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JDD

DRUGS • DEVICES • METHODS

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

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QUICK POLLS

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

Release Date: March 1, 2012
Termination Date: February 28, 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 the use of fillers for facial volumization and rejuvenation, including anatomic considerations, and site-specific approaches to the lips, midface, lower face, and periorbital region.

- Describe strategies and best practice techniques for preventing and managing complications when using fillers.

- Accurately conduct regional assessment of the face and analyze how underlying structural tissue changes affect on the contours, shape, and proportions of the aging face.

- Apply an evidence-based approach to filler product selection and injection technique (including an understanding of neurotoxin efficacy, dosage, storage, onset, field of effect, and duration of action), filler rheology and other properties, product layering, and use of blunt cannulas.

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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Test is valid through February 28, 2013 (no credit will be given after this date).

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Course Director and Guest Editor
Hema Sundaram MD (Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax, VA)

Faculty Credentials
John P. Arkins BS (DeNova Research, Chicago, IL) Benjamin Ascher MD (Paris Academy, Paris, France), Jean Carruthers MD (University of British Columbia, Vancouver, BC, Canada), Hugues Cartier MD (Centre Medical Saint Jean, Arras, France), Laurie Casas MD (University of Chicago Medical Center, Chicago, IL), Joel L. Cohen MD (AboutSkin Dermatology and DermSurgery, Englewood, CO), Steven H. Dayan MD (Chicago Center for Facial Plastic Surgery, Chicago, IL), , David J. Gold-

berg MD JD (Mount Sinai School of Medicine, New York, NY), Mitchel P. Goldman MD (University of California, San Diego Medical Center, San Diego, CA), Haideh Hirmand MD (Cornell Weil Medical College/New York Presbyterian Hospital, New York, NY), Derek H. Jones MD (Skin Care and Laser Physicians of Beverly Hills, Beverly Hills, CA), Marina Landau MD (Edith Wolfson Medical Center, Holon, Israel), Corey S. Maas MD (The Maas Clinic, San Francisco, CA), Ellen Marmur MD (Mount Sinai School of Medicine, New York, NY), Gary D. Monheit MD (Total Skin and Beauty Dermatology Center, Birmingham, AL), Rhoda S. Narins MD (Dermatology Surgery and Laser Center, New York, NY), Oge C. Onwudiwe MD (Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax, VA), Berthold Rzany MD (Charité–Universitätsmedizin, Berlin, Germany), Nowell Solish MD (University of Toronto, Toronto, Canada), Hema Sundaram MD (Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax, VA), Jonathan M. Sykes MD (University of California-Davis Medical Center, Davis, CA), Patrick Trévidic MD (Private Practice, Paris France)

Peer Reviewer Credentials

Dale Abadir MD (Abadir Associates, Rye Brook, NY), Robin Ashinoff MD (Hackensack UMC, Hackensack, NJ), Martin Braun MD (Vancouver Laser and Skin Care Centre, Vancouver, B.C, Canada), Mariano Busso MD (Private Practice, Coconut Grove, FL), Nelson Lee Novick MD (Mount Sinai School of Medicine, New York, NY), Eli Saleeby MD (Private Practice, Coral Springs, FL), Irene J. Vergilis-Kalner MD (Skin Cancer & Aesthetic Surgery, New York, NY)

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The faculty/authors have the following disclosed conflicts of interest:

John P. Arkins BS has no relevant conflicts of interest to disclose.

Benjamin Ascher MD has no relevant conflicts of interest to disclose.

Jean Carruthers MD serves as consultant and research for Allergan and Merz, as well as consultant for Lumenis.

Hugues Cartier MD has no relevant conflicts of interest to disclose.

Laurie Casas MD has no relevant conflicts of interest to disclose.

Joel L. Cohen MD has been a consultant or clinical trial participant related to soft tissue augmentation agents for Allergan, Medicis, Merz, Galderma, and Mentor.

Steven H. Dayan MD has been a researcher, speaker, and consultant for Allergan, Medicis, and Merz.

David J. Goldberg MD JD has served as consultant for Sanofi-Aventis.

Mitchel P. Goldman MD has served as consultant and researcher for Mentor, Sanofi-Aventis, Allergan, Medicis, and Merz.

Haideh Hirmand MD has served as a speaker, teacher, and advisor for Medicis, as well as advisor for Merz.

Derek H. Jones MD has served as consultant, investigator, speaker, and board member for Allergan and Merz.

Marina Landau MD has served as speaker and teacher for Q-MED-Galderma.

Corey S. Maas MD has served as speaker and faculty for Paradigm Medical Communications and Cosmetic Surgery forum.

Ellen Marmur MD has no relevant conflicts of interest to disclose.

Gary D. Monheit MD has served as consultant and clinical investigator for Allergen, Ipsen/Medicis, MELA Sciences, Revance, Galderma, Mentor, Merz; as clinical investigator for Dermik, Contura, and Kythera; and consultant for MyoScience.

Rhoda S. Narins MD has served as consultant for Merz, independent-contracted researcher for Suneva, independent-contracted researcher and consultant for Allergan, investigator for Revance and Kythera, and investigator/advisor for Contura.

Oge C. Onwudiwe MD has no relevant conflicts of interest to disclose.

Berthold Rzany MD has served as consultant and speaker for Galderma, Ipsen, and Merz.

Nowell Solish MD has served as a consultant and speaker for Allergan and consultant for Medicis.

DISCLOSURES CONT'D

Hema Sundaram MD serves as a clinical investigator and/or consultant for Galderma, Medicis, Mentor, Merz, and Suneva.

Jonathan M. Sykes MD has served as speaker and researcher for Medicis, advisor for Allergan, speaker for Mentor and Sanofi-Aventis, research support for Myoscience.

Patrick Trévidic MD has no relevant conflicts of interest to disclose.

The peer reviewers have the following disclosed conflicts of interest:

Dale Abadir MD has no relevant conflicts of interest to disclose.

Robin Ashinoff MD has no relevant conflicts of interest to disclose.

Martin Braun MD served as a teacher for Dermik and Allergan.

Mariano Busso MD has served as an independent contracted researcher, consultant, speaker, and teacher for Merz.

Nelson Lee Novick MD has no relevant conflicts of interest to disclose.

Eli Saleeby MD has no relevant conflicts of interest to disclose.

Irene J. Vergilis-Kalner MD has no relevant conflicts of interest to disclose.

The planning committee of this activity, Olivia Ayes, Editorial Project Manager *JDD*, Ruben Mercado, Design Lead *JDD*, Dustin Harris, Junior Designer *JDD*, Melissa Kerr, Marketing Associate *JDD*, Luciana Halliday, Director of Sales *JDD*, Nick Gillespie, Assistant Publisher *JDD*, and Michelle Frisch, NACE, have no relevant conflicts of interest to disclose.

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

Hema Sundaram MD

Progress in any field may be considered a composite process, arising as it does both from what is new and also from a new interpretation of what is older. The acquisition of new knowledge, and also of greater understanding regarding what already exists, often seems to occur in leaps and bounds rather than as a continuum. A glance back at the evolution in our use of soft tissue fillers over the past decade and a half clearly reveals this pattern. The epiphanies that have catalyzed our progress include the advent of the first hyaluronic acid filler; the emergence of further products and with them a growing understanding of how best to leverage each one; and most recently, the development in Europe of new genres of filler with novel tissue integration properties, and the approval in the US of both new products and new indications for existing products. To paraphrase the Italian poet, Cesare Pavese, it is not the days we remember but the moments.

The aim of this two-part supplement publication is to both illuminate and debate those moments. The supplement is somewhat groundbreaking for the Journal of Drugs in Dermatology, in that it brings together three dozen of the world's experts from the U.S., Europe, Canada and Israel to discuss the state-of-the-art in soft tissue fillers in a fair-balanced, CME-accredited format. Part I, which you are reading now, includes a round table discussion on HA fillers that charts the clinical and scientific path that has led us from wrinkle-chasing to true volumetry. International case vignettes with commentary highlight a variety of applications for fillers—some currently available in the US, and some available elsewhere and on the American horizon. Topics covered include single-product and multi-product volumetry, anatomic and safety considerations, and the use of blunt injection microcannulas. Quick poll surveys provide an engaging snapshot of the faculty's personal approaches, with the first three surveys focusing on the palette of HA fillers. Part II of the supplement, which appears next month, contains two consensus documents—on current and emerging concepts in fillers and on the use of blunt injection microcannulas. Additional case vignettes cover facial fat compartments and individualized selection of filler techniques and products; and Quick Poll surveys provide further expert insights.

