTAS can over harvest in isolated areas; meaning, a single pass with a 1.2cm^2 punch area may leave only the equivalent of 20 follicular units/cm^2 in isolated areas.

from the middle of the donor area, the potential to over harvest isolated areas of the donor area, along with the unexplained high percentage of "missing grafts" remain concerns for the ARTAS.

Finally, I think Drs. Pathomvanich, Bhatti, Ng, and Vong treated us to some impressive results. It was a well-rounded meeting. What are your final thoughts, Brad?

Bradley Wolf concluded: It was exciting to see the energy of the new attendees from Asia, which was very well represented with 56% of the attendees from Asia. Now it's on to Chicago, September 9-13, 2015. Save the date! Good luck to our incoming president, Sharon Keene, and our program chair, Nilofer Farjo, who I am sure are busy right now working on ISHRS #23. I hope to see everyone there.

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