A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

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The New Face of Fillers: A Multi-Specialty CME Initiative (Part II of II)

ISSN: 1545 9616

August 2012 • Volume 11 • Issue 8 (SUPPLEMENT)

JO0812

Disclosure of Commercial Support

The New Face of Fillers: A Multi-Specialty CME Initiative (Part II of II) supplement to the *Journal of Drugs in Dermatology* has been made possible by unrestricted educational grants from Medicis and Allergan.

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AUGUST 2012 VOLUME 11 ISSUE 8 (SUPPLEMENT)

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CASE VIGNETTES

QUICK POLLS

THE NEW FACE OF FILLERS: A MULTI-SPECIALTY CME INITIATIVE (PART II OF II)

Release Date: August 1, 2012
Most Recent Review Date: July 16, 2012
Termination Date: July 31, 2013
Estimated Time to Complete this CME Activity: 2 Hours
Media/Method of Participation: Journal article, web-based post-test, and evaluation
Hardware/Software Requirements: Any web browser

Statement of Need

As the scope of aesthetic rejuvenation expands, there is an increasing need to enhance the skill and knowledge of aesthetic physicians. Physicians need up-to-date, evidence-based research and training that supports the best possible care in the field of soft tissue augmentation. The expansion of dermal fillers and injectables for facial rejuvenation, coupled with increased patient demand creates a critical need for physician training in minimizing potential complications, understanding the use of blunt cannulas, selecting optimal products, strategizing for specific facial zones, and incorporating evidence-based data regarding efficacy, longevity, and field of effect. Aesthetic physicians must possess the professional information and training, in the presence of experience and judgment, to provide optimal patient outcomes in the field of dermatology and facial aesthetics.

Educational Objectives

This activity is a multi-specialty, evidence-based initiative designed to increase the knowledge of aesthetic practitioners by providing them with the simultaneous integration of knowledge, skills, and judgment from thought-leader testimonials, science-based research, and evidence-based data to address the difference between present patient outcomes and those considered achievable in the field of aesthetic medicine.

Upon completion of this activity, participants should be able to:

- Identify strategies for individualized, evidence-based selection of soft tissue fillers and appropriate patient selection, including patients with both deep and superficial volumization requirements.
- Organize thorough global and regional assessments of the face and analyze the effects of structural tissue changes on the volume loss, contours, shape, and proportions of the aging face.
- Identify how structural and functional anatomical considerations can guide safe and efficacious facial volumization and strategies for preventing and managing potential complications from soft tissue fillers.
- Describe how targeting of specific tissue planes with specific injection techniques, including the use of blunt injection cannulas, can optimize the results of volumization with soft tissue fillers.

Target Audience

This activity is developed for dermatologists, residents in dermatology and aesthetic physicians with an interest in the use of fillers to provide optimal outcomes in facial aesthetics.

Accreditation Statement

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The New Face of Fillers: A Multi-Specialty CME Initiative: Supplement Part II of II

Hema Sundaram MD

It is both a pleasure and an honor to introduce the second and final part of this CME supplement publication on fillers. Part I, which was published with the March 2012 issue of the *Journal of Drugs in Dermatology*, traced an intriguing path back from our clinical observations to the underlying science that provides a rationale for the behavior of the various filler products that have successively become available for aesthetic use. This connection of the dots from experience to evidence is both clinically relevant and intellectually satisfying, and brings to mind Albert Einstein's aphorism that everything should be made as simple as possible — but no simpler.

While this empiric path is valuable, the understanding it engenders will always be somewhat incomplete, as we can only seek explanations for what we have already observed. In the next stage of our evolution, we are moving forward with clinical and scientific exploration in tandem and modifying our hypotheses to fit the data as they are obtained. This forward path is charted in this second part of the supplement, which includes roundtable discussions on new and emerging concepts in fillers; a consensus document and individual perspectives on blunt microcannulas; and case vignettes that illustrate our current understanding of facial fat compartments, special considerations for skin of color, and the vertical injection techniques for filler implantation. The inclusion of Quick Poll surveys on filler "hot topics" affords a glimpse into the personal philosophies of an international, multi-specialty faculty that is recognized for its passion for, and dedication, to the field.

It is my hope that this publication will offer some insight into how clinical knowledge and the identification of unmet needs for our patients are driving novel research and development. We are categorizing fillers now in ways that allow us to define their optimal applications — for example, based on their qualities of firmness vs. softness, elasticity vs. fluidity, tissue integration patterns, and water binding capacity. And we are learning to parse when and how these properties are germane to the choices of product and injection technique that we make during every office consultation. A more evidence-based classification also allows us to refine our strategies for pan-facial and regional volumetry, to shorten the learning curve with new products and incorporate them appropriately with existing ones, and to combine fillers and neuromodulators more effectively.

Besides illustrating the scientific method in action, this supplement captures a little of the debate that makes the world of fillers and volumetry so exciting. As Mahatma Gandhi said, honest disagreement is often a good sign of progress. Next year marks the tenth anniversary of the FDA approval of the first hyaluronic acid filler in the United States. Poised to enter a second decade of experience with a burgeoning palette of fillers, we can anticipate that both honest debate and simplification without over-simplification will continue to light the way in this most fascinating aspect of nonsurgical rejuvenation.

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July 2012

Fillers and the "Three Curves of Youth"

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ABSTRACT

A 40-year-old Asian female presented complaining of looking tired. She had no significant medical history and was in good health. She had received botulinum toxin injection in the glabellar area routinely over the last several years but had no history of injectable fillers.

J Drugs Dermatol. 2012;11(suppl 8):s9-s11.

INTRODUCTION

Americans spent nearly $10.7 billion on cosmetic procedures in 2011. Of that total almost $6.6 billion was spent on surgical procedures; $1.9 billion on injectable procedures; $1.8 billion on skin rejuvenation procedures. Recent data imply that patients are addressing aging changes earlier than in the past. Although baby boomers have traditionally "led the pack," recent statistics from the American Society of Aesthetic Plastic Surgeons show that "GenX"ers (age 35–50) had the most procedures—more than 4 million and 44% of the total while baby boomers (age 51–64) accounted for 28%.[1] Therefore, the patient presented here is in that younger demographic.

CASE VIGNETTE

A 40-year-old Asian female presented complaining of looking tired. She had no significant medical history and was in good health. She had received botulinum toxin injection in the glabellar area routinely over the last several years but had no history of injectable fillers. Before and after injection photographs are shown in Figure 1.

She was treated with one vial of poly-l-lactic acid (Sculptra Aesthetic) (9 cc dilution, hydrated 48 hours) in the temples (3 cc total), midface (4 cc total), pyriform aperature (1 cc total), and mandible (1 cc total). A 25-gauge, 1.5 in needle was used in all locations except the pyriform and mandibular area. In this location, a 26-gauge, 5/8 inch needle was used. A reflux maneuver was performed before all injections to prevent inadvertent injection into the vasculature. Note the improvement in the position of the nose and upper lip, as well as decreased shadows in the central face (Figures 2-4).

Next, Restylane (2 cc total) was injected with a 27-gauge cannula in the medial brows and forehead (see Figure 3). (A small area in the mid/lateral brow—lateral to the supraorbital neurovascular bundle—was anesthesized with 1% xylocaine injected with a 30-gauge needle. The needle was withdrawn, and as there was no bleeding in the area, a 22-gauge needle was injected into the same opening just to the level of the deep dermis. This was then withdrawn, and the 27-gauge cannula inserted through this opening.) Note the projection of the brows and the contour of the forehead.

FIGURE 1. A 40-year-old female treated with poly-l-lactic acid, hyaluronic acid, and botulinum toxin. Frontal view **a)** baseline and **b)** six weeks after treatment. Right oblique view **c)** baseline and **d)** six weeks after treatment.

Next, 0.8 cc Juvéderm was injected into the deep fat pad of the lower lip only (nothing was placed in the top lip—change in length and shape is from supraperiosteal treatment of the pyriform aperture) as well as the submentalis fat compartment with a 27-gauge cannula utilizing the same technique detailed (Figure 5). Note how the increased length of the chin here, in conjunction with the "shortening" of the upper lip, create a "golden" ratio of 1:1.6 in the lower third of the face. Note also that injection into the deep fat pad of the lips serves to evert the lip, as well as give a gradual change at the "white roll" not achieved as well with injection into the vermilion border alone. Finally, 25 units of botulinum toxin (Botox Cosmetic) was injected into the

FIGURE 2. Augmentation around the pyriform aperature in a patient with congenital hypoplasia (as well as in older patients with bony remodeling) provides underlying support for the overlying soft tissue envelope improving the position of the nose and upper lip and the prominence of the philtrum and cupid's bow as seen in this patient status post solid polyethylene pyriform implant. 2a) Baseline 2b) Status post surgical implant 2c) Schematic illustration of implant position. Caution must be exercised in this area to avoid inadvertant injection into the angular artery. A low viscosity product like PLLA injected with a 26-gauge, 5/8-inch needle allows for reflux prior to injection of product and is the safest choice in my hands.

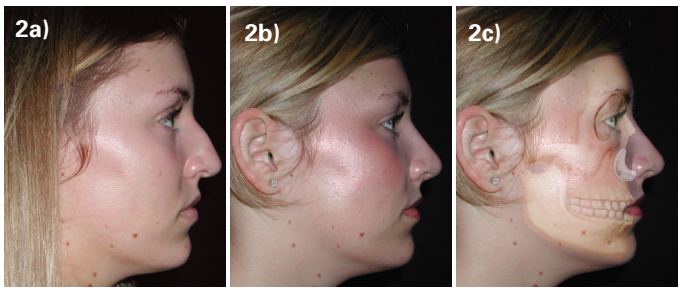

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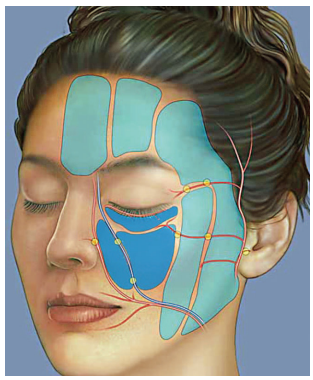
FIGURE 3. This schematic illustrates some of the superficial fat compartments of the face. The patient presented here was treated with PLLA in temple (deep to the deep temporalis fascia) and with 2 cc of hyaluronic acid under the brow as well as in the forehead fat compartments.



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depressor complex in the glabella only. Note the improvement in the "three curves of youth" the forehead and cheek contours, as well as a straighter, more defined jawline. Upon observation of these photographs during the preparation of this manuscript, it appears that this patient would benefit from botulinum toxin injections into the masseter muscles bilaterally, and this will be discussed with her on follow-up exam.

DISCUSSION

In order to solve any problem, one must first define the problem, come up with a solution, and then successfully execute the solution.

The youthful face has an ample amount of volume that is evenly distributed, which displays a smooth transition from one area to another and confers a well-rounded 3-D topography delineated by a series of arcs and convexities.[2] A youthful face also represents a point in time when a particular set of

FIGURE 4. a-c) The deep medial cheek fat (red arrow) lies under the orbicularis oculi at its superior border. It is bordered laterally by the medial fat compartment of the suborbicularis oculi fat (SOOF), which is bordered laterally by the lateral fat compartment of the SOOF as seen in Figure 4a. The presence or absence of this deep medial cheek fat is a primary determinant of the anterior projection of the face. Note that the "V shaped deformity" in the infraorbital area as well as the nasolabial fold improved with injection into this fat compartment alone (Figure 4b-4c). This example illustrates the concept of how loss of volume in one compartment may lead to visibility or pseudoptosis of another. The patient presented here was treated with PLLA in the deep medial cheek fat pad.

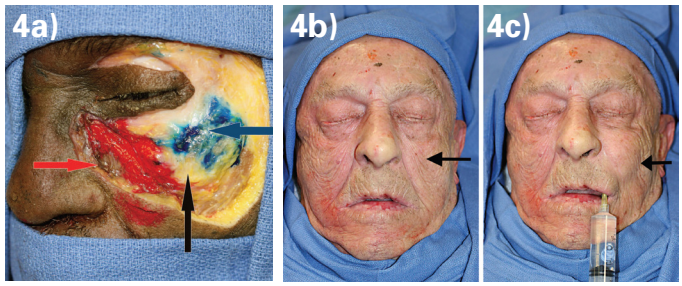

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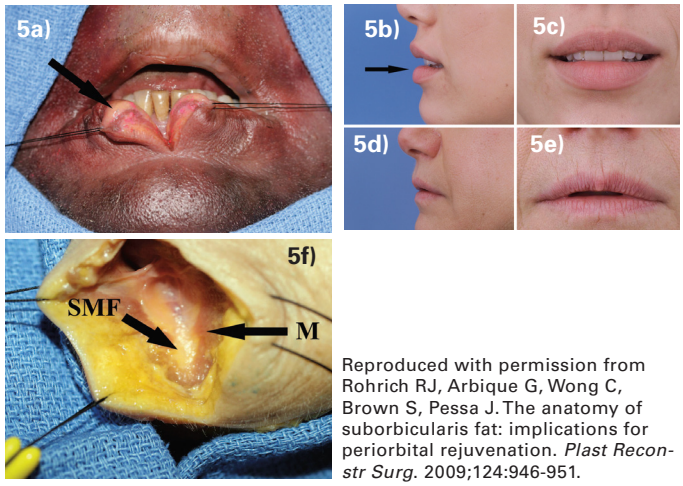
FIGURE 5. 5a) Vertical sectioning of the lower lip in a dissection of a cadaver specimen of an aged individual shows ample deep submuscular fat. This specimen's lower lip showed anterior projection and eversion similar to that typically seen in a much younger individual (5b,c) rather than that typical of an aged individual (5d,e) likely due in part to the presence of this deep fat. The submentalis fat compartment (labeled SMF below) deep to the mentalis muscle (labeled M below) is pictured in Figure 5f. Augmentation/restoration of deep volume here helps to soften the labiomental crease. The patient presented here was treated in the deep fat pad of the lower lip as well as in the submentalis fat pad with 0.8 cc of hyaluronic acid. She was also treated with 0.4cc PLLA/side placed deeply on the anterior mandible between the depressor anguli oris and the mentalis. A reflux maneuver was done before injection to avoid inadvertent intravascular injection. Taken together, these injections serve to "lengthen" the chin.



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skeletal proportions is ideal for their overlying soft tissue envelope—a place we likely grow into from infancy and away from with age.[3,4]

In addition to gains in technical insights that have improved our understanding of how to use the currently available products to best advantage, where to use these products to best advantage in facial filling has also improved enormously with ever-evolving insights into the changes observed in the aging face. Current literature reveals that these changes are occurring in all tissue structures of the face and that these changes are interdependent (i.e., a change in one area may lead to a cascade of predictable, secondary events).[5] The central role of volume loss and deflation in the aging face has been eloquently illustrated by Lambros in a longitudinal photographic analysis of more than 100 patients spanning an average period of 25 years.[6] This work, in conjunction with the work on changes seen with age related skeletal remodeling postulated by Pessa et al[4] and now supported by numerous studies[7,8] as well as the landmark studies carried out at University of Texas Southwestern by Rohrich, Pessa et al in the anatomy of facial fat and its contribution to the changes observed in the aging face[9-12] are truly "game changers." The value of this work lies in its implications for treatment. Although the sequence of events as we age is predictable, it's pace is not. This holds true not just between individuals, but between different structural layers in one individual as well. Recognition of where volume has been lost (or sometimes lacking in the first place) in each individual will greatly enhance our ability to achieve optimal and natural-looking results, by enabling us to treat the specific morphology of a particular individual at a particular point in time with site-specific corrections. In my experience, this anatomically based approach to individual facial morphology seems to almost effortlessly improve the shape, contours, topography, and proportions of the face treated in this manner.

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COMMENTARY

Dr. Fitzgerald has eloquently portrayed the next era of cosmetic medicine with the use of non-invasive regimens using neuromodulators and the highly selective use of current U.S. FDA-approved fillers. This is based upon her tremendous knowledge of how the human face ages anatomically. Her astute analysis of this patient's early aging process and how she's approached it is undeniably the next era of how to maximize the use of FDA fillers and neuromodulators.

The selective use of poly-l-lactic acid in the midface pyriform aperture, mandible, and temporal areas (the earliest areas to show aging, as shown by anatomic studies done at the University of Texas Southwestern) portray how subtle improvements in these key anatomic areas will rejuvenate a patient's appearance in a natural manner. The ability to astutely perform a combination of injecting Juvéderm to the deep fat compartment of the lip to enhance overall upper lip shape as well as in submentalis fat to give more proportionality to the lower face is remarkable. Dr. Fitzgerald has set a high bar for this new era of non-surgical facial rejuvenation with her astute facial analysis and choice of optimal fillers.

The key to future aesthetic non-surgical rejuvenation with neuromodulators and fillers so eloquently demonstrated by Dr. Fitzgerald's work is a precise analysis of the early aging process and the capability to restore the deep facial anatomy, specifically, the deep facial fat compartments. Dr. Fitzgerald is to be congratulated for her incredible analysis and expertise in the unique use of multiple different fillers and neuromodulators to achieve a natural-looking, youthful face.

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New and Emerging Concepts in Soft Tissue Fillers: Roundtable Discussion

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ABSTRACT

In the years since the U.S. FDA approval in 2003 of the first hyaluronic acid (HA) filler, a number of other HA products have become available for use in the U.S., in addition to products composed of calcium hydroxylapatite (CaHA), poly-L lactic acid (PLLA) and polymethyl methacrylate (PMMA). This roundtable discussion between two US-based dermatologists, a European plastic surgeon, and a US-based plastic surgeon provides an overview of commonly used alloplastic filler products and examines how new strategies for soft tissue augmentation are developing as filler options continue to expand.

J Drugs Dermatol. 2012;11(suppl 8):s12-s25.

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NEW AND EMERGING FILLER PRODUCTS IN THE UNITED STATES

HS: ***The latest alloplastic filler to be approved by the U.S. FDA, in the fall of 2011, is a hyaluronic acid (HA) with a cohesive polydensified matrix structure (Belotero Balance). The product that is likely to be approved next, which is currently under study (Juvéderm Voluma), is also an HA. What are the physicochemical characteristics of the latest HA product to be approved and how do they affect its clinical behavior during and after implantation?***

DC: The main difference between cohesive polydensified matrix HA—Belotero Balance—and filler products with a different type of structure is that the degree of cross-linking is not uniform. The filler is softer in some areas because the cross-linking is weaker or even absent. The non-uniform structure of cohesive polydensified matrix HA makes it softer in some areas and stiffer in others. The product is described as more resilient, in that it is readily able to return to its original shape after some kind of distortion or modification. This may make it adaptable to areas with uneven pressure, such as where we have sphincteric facial muscles. In contrast, Juvéderm Voluma and all the other Juvéderm products are crosslinked more uniformly. These are theoretical differences in the products. In clinical practice, what we see now is that a product that is stiffer does not necessarily last longer.

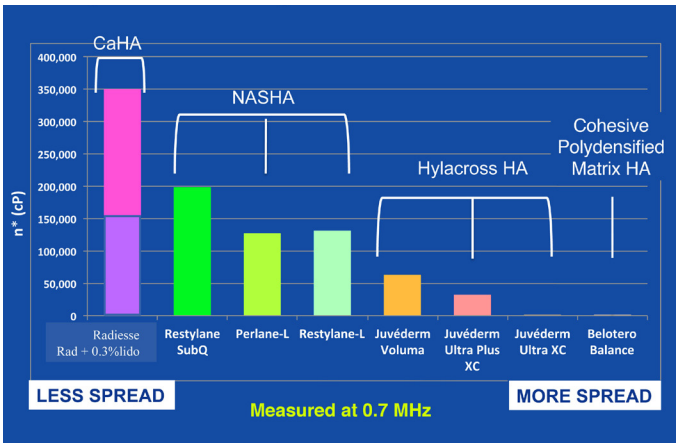
HS: Clinical studies with an evidence level of II show the longevity of cohesive polydensified matrix HA (Belotero Balance) to be comparable to that of NASHA (non-animal stabilized HA) (Restylane) and Hylacross HA (Juvéderm Ultra) when injected into the nasolabial folds.[1,2] One of these studies was a randomized, split-face controlled study that directly compared cohesive polydensified matrix HA to NASHA and Hylacross HA and found that they all provided equivalent clinical results 12 months after mid to deep dermal implantation.[3] All these products have a high total HA concentration—between 20 and 24 mg/mL. They vary in the type and degree of HA cross-linking and in how firm or how soft they are, with NASHA being the firmest of these products and cohesive polydensified matrix HA being the softest.

PL: I have some experience injecting Belotero Balance. It's a product that is very well injected superficially, and thanks to Dr. Cassuto's wonderful work that he did on the histology, we know that it has a smooth distribution within the dermis. My understanding is that a lot of the unique properties of this product are due to the relatively high concentration or content of free HA, yet the HA is of very large molecular weight. So it doesn't behave like the standard free HA that we think of in terms of just being a lubricating agent. It really behaves as a structural product, so to speak. And I think that's the unique nature of cohesive polydensified matrix HA.