Our growing appreciation of the multi-faceted aging process and the key role that facial volume loss plays enables us to optimize our use of fillers. Conversely, exploration and refinement in our filler strategies enhances our understanding of aging and how best to address it as our aesthetic toolbox expands.

The burgeoning spirit of collaboration between the core aesthetic specialties and the dialogue it has engendered have been vital to this understanding, and are reflected in the multispecialty composition of the supplement faculty. I trace so many of my own epiphanies to this dialogue, during the teaching assignments that I have been privileged to share with my esteemed dermatologist colleagues and also with colleagues from the fields of plastic surgery, facial plastic surgery and oculoplastic surgery.

I derive inspiration and education every year from the American Academy of Dermatology (AAD) and American Society for Dermatologic Surgery (ASDS) meetings. This has been

complemented by my experiences at the annual meeting of the American Society for Aesthetic Plastic Surgery (ASAPS), where I was introduced to blunt injection microcannulas, and the International Master Course on Aging Skin (IMCAS) congress in Paris, where I first discovered automated injection devices. My interactions at another multispecialty conference, the Vegas Cosmetic Surgery symposium, have engendered fruitful discussions and fresh ideas. There is perhaps no better learning experience than to see how thought leaders from the four core specialties approach the same problems from different perspectives.

It is my hope that this supplement will provide a little of that same experience to its readers and that it will be of value to all clinicians who have an interest in fillers. It provides a unique and fascinating overview of the philosophy and practices of an international faculty that has been instrumental in shaping our current, cutting-edge concepts of volumetry, and is actively engaged in the research and scientific inquiry that will undoubtedly define our future.

Hema Sundaram MD
Medical Director, Sundaram Dermatology, Cosmetic and Laser Surgery,
Rockville, MD and Fairfax, VA
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The Subliminal Difference: A New Treatment Philosophy

Steven H. Dayan MD[a,b,c] and John P. Arkins BS[d]
[a]Chicago Center for Facial Plastic Surgery, Chicago, IL
[b]Department of Otolaryngology, University of Illinois at Chicago, Chicago, IL
[c]School of New Learning, DePaul University, Chicago, IL
[d]DeNova Research, Chicago, IL

ABSTRACT

The female face of youth is exemplified by a petite lower one-third of the face as opposed to the aging face that is evident by jowling and a squaring of the jaw more representative of a masculine appearance. By placing fillers in the cheeks and infraorbital areas, it deemphasizes the lower one-third and allows unimpeded attention to the eyes, which are the first facial feature to be evaluated during impression construction. We present the case of a 37-year-old female desiring a more youthful appearance through non-surgical intervention.

J Drugs Dermatol. 2012;11(suppl 3): s10-s11.

INTRODUCTION

For the last two decades, we have targeted wrinkles and folds with minimal regard to the context within which those characterizing features are gained. Perhaps we should set our sights more globally on shaping a face based upon the evolutionary forces that compose beauty and attraction. As a female ages, her cheeks descend, forming deep hollows around the eyes. Jowling occurs as the cheek fat pad falls over the jawline, causing the chin to become square-like, and the aging female face masculinizes. It is these physical traits that the human mind interprets as aging, infertile, and of diminished attractiveness. By placing fillers in the cheeks and infraorbital areas, it deemphasizes the lower one-third of the face and allows unimpeded attention to the eyes, which are the first facial feature to be evaluated.[1]

CASE VIGNETTE

We present the case of a 37-year-old Caucasian female desiring a more youthful appearance. Her past medical history was noncontributory. Upon physical examination, moderate rhytids of the forehead, glabella, and perioribtal area were noted, as well as mild malar volume loss.

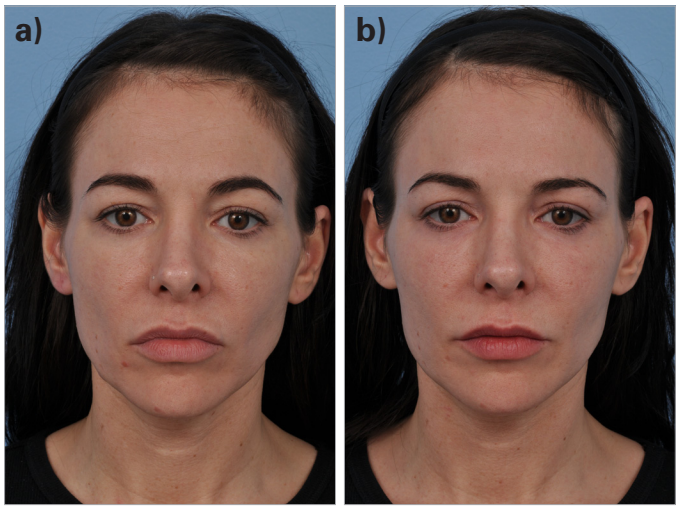
We performed a minimally-invasive approach to pedestal the eyes, deemphasize the lower third of the face to convey a more youthful appearance (Figure 1a). The area was cleansed with alcohol and betadine, and no topical or injectable anesthetics were given. After informed written consent was obtained, onabotulinumtoxinA (Botox Cosmetic) was reconstituted with 3.3 cc of saline to create a final dilution of 3U per 0.1 cc. Ninety units were injected into the procerus, frontalis, corrugators, orbicularis oculi, and masseters. Additionally, 2 mL of a 1 mL hyaluronic acid (HA) (Restylane), 0.1 cc of saline and 0.1 cc of 1% lidocaine preparation was injected into the temple area using a 22-gauge, 70 mm blunt-tip cannula. The malar areas were treated with 2 mL of a mixture of 1 mL HA, 0.2 cc saline, and 0.1 cc 1% lidocaine using blunt-tip cannula. After the filler was injected, the HA was manually molded to ensure proper placement.

The patient tolerated the procedure well with minimal to no edema or bruising based on patient report and seven-day video diary. At a two-week follow-up appointment, there was improvement in facial volume loss and a decrease in facial rhytids of the upper third (Figure 1b). The patient stated that immediately following the treatment, she was able to return to her daily activities and did not experience any bruising or pain as previously noted with other cosmetic procedures.

CONCLUSIONS

In its most basic form, beauty serves as a subconscious form of communication, signaling our health and vitality. It is the less than one millimeter change in the corner of the mouth, eyebrow position, eyelid aperture, and homogeneity of the skin

FIGURE 1. a) The patient prior to the procedure. **b)** At a two-week follow-up appointment, there was improvement in facial volume loss and a decrease in facial rhytids of the upper third.



that stimulates, attracts, and influences mood—not overtly obvious augmentations.[2] These visceral calling signals have been instilled into our brains and bodies through the emotionless process of natural selection. Understanding the subtleties of beauty through the evolutionary lens in which it was shaped is paramount to successful outcomes. It is imperative that we understand the different rheological properties inherent to the various fillers.[3,4] By mixing the product with lidocaine or saline, we can thin the filler, thereby reducing its viscosity and further modifying its properties to exploit its unique advantages similar to an artist working to create a specifically desired texture, tone, and depth of a color.

Incorporating this philosophy to widen the eyes, treat the temples, strengthen the jawline, and narrow the cheeks deemphasizes the lower third, draws attention to the eyes, and follows an evolutionary strategy of beauty. Using blunt tip cannulae, reducing viscosity of the fillers and bimanual molding allows a facial makeover in minutes with immediate results, minimal discomfort and virtually no bruising. Patient satisfaction is maximized.

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ADDRESS FOR CORRESPONDENCE

Steven Dayan MD
845 N. Michigan Ave.
Suite 923E
Chicago, IL 60611
Phone:.....(312) 335-2070
Fax:.....(312) 335-2074
E-mail:.....sdayan@drdayan.com

COMMENTARY

I applaud Dr. Dayan on this subtle yet significant example of natural cosmetic surgery. The word "subliminal" is clever and bold. It is true that we are accustomed to dramatic changes between pre and post cosmetic surgery pictures. Here we need to look back and forth to appreciate the well chosen enhancements. Once you see how the brow is lifted, the corners of the lips are uplifted, the cheeks are fuller yet high, and the quality of her skin is tighter and smoother—then it becomes obvious which is pre and which is post. She looks happier, healthier, more approachable. From a Darwian psychology or evolutionary biology perspective, she wins. There are several fields of academia focused on the role of aesthetics in the animal world. Game theory suggests that the more beautiful specimen wins the better mate and ensures the survival of its DNA. This example provides us with a new face of subtle yet subliminal cosmetic surgery using the newest techniques (i.e., cannula to reduce bruising) while utilizing a judicious amount of product to achieve a lovely effect.