HS: The tissue integration studies to which we are referring were performed by injecting small boluses of different HA fillers into the dermis of non-facial skin and then taking biopsies for histopathological evaluation. We learned that different HA fillers distribute quite differently in the dermis, both immediately after implantation and weeks to months afterwards. Restylane, which

is manufactured with NASHA (non-animal stabilized HA) technology, stays as a fairly well-defined bolus, whereas Belotero, a cohesive polydensified matrix HA, distributes homogenously through the dermis. And then Juvéderm Ultra, which is manufactured with Hylacross technology and has particles of variable shape and size,[4] falls somewhere in between. Ultrasound imaging after HA implantation has confirmed this pattern of filler product distribution.[5] Essentially, this is a map of viscosity. A filler product will remain where it is placed if it has higher viscosity like Restylane, whereas it will tend to spread out if it has lower viscosity like the Juvéderm and Belotero products (Figure 1).

FIGURE 1. Complex Viscosity of CaHA and HA Fillers
Measured at 0.7 Hz. Purple bar inset on pink bar for Radiesse (CaHA) shows complex viscosity of Radiesse + 0.3% lidocaine. HA products are grouped by generic family name. Restylane Sub Q and Juvéderm Voluma are currently not approved for use in the U.S. Refs. Sundaram H, Voigts B et al. *Dermatol. Surg.* (2010) and Data on file, Merz.



TF: I was fortunate to be able to collaborate with Swiss colleagues on an intradermal implantation study comparing Restylane, Juvéderm, and Belotero.[6] Subjects consented to have the filler products implanted as intradermal injections into their buttocks. After seven days the intradermal implants were biopsied and the histology of the products was examined by an independent dermatopathologist. What we found was that each type of HA has a predictable histologic behavior in the skin. Restylane demonstrated deposition in big pools, often deep in the reticular dermis, with the papillary and superficial reticular dermis free of HA. Juvéderm was deposited throughout all the thickness of the reticular dermis but still in clumps, with the papillary dermis free of filler. Belotero penetrated into the dermis in a diffuse, evenly distributed manner, except in the papillary dermis, which remained free of exogenous material. This is why Belotero Balance makes a very good superficial filler—because it integrates with the patient's own dermis and lifts up nicely the small fine wrinkles.

DC: Belotero is the first product after collagen that can be injected very superficially. So it's the first time after losing all the collagen products that we can go back and solve some of the very superficial problems with the same technique that we used in the past with Zyderm and the other collagens, including Evolence Breeze, which you didn't get to use in the U.S. And this is thanks to that uneven cross-linking that does reduce stiffness of the Belotero product, maintaining a lot of resiliency after it's out of the needle, and it sits in the tissue.

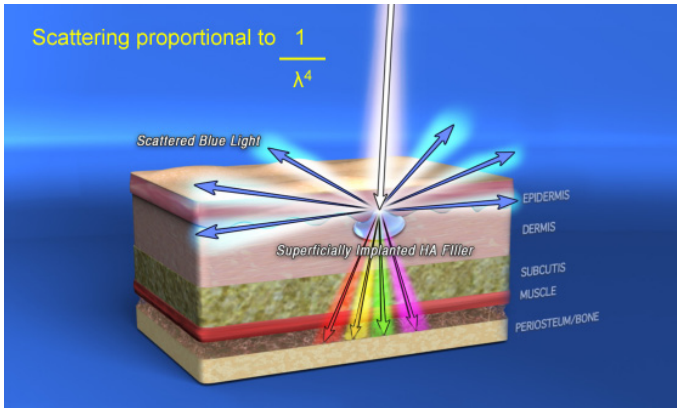
HS: By superficial injection, we mean injection into the dermis or the superficial subdermal plane. As a slight qualification, we have had another product in the U.S. that could be used in the same way as collagen. Dr. Lorenc and I have experience with it. This is Prevelle Silk, which is a low concentration, fully hydrated HA. Its total HA concentration is about 5.5 mg/mL. What's interesting is that almost all of that is insoluble crosslinked HA, as shown in the seminal rheology paper published by Kablik and Monheit.[7] Of course, because it's a low concentration product, it has a lesser longevity than Restylane, Juvéderm, or Belotero. In general, the longevity of Prevelle Silk will be about four months—a month or so longer than for the Zyderm or Cosmoderm collagen products.[8]

PL: I agree. We are gaining a better understanding of products and how to customize them. Prevelle Silk is nice to put in the tear trough. Usually I combine it with a neurotoxin around the eyes, so I think I get four months, maybe even sometimes five months of longevity. What's attractive is that you really have very little swelling. I think Prevelle Silk works well in specific areas—in the lip, for instance, if you just want to just enhance it just a small amount. Having said that, I've begun more and more to customize my HAs by diluting them almost routinely. For instance, I dilute Restylane about 50% of the time in the tear trough, with an equal volume of lidocaine so it has a final concentration of about 10 mg/mL.

HS: HA dilution with lidocaine or saline has come up in discussions with several other key opinion leaders. Dr. Susan Weinkle, president of the American Society for Dermatologic Surgery, remarked the other day during a discussion on fillers that it's all the fad these days to dilute. We should first make it clear that dilution of HAs is not recommended by any of the manufacturing companies, and all HA products are approved and labeled for use only as they are packaged. Therefore, patients should be apprised prior to injection that the use of a diluted HA product is off FDA labeling. I do not dilute HAs myself. I customize the concentration of the HA products I use by selecting Restylane, Juvéderm, or Belotero when I need a high concentration product and by selecting Prevelle Silk when I need a low concentration product. One of the rationales given for HA dilution by those who do it is that it reduces or eliminates the risk of the Tyndall Effect. This is because dilution decreases the number of particles per unit volume, which greatly reduces or eliminates the light scattering that causes the blue skin discoloration of the Tyndall Effect (Figure 2).

TF: I dilute HAs or calcium hydroxylapatite for deep placement

FIGURE 2. Tyndall Effect (Rayleigh Scattering)
Light scattering is inversely proportional to the 4th power of the light wavelength. Therefore, shorter wavelength blue light is scattered the most back to the observer's eye, and the superficially implanted bolus of particulate HA filler imparts a bluish appearance to the overlying skin.



Courtesy of Hema Sundaram MD.

into the fat pads of the face. I find that if I dilute the product at least 1:1 with lidocaine, I can really inflate the fat pads, and then massage the filler product throughout the pads. This has two benefits. First the over-diluted product shows patients where they are headed with filling—I can show them that they are really re-volumized and any concern can be mitigated by explaining that the filler will go down and blend in. Second, the massaging of the filler after the diluted product is in place helps distribute the material much more evenly for a very nice effect.

HS: One interesting question is whether dilution will affect the product's longevity, since it reduces the total HA concentration.

DC: We cannot assume that longevity is directly proportional to concentration. There are too many variables to take into account.

HS: It is true. And dilution may affect different HA products differently. We know from the paper by Kablik and Monheit that the water absorptive capacity of Restylane is limited.[7] The product is composed of relatively uniform particles suspended in a fluid phase. I have discussed with Dr. Kablik that dilution might not affect this product significantly in the long run because the diluent would remain in the fluid phase without affecting the integrity of the particles, and it would tend to be resorbed after implantation of the product into tissue. In contrast, Juvéderm Ultra and Ultra Plus have higher water absorptive capacity and less prominent particles which vary in size and shape, so dilution might have different effects. This is all hypothetical. The only way to know how dilution affects a HA product is to perform a controlled study.

DC: The reason I have embraced this dilution of HAs is that it's not uncommon for me to get nodules or lumps using them in the tear trough. And it's one of those things that my patients tend not to accept at all. I went through an exploratory phase trying to find the perfect product for tear trough injection. Porcine-derived crosslinked collagen (Evolence Breeze) seemed to work beautifully because it was very smooth and really had no hydrophilic effects. So that was my way of thinking, and that was the reason that I started to explore dilution of HAs.

TF: I agree. I have also experienced lumpiness in the tear trough, and there were some swelling issues. I dilute most of my deeper fillers at this point. And the diluted fillers flow nicely through blunt-tipped cannulas.

HS: In the poll on reasons for HA dilution that appeared in Part I of this supplement publication, 38% of the 33 faculty respondents stated that they dilute Juvéderm or Restylane to facilitate superficial injection, 26% to reduce filler nodules or contour irregularities, and 17% to reduce risk of the Tyndall Effect. 88% of the respondents reported that they use diluted or low concentration HAs in fewer than 50% of patients.[9] We now have three types of product that we can inject superficially with a lower risk of nodules and of Tyndall Effect. The first is Belotero Balance, which has a total HA concentration of 22.5 mg/mL and can be injected superficially with little or no risk of nodules or Tyndall Effect because of its specific, homogeneous tissue integration properties. Based on the evidence from studies of this product we expect it to have comparable longevity to undiluted Restylane or Juvéderm.[1,2] The second option is Prevelle Silk, which has a total HA concentration of 5.5 mg/mL and a longevity about half that of Restylane and Juvéderm. It is a soft product that also carries little or no risk of nodules or Tyndall Effect. And the third option is to dilute Restylane or Juvéderm to reduce its HA concentration.

TF: I agree that Belotero Balance is a very useful superficial filler because there is no Tyndall effect. Since the product diffuses into the dermis there are no pools of material to effect light scatter.

DC: I think that longevity is not only a matter of concentration and size of molecules. That's what an engineer would think. When you're a practitioner, you also know that different areas of the face have different mechanical stress in different directions. It is not necessarily true that a stiffer or a more concentrated product will last longer. If you take a bar of glass and a bar of chewing gum, the glass is more concentrated but it will break more easily than the chewing gum. This is because the glass is too stiff to resist; it's not resilient. So I think that we also have to consider that in a very static area of the face such as the temporal region, a stiffer product can do better, even though it can be felt and may be lumpier. Whereas in a highly mobile area like the tear trough or around the mouth, where you have the stress of a sphincter muscle, then a softer product can be more durable because it will accompany the movement, instead of resisting it.

PL: I agree. I think that when I dilute Restylane, in effect, I'm

delivering a lesser amount of almost the same product. My experience was also that I wanted to minimize the likelihood of getting lumps and nodules in the tear trough. In my mind, I'm just delivering a lesser amount of a product with the same structural component and therefore decreasing the possibility of nodules and lumps. I do concur that Belotero Balance, from my experience and knowing a little bit about its characteristics, is a soft, resilient, persistent product that's ideally suited to an anatomically unique area such as the tear trough.

HS: Whereas a firmer HA product such as Restylane or Perlane is ideally suited to deep implantation in areas such as the midface, nasolabial folds and temples where its lifting capacity is of value. When assessing the resilience of a product, it may be useful to consider its balance of elasticity versus fluidity. This can be done with a rheologic value known as tan delta, which is calculated as viscosity, measured as the viscosity modulus or G double prime (G"), divided by elasticity, measured as the elastic modulus or G prime (G') (Figure 3).

Belotero Balance has a high tan delta, which indicates a predominance of fluidity over elasticity. This makes it suitable for injecting superficially, as it will flow readily through the intradermal and superficial subdermal tissue planes and can be molded easily after implantation to achieve a smooth effect. In contrast, Restylane and Perlane have a low tan delta, indicating that elasticity is more predominant, which makes them more suited to deep implantation for lifting and vectoring effect. A firm filler will be less palpable if it is placed deeply, in the subcutaneous and supraperiosteal tissue planes, rather than superficially, and its tendency to flow less confers contour stability after implantation.

PL: I just wanted to mention an article by Fischer in 2009 that looked at what free HA does to fibroblasts in vitro.[10] The fascinating thing is that it stimulates proliferation of fibroblasts. So I just wanted to go back to the concept of what we're doing with HA, and specifically that free HA may promote collagenesis. I think there's something to it. This article gives some credence to the belief that we are doing something to fibroblasts, and possibly collagen, by injecting HA, and specifically free HA in this case.

HS: That's an interesting point. To clarify, free HA is non-crosslinked or unmodified. We consider soluble HA in a filler product to comprise free, unmodified HA plus some crosslinked or modified HA that has been degraded into fragments during the manufacturing and heat sterilization process,[11] whereas insoluble HA in a product is crosslinked. If we go back to the paper by Wang, Voorhees, and colleagues,[12] which looked at collagen upregulation after injection of HA (Restylane) into the forearm, the time point at which this was examined was after 14 days. Collagen upregulation was attributed to stretching of fibroblasts, though we do not have any high level evidence that this is the actual mechanism of collagenesis. Even soluble HA of low molecular weight

FIGURE 3a. Elastic Modulus (G') of CaHA and HA Fillers
Measured at 0.7 Hz. Blue bar inset on pink Radiesse bar shows G prime of Radiesse + 0.3% lidocaine HA products are grouped by generic family name. Refs. Sundaram H, Voigts B et al. *Dermatol. Surg.* (2010) and Data on file, Merz.

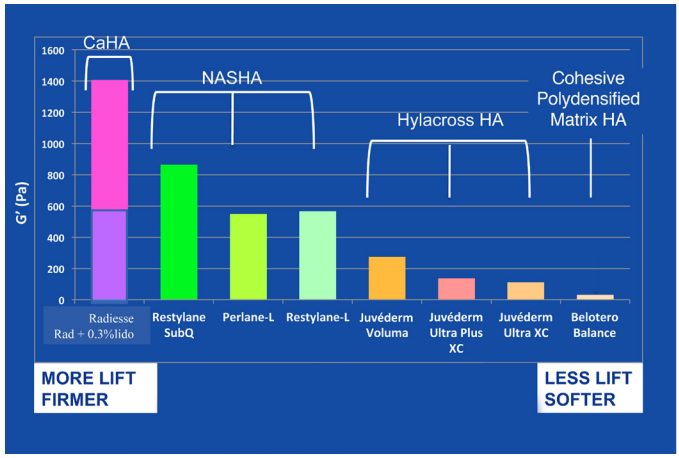
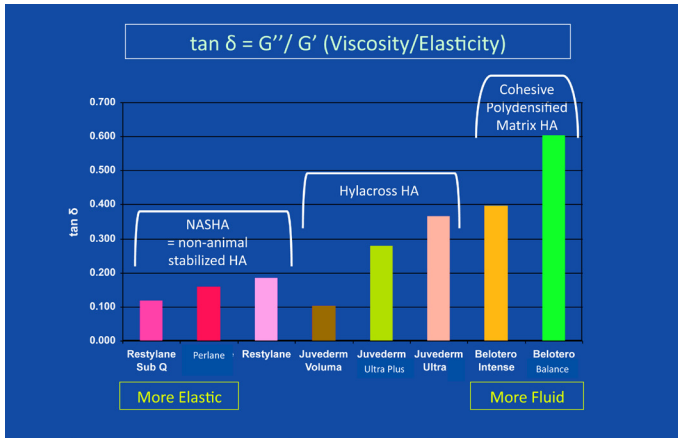


FIGURE 3b. Tan Delta of HA Products.
Tan delta is calculated as the Viscosity Modulus (G double prime or G") divided by the Elastic Modulus (G prime or G'). HA products with a low tan delta are firmer or more solid gels, whereas HA products with a high tan delta are more fluid gels. HA products are grouped by generic family name. Restylane Sub Q, Juvéderm Voluma and Belotero Intense are currently not approved for use in the US. Refs. Sundaram H, Voigts B et al. *Dermatol. Surg.* (2010) and Data on file, Merz.



will persist in the tissue for two weeks or so after implantation. So it is theoretically possible that it could play a role in induction of collagenesis after implantation of a HA gel filler. The value of soluble HA has been discounted previously; it has been considered not to play any part in filler longevity. However, we may need to re-examine this concept if triggering of collagenesis occurs within the time period when soluble, low molecular weight HA is still present in the tissue. Now we have Belotero Balance, which has a significant proportion of high molecular weight soluble HA, and I think we have to define what the longevity of that

is. Hypothetically, it should not have a lesser longevity than that of low molecular weight soluble HA.

DC: I'd like to say two things about this. The first one is that we still don't know what the real mechanism is by which HA influences tissue. Personally, I don't believe that it's due to stretching of fibroblasts. I don't think that fibroblast stretching is something reproducible. But there are many other mechanisms by which HA can influence the synthesis of new collagen. We still don't know which kind of HA can do that but free HA could definitely do something. I think that if we leave aside Restylane for a moment and we look at the other HA products, dilution could make them more available for any kind of interaction by increasing the contact surface.

HS: I also feel that stretching of fibroblasts may not be the mechanism by which HAs stimulate collagenesis. Do you consider dilution a possible method of making less particulate HA products such as Juvéderm more available for tissue interaction?

DC: Yes. Also, I agree that Belotero Balance should be injected superficially. However, there is another product that is approved for use in Europe but currently not approved in the U.S., called Belotero Intense, which is injected more deeply. In my experience, it has the same kind of longevity as Restylane and Juvéderm, and it is very unlikely to cause any lumps. There are also other volumizing HA fillers in Europe that can be injected deeply with blunt cannulas and barely be felt after injection.

HS: Belotero Intense can be used for multi-plane or sandwich volumetry with Belotero Balance. The Intense product is implanted subcutaneously and supraperiosteally, and then the Balance product is implanted into the intradermal and superficial subdermal tissue planes. Other families of HA fillers that include distinct products designed for either deep or superficial placement in tissue with relatively low palpability after implantation include the Emervel (Galderma) and Teosyal (Teoxane) ranges, which are currently under study in the US, and thus potentially on the horizon for American injectors. These products are softer than Radiesse, Restylane, and Perlane and therefore more moldable after implantation. Radiesse, Restylane, and Perlane are more suited to sculpting because they are firmer products.

PL: I think it's important for us to discuss these differences in particular products so that physicians understand how they can incorporate them into their practices really to benefit the patient. In my mind, Belotero Balance is not just the fifth HA to market in the U.S.; it has unique properties. I think it's ideally suited for injection of the tear trough, and also of the vermilion border. It has unique tissue integration, and the longevity is better than with very light products.

HS: A soft product such as Belotero Balance is suited to these anatomically unforgiving facial regions and will have better longevity than the low concentration (or light) soft product, Prevelle Silk. In the poll on the use of diluted or low concentration HA in Part I of this supplement publication, 26% of the 33 faculty respondents stated that they use it for the tear troughs and periocular regon and 21% for the lips.[9] Is it possible that the availability of Belotero Balance may decrease the incidence of dilution of Juvéderm and Restylane?

DC: The main reason for filler dilution in the U.S. is the limitation in product choices. It began as a way to meet needs that are not met by the current range of products. The other reason for dilution, and the reason I do it, is with the aim of increasing availability of HA to the tissue in order to try and exploit the stimulating actions of the HA molecules. If it can be proven that this is an effect of dilution, people may do it more.

PL: Another obvious reason for dilution is for pain control. I think we all accept the fact that the patient's perception of pain is lessened if you incorporate lidocaine into the filler.

HS: Prevelle Silk was the first currently available product to be manufactured with lidocaine. The Restylane, Perlane, and Juvéderm products are now also available with lidocaine added during the manufacturing process, as is the permanent filler, Artefill (polymethyl methacrylate). Belotero Balance and Radiesse (calcium hydroxylapatite) are manufactured without lidocaine, and this is often added immediately prior to injection. A protocol for dilution of Radiesse to give a final lidocaine concentration of 0.3% is approved by the U.S. FDA and also in Europe. Lidocaine is also commonly added to Sculptra (poly-L lactic acid) during reconstitution.

PL: I think that one of the most important reasons for dilution is for customization of the product. For me, this translates not only to HAs, but also to Radiesse, where I use three different dilutions, depending on which anatomical area of the face I'm treating. I think this customization really allows me to address and think about different areas of the face in different ways. My concept is to customize the dilution to match the area of the face that I'm trying to inject.

EVOLUTION OF STRATEGIES FOR PATIENT ASSESSMENT AND FORMULATION OF FILLER TREATMENT PLANS

HS: Patient assessment may be considered the key to formulating individualized treatment plans. Facial aging affects multiple tissue planes. How does structural and functional analysis of the affected tissues inform the process of selecting filler products and techniques to fulfill the treatment plan?

DC: We have to try to assess why a patient is unhappy with her nasolabial folds or her wrinkles, and we have to understand that she's expressing her discomfort using what words she can. What we should do every time is to assess the kind of aging and the kind of changes that all the different tissues have undergone. In the last ten years, plastic surgery litera-

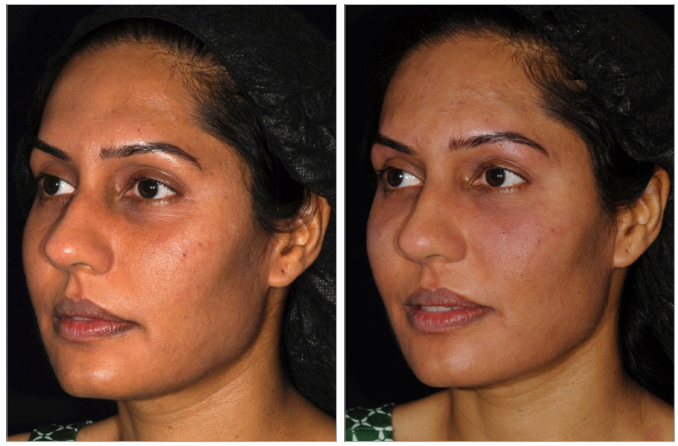
ture has shown us the dynamic changes of all the tissue layers, mainly bone and fat. The condition of the skin should also be assessed, not just by looking at it, but by something like the snap test that we do in plastic surgery on the lower lids to assess the quality of the tissues—it must be done everywhere. And the quality of the superficial facial muscles should also be assessed only after that.

HS: I also routinely perform a snap test to assess skin elasticity and quality in the periocular region—and also in the upper, mid, and lower face, and the neck. This simply entails grasping and elevating a small portion of the skin between the thumb and first finger, and then releasing the skin while observing how quickly it returns to its original position. The skin snap test can help to guide the injection strategy for both fillers and neuromodulators. In regards to really assessing the aging process and interpreting what patients express in this context, rather than just using what they complain of as a template for the treatment plan, the patient who comes in complaining of nasolabial folds is a good example. These days, our instinct is to inject the midface, rather than just blindly following what the patient says and chasing the nasolabial folds. We understand that the folds are due to midface deflation, and so we re-inflate the midface to efface the nasolabial folds. A second example is when patients complain that their noses have become bigger with age. Of course, there are structural changes in the nose with age, but a lot of the perceived change is due to midface deflation. We don't necessarily re-sculpt the nose as a primary means of addressing the patent's complaint. Again, we re-inflate the midface, and then the nose looks smaller again. In fact, patients often spontaneously comment on this improvement after filler injections to the midface.

DC: Yes, and I think one of the greatest examples is the lips. The importance of maxillary and mandibular bone reabsorption is often underestimated. Those are the two main supporting structures for both lips. Too many times, we see lips being augmented, instead of being restored by replacing the deep mandibular or maxillary volume that has been lost. If you augment lip volume on the foundation of reabsorbed bones, it's much easier to get that horrible duck-lip effect that we see so often. Another example is when injectors that have understood how to tackle the nasolabial folds from the cheek area forget that everything from the temporal area up to the frontal bone should also be treated in order to maintain facial harmony. Whereas in the past, filler treatments ended with an enlarged perioral area, lips and nasolabial folds and the rest of the face stayed shrunken, now it's the midface that gets enhanced. But above, from the temporal area up, the face is still shrunken. So this is what I mean by evaluating the whole face at all levels and all depths and for all tissues, to try to find the right solution.

HS: There is increasing recognition that volume loss from the temporal fossae is a cardinal feature of facial aging that can be addressed by the injection of fillers. Volume restoration to the forehead may be our last frontier—the final part of the treatment plan with fillers that we must recognize and implement. And when it is done appropriately, the results are dramatic and very pleasing (Figure 4).[13]

FIGURE 4. Volume Restoration with Non-Tyndall HA to the Forehead and Periocular Regions.
Before (left) and Immediately after (right) injection of HA. Patient had already received deep, supraperiosteal and subcutaneous injection of NASHA (Perlane and Restylane) to mid and lower face in a previous session. Note significant aesthetic improvement after addition of relatively small volume of low concentration fully hydrated HA (Prevelle Silk) superficially to the forehead with a sharp needle, supraperiosteally to the lower and upper eyelids with a blunt microcannula, and superficially to the lower eyelids with a sharp needle. From Sundaram H, Carruthers J. The Glabella and Central Brow. In: Carruthers J, Carruthers A, eds. *Procedures in Cosmetic Dermatology series: Soft Tissue Augmentation*. New York: Elsevier, 2013.



Courtesy of Hema Sundaram MD.

PL: I agree completely. I think that we should also reference the work of Pessa and Rohrich,[14] who have changed our way of thinking about deflation of the face and the importance, for instance, of re-volumizing the deep medial compartment of the face to lay the groundwork for superficial treatment on top of that. I also want to reference what I refer to as the direct and the indirect effect of a filler. A perfect example is that you will either lessen or completely eliminate the need to augment the nasolabial fold if you volumize the malar eminence or the pyriform area. I think an injection in the pyriform area is probably the most cost-efficient injection for a patient. You can put in 0.3 cc of a product—whether it's calcium hydroxylapatite (Radiesse) or a heavier HA—and you can have a very pronounced and natural-looking effect on the patient.

DC: I think that it is very important to understand that fillers have two roles. One is to make up for lost or missing volume. The other role is to try to induce some kind of regeneration. And we know that different fillers do this, including calcium hydroxylapatite and poly-L lactic acid (Sculptra). In my opinion, we also have

the hyaluronic acid fillers in this group, even though different HAs may cause different regenerative processes.

HS: I tend to use calcium hydroxylapatite and NASHA (Perlane) in the midface. My strategy for the nasolabial folds is to re-volumize the midface with microaliquots and then inject the pyriform area, after which barely any filler may be needed for the remainder of the nasolabial fold. Of course, there is the caveat that the upper face must also be re-volumized to avoid ending up with a "chipmunk cheek." Fitzgerald and Vleggaar have been instrumental in bringing the work of Pessa and Rohrich to dermatologists' attention.

PL: Their articles on re-volumization, especially on supraperiosteal placement of poly-L lactic acid, have completely changed the way that I approach patients in my practice—obviously, for the better.[15]

EVOLUTION IN STRATEGIES FOR FILLER INJECTION

HS: What are our preferred product and area-specific techniques for filler implantation?

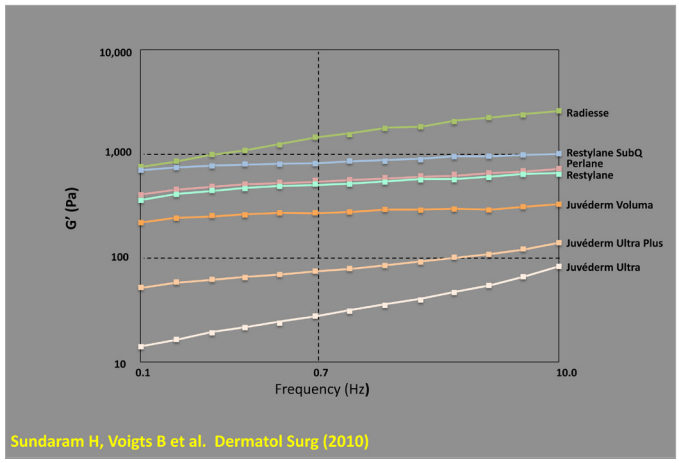
PL: As we discussed, examination of the patient and an understanding of what we are looking at are critical. When volumizing, I always think in terms of many different layers—not just one layer any more. In the deep, supraperiosteal layer, I use either poly L-lactic acid or calcium hydroxylapatite. And then I usually layer HAs on top of that. I use different types of HAs, depending on what I'm trying to achieve. Specifically now, with the introduction in the U.S. of Belotero Balance, I think in terms of having a third layer.

HS: We can place products with a higher G prime deep down, such as Radiesse and Perlane or Restylane—and also Sculptra, which has the lifting effect of a high G prime filler due to its stimulation of collagenesis. When selecting a product for superficial injection, I consider product viscosity to be important: The low viscosity and lack of Tyndall Effect with Belotero Balance make it advantageous for intradermal or superficial subdermal implantation.

TF: My techniques are evolving, as are most dermatologists' and plastic surgeons' when it comes to fillers. Now, most of my patients are getting two types of fillers at the same session—CaHA (Radiesse) or sometimes poly-L lactic acid (Sculptra) deeply for re-volumization, and then a HA such as Juvéderm for the treatment of wrinkles and folds. Each time patients come back, I continue the layering of the face to slowly restore the lost volume of deeper soft tissue and then to treat the wrinkles they are concerned about. Poly-L lactic acid is very useful in the severely volume-depleted patient. I have been pleased with the slow restoration it can provide with deep implantation.

DC: I think that we all agree on how deep every product should be injected. We just need to couple that with the real need, which we should assess in each face. We need to customize and personalize to each different face and ask what should be added, or which tissue should be replaced. Once we have assessed whether the problem is lack of fat or bone or muscle or skin thickness, this determines automatically what we're going to inject and where. My tendency, which is the general tendency in Europe, is to use only hyaluronic acid. We have enough hyaluronic acids that can be placed supraperiosteally. You're going to have Juvéderm Voluma, and there are also a lot of other choices in Europe. For example, we have a volumizing HA called Modélis (Anteis). And then we have the new Emervel Volume (Galderma).

FIGURE 5. Elastic Modulus (G') OF CaHA and HA Fillers
Linear plots show the elastic modulus of various CaHA and HA fillers at different rheometric testing frequencies. From Sundaram H, Voigts B, et al. *Dermatol Surg* (2010). For comparison, the elastic modulus of the five Emervel HA products is lower than the elastic modulus of Restylane, Perlane, Restylane SubQ and Radiesse, ranging from 34.5 to 213.8 Pa at a testing frequency of 2 Hz, From Segura S, Anthonioz L et al. *J Drugs Dermatol* (2012).



HS: These are all excellent products for volumizing. They have a lower G prime and viscosity than calcium hydroxylapatite (Radiesse) and the NASHA fillers (Restylane and Perlane) (Figure 5).[16,17] As new filler products are approved for use in the U.S., we may move towards a model where we use moldable products with good tissue integration properties, such as Belotero Balance, Emervel and Juvéderm Voluma, for optimal volumizing in multiple tissue planes. Products with higher G prime and viscosity such as Radiesse, Perlane, and Restylane may be used deeply for maximal lifting and vectoring—as may Sculptra due to its stimulation of collagenesis.

HS: One of the basic techniques of filler implantation is serial puncture, via which small microaliquots or larger boluses of product can be laid down in the tissue. An example is the "Tower Technique" described by Bartus, Sattler, and Hanke.[18] The other basic technique is threading, via which ribbons or

lines of product are laid down. How do we employ these specific techniques for different facial regions?

PL: Of course, it varies depending on the region of the face. I have some experience with an assisted injection device that is controlled by a foot pedal, and I love to use that for the Tower Technique, because it allows me to deposit filler aliquots in an almost continuous vertical way. I think this works extremely well in the pyriform and malar areas. I always was a bit hesitant as far as the threading technique goes. I recently watched calcium hydroxylapatite being injected in this way at a symposium. My question is always how it will look in the long term, several months down the line, when you have skip areas between the threads. I think there's a fine line between being too deep and too superficial with the threading technique. I like a more vertical orientation and the positioning of products in a specific way.

HS: I am also using this particular assisted injection device (Artiste, Nordson Micromedics), and I've been impressed with the results and the improvement in patient comfort compared to manual injection. I use the device with blunt cannulas or sharp needles. For fillers implanted in the subcutaneous and supraperiosteal planes, I prefer to inject in microaliquots as I also feel that this provides product placement within a precise tissue plane. I will even do this in the perioral region, including the deep fat compartment of the lower lip, with molding of the product after injection to achieve a smooth effect. The only areas where I routinely use the threading technique are the pre-jowl sulcus where I inject calcium hydroxylapatite with retrograde flow and NASHA with anterograde flow, and the periocular region where I inject HA, usually with anterograde flow. Sometimes I will inject short threads of one of these products at and above the temporal hairline with the needle angled upwards and laterally to achieve a vectoring effect. For fillers implanted intradermally and in the superficial subdermal plane, I commonly use retrograde threading technique through a sharp needle with a length of 13 mm to 38 mm, as I find this facilitates flow of the product and enables it to be laid down precisely in thin sheets.

DC: I've used an assisted injection device for more than two years. I think that the most important thing about these devices is that they teach us to inject in a more comfortable way for our patients by controlling the pressure much better than we can manually. They diminish the pain immensely. Besides the pressure issue, the assisted injection device is very helpful whenever you have to be precise in your filler placement, for example when chasing the very superficial wrinkles around the lip. When you start exerting pressure during manual injection after you've placed the tip of the needle in the skin, there's always a slight movement of the needle that is difficult to avoid. If you just have to concentrate instead on keeping the needle in place with your foot activating the pedal of the injection device, and you don't have to apply any pressure at all, it makes life much easier, and you end up wasting less product by over-pushing. That is my experience.

In regards to product placement, I try to assess first where I want to put it, and then customize and adapt the technique. This depends on the biological age of the patient's tissues. When I have patients with good overlying soft tissues and I need to place a product deeply, then I don't mind injecting a bolus, such as in the pyriform fossa and the higher eminence of the zygomatic bone. There are some areas in which you must thread the product such as the lower eyelid, whether you are over the periosteum or superficially, the lower cheek area—and the pre-auricular area, where we see a lot of wasting, especially years after face lifting. Replacing volume in front of the ear is a real cure for submandibular sagging skin.

HS: Dr. Cassuto, you have made a very important point, which is that it is physiological or biological age of the tissues that matters more than chronological age, when we are assessing patients and formulating injection strategies. Dr. Lorenc, do you have any comments on vectoring?

PL: I think there is such an entity as vectoring. When I volumize the face I always start from above and move down, to see what kind of an effect I will get. For instance, if I increase malar prominence and really volumize the midface, I want to see what kind of an effect it has on the nasolabial fold and on the lower face—in effect, what kind of vectors I am instilling in the patient. I tend to believe that volumizing has more of a vectoring effect than just putting in superficial threads in a fanning arrangement.

HS: When you are performing pan-facial volumization, is there a specific order in which you address the facial regions? From what you are saying, it appears that you would tend to start with the midface.

PL: When I volumize the face I always start from the midface, at the malar eminence and then the cheek. Then I go to the pre-jowl sulcus to see what happens to the nasolabial fold. And sometimes there is the pyriform area, which is also one of the really important injections. It's a supraperiosteal injection, to reinflate that medial deep fat compartment of the face. I think the temple is a separate sort of anatomical area. Volumizing the temporal hollow has very little effect on the lower face, so that you can do it first or you can do it last.

HS: My strategy is remarkably similar. Invariably, I will start with the midface, and I will include the pyriform area when I inject the midface. Then I inject the pre-jowl sulcus. Then I proceed to the lower eyelid and the upper eyelid. These days, the nasolabial fold is one of the last areas I inject. It may even be after I address the temple, and the brow and the forehead. Our sense is that injection of the midface and lower face has a significant impact upon the nasolabial fold. This may be considered a type of vectoring, because we're exerting upward and downward forces on the nasolabial fold as we reinflate the face. We don't want to volumize the nasolabial fold prematurely if it can be largely addressed through efforts in other areas of the face.

DC: This was more or less my approach before I started using blunt cannulas. Since then, my cannula entrance point is lateral to the lateral canthus or in the inferior part of the temporal area. And, from there, I can reach all the points I need. So I don't need to start from a certain point. I usually start by trying to restore the orbital circle, by putting a very thick hyaluronic acid over and all around the orbital margin. After that, it depends on how much the patient can tolerate in one session, as far as the change of self-image is concerned, and it also depends on the economic impact to the patient of what I'm doing. I may go down along the cheek, down to the pyriform fossa, which can easily be reached with a 22-gauge microcannula that is 50 mm to 80 mm long. I think that we are all ending up filling up the same areas, because we have learned from the same papers that these are the areas where volume is being lost with aging. So we are simply putting back what is missing.

COMBINATION OF FILLERS WITH BOTULINUM NEUROTOXINS

HS : How are we combining fillers with neurotoxins?

HS: I have evolved in my practice towards using lower doses of neurotoxin in the upper face than I used to. I started off doing this in the frontal region because it was my anecdotal observation that some patients who receive maintenance treatment with injection of neurotoxins over years have a tendency to develop localized or focal atrophy of the Frontalis muscle.[13] Of course, it is a quite thin, sheet-like muscle to begin with. Some patients have diffuse or localized volume loss from the forehead as a manifestation of aging that is unrelated to prior treatments; I reduce neurotoxin dosage for these patients to avoid exacerbating the pre-existing volume deficits by causing atrophy of Frontalis. When using these lower doses of neurotoxin, I tend to add a HA filler to correct the volume deficit. Even for the periocular region, I often use lower doses of neurotoxin in combination with a HA filler, which I inject both supraperiosteally and more superficially. My aim with neurotoxin treatment here is to reduce shearing forces on the filler and thus enhance its aesthetic effects and increase its longevity, rather than to obliterate the crow's feet.

PL: My practice has evolved in exactly the same way. I think we need to give credit to the patient for this. Patients are driving what we are doing for them; over-aggressive neurotoxin to the face is so passé, and my patients don't want that anymore. It's more about refinement. I agree that we have to be very careful to avoid atrophy. I transitioned because I think I get a much more natural, more aesthetic look by routinely combining fillers with neurotoxins in one sitting. I think that's just an obvious and natural request that patients have.

DC: I agree completely. I can describe this evolution that we've all gone through with different words, according to what I call a diagnostic approach. Just because neurotoxin can influence wrinkles in some areas, it doesn't mean that muscle is the problem there and that we should treat the muscle. For example, when a patient needs the activity of Frontalis to lift up the brows and prevent drooping of the eyelids, the wrinkles on the forehead are functional. The use of neurotoxin on functional rhytids is absurd. Now we understand when the diagnosis is lack of volume, and we're replacing the volume instead of misguidedly trying to paralyze a muscle that is only doing its job, which would worsen the pre-existing eyebrow and eyelid ptosis. Another example is when we have older patients with accentuated periocular aging. The crow's feet become very long lines that reach down into the cheek. For many years, the solution that was advocated was a second, more peripheral line of neurotoxin injection points. This is dangerous, because these peripheral injection points are close to functional muscles like the temporalis and the zygomaticus. Now, since we understand that the bone and fat in this area have been lost, and that the crow's feet have become longer due to this reduction in volume. If we first replace the volume and then treat the crow's feet with neurotoxin, everything looks much better. I think it's a more diagnostic approach: if we try to target more the cause of the problem, instead of just the problem itself and understand that we have to treat more tissues than just skin and muscle, we'll definitely use more substances.

HS: Is it fair to say that the evolution in our understanding of fillers has secondarily allowed us to refine our techniques with neurotoxin?

PL: Yes, this is very fair.

HS: Do you feel that it's beneficial to be using filler and neurotoxin on the same day, or do you feel that it's beneficial for some patients to volumize first and then reassess to see what needs to be treated subsequently with neurotoxin?

DC: Are you referring to treatment in the same area?

HS: Yes and no. I think we've established that we could restore volume to one area and impact the rhytids in an adjacent area. Could this modify the neurotoxin injection strategy for that adjacent area, in terms of dose and perhaps even the placement of injection points?

DC: Again, I think it depends on our assessment. We should be very cautious in order to avoid overcorrection of volume or overparalysis of a muscle. We should always evaluate whether or not the effect of each treatment confirms our initial, pre-treatment assessment. From this point of view, I think it's ideal to inject the products one by one, in different sessions. Obviously we must compromise sometimes for logistical reasons, such as when patients are traveling long distances to see us, and then we do more than one thing in one session. In that case, I think that working on one distinct area with fillers and another with neurotoxin makes more sense than working with both in the same area.

HS: In regards to sequential treatment with neurotoxin and fillers, I just want to point out that there is a difference between onset of effect and reaching the end result with a neurotoxin. In some patients, I have observed that it takes a number of weeks to reach the end result, as weakening of one set of muscles necessitates a rebalancing in the activity of the opposing muscles. These days, if I am treating a patient in sequential sessions, I prefer to inject fillers first and then neurotoxin. But if I am doing things the other way around, perhaps based on patient preference, in order to say accurately that I'm sequentially treating with neurotoxin and fillers, I want not just the onset of effect of the neurotoxin but to have reached the fulfillment of that effect, or the full result, in order to determine how the neurotoxin will influence my filler strategy.

PL: Jean and Alistair Carruthers showed that there is greater filler persistence if muscle activity is also decreased with neurotoxin.

HS: This was a randomized study with two arms, comparing the effect of NASHA (Restylane) alone to the effect of the NASHA plus neuromodulator.[19]

DC: The end effect of the neurotoxin does take a few days. And then you need a longer time until the brain starts to adapt so that the contraction of other muscles in the same area goes away. But it's enough to have a slight limitation of contraction of the sphincteric muscles of the periocular or perioral region in order to avoid damaging a superficially placed filler. For that, you don't need to wait for the full-blown effect of the neurotoxin; a few hours from the onset of effect is enough to avoid mechanical breakdown of the filler.

HS: Absolutely. This is certainly the case if we are aiming to decrease muscle hyperactivity in order to decrease potential damage to a filler that is implanted into the same area, especially if that filler is implanted superficially. The second reason for sequential treatment is if we are striving to minimize our use of both neuromodulator and filler, which is an economic consideration for patients as well as an ethical consideration for us as physicians. If I really want to really know how little filler I can use after neuromodulator, then I want more than just an onset of neuromodulator effect.

EVOLUTION IN UNDERSTANDING AND IMPLEMENTATION OF MULTI-PLANE "SANDWICH" VOLUMETRY

HS: Do you think that our expectations of longevity should differ for a superficially implanted filler because it may be subject to more shearing forces and enzymatic activity than a deeply implanted filler?

PL: Longevity of a filler product is multifactorial. I think that different contractile forces are exerted upon a filler that is injected more superficially. For instance, if you inject a product supraperiosteally into the pyriform area, it behaves very differently than if you put it into a superficial line in the periorbital area, where it's constantly being affected by contracture. So I think that we have to be very clear and discuss different filler persistence based on different anatomical placement.