Ellen Marmur MD
Mount Sinai Medical Center, New York, NY

Vascular Compromise After Hyaluronic Acid Cheek Augmentation

Joel Cohen MD[a] and Oge Onwudiwe MD[b]
[a]AboutSkin Dermatology and DermSurgery, Englewood, CO
[b]Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax,VA

ABSTRACT

Soft tissue augmentation agents are used for facial rejuvenation millions of times each year throughout the world. Fortunately with the use of approved substances as well as a keen knowledge of the underlying anatomy, vascular compromise is a very rare circumstance. It is imperative, however, to be familiar with potential side effects of filler agents, and specifically the signs and symptoms of vascular compromise.

J Drugs Dermatol. 2012;11(suppl 3): s12-s14.

CASE VIGNETTE

This patient received the hyaluronic acid filler (Juvederm® Ultra Plus XC) to the midface for cheek and infra-orbital augmentation (Figure 1). The filler was delivered with the pre-packaged 30 gauge needles. No blanching to the treatment area was ever appreciated at the time of injection. Immediately post-procedure, only minimal swelling was noted. Five days later, the patient returned to the office with a chief complaint of persistent purple discoloration to the left cheek and mild discomfort to the infra-orbital area. He did indicate, however, that the discomfort began on the day of the injection. Upon examination, he had a violaceous discoloration of the cheek in the distribution of the infra-orbital artery. There was no evidence of epidermal ulceration or necrosis. After conferring with other cosmetic physicians, the treating physician elected to handle this presentation as a likely delayed vascular compromise case with perhaps some element of venous congestion. In order to hopefully prevent impending necrosis, treatment was initiated following steps from some published reports of similar cases.

Management

One published protocol for treating vascular compromise includes immediate warm to hot compresses to the affected area, gently massaging or tapping the area, applying transdermal nitroglycerin ointment (Nitropaste) as well as starting oral aspirin—all in an effort to help facilitate vasodilation, break-up product aggregation and prevent vessel occlusion.[1]

When a hyaluronic acid filler is used, however, there is fortunately the option to try to dissolve the filler with the enzyme hyaluronidase. Hyaluronic acid itself is a glycosaminoglycan polysaccharide composed of alternating residues of the monosaccharides d-glucuronic acid and N-acetyl-d-glucosamine. The enzyme hyaluronidase is a non-ATP dependent enzyme that degrades complex hyaluronan sugars. It works by splitting the glucosaminidic bond between C1 of the glucosamine moiety and C4 of glucuronic acid.[2] Hyaluronidase use to specifically dissolve a filler product represents an off-label use of a product that has been approved by the U.S. Food and Drug Administration (FDA) only as an adjunct to increase the absorption and diffusion of injected drugs such as anesthetics, contrast for subcutaneous urography, and the enhancement of fluid absorption in hypodermoclysis.[3] There are a number of hyaluronidase products currently available on the market. Their origin varies from animal to human and are reviewed in the article written by Lee et al.[3] Reports have shown the effectiveness of hyaluronidase in degrading hyaluronic acid filler in both the emergent and non-emergent setting.[4-7] A comprehensive protocol has been recently suggested by Dayan et al which adds details to the above previous standard including employing the use of topical oxygen therapy.[7] In vitro studies have shown that depending on the concentration of hyaluronidase and the concentration of the filler used, the onset of activity can occur as early as 30 minutes after injection of the enzyme.[8] One case report showed an even earlier onset of ten minutes.[9]

FIGURE 1. Dusky and violaceous discoloration of left cheek five days after cheek augmentation with hyaluronic acid filler.

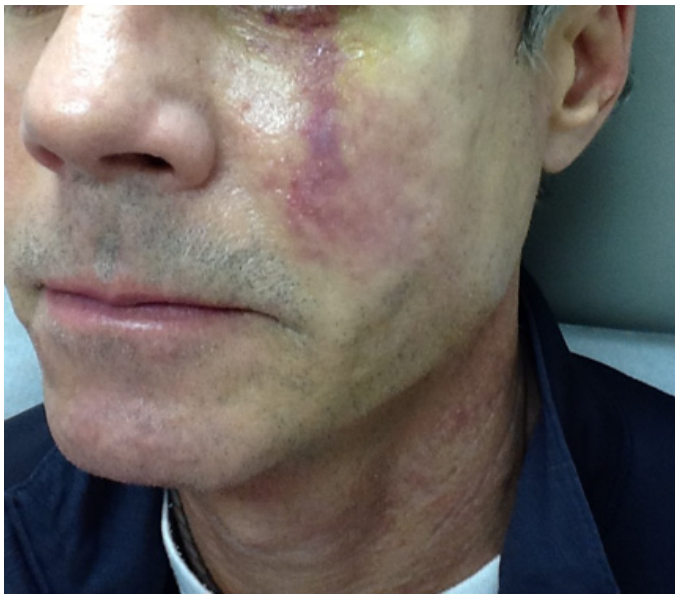

Photo courtesy of Ken Edelson MD

FIGURE 2. Superior labial artery can sometimes have a tortuous course, as seen in this photo taken from a Mohs surgery patient.

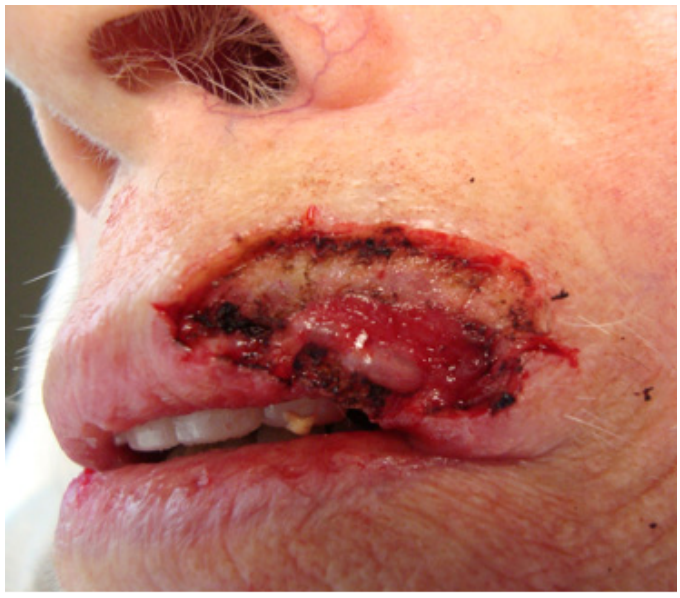

Photo courtesy of Joel Cohen MD

So, while soft tissue augmentation of the face is performed safely and effectively millions of times a year around the world, there are rare circumstances when placing fillers could disrupt blood supply to adjacent areas leading to cutaneous necrosis. Injection necrosis is a rare but serious potential complication caused by either compression of the vascular supply by the filler product or intra-arterial occlusion.[10] It is important for physicians to not only fully understand the anatomy of the area of treatment, but also to recognize the signs of vascular compromise and have the necessary treatment strategies in place to treat such complications. Although the most common site of tissue necrosis after filler injection is the glabella, caution should also be taken in many other regions such as the nasolabial fold (most specifically its superior aspect as it joins the alar groove area), upper and lower lip [with respect to the superior and inferior labial artery (Figure 2), as well as the nose (especially if the patient has had previous surgery to the area making the vascular supply of the area less predictable].[11] It is possible that the recent attention to the use of blunt cannulas being adopted for injecting some regions (in particular cheeks, infra-orbital hollows, temples, and dorsal hands) may potentially decrease the risk of necrosis to these specific areas.[12] As with any procedure, patients should also be thoroughly explained the potential risks of filler injections.[13] Specifically, patients should be educated on the warning signs and symptoms of vascular compromise such as pain along with a patchy purple discoloration (especially for higher risk areas such as the glabella) as all vascular complications will not present in the immediate peri-procedure period. Reports have shown delayed presentations of vascular compromise post-filler augmentation of the face surprisingly up to four weeks after treatment.[7]

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ADDRESS FOR CORRESPONDENCE

Joel L. Cohen MD
499 E. Hampden Ave. Suite 450
Englewood, CO 80113
Phone:.....(303) 756-7546
E-mail:.....jcohenderm@yahoo.com

COMMENTARY

Soft tissue augmentation of the face has grown in popularity and demand in the past decade. Since the U.S. FDA approval of the first HA in December 2003, the number of approved hyaluronic acid fillers in the U.S. has increased, as has the public interest for these products. Additionally, other facial fillers, such as calcium hydroxylapatite and biostimulators, such as poly-L-lactic acid, have become FDA-approved, giving the patient and practitioner therapeutic options to augment facial soft tissue deficiency.