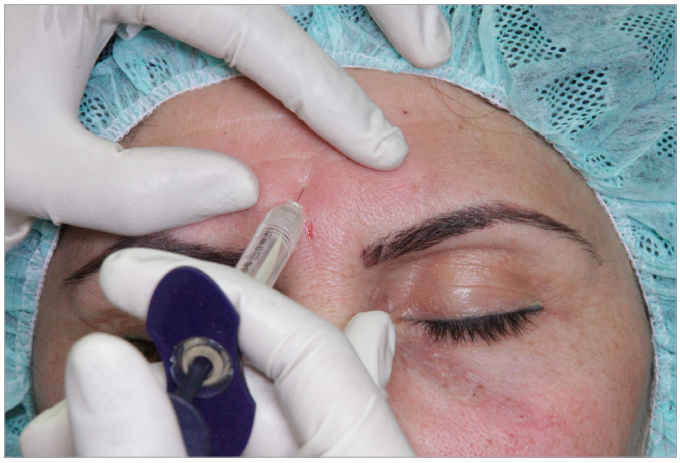
DC: I agree that this is multifactorial. We can establish some sort of correlation. I only place fillers deeply with blunt microcannulas now, and I use rather thick cannulas (22 gauge). In my personal, anecdotal experience, that is less painful than using thinner cannulas and it causes less trauma to the tissues. A 22-gauge cannula is less flexible, so it goes exactly where you want. I think that anything smaller than that, even if it's manufactured as blunt, can still be quite traumatic, and that more pain means more trauma to the tissues. There can be a little bleeding now and then with smaller cannulas, which I have not experienced with a 22 gauge. If there is more trauma, and maybe some very small broken capillaries, there could be more tissue inflammation, and that might reduce longevity of the filler.

HS: This is an interesting concept. There is certainly a need for more evidence regarding the effect of post-implantation inflammation on filler integrity and longevity. Some degree of inflammation might actually be necessary for collagenesis to occur. My feeling is that water binding may play a greater part in HA longevity than is realized. HA molecules unfold as they start to degrade, and this will expose more water-binding sites. So the happy thing about HAs is that as they start to degrade, they pull in more water and this can contribute to the corrective effect. I've started looking closely at my patients four or five months after I've injected them with Restylane or Juvéderm and, to me, they have more of a soft, tumescent look than they did soon after injection. I think that there is more water binding occurring in the later stages of the life span of these fillers than at the beginning. It's an anecdotal observation, but it is borne out by the science. The current perception is that the longevity of a HA is primarily determined by its concentration of crosslinked or insoluble HA. As we discussed before, the advent of new HAs with different structures may cause us to rethink or refine this theory. We need a greater understanding of the behavior of the high molecular weight soluble HA that is prominent in a product such as Belotero Balance, which evidence level II studies have shown to have comparable longevity to Restylane and Juvéderm after nasolabial fold implantation. We also need to gather more evidence regarding the time course of collagenesis after HA implantation, and to determine which components of the HA product could be initiating and sustaining collagenesis.

PL: Unfortunately we do not have a better model for filler longevity and persistence than the nasolabial fold, which is where all the pivotal studies have been done. Yet this translates into zero when it comes to what we're doing in practice, because it is almost irrelevant to what we're doing clinically.

DC: I totally subscribe to this.

FIGURE 6. Superficial Blanch Injection Technique for Glabellar Rhytides
Retrograde intradermal injection of non-Tyndall small gel calibration HA (Emervel Touch). Transient skin blanching at the point of injection (circled) is a result of intradermal placement of the filler. Stretching of the skin with the fingers of the non-dominant hand in a perpendicular direction to the rhytides facilitates this intradermal placement.



Courtesy of Hema Sundaram MD.

HS: It would be helpful to gather more data on the longevity of deeply implanted versus superficially implanted fillers. But this may be challenging because there are so many factors that influence filler longevity.

HS: In conclusion, let's consider volumetry versus "wrinkle-chasing". The move away from "wrinkle-chasing" in the US started in 2003 when the first HA, Restylane, was approved by the U.S. FDA. With the approval of the latest HA, Belotero Balance, we now have a high concentration HA that can be injected superficially. Could this lead to something of a "wrinkle redux"—a return to wrinkle-chasing—or, instead, to a further evolution in our concepts of volumetry?

DC: We have to go back again to the diagnosis. Why is a wrinkle there? If we try to understand why it is there, then we can treat the cause instead of just chasing it. It is very tedious to perform serial, superficial punctures, although it becomes less tedious with an assisted injection device. However, if it is done consistently, the results are excellent in the long run, and probably comparable to a very strong laser resurfacing. We wouldn't want to use highly crosslinked HA products here because they could cause persistent lumps if they are injected into the superficial dermis.

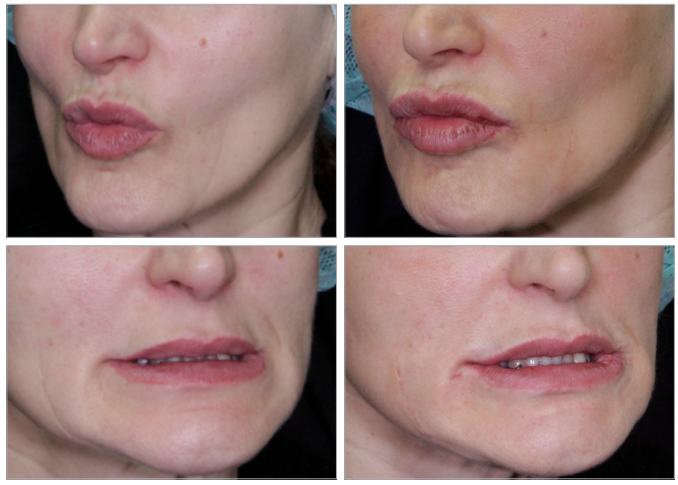
HS: I do use serial punctures to fill glabellar rhytids. The dermis is an anatomically safe plane in which to inject the glabella and forehead. There is transient skin blanching when the filler is injected intradermally, and this serves as an indication of appropriate filler placement (Figures 6 and 7).

In the perioral region, I will often lay down a superficial sheet of product parallel to the vermilion border using retrograde threading technique, to efface the fine rhytides, rather than attempting to fill them individually. I find that this gives a better result. I also use this technique for fine rhytides in the submalar region. I consider this to be superficial volumetry, rather than wrinkle-chasing, with a horizontal vector due to the flowing nature of the filler product (Figures 8 and 9).

FIGURE 7. Before and 30 Minutes After Injection of Glabellar and Forehead Rhytides with Superficial Blanch Injection Technique
Retrograde intradermal and superficial subdermal injection of non-Tyndall cohesive polydensified matrix HA (Belotero Balance). Transient skin blanching at the point of injection has resolved 30 minutes after injection.

Courtesy of Hema Sundaram MD.

FIGURE 8. Before and 30 Minutes After Superficial Sheeting Injection Technique to Perioral and Submalar Regions
Retrograde intradermal and superficial subdermal injection of non-Tyndall cohesive polydensified matrix HA (Belotero Balance). Transient skin blanching at the point of injection has resolved 30 minutes after injection. Note improvement of fine rhytides in perioral and submalar regions.

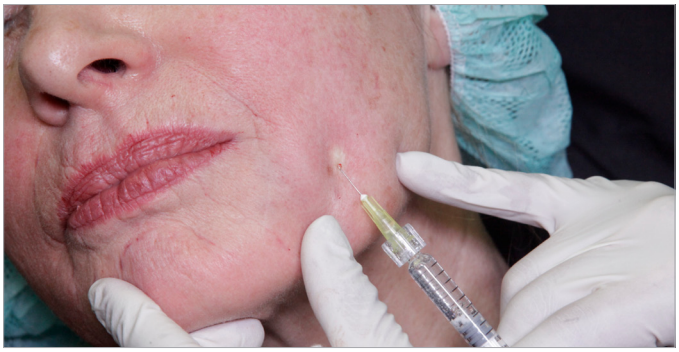


Courtesy of Hema Sundaram MD.

TF: Belotero Balance is good for fine lines that are so small that you risk an uneven result with other HAs. It can be injected out of the syringe with a 32-gauge needle and magnifiers can be used to place the material directly into the dermis.

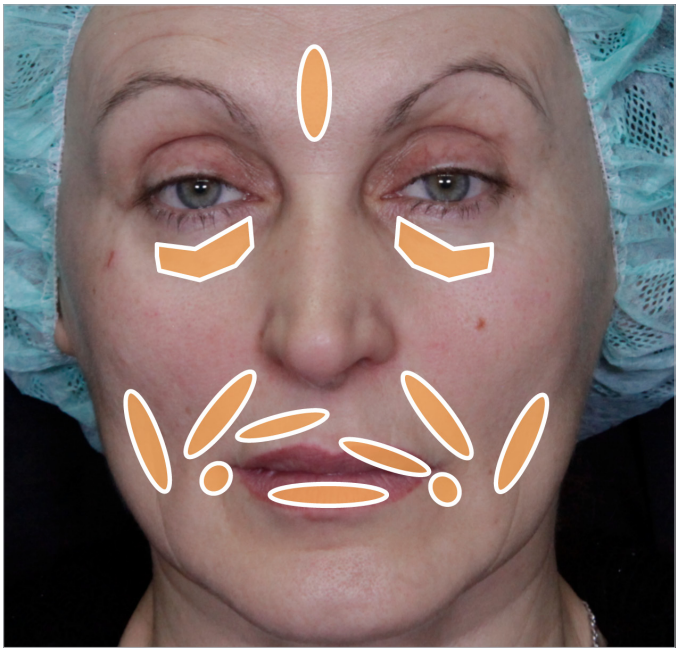
PL: I am thinking now in three dimensions. I volumize deeply with products such as Radiesse, which has a very high G prime, or Sculptra. Then I transition to heavier HAs such as Restylane

FIGURE 9. Superficial Blanch Injection Technique to Submalar Fine Rhytides
Intradermal and superficial subdermal injection of cohesive polydensified matrix HA (Belotero Balance). Note transient skin blanching at the point of intradermal injection of the filler. Stretching of the skin with the dominant and non-dominant fingers of the non-dominant hand perpendicular to the rhytides facilitates this intradermal placement.



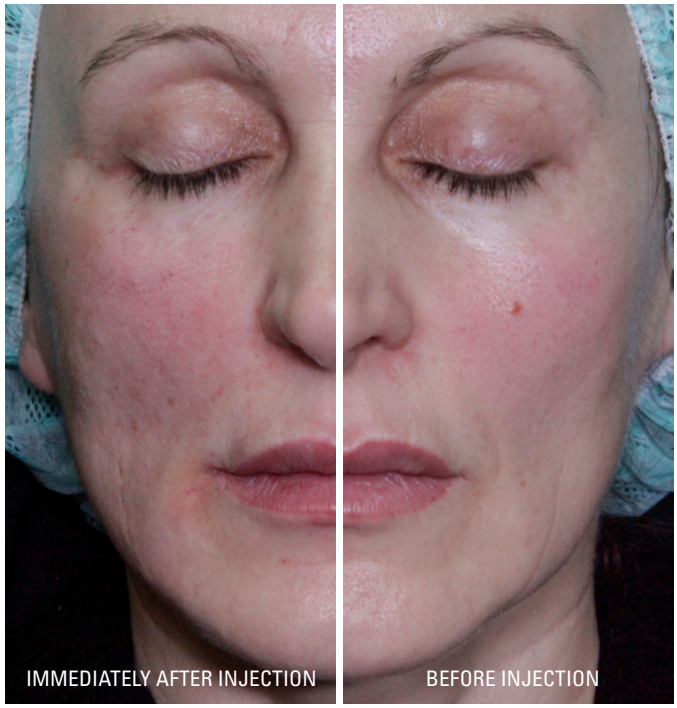
Courtesy of Hema Sundaram MD.

FIGURE 10. Multi-Plane Injection Strategy Using CaHA (Radiesse) and Cohesive Polydensified Matrix HA (Belotero Balance)
CaHA was injected supraperiosteally and subcutaneously to the mid face, pre-jowl sulci and nasolabial folds. Cohesive polydensified matrix HA was injected into the orange shaded areas. HA was injected into the intradermal and superficial subdermal planes of the nasolabial, perioral and submalar regions, the vermilion borders, lower eyelid, and glabella with a 27G, 13 mm sharp needle. A 27G blunt microcannula was used to inject the HA supraperiosteally into the lower eyelid. HA was injected submucosally into the vermilion lips with a 27G, 13 mm sharp needle.



Courtesy of Hema Sundaram MD.

FIGURE 11. "Sandwich" Volumetry: Same Patient Immediately after Half-Face Multi-Plane Volumetry with CaHA and Cohesive Polydensified Matrix HA
Right side of face immediately after injection of lower eyelid, temple, midface, nasolabial fold and oral commissure, vermilion lip, and lower face. Left side before injection. Note smooth integration of the CaHA and HA products with lack of ecchymosis and tissue edema, and lack of Tyndall Effect with intradermal injection of cohesive polydensified matrix HA.



Courtesy of Hema Sundaram MD.

or Juvéderm, and it's quite likely that I will inject in two or three layers when I'm trying to rejuvenate the face. Now, I have the opportunity to layer a product like Belotero Balance on top.

HS: This layering of fillers in the superficial and deep tissue planes has been described in Europe as a "sandwich" technique. For most injectors in the US, it's a new paradigm of volumetry. We can take products like calcium hydroxylapatite, NASHA or Hylacross HA, or poly-L lactic acid, and implant them deeply, in the subcutaneous and supraperiosteal planes. They are very well suited to this. Now we have a product of comparable longevity—cohesive polydensified matrix HA—that is appropriate for superficial implantation, in the intradermal and superficial subdermal planes. So we can start to triage our filler products for superficial or deep implantation, rather than doing what has been done before, which is take a product that is more suited to deep implantation and attempt to modify it by dilution, to make it less unsuitable for superficial implantation (Figures 10, 11, and 12).

PL: It is about layering different products, and being cognizant of what they do, based on their properties. The more products

FIGURE 12. "Sandwich" Volumetry: Same Patient Before and 30 Minutes After Pan-Facial Multi-Plane Injection of CaHA and Cohesive Polydensified Matrix HA
Note improvement in facial contours and fine rhytides.

Courtesy of Hema Sundaram MD.

FIGURE 13. "Sandwich" Volumetry: Before and 3 Weeks After Multi-Plane Injection of CaHA (Radiesse) and Low Concentration Fully Hydrated HA (Prevelle Silk)
Patient also received injection of abobotulinumtoxin A (Dysport) to the upper face, lower face and neck. Note improved skin reflectance and lack of Tyndall Effect with intradermal implantation of fully hydrated HA. The longevity of correction with this HA product is about half the longevity of correction with cohesive polydensified matrix HA or small gel calibration HA.

Courtesy of Hema Sundaram MD.

come to market, the more specific they are, and the more we can expand that way of thinking.

HS: Our understanding of age-related facial volume loss is that it is a multi-planar process. So it makes sense to restore the volume to different tissue planes. In my experience, the addition of superficial volumetry optimizes results for many patients and can also improve skin reflectance and texture. With increased clinical experience and the gathering of more evidence, the potential benefits of multi-plane or sandwich volumetry in regards to volume efficiency and longevity of results may be elucidated more precisely (Figure 13).

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LETTER TO THE EDITOR

New and Emerging Concepts in Soft Tissue Fillers

The use of combination therapy in comprehensive, non-surgical facial rejuvenation has become the standard of care, with carefully selected injectable fillers for varied applications used in coordination with neuromodulating agents and other modalities. The various methods of delivery of these filling agents illustrate the importance of optimal technique and application. These can vary dramatically depending on the product chosen and the target tissue to be injected. One issue that is not completely addressed with subdermal filler treatments is loss of skin elasticity and textural quality (including the treatment of fine lines), which can be tackled by the addition of a true dermal filler that can be effectively and aesthetically directed into the mid to superficial dermis. Examples of these options include newer products such as Cohesive Polydensified Matrix HA (Belotero Balance) or reconstituted Hylacross HA (Juvéderm) and other HA agents,[1,2] whereby existing concentrations of these formulations are reduced by dilution so that they can be more easily injected with fine (32 gauge) needles into the more superficial dermis to more directly affect some of the aging skin changes using injectable agents. Mounting evidence suggests that the long-lasting results with this approach are due to a beneficial biologic effect at the level of the dermis (collagen stimulation) that is beyond the traditional understanding of "space-filling" or hydrophilicity using these agents. Regarding skin turgor, it is my opinion that the addition of effective dermal filling with the appropriate agents such as these aforementioned options is an essential component of comprehensive treatment and next-level results. Simple reflation with subdermal filling agents will generally not improve the appearance of skin texture, and attempts to do so may result in distortion or over-inflation and suboptimal outcomes. The high volumes of existing filler products that are commonly administered are more than is typical for the average patient in my personal practice, and it has been my observation that repeated reflation with such high volumes appears to have a diminishing effect (oftentimes adverse) with time. Yet in many patients, significant and perceptible improvement in facial appearances may require this sort of volume at what would (also) usually not be considered an insignificant cost. Ultimately, it is now better understood that facial aging is a complex and dynamic process. The most comprehensive and aesthetic solution will require a higher level of understanding of this as well as the true long- and short-term biologic effects of our selected injectable agents used in combination and delivered with optimum technique to address these complexities.

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Hyaluronic Acid Fillers on the Horizon: Roundtable Discussion

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ABSTRACT

In this roundtable discussion, the physicochemical properties and potential clinical applications of two new ranges of hyaluronic acid fillers are reviewed. These fillers display enhanced tissue integration after implantation due to novel manufacturing processes, and one of the ranges is customized for specific clinical applications by variation of filler gel calibration and cross-linking.

J Drugs Dermatol. 2012;11(suppl 8):s26-s28.

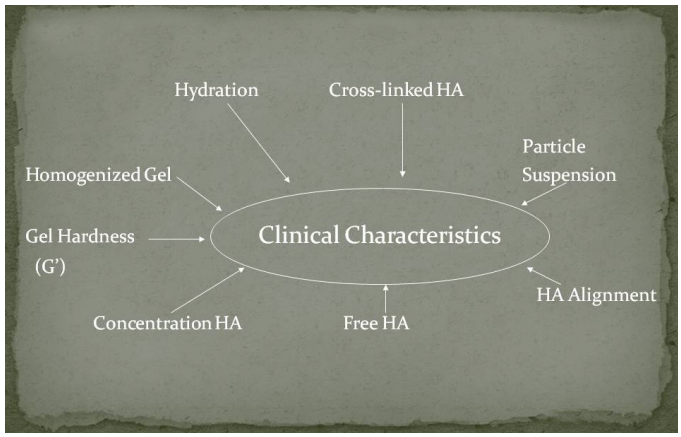
Discussants
Gary Monheit MD Dermatologist (GM)
Philippe Kestemont MD Facial Plastic Surgeon (PK)
Hema Sundaram MD Dermatologist (HS)

HS: The next generation of hyaluronic acid (HA) fillers is characterized by enhanced tissue integration. This is a manifestation of new manufacturing processes such as Cohesive Polydensified Matrix (CPM) or Optimal Balance Technology (OBT). You both have unique insights into these fillers by virtue of your service as principal investigators on some of the pivotal studies. How do you distinguish these new filler products from existing ones, in terms of rheology and other physicochemical properties, injection experience, and clinical behavior?

GM: The advances in injectable soft tissue filling material are paralleled by an expansion in our knowledge, as clinicians, of the composition, the rheology, and thus the relationship between physical properties and clinical results. HA fillers are on the forefront in clinical usage and our understanding of the product is essential. The flow characteristics in all tissues, malleability after injection, natural-looking incorporation into tissue due to hygroscopic nature, and reversibility by hyaluronidase, make HAs the most popular of present injectable fillers. Presently, we have three families of fillers with unique characteristics—Juvéderm, Restylane, and Prevelle, which have different physical characteristics and thus perform differently in various tissues. The varying manufacturing methods make significant differences in HA modification, cross-linking, calibration, and concentration. These differences account for the characteristics we note in flow through the needle, viscosity, duration, firmness, ability to lift tissue, malleability, and softness.

Modification refers to the changes the cross-linkers give to natural HA. The cross-linker—BDDE—will link to HA either as a pendant or as a bridge cross-linker. The former will give a softer, more malleable product, while the latter gives a firmer, more robust product. Calibration is the measure of particle size, whether homogenous such as for the Restylane family, or heterogeneous as with Juvéderm. The larger particle size is designed for deeper injections, while the smaller size is for more superficial filling. The concentration of HA particles has the greatest import in injectability and longevity. The measure of gel hardness or "elastic modulus" (G') is determined mainly by concentration and cross-linking. These measurements—degree of modification/cross-linking, calibration, and concentration—are the tools we can use to characterize differences in fillers and determinants as to where a filler will be used (Figure 1).

FIGURE 1. Variables in Hyaluronic Acid (HA) Products.



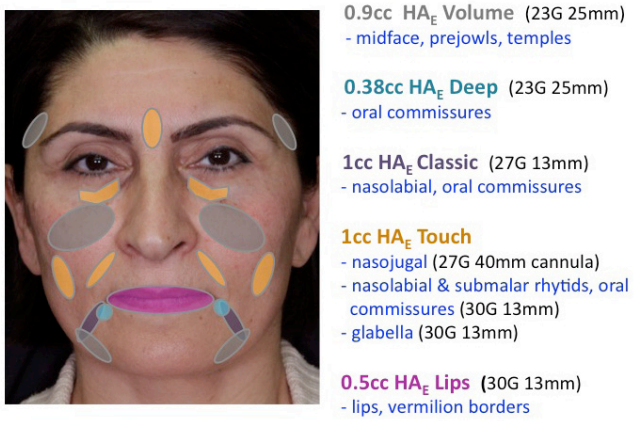
Courtesy of Gary Monheit MD

As new injectable HA fillers are vcoming into the U.S. market, we now have the tools to study them and find their place with other fillers. The quest for an ideal filler aims to find an optimal balance of the three major determinants: cross-linking, concentration, and calibration. These factors are the key to the clinical factors we wish to control: erythema, inflammation, resorption/longevity, implant distribution, and gel hardness.

The Belotero filler family (Merz) was developed with similar technology to Juvéderm. It has been modified to include a superficial and a medium-depth filling gel based on differences in cross-linking and concentration. The unique manufacturing technology—Cohesive Polydensified Matrix (CPM)—consists of two separate cross-linking processes that give additional pendants and cross-linkers to the HA gel. This enhances a balance of softness and malleability. The product, Belotero Balance, which was approved recently by the FDA for aesthetic use, has an HA concentration of 22.5 mg/mL and exhibits a firm, robust character.

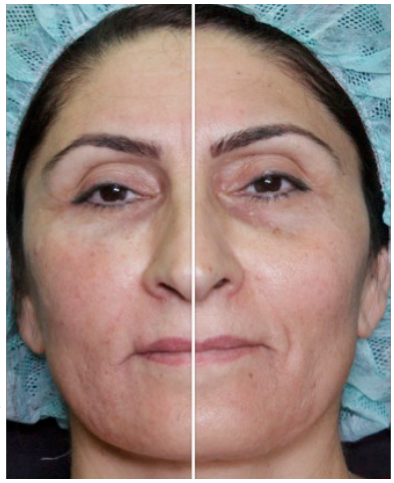
PK: HA fillers, such as the Emervel family (Galderma), provide a new technology with both variable and controlled cross-linking and calibration. The Optimal Balance Technology is characterized by "the three C's": cross-linking, calibration, and concentration. As physicians, we can select the right combination for each clinical indication. All the products in the family have an HA concentration of 20 mg/mL. The products with larger particle size are for deeper injection to provide a stable implant. The products with smaller particle size are for superficial injection to provide a spreading effect. High cross-linking gives firmness for very mobile areas to better resist to deformation and ensure stability of the implant. Low cross-linking gives softness for less mobile areas and to provide a comfortable outcome. The broader range of product textures enables physicians to achieve very sophisticated results (Figures 2 and 3).

FIGURE 2. Injection strategy for a 53-year-old woman with Fitzpatrick skin type III using a range of hyaluronic acid (HA) products (Emervel) that are customized for specific clinical applications by variation of gel calibration and cross-linking. Product with heavy cross-linking and large gel calibration (HA_E Volume) was implanted supraperiosteally and subcutaneously. Product with heaviest cross-linking and medium gel calibration (HA_E Deep) was implanted subcutaneously. Product with moderate cross-linking and small gel calibration (HA_E Classic) was implanted into the superficial subdermal plane. Product with minimal cross-linking and small gel calibration (HA_E Touch) was implanted supraperiosteally and in the superficial subdermal plane into the lower eyelid with a blunt-tipped microcannula (Pix'L) and intradermally to the other areas with a sharp needle. Product with heavy cross-linking and low gel calibration (HA_E Lips) was implanted submucosally to the vermilion lip. Gauge and length of blunt-tipped microcannula used for filler implantation into lower eyelid and gauges and lengths of sharp needles used for filler implantation into other regions are shown in parentheses.



Courtesy of Hema Sundaram MD

FIGURE 3. Patient after half-face treatment with five "customized" hyaluronic acid (HA) products of different gel calibration and cross-linking. Right side of face immediately after injection of lower eyelid, temple, midface, nasolabial fold and oral commissure, vermilion lip, and lower face. Left side before injection. Note smooth integration of the HA products with lack of ecchymosis and tissue edema, and lack of Tyndall Effect with subdermal and intradermal injection of the product designed for superficial implantation into the lower eyelid, nasolabial and submalar rhytids, and oral commissure.



Courtesy of Hema Sundaram MD

The products have homogenous texture due to homogenous gel calibration. This provides consistent extrusion force, homogenous tissue integration with less massage required and homogenous gel degradation.

HS: Do you feel these new products are a valuable addition to the aesthetic toolbox, and if so, how do you envisage them being incorporated into treatment paradigms for volumetry, both alone and in combination with existing products?

PK: The new generation of HA fillers is a real advance. Rather than treating the aging face with a single product, there is a specific HA product for each region of the face that is efficient, durable, and safe. We have new anatomical concepts of the aging face. The first goal is to limit facial muscular action. Skin muscles are responsible for wrinkles, but also for mobilization of fat tissue and then the change in facial volume over time. Botulinum neurotoxin is the main treatment for muscular activity. After that, we have to restore volume, region by region, with specific fillers. We don't need the same product with the same cross-linking for a malar projection as for a lip. The injection of a tear trough with a fine needle or a fine cannula is different to the injection of a nasolabial fold. The cross-linking, the calibration, and the concentration of these new HAs are different according to their intended utilization.

For example, for volumetry of the lip, the best product is safe as shown by clinical studies, durable due to ideal concentration and cross-linking, easy to inject with a fine needle or cannula (30G) due to ideal calibration, and comfortable due to the incorporation of lidocaine. For malar projection, the injection plane is deeper, the cannula used is larger (22G or 18G), and patients also appreciate the lidocaine. In summary, these new HAs are not "gadgets," but efficient tools for volumetry, alone or in association with botulinum neurotoxin.

GM: Emervel has been developed as a family of products that give a range of HA fillers tailored for different critical areas. By modifying the cross-linking and calibration, the products developed are specific for clinical usage. The product with minimal cross-linking and small size calibration is designed for superficial injection. The product with moderate cross-linking and small size calibration is for shallow folds. Heavy cross-linking and medium size calibration produce a product for deeper grooves and subcutaneous tissue. Heavy cross-linking and large calibration size give a volumizing product.

The key to successful use of all HA products is to understand the basic components of the HA gel fillers. Cross-linking, necessary for firmness and lift, causes significant inflammation if overdone. Small particle size is designed for superficial injections as the product lies flat and is malleable, while large particle size will hold up deeper structures—but if the particles are too large, this can cause nodules. High HA concentration is needed for longevity and durability, but too concentrated a product can create nodules, granulomas, and inflammation. An understanding of these key factors will allow the clinician to use all HA gel fillers correctly for each clinical situation.

FURTHER READING

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COMMENTARY

This roundtable discussion reinforces what clinicians have believed since multiple dermal fillers first became available (ie, no one product is great for every area of every face). The concept of matching fillers of different filling capacity to different treatment areas is not new and has always been a part of the "culture" of dermal fillers. The original dermal filler, bovine collagen, came in three strengths—Zyderm 1, Zyderm 2, and Zyplast—which were each meant to treat specific wrinkles of varying depth. Additionally, all three of the hyaluronic acid (HA) gel "families" noted in this round table have created several strength products within their own family to try and treat various facial areas with greater efficacy. This is generally done by changing only one variable, such as cross-linking or particle size, yielding products that are thinner or thicker than their counterparts. These various HA products have allowed injectors to achieve better clinical results than were possible with collagen-based products, particularly as we have developed a better understanding of the niche for each product. In particular, the lifting nature of HA fillers has ushered in the concept of facial volumizing as a treatment for the aging face rather than just filling wrinkles.

The most intriguing concept presented in this roundtable is the idea of manipulating multiple variables in a family of fillers to further refine them. This appears to allow products to be more than just thin, medium, and thick, but also to be soft or firm. Having the choice of these different characteristics would allow clinicians the opportunity to fine-tune their injections even further than what they are currently capable of. Remember, though, artists don't necessarily only need better paint to create a masterpiece, they also need a better sense of aesthetics. Every aging face doesn't need 4 cc of fillers to look better, even if the products are soft and thin!

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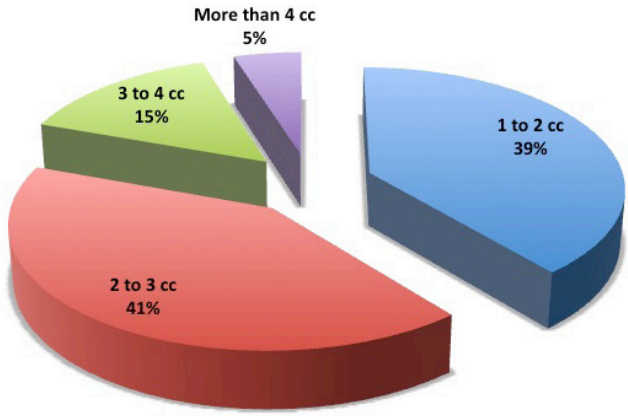
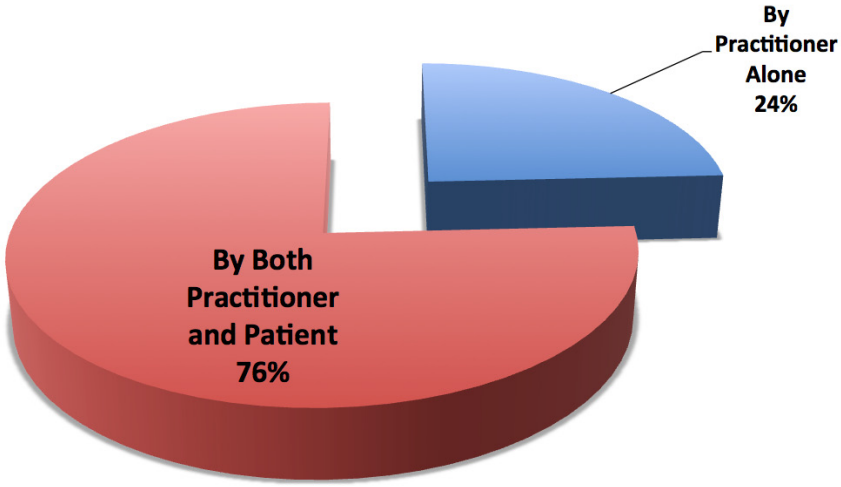
Quick Polls

QUICK POLL: Faculty Usage of Filler Volume in a Single Session



Faculty were asked what volume of filler they inject during a typical treatment session. Chart indicates the percentage of faculty who inject each of the filler volumes shown.

QUICK POLL: Injected Volume: Decision-Making



QUICK POLL RESPONDENTS

D=Dermatology F=Facial Plastic Surgery O=Oculoplastic Surgery P=Plastic Surgery

Benjamin Ascher MD (P), Magda Belmontesi MD (D), Vivian Bucay MD (D), Laurie Casas MD (P), Daniel Cassuto MD (P), Joel L. Cohen (D), Doris Day MD (D), Steven H. Dayan MD (FP), Luc Dewandre MD (P), Lisa M. Donofrio MD (D), Steven Fagien MD (OP), Julius W. Few Jr. MD (P), David J. Goldberg MD JD (D), Mitchel P. Goldman MD (D), Haideh Hirmand MD (P), Derek H. Jones MD (D), Mary Lupo MD (D), Marina Landau MD (D), Z. Paul Lorenc MD (P), Ellen Marmur MD (D), Gary D. Monheit MD (D), Rhoda Narins MD (D), Tatjana Pavicic MD (D), Jason N. Pozner MD (P), Nowell Solish MD (D), Hema Sundaram MD (D), Jonathan M. Sykes MD (FP), Amy Taub MD (D), Patrick Trévidic MD (P), S. Randolph Waldman MD (FP), Heidi Waldorf MD (D), Susan H. Weinkle MD (D), Sabine Zenker MD (D)

**Erratum: In Part I of the "The New Face of Fillers," Dr. Laurie Casas was erroneously listed as a dermatologist. Dr. Casas is a Board Certified Plastic Surgeon.*

Racial and Ethnic Differences in Skin Aging: Implications for Treatment with Soft Tissue Fillers

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ABSTRACT

Racial and ethnic differences in the age of onset, severity, and anatomical features of facial aging have been described. In addition, increased melanocyte lability and fibroblast reactivity are functional features that are characteristic of skin of color. These differences should be considered when treating patients with soft tissue fillers in order to achieve optimal results. Signs of facial aging in individuals with skin of color tend to be most pronounced in the periorbital and midface region with less prominent features of skin aging in the upper third of the face and a decreased tendency toward perioral rhytides and radial lip lines. As such, volumization of the midface while preserving individual and ethnic ideals of beauty is a key goal. Important treatment considerations include minimization of inflammation, epidermal injury, and bruising, which can lead to aesthetically displeasing sequelae.

J Drugs Dermatol. 2012;11(suppl 8):s30-s32.

CASE VIGNETTE

A 74-year-old African American woman presented with characteristic features of facial aging that are commonly seen in individuals of African descent with Fitzpatrick skin types IV–VI (Figure 1). The key features included: mild rhytids on the forehead, infraorbital hollowing, pseudoherniation of the orbital fat pad, dermatochalasis, midface volume loss, descent of the malar fat pads with resultant deepening of the nasolabial folds (the most prominent feature), absence of perioral rhytids and radial lip lines, minimal lip atrophy, dyschromia (hyperpigmentation due to melasma on the forehead and solar lentigines on the cheeks), dermatosis papulosa nigra, and enlarged pores and textural irregularities.

The aim of filler treatment would be to rectify the descent of fat pads into the midface, and the contiguous areas of volume loss. This requires careful examination of the patient and marking to highlight areas of relative fat excess and loss, respectively. For instance, the nasolabial folds are heavier, but the area above them is relatively thinned out. Infraorbital fat herniation can create a "saddlebag" like appearance, with a line of demarcation at the lower margin, which can be camouflaged by judicious application of filler. In the midcheek, atrophic areas can be repleted, with the filler functioning to fill the upper margins of fat pads, and the thicker areas can be avoided so that they are not made more protuberant. Injection of filler in the temple area and the upper lateral face can also help to pull up the midface, as well as slightly soften the nasolabial fold. On the lower face, jowling can result in a notch between the lower lateral cheek and the relatively fixed chin margin; this can be treated with focal injection of a filler into the chin notch or "pre-jowl sulcus."

In patients with skin of color, the protective effects of increased eumelanin contribute to delayed and less pronounced features of photoaging. As a result, features of intrinsic aging (including midface volume loss and descent of the malar fat pads) tend to be more pronounced than those of extrinsic aging (including laxity and rhytids). Dyschromias—both as a feature of photoaging and a risk of aesthetic procedures—are major consideration when treating patients with skin of color. Melasma, mottled pigmentation and other nonspecific dyschromias are common aesthetic concerns in patients with Fitzpatrick skin types IV–VI. In addition, labile melanocyte responses are associated with an increased risk of pigmentary abnormalities following injury or inflammation in richly pigmented skin.

As such, optimal approaches to aesthetic procedures in patients with skin of color hinge on minimization of injury and inflammation. In the context of injectable soft tissue fillers several techniques are beneficial in achieving this goal, including: selection of products that have minimal reactivity (i.e., are unlikely to induce an inflammatory response); minimizing of needle punctures—threading and fanning are preferred over serial puncture; and treating erythema associated with injection of fillers with a topical corticosteroid to reduce inflammation promptly.

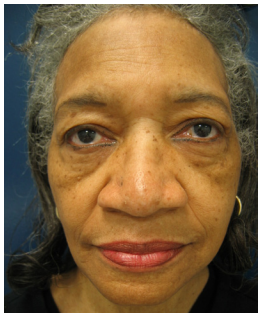
Another consideration when treating skin of color is the tendency for discoloration associated with the Tyndall effect and hemosiderin deposition to be more conspicuous (i.e., darker) in highly pigmented skin compared to less pigmented skin types. As such, avoidance of superficial placement of product and bruising are especially important.

DISCUSSION

Racial/Ethnic Differences in Facial Shape and Skin Texture

Beyond issues of color, there are differences in facial shape, fat pad location, and skin texture in aging patients of different eth-

FIGURE 1. A 74-year-old African American woman with characteristic features of facial aging.



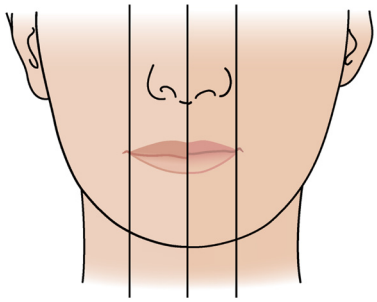
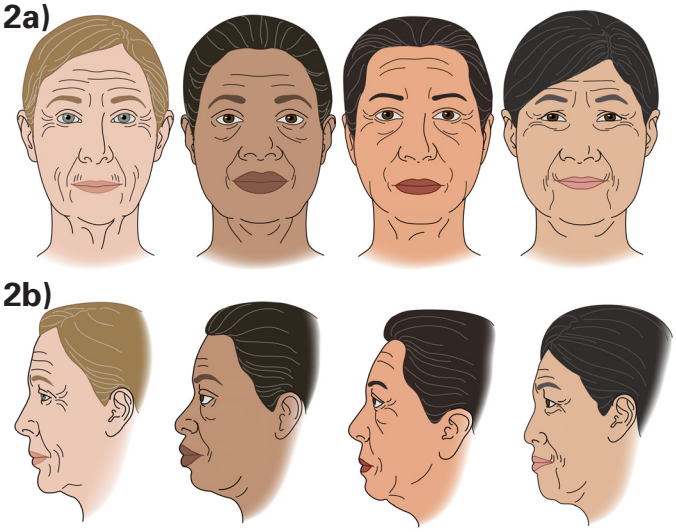


FIGURE 3. Mandibular width in Asian women (left) is wider than in Caucasian women (right).

FIGURE 2. Features of facial aging in Caucasian, African American, Latino, and Asian women, from left to right. **a)** Frontal view. **b)** Lateral view.



nicities. Specifically, key angles and proportions, including the nasofrontal angle, nasolabial angle, alar width as a proportion of intercanthal distance, and the width of the columella relative to the nasal lobule may vary. For instance, in the periorbital region, Japanese, Latino, and Caucasian women may have different wrinkles scores with eyes opened and closed, respectively[1]; on the other hand, other Asian women, and African American women may have more stable wrinkling that does not vary with eyelid position. So in the former group, it is very important to assess eyes in both the open and closed positions before placing filler.

As seen in Figure 2, from front and side views, typical aged Caucasian, African American, Latino, and Asian women have different facial architecture. The Caucasian woman has more fine perioral and periorbital fine rhytids, and the malar eminence and corneal surface lie in the same vertical plane. On the neck, the Caucasian face shows skin sagging and jowling, with effacement of the cervicomental angle to skin laxity. In the African American face, the head height is relatively shorter, as are the nose and ear lengths, but the alar, eye fissure, and mouth widths are relatively greater.[2-4] Aging particularly affects the midface, with laxity of the eyelids, pseudoherniation of the infraorbital fat pads, and pooling of excess tissue and fat pads in the midcheek area.[4] In younger African American women, the cheek is recessed relative to the eye position, so age-related accumulation of redundant fat in the midcheek is clear evidence of aging. On the neck, rather than skin laxity, African American women develop accumulation of submental fat and protuberant thick skin that also soften the cervicomental angle. Jowls are composed not of sagging, fine skin but rather the same heavy tissue that permeates the midface.[4] Latino women have more sebaceous skin than Caucasian women and tend to have a rounder face, with heavy eyelids and a prominent midface and cheek area.[5] Nasal length is abbreviated, the alar region is wider, and the chin is relatively recessed. With aging, the Latino face, like the African American face, becomes thicker and heavier in the midcheek area, with notable nasolabial folds and fat pad accumulation; this is combined with eyebrow and eyelid drooping and hooding, including lower lid fat herniation. There is excess mandibular and submandibular skin and soft tissue.[5] In contrast, Asians have less wide mouths, elongated intercanthal width, and significantly wider lower nasal margins.[3] The wider mandibles of Asian women (Figure 3) are important to recognize so that this element is not exacerbated with further filler injections and is possibly improved with neurotoxin injections to relax the masseter.

CONCLUSION

Signs of facial aging in individuals with skin of color tend to be most pronounced in the periorbital and midface region, with less prominent features of skin aging in the upper third of the face and a decreased tendency toward perioral rhytides and radial lip lines. As such, volumization of the midface while preserving individual and ethnic ideals of beauty is a key goal. Important treatment considerations include minimization of inflammation, epidermal injury, and bruising, which can lead to aesthetically displeasing sequelae.

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COMMENTARY

I applaud the efforts of Dr. Alexis and Dr. Alam for their outstanding review of the patient presented and keen aesthetic observations regarding skin of color. The patient shown illustrates commonly found aging sequelae for the woman of color: brow ptosis, upper eyelid involution, secondary tear trough formation, mid-facial atrophy with ptosis and jowl formation.