The ease of injection and availability of these products often lures practitioners into a sense of confidence without full appreciation for potential complications. The article by Cohen and Onwudiwe entitled "Vascular Compromise After Hyaluronic Acid Cheek Augmentation" presents a case report of a patient who presented with vascular compromise of the cheek skin and superficial soft tissues five days after midfacial injection of hyaluronic acid filler. The case is well presented and illustrates the potential vascular compromise that exists with any soft tissue injectable filler.

The case report outlines the important features that alert the physician to impending soft tissue necrosis including pain and early patchy discoloration. The mechanism of the compromise can be either pressure to adjacent vasculature or via an embolic phenomenon. In either case, treatment must not be delayed. This article also reiterates the need for a treatment algorithm (as previously outlined by other authors), which should be ready to be initiated should the practitioner suspect vascular compromise.
This article emphasizes three important points relating to complications with facial fillers:
1.) Early recognition is key. The symptoms and signs should be suspected.
2.) A treatment algorithm should be well known and should include hyaluronidase for all HA fillers
3.) Treatment should not be delayed

Jonathan Sykes MD
University of California-Davis Medical Center, Davis, CA

Clinical Experiences With Hyaluronic Acid Fillers: Roundtable Discussion

Hema Sundaram MD,[a] Gary D. Monheit MD,[b] Mitchel P. Goldman MD,[c]
Corey S. Maas MD,[d] Nowell Solish MD[e]

[a]Dermatology, Cosmetic, & Laser Surgery, Rockville, MD
[b]Total Skin and Beauty Dermatology Center and University of Alabama at Birmingham, Birmingham, AL
[c]University of California, San Diego, San Diego, CA
[d]The Maas Clinic and the University of California San Francisco, San Francisco, CA
[e]University of Toronto, Toronto, Canada

ABSTRACT

Hyaluronic acid fillers are a versatile genre that may be used for safe and efficacious volume restoration to the face and body with a variety of techniques. Understanding of the manufacturing processes for different products, and how these determine their physico-chemical characteristics and consequent clinical behavior, can aid in the selection of appropriate products and injection techniques for each application and also help to prevent some complications.

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EVOLUTION IN UNDERSTANDING AND USE OF HYALURONIC ACID FILLERS

HS: ***How have we seen hyaluronic acid (HA) fillers evolve, in terms of the variety and specific characteristics of available products?***

GM: HAs were the evolution that directly followed collagen. Our first HA, approved by the FDA, was Restylane, which changed a lot of our concepts because of the unique characteristics of hyaluronic acid. We saw these characteristics clinically before we understood them scientifically. We appreciated the product's natural feel, the way it incorporated itself, and its gradual breakdown. This was followed in a number of years by Juvéderm, which incorporated some of the features of Restylane but some differences.

HS: Restylane was FDA-approved for aesthetic use in 2003. With the arrival in the U.S. of this first HA product, there was a paradigm shift in our use of soft tissue fillers: we no longer focused on filling individual wrinkles but moved towards pan-facial volumetry—filling many facial areas at once to restore youthful contours, and even to enhance facial contours beyond what they had been in youth. Further HA products were FDA-approved in the ensuing years, including Juvéderm Ultra and Ultra Plus in 2006, Perlane in 2007, Prevelle Silk in 2008, and Belotero Balance in 2011. All these products are non-animal derived.

NS: We have a larger number of HA fillers to choose from, and we have learned the subtle differences between them. In the beginning, I used the same product in every person and area. This has changed.

GM: As we started using these products, we noted clinical differences. Through the work of manufacturing companies, we were given the concept of why there were differences in these HA products and what these differences were. HA is a glycosaminoglycan that is found naturally in most tissues of our body. But it has very little stability or longevity. It's the modifications that are made by industry that first make the differences and make it an acceptable filler. It is understanding these modifications that allows us to use each HA product in its proper way.

HS: If unmodified HA is injected into the dermis, it has a half-life of no longer than two weeks. The HA molecule must be modified

by crosslinking in order for it to persist after injection. Different HA products have different methods, types and percentages of crosslinking. All HA fillers are gels, by virtue of having a solid (particulate) phase suspended in a fluid phase. Their physicochemical structure is established during the manufacturing process; besides crosslinking, it depends on other factors including the concentration of the HA molecules and the proportion of the overall gel that the fluid phase constitutes—known as the gel-to-fluid ratio.

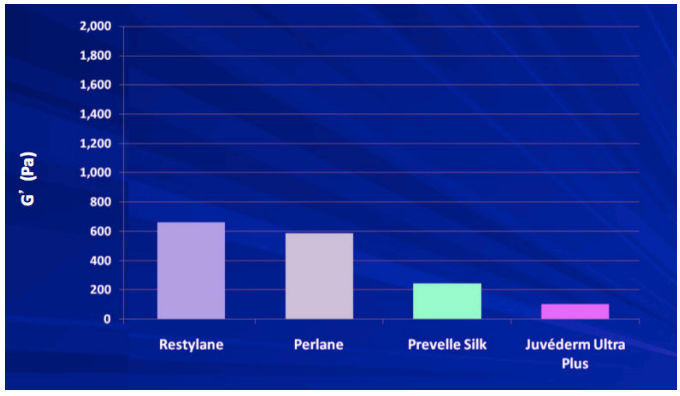
GM: Crosslinking is a specific bond that holds together two strands of HA. One type of crosslinker is the bridge that suspends two strands of HA; the more bridging between the strands, the closer together they become and the stiffer and more robust the product is. The second cross linker, the pendant, flows in the breeze—the more pendants, the more malleable and soft the product. Another factor is HA concentration, measured in milligrams per milliliter, including both soluble and insoluble HA. Soluble HA is added during manufacturing so that the product can be pushed through the syringe more easily. It liquefies it, to some degree. The amount of bridging determines how much soluble HA is needed. Stiffer products do need some soluble HA, which goes away and adds nothing to the stability or robustness of the product. It's only the insoluble HA that stays. If we add concentration and cross linking together, we come up with a characteristic called G prime. G prime is the amount of force required to produce a given amount of deformation. It represents the firmness or robustness of the gel.

HS: One thing we're learning is that the soluble component of an HA filler probably comprises unmodified HA and also some modified HA that has been heat-degraded into fragments during the manufacturing and heat sterilization process. Fragments of modified HA with lower molecular weight would behave in a similar way to the unmodified HA that is added to the product to optimize its extrusion force from the syringe and needle during injection. Depending on the manufacturing process, there can also be varying amounts of higher molecular weight soluble HA, and we need to further characterize how this behaves. Two weeks would be the maximum time that the lower molecular weight soluble HA would persist.

GM: Very much so. And that's why with some HA products, we see a drop in correction of nasolabial folds or wherever we're injecting in about a two week period. In studies, it's at the two-week point that we usually give a re-injection, if needed.

HS: Dr. Monheit, the seminal paper on the physicochemical properties of HA fillers was your own with Kablik.[1] This examined the rheologic (flow-related) properties, types of crosslinking and other characteristics of various HA products (Figure 1).

FIGURE 1. Elastic modulus (G)' of cross-linked HA fillers.



Measured at 5Hz
From Kablik J, Monheit GD, Yu L, Chang G, Gershkovich *J. Dermatol Surg.* 2009; 35(suppl 1):302S-312S.

GM: Another characteristic we talk about is swelling, which is determined by how much the HA is hydrated by water or how much it is deprived. HA has the capacity to absorb fluid either internally or externally. The partially hydrated HAs will have more correction and more swelling by the second and third day than they do initially because of water absorption. This has been demonstrated in the test tube and must be separated from post-injection trauma, which can cause a different kind of swelling. If the HA is fully hydrated externally, there's very little swelling.[1]

HS: There seem to be two components to tissue swelling after injection—first, an inherent tendency of each product to absorb water to a greater or lesser degree and to swell and second, swelling related to injection technique and other aspects of the injection process. All HA fillers are hydrophilic. Restylane, Perlane, Juvéderm Ultra and Ultra Plus, and Belotero Balance have higher water binding capacities due to their higher HA concentrations (20 to 24 mg/mL) and tend to pull in water after injection. Prevelle Silk has a low HA concentration (5.5 mg/mL), so it has a lower total water-binding capacity and is already fully hydrated prior to injection.

GM: The last important consideration is particle size. Products have varying particle sizes, and I think we can agree that there are particles in every filler.