We know that aging, regardless of racial or ethnic considerations, consists of three primary components: wrinkle/skin atrophic change, volume loss, and ptosis of facial tissues. Skin of color tends to be resistant to skin atrophic/actinic effects, but volume and ptosis are key players in this select group of patients.[1] It is important to emphasize the technical points mentioned in the review, specific to avoiding unnecessary trauma to the skin and appropriate treatment/prevention of post-inflammatory hyperpigmentation. Specifically, the injector should avoid serial puncture where possible and preferentially place fillers deeper to avoid dermis/epidermal disruption.[2]

I agree with the use of fillers to restore volume to the cheeks, creating a mid-facial lift, then look to lower facial depressions secondarily, such as the nasolabial and marionette folds. Finally, addressing ancillary issues, such as dermatosis papulosa nigra, completes the picture of nonsurgical optimization. One must remember that the nonsurgical modalities described above can be combined with strategic surgical intervention to create a blending I refer to as part of the continuum of beauty, to achieve synergistic improvement with less recovery time.

In conclusion, appropriate understanding of aging sequelae in skin of color can lead to nonsurgical treatments that yield powerful enhancement in facial aesthetics.

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Blunt-Tipped Microcannulas for the Injection of Soft Tissue Fillers: A Consensus Panel Assessment and Recommendations

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ABSTRACT

As blunt injection microcannulas increase in popularity, clinicians may find it of value to have a systematic review of their current uses. This consensus document is derived from a roundtable discussion between a multi-specialty faculty comprising two U.S.-based dermatologists, one U.S.-based plastic surgeon, and one European cosmetic surgeon, all of whom were early adopters of blunt microcannulas for alloplastic fillers. The purpose of this consensus document is to provide an overview of the utility and clinical applications of blunt microcannulas, guidelines for their safe and efficacious use, and recommendations for the further evidence that needs to be accrued to substantiate the claims that have been made in regard to their superior safety profile and other benefits.

J Drugs Dermatol. 2012;11(suppl 8):s33-s39.

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INTRODUCTION

Blunt-tipped cannulas have been used for the injection of autologous fat for volume restoration since the early part of the last century.[1,2] In recent years, blunt microcannulas of varying gauges and lengths have become available for the injection of alloplastic fillers.[3] Use of these microcannulas was first described in Europe, and they have subsequently been introduced to the United States and other countries.

A number of advantages have been ascribed to the use of blunt microcannulas rather than sharp needles for the injection of fillers. These include the elimination or near elimination of post-injection bleeding and ecchymosis, a decrease in the number of injection entry points, elimination of the risk of inadvertent intravascular injection, and decreased patient discomfort during injection. It has also been hypothesized that the back-and-forth passage of the microcannula through tissue may stimulate collagenesis.

As blunt-tipped microcannulas increase in popularity, clinicians may find it of value to have a systematic review of their current uses. This consensus document is derived from a roundtable discussion between a multi-specialty faculty comprising two U.S.-based dermatologists, one U.S.-based plastic surgeon, and one European cosmetic surgeon, all of whom were early adopters of blunt microcannulas for alloplastic fillers. The purpose of this consensus document is to provide an overview of the utility and clinical applications of blunt microcannulas, guidelines for their safe and efficacious use, and recommendations for the further evidence that needs to be accrued to substantiate the claims that have been made in regard to their superior safety profile and other benefits.

Overview of Available Blunt Microcannula Products and Faculty Experience With Them

The faculty's experience with blunt microcannulas for injection of alloplastic fillers ranges from two to three years, with all faculty members noting that they were introduced to them in Europe. For several years before this, they have used blunt cannulas of various gauges for the injection of autologous fat. The products that they have used for alloplastic fillers are blunt-tipped, disposable surgical steel microcannulas available in a range of gauges and lengths and designed for single-time use. Three brands of blunt-tipped microcannulas are currently approved by the U.S. Food and Drug Administration (FDA) as 510(k) Hypodermic Single Lumen Needle devices: DermaSculpt (CosmoFrance), Merz (Merz Aesthetics), and Magic Needle (Needle Concept). Several other brands are available in Europe and elsewhere. While the approval of blunt microcannulas enables them to be used for fluid injection or aspiration, it should be noted that injection of soft tissue fillers with them is considered off-label by the FDA, in that each filler product is specifically approved for use with the sharp needle(s) that are packaged with it. Patients should be apprised of this off-label usage as part of the informed consent process before filler injections.

The faculty all have experience using DermaSculpt microcannulas, and three [Pozner, Sundaram, Weinkle] have also used the Merz brand. Other brands with which the faculty specifically cited experience include Magic Needle [Weinkle], Pix'L (Thiebaut) [Sundaram], and Softfil (Soft Medical Aesthetics) [Pozner, Sundaram, Weinkle]. All the faculty have experience using blunt microcannulas to inject a number of hyaluronic acid (HA) filler products available in the U.S.: NASHA (Restylane and Perlane, Medicis), Hylacross HA (Juvéderm Ultra and Ultra Plus, Allergan) and Cohesive Polydensified Matrix HA (Belotero Balance, Merz). One [Sundaram] has also used microcannulas to inject low-concentration hydrated HA (Prevelle Silk, Mentor). Three of the faculty [Pozner, Sundaram, Weinkle] have also used blunt microcannulas to inject calcium hydroxylapatite (Radiesse, Merz) and poly-L lactic acid (Sculptra, Valeant), and two [Pozner, Sundaram] have used them for polymethyl methacrylate (Artefill, Suneva).

The entry point for the blunt microcannula is first made with a sharp "pilot" needle, and then the microcannula is carefully inserted and maneuvered until the desired tissue plane is reached. The faculty note that some brands of microcannula (e.g., DermaSculpt, Magic Needle) are supplied with pilot needles of appropriate gauge for each gauge of microcannula. Injectors provide their own pilot needles for other brands (e.g., Merz). Three of the faculty [Dewandre, Pozner, Sundaram] typically use a 26-gauge sharp pilot needle to make the entry point for a 27-gauge microcannula, and a 23-gauge sharp pilot needle for a 25-gauge microcannula. Two [Pozner, Sundaram] note that since the gauge of the pilot needle is close to that of the microcannula, stretching of the skin facilitates passage of the microcannula through the entry hole. This may be achieved by retraction of the skin with the fingers of the nondominant hand while guiding the microcannula with the dominant hand, or with the help of an assistant. Another technique (Weinkle) is to use a larger-gauge pilot needle (e.g., a 21-gauge needle for insertion of a 25-gauge microcannula). The faculty have found that if it is difficult to locate the entry hole after the initial puncture has been made with the pilot needle, gentle rubbing of the area with sterile, gloved fingers can produce slight bleeding through the entry hole that serves to locate the microcannula insertion site. Filler is injected through blunt microcannulas with anterograde or retrograde serial threading or microthreading injection technique. The faculty notes that serial puncture or microaliquot injection techniques can be used with sharp injection needles, but not with blunt microcannulas.

The faculty notes differences in the degree of flexibility vs. rigidity of microcannulas that can impact their clinical behavior. For example, one of the brands currently approved for use in the U.S. (DermaSculpt) is markedly flexible. Another brand that a faculty member [Sundaram] has used in Europe (Pix'L) is available in a flexible form (Pix'L) and also in a reinforced, more rigid form (Pix'L +) intended for periorbital use. Longer microcannulas (38 mm, 50 mm, or more) tend to be more flexible, while shorter, 25 mm microcannulas are more rigid. A microcannula with a 30 or 27 gauge will tend to be more flexible than one with a gauge of 22. The specific design of a microcannula and its flexibility or rigidity may determine its passage through tissue and injection characteristics. The faculty feel that longer experience and more systematic appraisal are needed to define further how these differences might influence microcannula selection and clinical performance (Figure 1).

Consensus Recommendation #1

Patients should be apprised as part of the informed consent process before treatment that, while the use of blunt injection microcannulas may confer some benefits in the clinician's opinion, the injection of soft tissue fillers with them is considered off FDA labeling.

Consensus Recommendation #2

In regard to the selection of specific types and sizes of blunt microcannula for different clinical applications, comparative study data are needed to adopt an evidence-based rather than anecdotal approach.

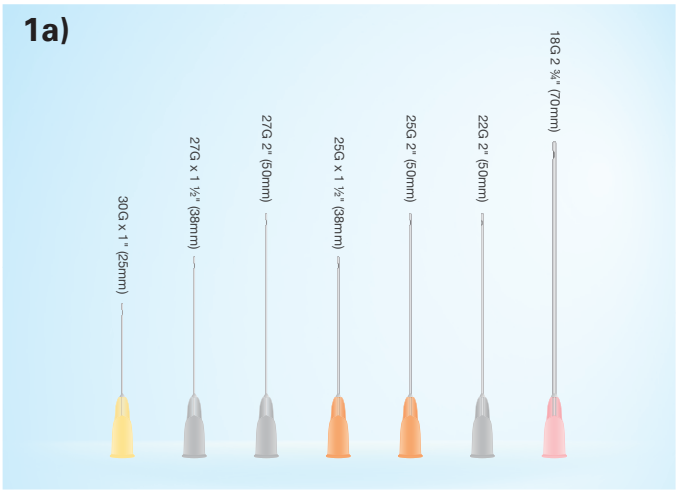
Consensus Recommendation #3

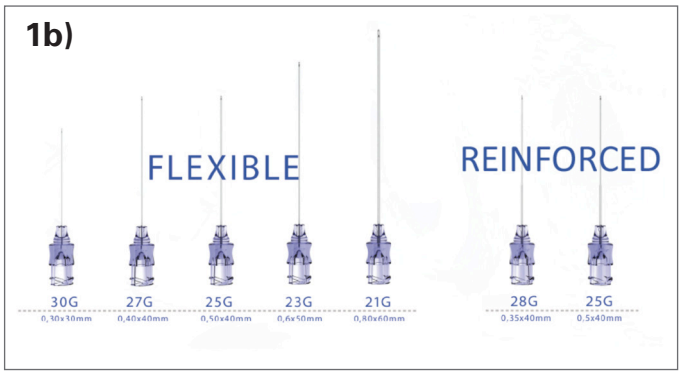
Recommended entry points for blunt-tipped microcannulas when injecting the face (Figure 2).

Evolution in the Use of Blunt Injection Microcannulas and Their Impact Upon Injection Technique

The faculty believes that a great benefit of working with blunt microcannulas is the ability to achieve effective volume restoration with fewer injection entry points. Blunt microcannulas also demonstrate the value of using a longer tool for filler injections and allow the refinement of technique for doing this. Three of the faculty [Pozner, Sundaram, Weinkle] note that their experience with longer microcannulas has serendipitously led them to find utility in long sharp needles for areas that need more precision or definition, or when injecting into the upper half of the dermis, which has increased tissue resistance compared to the subdermal planes. The panel most commonly utilizes the 27-gauge, 1¼ in, 31 mm long sharp needle when injecting calcium hydroxyapatite (CaHA) into the midface. For poly-L-lactic acid (PLLA), the 22-gauge, 70 mm blunt microcannula [Pozner] and 25-gauge, 1½ in, 38 mm needle [Weinkle] are favored. One of the panel [Sundaram] is increasingly using a 22-gauge microcannula with a length of 50 mm or longer for filler implantation to all facial areas. With both, the panel recommends prewarming of PLLA and dilution in a syringe with a volume at least 1 cc larger than the total product volume to decrease the risk of microcannula or needle clogging.

FIGURE 1. a) Range of flexible blunt-tipped microcannulas approved for use in the U.S., Europe, and elsewhere (DermaSculpt). **b)** Range of flexible and more reinforced blunt-tipped microcannulas approved for use in Europe and elsewhere (Pix'L and Pix'L +).

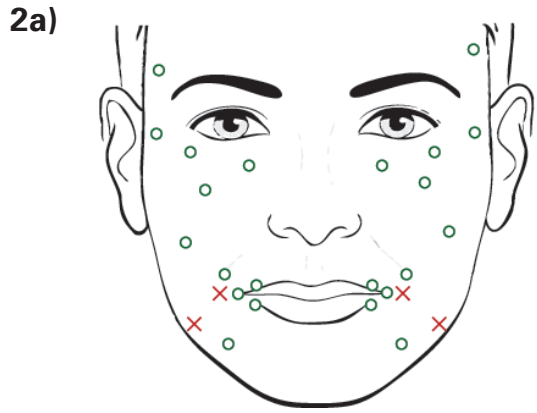


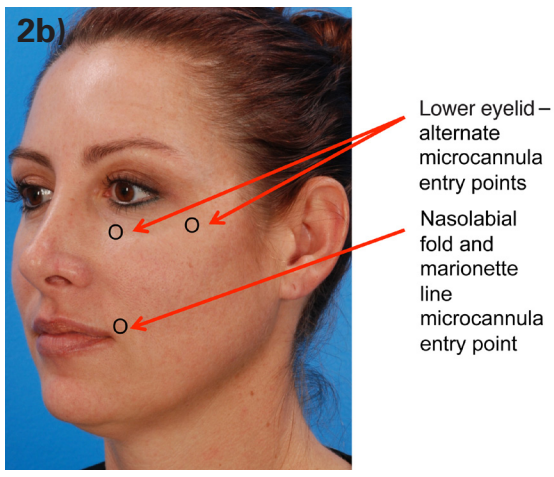


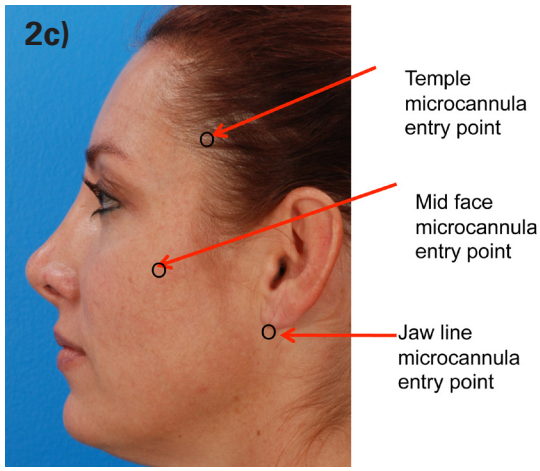
The faculty panel also finds that slight dilution of HA fillers with lidocaine or saline helps to decrease extrusion force during injections through microcannulas with a diameter that is smaller than 22 gauge. They consider lidocaine without epinephrine to be the diluent of choice. Epinephrine is avoided because it produces a burning sensation when administered [Weinkle], and the skin blanching it induces might mask signs of vascular compromise during or immediately after filler injection [Sundaram]. The faculty feels that there is little or no tissue trauma caused by the appropriate use of blunt microcannulas that are 27 gauge or larger in diameter, and thus epinephrine is not needed to promote local vasoconstriction.

The panel's consensus is that the greatest utility of blunt microcannulas is for deep, subdermal implantation of fillers to the face, using techniques similar to those developed for autologous fat grafting. A blunt microcannula can cover a significant surface area from one entry point and fanning injection technique allows broad, multi-directional distribution of the filler

FIGURE 2. Consensus recommendations for blunt microcannula entry points to the face. **a)** Possible entry points for injecting the lower eyelids, temples, midface, nasolabial folds, lips, chin, and oral commissures/marionette lines are indicated by open circles. Depending on microcannula length, as few as two to four entry points in total may be required for pan-facial treatment. Areas where microcannula entry points are not recommended are indicated by red crosses (Depressor Anguli Oris muscle and insertion of Platysma muscle on the mandibular angle). **b-c)** Indication of how microcannula entry points may be selected for a specific patient based on desired areas of filler injection.







Images courtesy of Jason Pozner MD.
Recommended microcannula entry points by panel consensus.

TABLE 1.

Preferred Blunt Microcannulas for Specific Areas and Products

Area	Microcannula Diameter and Length	Preferred Filler Product(s)
Lower eyelid	27 or 25-gauge, 38 mm	HA (may be diluted)
Upper eyelid and around eyebrow	27-gauge, 25-, or 22-gauge or 38 mm or longer	HA (may be diluted)
Midface	25 or 22-gauge, 38 mm or longer	HA, CaHA, or PLLA
Temple	25 or 22-gauge, 38 to 70 mm	CaHA, PLLA, or HA
Lower face	25 or 22-gauge, 38 mm or longer	CaHA or HA
Lips	27-gauge, 38 mm	HA
Hand (dorsum)	25 or 22-gauge, 38 mm or longer	CaHA or HA
Décolleté	25-gauge, 38 mm	HA

product. The faculty notes that sharp needles are valuable for precise injection of smaller volumes and for superficial injection, as when effacing fine rhytides. The panel believes blunt microcannulas to be superior in every respect to sharp needles for injection of fillers into non-facial areas such as the dorsum of the hands (Figure 3) and the décolleté. In summary [Sundaram], filler implantation to non-facial areas is viewed as essentially a process of bulk volume restoration, whereas implantation to the face has the objective of bulk volume restoration, and also of smaller volume "fine tuning." The latter may require injection techniques other than subdermal threading and fanning, such as serial puncture and/or intradermal injection.

Consensus Recommendation #4

Blunt microcannulas may be considered the preferred option for implantation of soft tissue fillers to non-facial areas such as the hands and décolleté, and a valuable option for deep (subdermal) filler implantation to the face.

Area-Specific and Product-Specific Strategies for the Use of Blunt Microcannulas

For injection of the temples, three faculty [Dewandre, Pozner, Sundaram] prefer the blunt microcannula technique, with gauge and size ranging from 22-gauge, 70 mm to 25-gauge, 50 mm. This is considered to permit safer injection in both the superficial and deep tissue planes. Two of the faculty [Sundaram, Weinkle] also inject the temples on occasion with sharp needle serial puncture, only in the supraperiosteal plane to avoid damage to the temporal branch of the facial nerve and other vital structures that lie more superficially. They employ a vectoring or fanning technique to deliver the filler product above the hairline for lifting effect. The panel most commonly selects CaHA or PLLA for injection of the temples.

For the periocular region, the consensus of the panel is to use a smaller diameter blunt microcannula for deep (supraperiosteal) implantation of HA fillers. One faculty member [Sundaram] finds that a short microcannula (27-gauge, 25 mm) provides better control when injecting the upper eyelid and below the eyebrow, due to its greater rigidity. She also uses a 22-gauge, 50 mm microcannula more frequently for filler implantation to multiple facial areas. including the periocular region, for which with the entry point is placed in the superolateral midface to allow access to both the lower eyelid and the lower forehead above the eyebrow. Another faculty member [Weinkle] does not inject the upper eyelid but also prefers a shorter, more rigid microcannula to inject along and above the eyebrow.

For the midface, the panel prefers 25-gauge, 50 mm or 22-gauge, 50 mm microcannulas. HA, CaHA, and PLLA are the most commonly used filler products. Three of the faculty members [Pozner, Sundaram, Weinkle] also find sharp needle injection to be of value for correction of focal volume loss with CaHA or HA; this is most commonly done with serial microaliquot technique.

For the lips, the faculty notes that blunt microcannulas or long sharp needles may be used, with the latter often conferring a greater deal of precision.

One faculty member [Sundaram] regularly injects the forehead with fillers but uses a sharp needle to inject non-Tyndall HA (Belotero Balance or Prevelle Silk) into the dermal or superficial subdermal tissue planes.

FIGURE 3. Consensus recommendation for blunt microcannula entry point for the dorsum of the hand in the finger web between the middle and fourth fingers (black circle). Alternatively, two entry points may be made, the first between the index and middle fingers and the second between the ring and little fingers (white circles).

Images courtesy of Jason Pozner MD.
Recommended microcannula entry points by panel consensus.

For injecting the hands, the panel prefers the 25- or 22-gauge blunt microcannula, with CaHA (Radiesse) as the filler product of choice and NASHA (Perlane) as a second option. The panel recommends dilution of CaHA with lidocaine to give a final concentration of 0.45%, with further addition of lidocaine or 0.9% saline as considered appropriate to lower viscosity of the filler and facilitate its spread through the tissue after implantation.

The panel notes that microcannula selection may also be product-specific. For example, one faculty member [Dewandre] typically uses 27-gauge and 30-gauge microcannulas for low- and medium-density HA products such as Juvéderm Ultra and Ultra Plus, Restylane, and Perlane, 25-gauge microcannulas for CaHA (Radiesse) and PLLA (Sculptra), and 22-gauge microcannulas for high-density products such as the HA fillers, Juvéderm Voluma and Restylane Sub Q, and for polymethyl methacrylate (PMMA, Artefill).

Consensus Recommendation #5

Preferred blunt-tipped microcannulas for specific facial areas and filler products (Table 1).

Clinical Considerations: Efficacy, Safety, Tolerability, and Potential Patient Benefits of Blunt Microcannulas

Inadvertent Intravascular Injection or Neurovascular Damage

The clinical benefits attributed to blunt microcannulas include elimination or near elimination of the risks of inadvertent intravascular injection and of injury to vital neurovascular structures within the areas of injection. The panel is in general agreement that a blunt microcannula of 27 gauge or above is unlikely to penetrate blood vessels or nerves if it is used with appropriate technique but, rather, will push them aside as it traverses the path of least resistance through the tissue. Two of the faculty [Pozner, Sundaram] feel that the most narrow microcannula, of 30 gauge, might have the potential to cause neurovascular injury or even to penetrate a blood vessel if passed through tissue with inappropriately high speed and/or force.