HS: The manufacturing process and microscopic examination of finished products bear out the fact that HAs are all particulate to some extent.[2] There are differences in the diameter of the particles and in how distinct or uniform they are. Conventionally, we refer to Restylane as small particle HA, Perlane as large particle HA, Juvéderm Ultra and Ultra Plus as "nonparticulate" HA, and Belotero Balance as cohesive polydensified matrix HA. In fact, the Juvéderm products do have particles, but they are more variable in shape and size.[2]

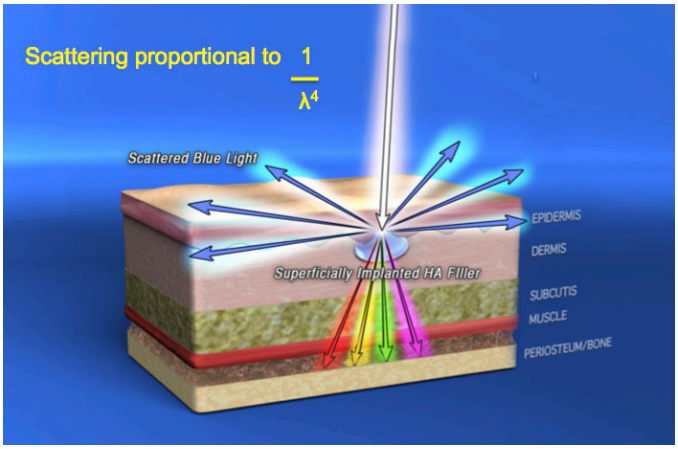
EXTRAPOLATING FROM SCIENCE TO CLINICAL EXPERIENCE

HS: ***How are we leveraging the physicochemical characteristics of different HA products, based on science and also on clinical experience of how products behave and perform?***

MG: One of the cardinal features of using bovine or human collagen was to overfill the lesion and to place the collagen intradermally. With HAs we needed to relearn our technique so that injections were placed deeper and overfilling was not attempted. With proper injection, we avoid a Tyndall effect, and we also avoid lumpiness and overfilling. Restylane and Juvéderm tend to not be placed superficially in the skin because of the Tyndall effect, whereas Prevelle Silk can be placed more superficially without the fear of a Tyndall effect.

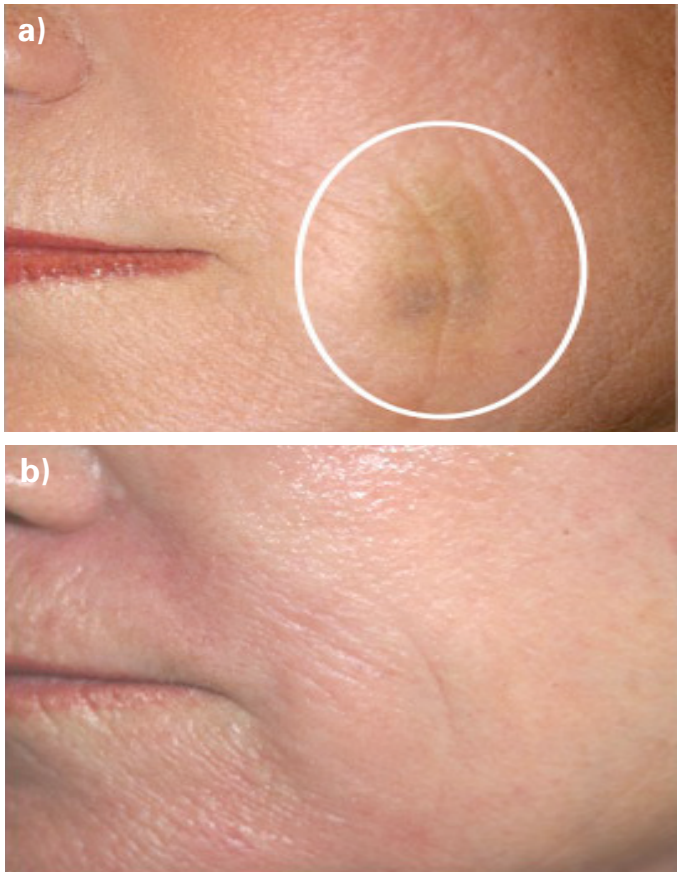
HS: The Tyndall effect, more correctly described as Rayleigh Scattering,[3] is the problem of persistent bluish skin discoloration after implantation of an HA filler into the superficial dermis or the epidermis (Figure 2). This superficially implanted filler bolus is translucent but disperses light beams penetrating the skin surface in many different directions - a process known as light scattering. The intensity of the scattered light is proportional to the fourth power of the frequency of the light waves. Because blue light has a shorter wavelength of 400 nm, and thus a higher frequency than red light, which has a wavelength of about 700 nm, the filler material scatters blue light about ten times more strongly than red light. This blue light then traces a visible path back to the skin surface. Rayleigh Scattering is also the reason that the colorless sky appears bluish, due to stronger scattering of blue light than red light. The misplaced filler may be removed by extrusion after needle incision or by the injection of hyaluronidase to dissolve it (Figure 3).[4]

FIGURE 2. Tyndall Effect (Rayleigh Scattering). Light scattering is inversely proportional to the fourth 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

FIGURE 3. Removal of misplaced HA filler with hyaluronidase. **a)** A 57-year-old woman who presented reporting injection of particulate HA into fine lines of the left cheek 1 month previously. Note focal bluish skin discoloration (Tyndall Effect) within area of ecchymosis, induration, and elevation (ringed). **b)** The same patient 14 days after injection of 20 units ovine hyaluronidase. Patient reported that complete resolution of skin discoloration and induration occurred within 48 hours of hyaluronidase injection.



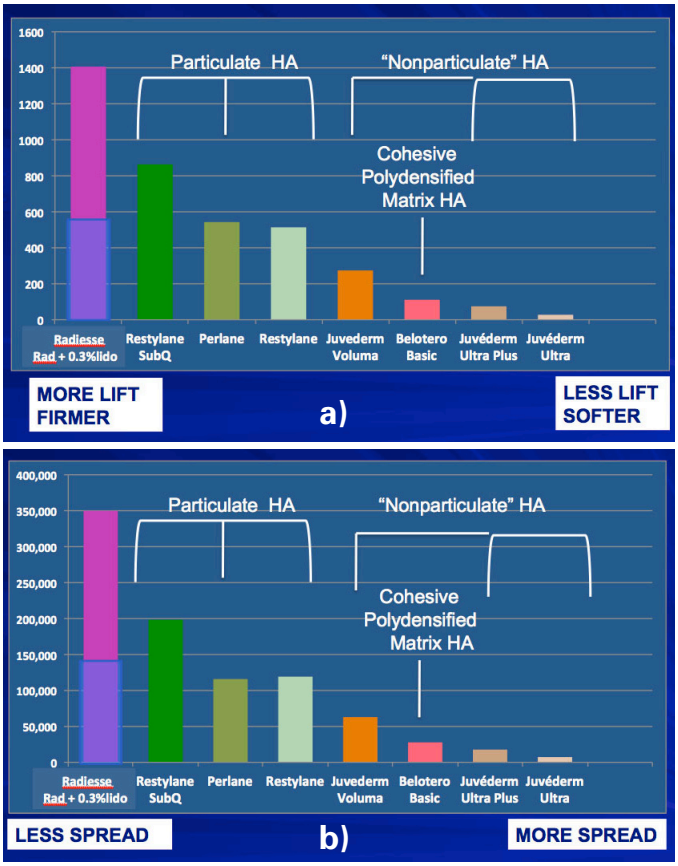
Courtesy of Hema Sundaram MD

Prevelle Silk does not cause the Tyndall effect even when implanted superficially because its HA concentration is sufficiently low, and its low viscosity causes it to spread into the tissue, such that significant light scattering does not occur. Belotero Balance is a high concentration, low viscosity HA with homogeneous tissue distribution due to its cohesive polydensified structure,[5] and the Tyndall effect has not been reported after over seven years of use outside the U.S.

MG: The next point regarding HAs is injecting them on label and off label. We often inject HAs off label to do what we feel is practical and appropriate for our patients.

HS: The FDA on-label indication for these HA products is that they are intended for temporary correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. One product, Restylane, also has approval for lip augmentation.

FIGURE 4. a) Elastic modulus (G') of CaHA and HA fillers. **b)** Complex viscosity of CaHA and HA fillers. Blue bar inset on pink Radiesse bar shows G prime of Radiesse and 0.3% lidocaine. HA products are grouped by generic family name.



Measured at 0.7 Hz.
From Sundaram H, Voigts B, Beer K, Meland *M. Derm Surg.* 2010;36(suppl 3): 1859S-1865S.
Data on File, Merz.

MG: One evolution in using HA fillers is mixing them with lidocaine to decrease pain or normal saline to make them flow more easily. Early on when using HA fillers, physicians minimized pain on injection with topical anesthetic which often was not effective, or even field blocks or nerve blocks which in and of themselves were painful. But many physicians started mixing lidocaine into the HA, not knowing exactly the consequences of manipulating the filler. Then, various companies came out with HA fillers with lidocaine already mixed in.

NS: The addition of lidocaine has helped with pain control by reducing discomfort significantly and has almost completely eliminated the need for local anesthetic. The occasional patient still wants local mini-blocks for lip augmentation, but otherwise, topical anesthesia and fillers with lidocaine work in the vast majority.

HS: It was an epiphany to see how dramatically a filler containing lidocaine improved patient comfort both during and after injection. Prevelle Silk was the first marketed HA product containing lidocaine. Dr. Monheit's study evaluated the reduction in pain with this filler in comparison to a similar filler, Captique, that did not contain lidocaine. Many clinicians then began adding small volumes of lidocaine suspension to the other HA fillers; this was done immediately prior to injection because the long term stability of the filler after in-office lidocaine addition is not known.[6]

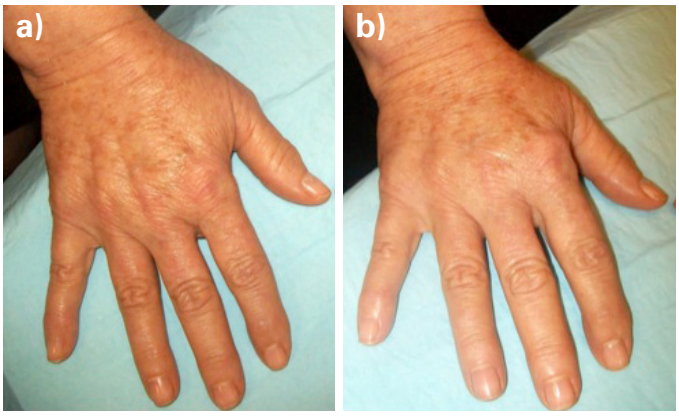
Adding lidocaine suspension to a filler just before injection will lower its G prime and viscosity because it dilutes the filler. This reduction has been quantified[7] for another genre of filler—calcium hydroxylapatite (CaHA) (Radiesse)—when the lidocaine is added in accordance with an FDA-approved mixing protocol.[8] The addition of lidocaine reduces extrusion force, but does not seem to adversely impact tissue lifting properties, since the CaHA still has high to medium G prime and viscosity (Figure 4).

Formulations of Juvéderm Ultra and Ultra Plus, Perlane and Restylane that already contain lidocaine have now been approved by the U.S. FDA and in Europe. Because lidocaine is added in crystalline form, the products are not diluted, and they have the same G prime and viscosity as when they are manufactured without lidocaine. However, there are clinical situations where it is still beneficial to dilute these products with lidocaine suspension or saline solution just before injection. The resultant reduction in G prime and corresponding reduction in extrusion force allows the product to be injected more superficially into finer rhytides through a smaller gauge needle. There is also a reduction in viscosity, resulting in increased spreadability, which can enhance filling and contouring in anatomically unforgiving facial zones and also in the dorsum of the hands. These rheologic changes can be titrated by the addition of more or less diluent (Figure 5).

A significant reduction in G prime could theoretically impact longevity, although we consider longevity to have multifactorial etiology, in that it is partly inherent to the physicochemical characteristics of the filler, but also dependent on implantation site and even on the individual patient. CaHA and particulate HA fillers have limited water-binding capacity; thus it might be expected that the diluent would be resorbed completely or to large extent after implantation and have little ultimate impact on those aspects of performance or longevity that depend on G prime and viscosity. There could be a decrease in longevity if resorption of a significant volume of diluent after implantation results in undercorrection of volume loss. Full correction during the first treatment or at a subsequent touch-up session will prevent this problem. Another method of rheologically changing an HA filler is to shear it through a 32 gauge needle. Depending on the shearing force, this may temporarily decrease G prime and viscosity during injection, or it may cause permanent physicochemical alterations (Figure 6).

NS: The ability to add lidocaine helps me change the HA to meet my needs. For example, very small lines that used to be very dif-

FIGURE 5. Titrating viscosity and G prime via filler dilution. **a)** Right hand before injection. **b)** Right hand immediately after injection of calcium hydroxylapatite and 0.4% lidocaine for patient comfort and to increase filler spread.



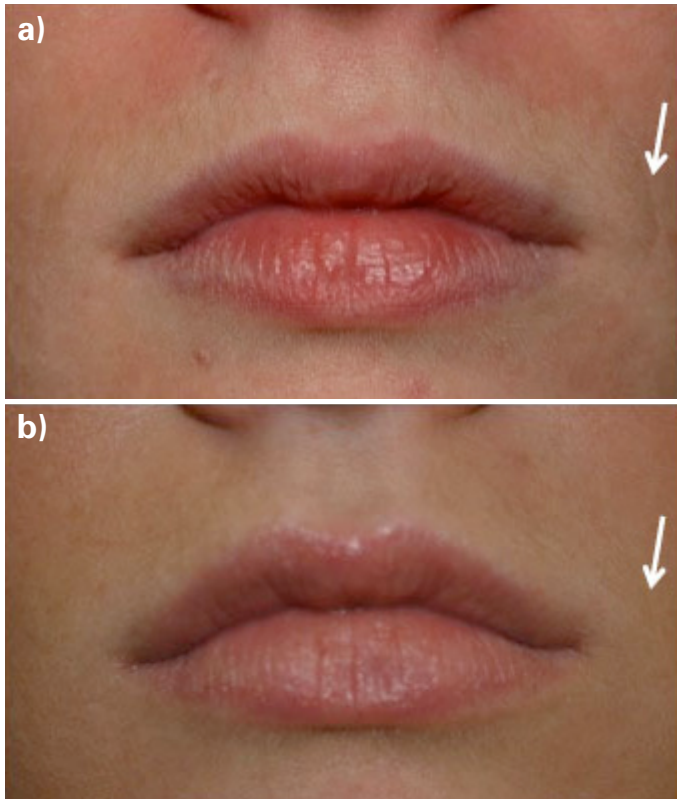
Courtesy of Hema Sundaram MD

ficult to treat can be improved by diluting the normal HA that I use. Very small upper lip lines and sleep lines work well with diluted product. Larger areas like the temples where there is a risk of uneven appearance of the product also do better with diluted HA.

CM: As we evolved to HAs, we changed from using fillers intradermally. In addition to the Tyndall effect, there was also what I call the "corn row" effect, where you create a little corn or mole row, and then in the middle of it is your little wrinkle. We found that we could go subdermal and get plenty of correction and long term duration of effect. So a big transition in the learning experience was that Restylane and Juvéderm, while they can be used intradermally with great caution, are more commonly used subdermally.

HS: We are often a lot deeper with HAs than we realize. To be truly intradermal, you usually have to see tenting or outlining of the needle through the skin, and the needle has to be at a much smaller or more acute angle to the skin surface than we are accustomed to when injecting HAs. When injecting into the superficial dermis, there will be visible skin blanching and the gray of the needle will typically be visible through translucent skin. We have to make a conscious, purposeful effort to inject intradermally. Restylane and Juvéderm are very forgiving of subdermal injection, and I find anecdotally that their longevity is better with deeper injection. Another consideration is that the dermis is not a sealed unit; we may presume it's structurally quite porous in its lower, reticular portion. There is histopathological evidence that particulate HA eventually settles down into deep dermis and even below this, even if it was originally injected higher. Given the structure of the dermis, I think it's also reasonable to presume that post-injection tissue massage might cause some of a highly concentrated HA placed in the mid to deep dermis to drop down to the subdermis. So for all these reasons, we're invariably placing Restylane and Juvéderm deeper than we perhaps even think we are.

FIGURE 6. Decreasing filler G prime and viscosity by needle shearing. **a)** Before and **b)** one month after injection of 0.8 cc small particle HA via a 32G needle into vermilion borders and fine nasolabial rhytides (arrowed). Note lip enhancement without appreciable augmentation, with improved symmetry of the lips, maintenance of appropriate upper to lower lip height ratio, enhanced definition of philtral column, shortening of distance from columella to upper vermilion border, and improved light reflectance at vermilion borders due to enhancement of vermilion white roll. Shearing of particulate HA through a small gauge needle decreases G prime and viscosity, making the particulate HA more suitable for injection into fine lines and the vermilion lip border.