Vascular Compression

The panel notes that the use of blunt microcannulas does not by itself decrease the risk of vascular compromise due to compression by injected filler, as this is technique-dependent. To avoid excessive extrusion force when injecting fillers through blunt microcannulas that are invariably longer than the typical 13 mm to 19 mm sharp needles, a larger gauge is selected. In general, a microcannula of 27-gauge or larger diameter is used in place of a 30-gauge sharp needle, and a microcannula of 25 gauge or larger diameter in place of a 27-gauge sharp needle. The decreased extrusion force facilitates increased flow of filler product that can cause deposition of inappropriately large filler boluses if the injector is unused to the small volume micro-threading technique that is best suited to microcannulas. One faculty member [Sundaram] considers the angular artery during its course through the area of the pyriform aperture and medial midface to be one of the vital structures at greatest risk of compression due to overinjection of fillers. This compression may be likened to a compartment syndrome.

Ecchymosis

The decreased or eliminated risk of piercing a blood vessel with an appropriately used blunt microcannula compared to a sharp needle results in a significantly decreased risk of ecchymosis, which may be particularly noted in regions such as the nasojugal fold, the upper eyelid and the pre-jowl sulcus. In the faculty's experience, ecchymosis with blunt microcannulas is minimal and, for many patients, nonexistent. If ecchymosis does occur, it may be at the insertion site of the pilot sharp needle, or in areas of increased tissue resistance if the microcannula is applied with inappropriate force. Increased tissue resistance may be due to fibrosis, in patients who have previously had face-lifting surgery or multiple injection sessions with collagen-stimulating volumizers such as PLLA. These situations may be considered relative contraindications to the use of blunt microcannulas.

Tolerability

In the faculty's experience, the tolerability of blunt microcannulas is equal to or better than that of sharp needles. Anecdotally, patient discomfort is reduced to the level where topical anesthesia alone consistently suffices even for injection of the lips, and local nerve blocks are not necessary. There may be some discomfort during injection, especially if a microcannula is passed multiple times through a zone of tissue fibrosis. One faculty member [Weinkle] has observed that some patients dislike the noise of a blunt microcannula passing through tissue and recommends forewarning patients of this and playing music to provide auditory distraction during the injection procedure.

Collagenesis

It has been suggested that back-and-forth passage of a blunt microcannula multiple times through an area may stimulate collagenesis. This theory is persuasive by extrapolation from the collagenesis observed with repeated back-and-forth passage of cannulas during liposculpture. However, the panel notes that collagenesis induced by liposculpture typically results from a much larger number of "tunneling" passes through the tissue than would be performed when injecting alloplastic fillers with microcannulas. Given the current lack of evidence for the hypothesis that injection of fillers with blunt microcannulas stimulates collagenesis, the panel recommends controlled studies of microcannula vs. sharp needle injection if it is desired to substantiate this hypothesis. If blunt microcannula use does, indeed, stimulate significant collagenesis, an interesting

consideration is whether previous repeated treatment sessions with microcannulas might at some point be deemed a relative contraindication to their future use, due to the resultant increase in tissue resistance.

In general, the faculty notes that more experience is needed to determine the long-term effects, if any, of using blunt microcannulas.

Consensus Recommendation #6

Blunt microcannulas may be preferred to sharp needles to decrease or eliminate the risk of inadvertent intravascular injection or neurovascular damage, and to decrease the risk of ecchymosis. These safety benefits are contingent upon appropriate use, specifically including the avoidance of inappropriate speed and force as a blunt microcannula is passed through the tissue.

Consensus Recommendation #7

Previous facial surgery or repeated injections with collagen-stimulating fillers may constitute a relative contraindication to the use of blunt microcannulas, due to tissue fibrosis.

Review of Blunt Microcannula Studies to Date and Identification of Further Data that Need to be Obtained to Provide Evidence-Based Substantiation of Clinical Claims

Peer-Reviewed Study Publications

A recent prospective phase II (pre-approval) randomized split-phased, double-blinded study was conducted to assess the safety and efficacy of a proprietary 21-gauge, 30 mm metallic blunt cannula when injecting HA filler into the nasolabial folds.[4] Twenty-five study subjects with a score of 2 to 3 bilaterally for the nasolabial folds (NLF) on the validated seven-point photographic Modified Fitzpatrick Wrinkle Scale (MFWS) were randomly assigned to receive an injection of 0.5 mL HA filler with the cannula to one NLF and with a 30-gauge (13 mm) sharp needle to the other NLF. On evaluation three days after injection, there was a bilateral decrease in MFWS score (indicating improvement in NLF). Study subjects reported decreased pain, hematoma, edema, and erythema on the side treated with the cannula.

The panel notes that the cannula used in this study is somewhat wider and shorter than the microcannulas they most commonly use for alloplastic filler injections (27-gauge, 38 mm). Further controlled studies would be needed to determine whether the specific safety, tolerability and efficacy profiles of this microcannula differ significantly from those of the wider, shorter cannula.

In another study,[5] 26 subjects with periorbital hollowing were injected with HA filler using the reinforced, rigid microcannula that was noted above as specifically designed for periorbital use (Pix'L + microcannula). Subjects were evaluated immediately after injection, 10 to 25 days afterward and three months after injection. Eighty-eight percent of subjects reported that they were satisfied or very satisfied with treatment. It was observed that there was even distribution of the filler product with excellent aesthetic improvement and a low rate of hematomas or post-treatment edema.

The claims of superior safety and tolerability and decreased risk of ecchymosis with blunt microcannulas compared to sharp needles are reviewed above. The panel is in general agreement with these claims, with the reservations that have been noted.

It has also been suggested that the use of blunt microcannulas increases volume efficiency and decreases treatment time. The faculty agrees that pan-facial volumization with PLLA is usually faster with blunt microcannulas than with sharp needles, but has not observed this consistently with HA fillers. In regard to this claim and also the claim of volume efficiency, the panel recommends controlled studies to provide a higher level of evidence than anecdotal observation.

Consensus Recommendation #8

Further controlled studies are needed for corroboration of early data suggesting that blunt microcannulas can decrease discomfort during filler injection.

Consensus Recommendation #9

Controlled studies are needed to substantiate or refute the hypothesis that blunt microcannulas increase the volume efficiency of filler treatment compared to sharp needles

Combination of Blunt Microcannulas and Sharp Needles: Rationale and Applications

All the faculty members frequently combine blunt microcannulas with sharp needles for the injection of alloplastic fillers. They consider microcannulas a first-line option for deep (subdermal) filler injection to areas of diffuse volume loss, such as facial troughs, the dorsum of the hands, and the décolleté. They add filler injection via sharp needles to precisely address areas of focal volume loss, such as in the midface in some patients, and also for more superficial injection in the intradermal and superficial subdermal tissue planes, as when effacing fine rhytides or the vermilion lip border. For example, one faculty member [Dewandre] routinely uses a 27-gauge, 38 mm microcannula for layered injection of HA to the vermilion lip, in combination with a 30-gauge, 13 mm sharp needle for vertical injection of HA to fine perioral lines. Another [Sundaram] frequently employs multi-plane "sandwich" technique, using a blunt microcannula of 22, 25, or 27 gauge, ranging in length from 38 mm to 70 mm where appro-

priate for supraperiosteal or subcutaneous injection of CaHA or NASHA, followed by intradermal or superficial subdermal injection of non-Tyndall HA for a sheeting effect or to efface fine lines, with a sharp needle of 30 or 27 gauge that ranges in length from 13 mm to 32 mm.

Consensus Recommendation #10

For many patients, a combination of blunt microcannula and sharp needle injection of fillers may represent the optimal balance of safety and efficacy, by providing minimally traumatic diffuse contouring plus precise shaping.

CONCLUSION

The panel finds blunt-tipped microcannulas to be a significant advance in nonsurgical rejuvenation and a valuable addition to the options available for injection of soft tissue fillers. With the caveat that the safety and efficacy of filler injections ultimately depend upon the knowledge and skill of the injector, distinct patient benefits that can be identified as a result of using microcannulas include improved safety, and a decreased risk of ecchymosis leading to a faster return to normal daily activities. Some patients also report improved comfort during injection.

The objectives of this consensus document are to generate an overview of the current use of blunt microcannulas by a faculty of relatively early adopters, and to provide the information and guidelines needed for their successful incorporation into aesthetic clinical practice. The consensus recommendations encompass best practice techniques for patient counseling and injection of alloplastic soft tissue fillers with blunt microcannulas, and also identify areas where controlled study data are needed in order to adopt a more evidence-based approach to their applications.

ACKNOWLEDGMENT

The faculty acknowledges the assistance of Oge Onwudiwe MD (Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax, VA) in the early stages of preparation of this manuscript.

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Utilizing Blunt-tipped Cannulas in Specific Regions for Soft-tissue Augmentation

To the Editor:

Cannulas, while long used in fat transfer, only began to become popular with dermal fillers in Europe over the past three years. After watching and then injecting with some of our overseas colleagues during the course of several European meetings during this time frame, I was hooked. At least in my hands, I have found them to be invaluable in several very specific regions, including the infraorbital hollows, the mid cheek, the dorsal hands, and the décolleté. It certainly makes at least theoretic sense that a blunt-tipped cannula could potentially bounce around a vessel, while a needle would pierce the vessel (Figure1).[1] I have found these flexible blunt-tipped cannulas to seemingly cause less bruising and swelling in these regions, while at the same time having many patients report less pain upon injection of these regions (Figure 2).

Two recent articles in the aesthetic literature seem to substantiate some of these perspectives. In a small observational study of 26 patients, Berros[2] reported that using cannulas for periorbital Restylane placement led to less irregularities, inflammatory reactions, and hematomas. In a double-blind study of 25 patients treated with Restylane in the nasolabial fold, Hexsel et al[3] reported that participants noted less pain, less edema, less redness, and fewer hematomas on the side that turned out to be the one injected with a cannula.

In 2008, a paper stemming from a study I participated in was published that indicated using a "fanning" injection technique was one of the principal factors associated with more swelling and bruising,[4] and I think many of us then began to rethink and thus change our injection approach to some areas where fanning was more commonplace—such as the cheeks. Using cannulas has brought me back to fanning in these 4 regions. I also feel a bit safer injecting the midcheek and infraorbital areas with a cannula, as arterial occlusion, though extraordinarily rare, has been reported in these areas with arteries well below the surface and not always predictable in their distribution (versus, for instance, the temporal artery, which has a more predictable course and can often be palpated).[5]

I absolutely do not think that cannulas are going to ever replace needles. In fact, needles are still necessary to make the small nick in the skin to introduce cannulas. In addition, I find needles to be essential in other regions, such as the lips (to focus on only injecting specific tubercles for a more "natural look" rather than threading a cannula in the lip, which releases aliquots more uniform in volume that could risk the "sausage look"), as well as for treatment of the temporal hollows (to pierce the layers needed to inject down very deep directly on the periosteum). In these regions of the lips, the temples, and also really the oral commissure, I prefer to use a needle with more of a vertical approach and try to precisely place small bolus injections to try to lift contour irregularities and concavities.

My approach to using flexible cannulas has been to mark the skin in areas that need to be filled. I then decide on one entry point for the cannula for the infra-orbital area and another entry point for the mid-cheek. I then gently insert a 25g-needle (0.5 inch) about 1/5 of the way into the skin so that just beyond the bevel is in the skin, and then I pinch the skin around that needle with my non-injecting hand. I then place the filler syringe with a 27G cannula (1.5 in) attached in my injecting hand, while still pinching with my non-dominant hand, and have my assistant pull out the needle while I am focusing on the nick in the skin that I need to then insert my

FIGURE 1. Traditional needle versus soft tipped cannula use. On the left, sharp needles can easily puncture blood vessels, causing bleeding. On the right, cannulas with blunt tips can be used with a lower risk of puncturing a blood vessel.

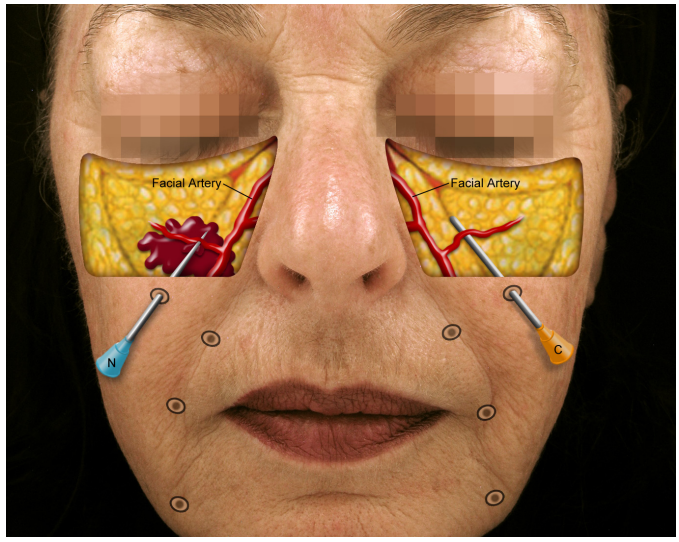

Image courtesy of Jake Nielson, Maria Kim and Joel L. Cohen MD

FIGURE 2.

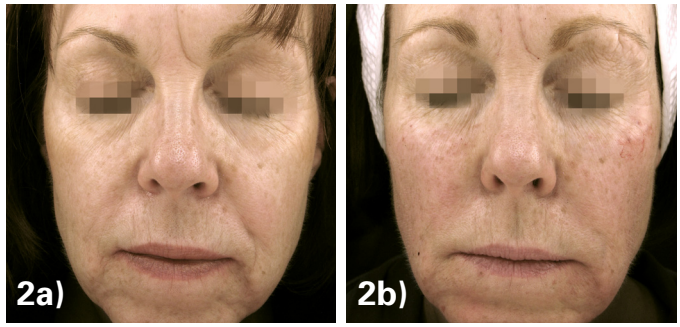

Photo courtesy of Joel L. Cohen MD

cannula through. This technique allows the injector to keep track of that nick, as occasionally it can be lost as you turn to the tray to get your filler and then turn back unable to find the entry site.

For the dorsal hands and décolleté, I do a very similar technique but use a 21G needle to make the entrance points and then use a 25G cannula (1.5 in for the hands and 2 in for the décolleté). Typically in these non-facial regions, I will use several injection sites (often 3–5) for access to areas of volume depletion. I continue to pinch the skin around the entrance site in order to tent it and provide for easy passage of my cannula below. Chlorhexidine prep can again be used in the area to help massage out any lumps or bumps in a smooth fashion, while others might use ultrasound gel, vitamin K or arnica cream, or even a gentle lotion.

Over the next few years, I think we are going to see many more cannula manufacturers enter the US market.[6] Currently, DermaSculpt and Magic Needle are both approved in the United States through the 510k process, but as these are not pre-packaged with the filler gel pack, it may still be a bit of a regulatory gray zone in terms of their actual use. Hopefully, over time, we will see some large, well-designed clinical studies to see if these flexible blunt-tipped cannula anecdotes as well as early reports of less bruising, swelling, and pain prove to be real in the form of highly powered actual data.

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Blunt-Tipped Microcannulas—A Personal Perspective

To the Editor:

Those of us accustomed to performing autologous fat transfer are no strangers to the use of injection cannulas. They afford placement of fat into planes that would be difficult to breach safely with a small-bore sharp needle. But now that blunt cannulas are gaining mainstream attention for "off the shelf" fillers, it is precisely safety issues that have me concerned. We tend to inject differently with a blunt cannula than with a needle. There is less movement, less subcision, and less fanning. The cannulas tend to be advanced along one plane, the filler ejected, and then the cannula withdrawn. This alone could account for the decrease in bruising seen in the Hexsel paper[1] when compared with a needle, but certainly the single incision vs. multiple stabs is also a factor. My fear is that the injector will feel that cannulas "are safer" since they are blunt, but little could be further from the truth.

A small gauge (20G or smaller) blunt cannula—especially if is nonflexible—is, in effect, a needle. It can puncture vessels, nerves, and the orbital septum. In the fat transfer literature, middle cerebral artery infarction as well as vision loss have occurred with the injection of fat with a large-bore blunt cannula. The premise of the insult being a high-pressure bolus injection that overcame the arterial perfusion pressure to become retrograde into the internal carotid system. So indeed even large (>20G) blunt cannulas can penetrate vessels. Since cannulas need a greater force to infiltrate the skin, the injector is more likely to inject with more force. Furthermore, the ease of injection through a cannula encourages a high-flow pressure via a bolus. There are aesthetic concerns with cannula use as well. Hyaluronic acids (HAs) are highly hydrophilic and cohesive. Cannulas (especially ones larger than 28G) push tissues aside and, in essence, make tracts. These tracts, when filled with HA products, can form cohesive lakes of product. This was certainly seen by many of us with large-particle non-animal stabilized HA products not available in the US injected through 18G cannulas. In addition, because of fibrous areas of the superficial musculoaponeurotic system, some areas/planes are difficult to breach intentionally with a blunt cannula. This can cause an uneven distribution and "bunching" of filler, especially upon animation.

So, in the interest of safety as well as aesthetic outcome, I recommend the following:

1.) Choose the smallest-bore flexible cannula possible.

2.) Keep the cannula moving, avoiding static injections.

3.) Inject small aliquots, avoiding high injection pressures.

4.) Inject into multiple planes, avoiding causing wide tunnels, to get the most even distribution of product and prevent pooling.

5.) Switch to a needle when appropriate.

6.) Know your anatomy!

In summary, I like injecting with cannulas. I think that in the right situation with the right filler and technique, they can offer a superior aesthetic outcome. Just don't become complacent with the assumption that they are safer than needles.

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Blunt-Tipped Microcannulas for Filler Injection: An Ethical Duty?

To the Editor:

Operator ability is the most important consideration for cosmetic procedures, regardless of the tools we use. In the case of fillers, ability is defined as knowing where and how to position the material. In regards to technique, different injectors may perceive different needs, such as bolus injection, fanning, threading, or cross-hatching. One should theoretically master all injection techniques and try to diagnose which is needed where (eg, at which level of the tissue). What's crucial is to understand where volume is most needed and then to plan how to put it there.

For placement of fillers very superficially in the dermis, I still consider sharp needles to be superior to blunt microcannulas. The selection of a tool for deeper dermal injections depends on the operator's manual ability. One should use what one is most comfortable with. I feel that good injectors should master both cannulas and needles and choose the most appropriate for the injections that they are performing. Once you acquire the ability to use blunt cannulas well, you will find it is much easier to stay within the dermis instead of inadvertently injecting subdermally as most of us commonly do.

For subdermal injection of fillers, I believe it is our ethical duty to try to use microcannulas whenever possible, for a number of reasons. First, blunt cannulas minimize the possibility of damaging subcutaneous nerves and blood vessels by pushing them aside instead of piercing through them. This is particularly so for cannulas that are 23G or larger in diameter. Second, the subcutaneous tissues are not wounded, but rather spread as in a blunt dissection, which—as surgeons recognize—is desirable to minimize tissue trauma and procedural pain and to optimize tissue healing. Minimizing tissue trauma will minimize post-injection hematomas and swelling and, ultimately, minimize post-procedural down time. However, blunt cannulas alone do not decrease the risk of damage to very superficial veins. All risk of bruising can be eliminated by inspecting the potential entry site with polarized magnification before initial insertion of the pilot needle and subsequent insertion of the cannula. Last but not least, being able to reach the whole hemi-face through one planned lateral entry point can really turn filler injection into a "lunchtime procedure."

I began to use blunt microcannulas for alloplastic fillers only two years ago. For ten years before that, I had performed fat grafting with larger cannulas. Until 2010, I used sharp needles for filler injections because I thought that microcannulas were superfluous and I could do a wonderful job with needles. I decided to try microcannulas after seeing the live demonstrations and presentations of my colleague, Dr. Benjamin Ascher. I understood that he was right, and I have never again used a sharp needle for subcutaneous filler injections, which comprise 80% to 90% of my total injection procedures.

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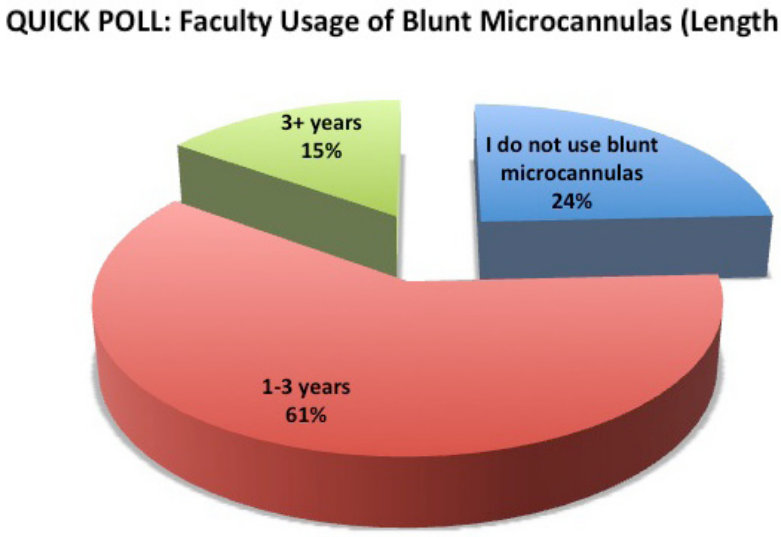
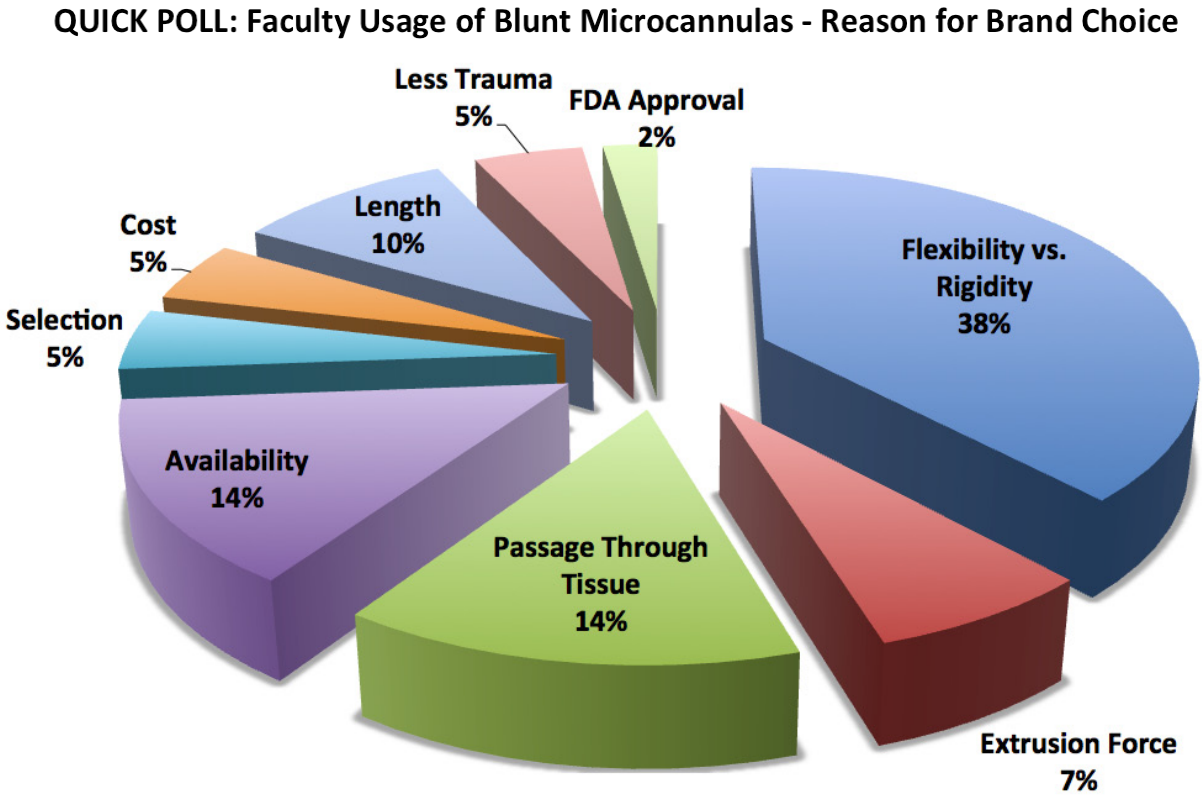
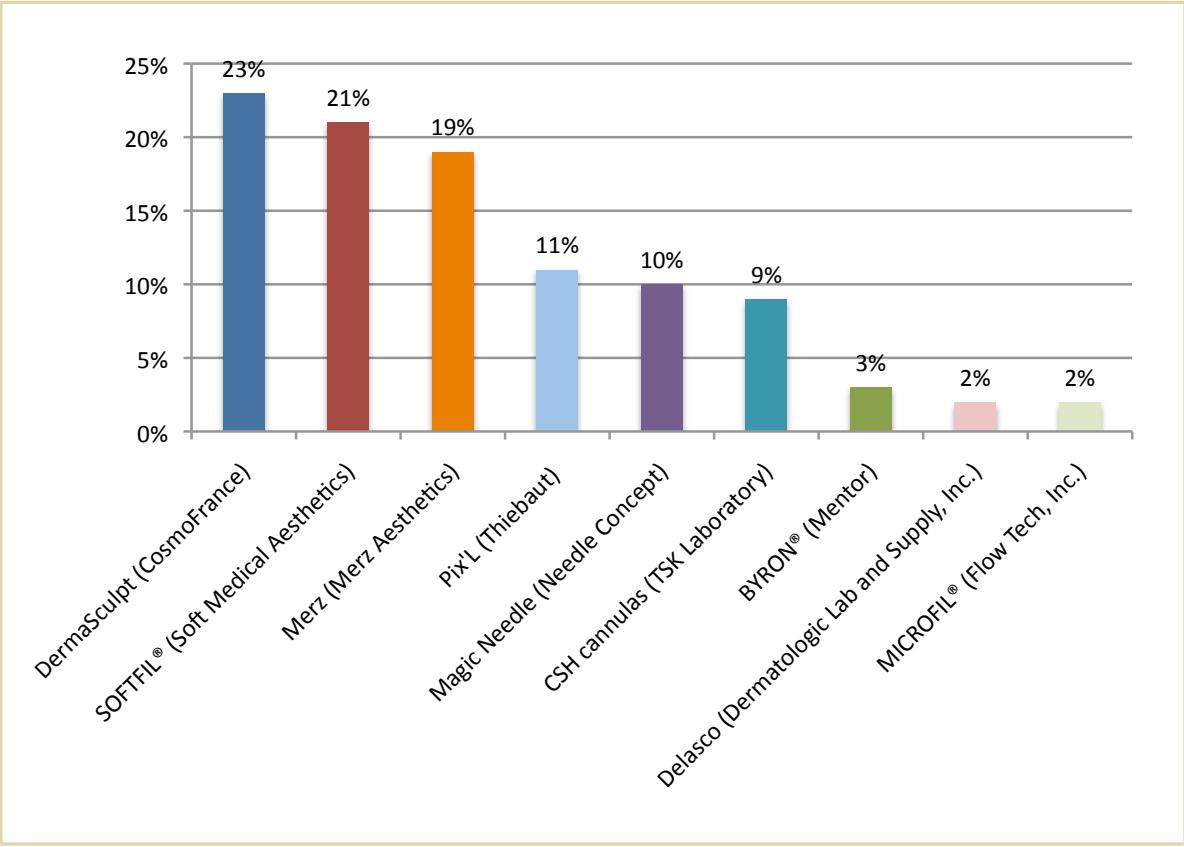
Quick Polls





QUICK POLL: Faculty's Present and Past Usage of Blunt-Tipped Microcannulas (by Brand)



QUICK POLL RESPONDENTS

D=Dermatology F=Facial Plastic Surgery O=Oculoplastic Surgery P=Plastic Surgery

Benjamin Ascher MD (P), Magda Belmontesi MD (D), Vivian Bucay MD (D), Laurie Casas MD (P), Daniel Cassuto MD (P), Joel L. Cohen (D), Doris Day MD (D), Steven H. Dayan MD (FP), Luc Dewandre MD (P), Lisa M. Donofrio MD (D), Steven Fagien MD (OP), Julius W. Few Jr. MD (P), David J. Goldberg MD JD (D), Mitchel P. Goldman MD (D), Haideh Hirmand MD (P), Derek H. Jones MD (D), Mary Lupo MD (D), Marina Landau MD (D), Z. Paul Lorenc MD (P), Ellen Marmur MD (D), Gary D. Monheit MD (D), Rhoda Narins MD (D), Tatjana Pavicic MD (D), Jason N. Pozner MD (P), Nowell Solish MD (D), Hema Sundaram MD (D), Jonathan M. Sykes MD (FP), Amy Taub MD (D), Patrick Trévidic MD (P), S. Randolph Waldman MD (FP), Heidi Waldorf MD (D), Susan H. Weinkle MD (D), Sabine Zenker MD (D)

**Erratum: In Part I of the "The New Face of Fillers," Dr. Laurie Casas was erroneously listed as a dermatologist. Dr. Casas is a Board Certified Plastic Surgeon.*

The Tower Technique and Vertical Supraperiosteal Depot Technique: Novel Vertical Injection Techniques for Volume-Efficient Subcutaneous Tissue Support and Volumetric Augmentation

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ABSTRACT

A 55-year-old Caucasian female with a past history of face-lifting surgery presented with early signs of soft tissue elastosis, volumetric deficiency in the periocular region, the nasolabial folds, the lips, and the lower face. Hyaluronic acid (HA) filler injections were performed with two novel vertical injection techniques that support and tense the subcutaneous connective tissue—the Tower Technique (TT) and the Vertical Supraperiosteal Depot Technique (VSDT). Vertical injection techniques are a volume-efficient means of delivering excellent, long-lasting results and patient satisfaction with minimal recovery time and are appropriate for volumetric augmentation even in patients who have subdermal fibrosis due to previous facial surgery.

J Drugs Dermatol. 2012;11(suppl 8):s45-s47.

CASE VIGNETTE

A 55-year-old Caucasian female presented reporting that she had a surgical face lift one year previously and was dissatisfied with the tired look that had developed shortly afterward. Her aim was to regain an attractive fresh-looking facial appearance. She had received botulinum toxin A treatments several times before at six monthly intervals. Clinical examination showed early signs of soft tissue elastosis, volumetric deficiency in the area of the suborbicularis oculi fat (SOOF) and orbital hollows, the nasolabial folds, the marionette lines, the upper and lower white lips (perioral region), and the lateral aspects of the red lip. Minor elastosis-related caudalization of tissue was also noted in the area of the true osteocutaneous retaining ligaments in the zygomatic and bucco-maxillary areas, as well as in the mandibular area. Additionally, a pronounced glabella fold was noted when the patient was asked to frown.

The patient was treated solely by injection with 6 mL of a hyaluronic acid (HA) filler (Juvéderm Voluma) and 50 units of onabotulinumtoxin A (Vistabel/Botox Cosmetic). The HA filler injections were performed by using the Tower Technique (TT) as well as the Vertical Supraperiosteal Depot Technique (VSDT) (Figure 1).

Tower Technique

This is an injection technique for soft tissue augmentation based on the anatomical circumstance that horizontal layers of tissue (fascia, connective tissue, muscle, fat, and dermis) are attached to each other with a limited lateral flexibility.[1-2] By injecting soft tissue filler material in a vertical manner while withdrawing the syringe, small depots of filler are placed between the layers. In effect, the thickness of the augmented section is increased in the same way that the body of a harmonica is stretched while it is being played. The small depots of filler are positioned in the tissue planes like multiple washers positioned in between each tissue layer. Due to little lateralization of the filler in the tissue, this technique allows the injector to build towers or columns in the soft tissue, which leads to a vertical extension or enlargement. The towers are

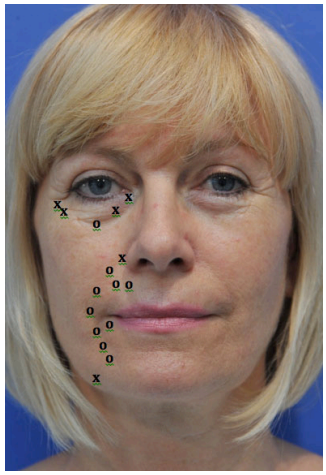


FIGURE 1. Hyaluronic acid filler injection strategy. Tower Technique injection sites are indicated by "o," while Vertical Supraperiosteal Depot Technique injection sites are marked with an "x."

usually placed in groups of lines, e.g., along the nasolabial fold, with the injection points about 0.5 cm to 1 cm apart. The injection is performed strictly vertically at a 90 degree angle to the base of the injection site. The TT is mostly recommended in sites where no bony base is present. This means that the towers are self-supporting, floating in a soft tissue section with no basal support needed. The recommended areas of use are the nasolabial folds, the marionette lines, the upper and lower lip, the cheek, and the gluteal area.

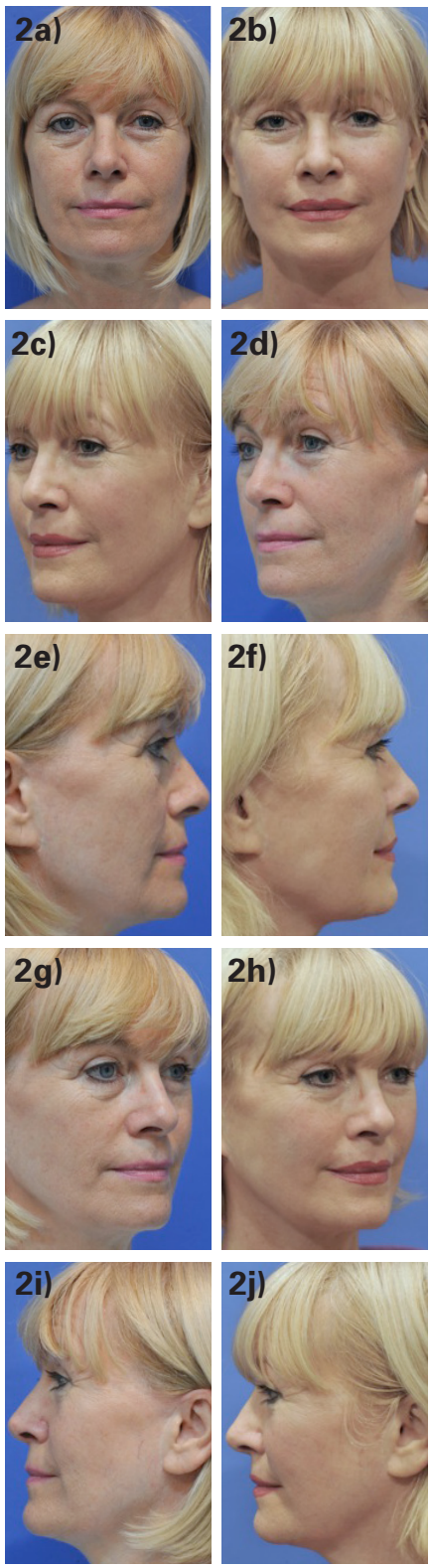
Vertical Supraperiosteal Depot Technique (VSDT)

In comparison to the TT, the VSDT uses only single, small depots of soft tissue filler material that are placed via a vertical injection on a location directly on the bone or, more exactly, on the periosteum. Due to the bony support, only very little material is needed in order to produce a pronounced correction at the skin surface. This can be observed in the area of the orbital hollow over the medial part of the orbital rim as well as in areas like the zygomatic bone. The intention in using this technique is to avoid overcorrection. Other areas of interest are the upper orbital rim in the area of the eyebrows, the bridge of the nose, the mandibular bone, and the entire forehead.

CONCLUSION

Vertical injection techniques are currently considered preferable for volumetric soft tissue augmentation. The purpose of this type of treatment is not to create ballooning "fat" faces, but instead to support and tense subcutaneous connective tissue elements. Volumetry occurs due to the amount of filler that is injected as well as the volume that derives from the water-binding capacity of HA filler. If the "sweet spot" of a decompensated area can be found and treated, minimal amounts of filler material are needed in order to obtain a successful correction. The long-lasting results that have been consistently observed might be explained by the low concentration of fibroblasts in the deeper soft tissue planes, since fibroblasts are the source for the patient's own production of hyaluronidase.

FIGURE 2. Before and eight weeks after injection of hyaluronic acid filler and onabotulinumtoxin A. **a-b)** Frontal view. **c-d)** Left lateral view. **e-f)** Left oblique view. **g-h)** Right lateral view. **i-j)** Right oblique view.



ACKNOWLEDGMENT

The faculty acknowledges Hema Sundaram MD for assistance in preparation of this manuscript.

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COMMENTARY

Targeting soft-tissue compartments in the face with vertical hyaluronic acid (HA) injection techniques is essential for good results. Dr. Sattler's 55-year-old patient has typical facial volume loss of aging. She had a face-lift previously, which pulled the skin tighter, but did not address the underlying facial volume deficiency. Although various filler materials could have been used in this patient, HA is certainly the most versatile and reversible.

The suborbicularis oculi fat is a well-defined soft-tissue compartment that can be augmented with HA just above the underlying periosteum. In my view, the infraorbital hollows are the single most difficult area to treat. Dr. Sattler has achieved success in this area using a combination of the Tower Technique (TT) and Vertical Supraperiosteal Depot Technique (VSDT). With both of these techniques, the injections are given perpendicular to the skin's surface. This minimizes trauma and the number of needle sticks, thereby limiting discomfort and morbidity from bruising and swelling.

The TT can be utilized to fill all of the tissue layers from periosteum to the lower dermis. The VSDT fills the space overlying the periosteum. The TT can be used in areas where there is underlying bone.

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1. Which of the following is a potential result of blunt-tipped microcannulas, when used appropriately?
   a. increased bruising
   b. decreased risk of intravascular injection
   c. increased risk of nerve injury
   d. increased number of injection points

2. Increased length of blunt-tipped microcannulas results in:
   a. decreased flexibility / greater rigidity
   b. decreased extrusion force when injecting filler
   c. fewer entry points for injection of multiple facial areas
   d. better ability to move the microcannula around facial angles

3. Recent statistics from the American Society of Aesthetic Plastic Surgeons (ASAPS) show that the following age group had the most cosmetic procedures performed:
   a. 20–35 years
   b. 35–50 years
   c. 51–64 years
   d. >65 years

4. A youthful face represents a point in time when:
   a. There are no "tear troughs."
   b. There are no "nasolabial folds."
   c. There are no "marionette lines."
   d. There is a particular set of skeletal proportions ideal for their overlying soft tissue envelope—a place we likely grow into from infancy and away from with age.

5. As we age, changes are occurring in:
   a. the skin
   b. the bone
   c. the fat
   d. all tissue structures of the face

6. Which of the following is typically the most prominent feature of facial aging in individuals of African ancestry with Fitzpatrick skin types IV–VI?
   a. perioral rhytids
   b. radial lip lines
   c. lip atrophy
   d. deepening of the nasolabial folds
   e. crow's feet

7. All of the following are reported racial/ethnic differences in age-related changes in facial architecture EXCEPT:
   a. greater skin laxity in Caucasians
   b. wider mandible in Asian women
   c. pseudoherniation of the infraorbital fat pads in African Americans
   d. wider mouth width in Asians
   e. prominent descent of the malar fat pads in African Americans and Hispanic/Latinos

8. The key elements determining filler characteristics from physical properties include the following EXCEPT:
   a. concentration
   b. cross-linking
   c. gel color
   d. calibration
   e. free hyaluronic acid

9. Which of the following is true about vertical injection techniques with hyaluronic acid fillers:
   a. The injections are all performed in the subdermal tissue planes.
   b. They can cause secondary improvement in superficial rhytides.
   c. The Tower Technique can be performed in patients who have had previous facial surgery.
   d. The Vertical Supraperiosteal Depot Technique is recommended for the upper orbital rim and the forehead.
   e. all of the above

10. In which of the following facial areas would it be appropriate to inject a soft tissue filler with the Tower Technique?
    a. nasal bridge
    b. orbital hollow
    c. marionette lines
    d. chin
    e. over the zygoma

continued on next page

11. Physicochemical and rheologic (flow-related) differences between hyaluronic acid (HA) fillers include which of the following:
    a. Restylane is a Non-Animal Stabilized HA (NASHA), Juvéderm Ultra is a Hylacross HA, and Belotero Balance is a Cohesive Polydensified Matrix HA.
    b. Belotero Balance has a low viscosity, whereas Restylane and Perlane have a high viscosity.
    c. Belotero Balance is a soft, flowing filler, whereas Restylane is a firm, lifting filler.
    d. Differences in the tan delta measurement indicate diferences in the extent of elasticity that is present in an HA filler.
    e. all of the above

12. Which of the following is true of alloplastic soft tissue fillers:
    a. Belotero Balance is best implanted supraperiosteally.
    b. Controlled studies show that Restylane, Juvéderm, and Belotero Balance all have comparable longevity after mid to deep dermal implantation.
    c. Addition of lidocaine to Radiesse raises its viscosity and makes it more difficult to spread.
    d. Juvéderm Voluma is best implanted intradermally.
    e. Emervel filler products designed for different clinical applications have the same HA concentrations, gel calibrations, and degrees of cross-linking.

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The New Face of Fillers: A Multi-Specialty CME Initiative (Part II of II)

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☐ I certify my actual time spent to complete this educational activity to be: _____

☐ I participated in the entire activity and claim 2 *AMA PRA Category 1 Credits*™.

Please answer the following questions by circling the appropriate rating:

1 = Strongly Disagree	2 = Disagree	3 = Neutral	4 = Agree	5 = Strongly Agree

Was timely and will influence how I practice
1 2 3 4 5

Enhanced my current knowledge base
1 2 3 4 5

Addressed my most pressing questions
1 2 3 4 5

Provided new ideas or information I expect to use
1 2 3 4 5

Addressed competencies identified by my specialty
1 2 3 4 5

Avoided commercial bias or influence
1 2 3 4 5

Impact of the Activity

Name one new strategy you learned as a result of completing this activity:

_____

Name one thing you intend to change in your practice as a result of completing this activity:

_____

Additional comments about this activity:

_____

Please list any topics you would like to see addressed in future educational activities.

_____

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