Courtesy of Hema Sundaram MD

MG: A histologic study performed after excisional surgery demonstrated that even when clinicians thought they were injecting into the superficial dermis, all injections of HA, at least in the nasolabial fold, were injected in the deeper dermis.[9]

CM: HA concentration is an important concept as it relates to the indication that you're treating. Prevelle Silk has a much lower concentration of HA—5.5 mg/mL versus the 20 mg/mL and 24 mg/mL for Restylane and Juvéderm, respectively. As Dr. Goldman pointed out, a lot of experienced injectors are taking existing products and diluting them when treating fine lines. You could see the more concentrated products if

FIGURE 7. Volume-efficient deep lifting with medium-high G prime and viscosity HA fillers. Right side immediately after subcutaneous injection of 1 cc large particle HA (Perlane) plus 1 cc small particle HA (Restylane) to malar, pre-jowl, and nasolabial fold regions, mid and lower face. The left side is untreated. Note lack of tissue ecchymosis and edema with slow, careful injection technique.

Courtesy of Hema Sundaram MD

you're intradermal; the less concentrated product appears, from our clinical experience, to be usable in the dermis and still not visible.

HS: We've developed the concept of rheologic tailoring. The low G prime and viscosity product is most suitable for fine lines, whereas the higher G prime and viscosity product provides more tissue lift and contour stability. Restylane, Juvéderm, and Belotero Balance are all high concentration HAs, and studies show their longevity is comparable, whereas Prevelle Silk has lower concentration and lesser longevity.

CM: There's not a great deal of variation in HA particle size in the United States. We don't have Restylane SubQ, which has very large particles. While in theory, larger particle size translates into greater duration, my experience is that the duration of Perlane and Restylane is pretty much the same.

HS: In fact, phase 3 FDA studies showed no significant difference in longevity between Perlane and Restylane—at least, based on the clinical criterion of improvement on the Wrinkle Severity Rating Scale (WSRS) after intradermal implantation into the nasolabial folds.[10]

CM: Cross linking is interesting science. But from a practical standpoint, I can't really tell the difference between HA cross-linked with BDDE versus other cross linking agents. I would agree that the amount of free HA in the product does seem to have an impact on how much swelling patients have. The more free HA, the more potential there seems to be to grab onto tissue water, and as a result, swelling outside of the typical inflammation-related swelling can be greater.

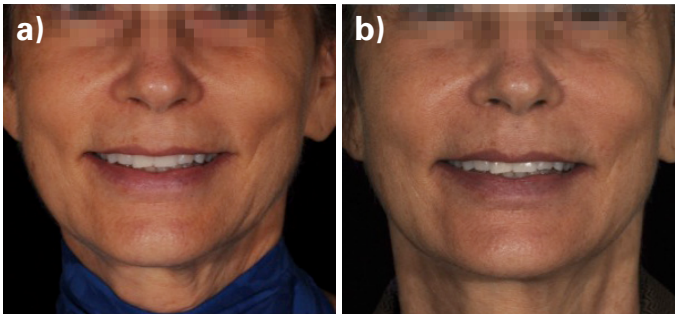
HS: I think we still have a lot to learn about the clinical implications of HA crosslinking. There is some limited evidence that different crosslinkers might impact HA degradation in vivo. What we do understand, as brought out in Dr. Kablik's and Monheit's paper,[1] is that pendant modification seems to result in a softer product, whereas bridging crosslinking produces a firmer product. If different products swell differently, that would presumably be due to variation in water binding capacity, which might relate to characteristics such as HA concentration or bridging versus pendant modification. I consider swelling to be multifactorial: first, filler-inherent swelling is mostly due to the difference between full and partial hydration. Second, swelling can be injection-related; short-term swelling may be related to rapidity of injection and fanning injection technique, as we learned from a paper by Drs. Glogau and Kane.[11] Third, swelling can be patient-related; anecdotally, I've found that a few patients manifest an injector-independent, urticarial type of swelling, predominantly after lip injection—and, indeed, this swelling responds to antihistamines or to intradermal or oral corticosteroids.

CM: I think the main thing that's evolved with HA fillers is that clinicians are, for the most part, injecting Restylane and Juvéderm subdermally rather than intradermally.

GM: I agree completely. We first quantified that when we were doing our studies, because all HA fillers are FDA-approved for dermal injection. But we learned that 80% is going into the subcutis even when we're trying to hit the deep dermis. And then we learned that we're doing more than just filling a wrinkle by putting it into the subcutis. Once we inject deeper, we can "volumize," which is that idea of replacing lost subcutaneous tissue and the lost structural tissue of the face with our filler in a volumetric way.

HS: My use of fillers has evolved so that I perform mass lifting volumetry and sculpting by deep injection of high to medium G prime and viscosity HA products—Perlane and Restylane—and also with the CaHA product, Radiesse. These products are volume-efficient, and they will stay put. I use Perlane and Restylane when I want a slightly rounded contour because these products pull in a little water, and I use Radiesse for more angular contouring. I use Juvéderm Ultra Plus or Ultra for mass lifting when patients request it or when they request a less palpable filler. I perform tension volumizing and filling of fine lines and borders with more superficial injection of lower G prime and viscosity products that do not have propensity to cause the Tyndall effect—Belotero Balance and Prevelle Silk (Figures 7 and 8).

FIGURE 8. Soft contouring, defining and lifting with low G prime and viscosity HA fillers and higher G prime and viscosity CaHA filler. **a)** Before and **b)** three weeks after 2.4 cc "nonparticulate" HA (Juvéderm Ultra) subdermally to mid and lower face, 1.5 cc fully hydrated HA (Prevelle Silk) to nasojugal folds, and intradermally to nasolabial rhytides and lower face, and 3 cc CaHA (Radiesse) subcutaneously and supraperiosteallly to mid and lower face. Patient has also received onabotulinumtoxin A (Botox Cosmetic) to upper and lower face.



Courtesy of Hema Sundaram MD

Although the trend has been more towards volumizing to improve overall facial contours, when patients come in for a consultation, they are sometimes still wrinkle chasing. The classic example is the woman who specifically requests fillers for fine rhytides on her upper lip even though, as clinicians, we may see volume loss throughout her face. Then it becomes a balancing act between volumizing through deep injection and the improvement in fine lines that they are requesting. When striking that balance, it is useful to have products in our aesthetic toolbox—a wonderful term that Dr. Monheit taught me—that we can inject deeply for contouring, and also products that we can inject intradermally to address wrinkles.

GM: The concept of volumization had to come to us first before it came to our patients. I think it occurred to me when I realized that there's only so much I can do to correct the nasolabial fold when I've got a malar fat pad hanging over it. I can keep trying to fill it, but I won't fill it. We originally learned through autologous fat filling that as we inject into the cheek and the upper face, and actually lift that malar pad off the fold, we're going to get correction that we couldn't achieve by just injecting into the wrinkle or the fold alone. What we're doing is re-inflating the area where the tissue has dropped, to bring it back into position. So rather than just volumizing, we're really sculpting. We're rebuilding structure. And, Dr. Sundaram, you're very correct in saying that is something we have to educate our patients into.

There are various ways we can do it. We can show them how, by adding volume around the malar area, the medial fat pads, we can lift the malar pad off the nasolabial fold. It's the same for areas such as the pre-jowl sulcus. And then I think they understand. Our understanding of the science of the products is that some are more robust, they have a higher G prime, their concentration is greater. They're great for volumizing, and that includes Restylane and Perlane. Probably Restylane is my favorite for the malar areas, while I like Juvéderm for volumizing in the lip—it's softer, and it spreads out more. We have learned, both through science and through our experience, what fillers are best for what areas; what we're going to use for volumizing and what we're going to use more superficially.

LONGEVITY AND NEOCOLLAGENESIS

HS: ***It has been postulated that longevity of a HA filler has a direct linear relationship with its concentration and percentage elasticity.[12] While concentration does appear to be important, is it realistic to mathematically quantify longevity, given all the product, technique, and patient variables we see when implanting an HA?***

GM: I can't see how it really would work in practical situations. We can make predictions in vitro, but what happens in vivo has many other variables that are not taken into account with a mathematical equation.

CM: Beyond the theoretical, there's just the practical observation, which is that the lower concentration HAs don't last as long as the higher concentration HAs. We know it's at best probably a few months for the 5 milligram per milliliter range. And when you're up in the 20 plus mg/mL range, it's going to be typically six months or longer duration. I'm not talking about how long the product actually exists in tissue; I'm talking about the clinical outcome or the indication for retreatment.

GM: An important factor, in addition to HA concentration, is cross linking. Heavier cross linking is going to pull these HA strands closer together and make them more resistant to degradation. I think that's why Juvéderm Ultra Plus has probably a more resistant and more robust effect than Juvéderm Ultra—because it is more highly cross linked.

MG: The early HA products, which were primarily used for orthopedic applications, were not very highly cross linked, and if you injected them into the skin, they didn't last very long. And as we got into products that were usable for our applications, they were certainly more cross linked and showed greater duration of effect. So I think we can make the conclusion that cross linking has an impact on longevity. Now, is there a limit to how much crosslinking, and is there a peak effect in cross linking? We really don't know.

GM: I've tried some experimental products that were so heavily crosslinked you couldn't get them out of the syringe. So I think that there is a limit to how much crosslinking (i.e., G prime) we can put in and still have a product that is clinically applicable. Also, there is more inflammation as a reaction to a solid mass

that's very heavily crosslinked.

HS: Basically a hard product hitting the soft tissue could potentially cause more tissue trauma. And perhaps there is less control over the rate of injection when we have an excessively high extrusion force.

HS: ***Let's consider the influence of HA particle size. Based on studies and our clinical experience with the particulate HAs currently available in the U.S., we're not really seeing a difference in longevity, correct?***
GM: Perlane has a larger particle size than Restylane, but I don't see a difference between the two in terms of longevity.

MG: I concur. My personal experience mimics the peer reviewed report by Drs. Dover, Rubin, and others[10] that there doesn't appear to be much difference in longevity between Perlane and Restylane. However, there may be a difference in the lift effect of large particle HA.

HS: There isn't a whole lot of difference between the G prime and viscosity of Restylane and Perlane. I agree with Dr. Goldman that I see a bit more lifting effect when using Perlane, and for that reason I like to use Perlane for lifting the mid and lower face and temples. But I attribute that to the fact that I tend to implant Perlane a bit deeper than Restylane, so perhaps that produces more tissue lifting effect. Whenever possible, I inject Perlane supraperiosteally or subcutaneously. The greater lifting effect of Perlane is perhaps more a function of the depth at which I'm placing it than of the product per se.[1,5]

HS: ***Do we consider depth of implantation to impact longevity? Do we feel that neocollagenesis may be more pronounced the closer we get to the periosteum?***
MG: I think that's a very interesting question. I believe there have been no clinical studies to answer it. We do not know the full effects of deep and even supraperiosteal injections of HAs presently available the United States.

GM: I think another factor is immobility of a product as it sits. When we're injecting filler supraperiosteally, there's no movement around it. And there's very little antigenic effect or enzymatic effect in that plane. I think all of us have observed the nasojugal folds. I also inject into the mental creases in the chin. I inject into the maxilla in order to build up the platform of the lip. Injections into those particular areas last over a year. Patients come back, and I can still see the correction is there. The injection area where results are shortest lived, no matter what we use, is the lip, where either we inject subcutaneously or into the muscle, and I think a lot of that is movement-controlled.

HS: The lips are more mobile, and this diminishes filler longevity even though we tend to inject submucosally. Here is an opinion regarding what actually gives correction with an HA product. First, there is the implanted HA itself. Second, there is bound water; this may vary in amount within the first two or so weeks because, as we've observed, there are differences in the degree of water absorption of these products. In my opinion, by the time we get to five months or longer after injection, a significant proportion of the corrective effect we're seeing may actually be due to bound water as HA molecules are unraveling and more water-binding surfaces are exposed. The third contributor to longevity of corrective effect is neocollagenesis. Our concept that neocollagenesis occurs with HA fillers is founded on an in vivo pilot study of a non-facial area—such as forearm skin—injected intradermally with Restylane, resulting in the intradermal deposition of parallel arrays of collagen fibers and upregulation of type I and type III procollagen gene expression.[13] We've just established from our prior discussion that, when working on the face, we tend to implant Restylane, Perlane, Juvéderm Ultra, and Juvéderm Ultra Plus subdermally rather than intradermally. We might wish to consider which of these three factors—the implanted HA itself, bound water and neocollagenesis—may be significant contributors to longevity of the corrective effect. We might also ask whether we need to further investigate the story of HA-specific neocollagenesis after subdermal implantation into the face? I am most convinced we can actually get neocollagenesis with a HA filler when we're implanting close to the periosteum.

CM: At least from clinical observations and patients reports, it does appear that there is a build-up of soft tissue correction over time with repeated injections. This may not be unique to HAs – it may be trauma-related, or there may be any number of different factors that result in this outcome.

GM: I'm not sure what the cause is. Is this a factor of HA or is this a factor of injection, trauma and/or swelling, and then going through the cascade of neocollagenesis, which can occur from anything? We've noted that just from subcision, which creates trauma with a little blood (as happens when we give injections of HAs), we get neocollagenesis, and we can elevate scars and other structures. I don't think we have a real model that proves that it is the HA itself that creates neocollagenesis.

HS: ***Do we feel that there is a difference in collagen synthesis potential of different levels of the dermis? In studies of topical rejuvenating agents, we often look at the superficial dermis (Grenz zone) to determine whether there is any impact on collagen synthesis.[14]***

MG: I think that neocollagenesis is due to stretching of the fibroblast. Regarding the depth, as long as there's a sufficient quantity of fibroblasts in the injected area that can be stretched, then we can make the assumption that that area will develop neocollagenesis.

GM: That makes sense. But also, let's look at a different filler that we know changes the texture of the surface skin even though we're injecting it deeper: poly-L-lactic acid (Sculptra). When we pan volumize—and we're mainly doing that subdermally—we know that we're increasing the dermis itself, and that's been measured.[15] But in addition I have seen, and I'm sure you have too, that there's a change in the texture of skin over a period of time, which is accounted for by neocollagenesis.

HS: And that's really interesting, isn't it: that we could implant poly-L-lactic acid—or calcium hydroxylapatite, for that matter—beneath the dermis and get a change in an anatomically distinct, higher level. Could there be passage of filler molecules in either direction between the dermis and the subdermis or even cytokine signaling?

OPTIMIZING CLINICAL OUTCOMES

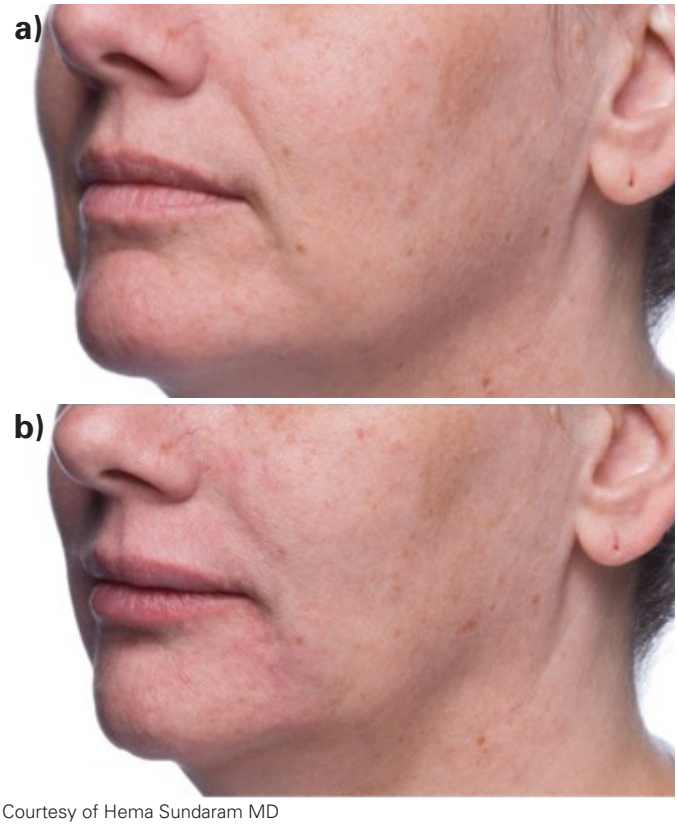
HS: ***How do considerations such as rheology, HA concentration and degree of hydration play out in the dialogue with patients when we're trying to meet their objectives?***

GM: We choose products with higher G prime for volumizing and putting deeper, and softer, more malleable products for areas that need more of a natural effect. What we can use in the lip may not be the same product we want to use in the nasojugal fold. In the nasojugal fold, we're looking for firmness, stability, and robust lift. And if it has a little more inflammation, that's okay, because we're putting it deep. In the lip we want the filler to spread out more, not to necessarily stay exactly where we put it. So it will feel and look more natural, and there'll be less inflammation.

HS: For both these areas I use high or low G prime products depending on the effect I want to achieve. When I want maximal lift and longevity in the nasojugal fold, I use Restylane, and I have seen the corrective effect last up to 15 or 18 months when this is implanted supraperiosteally. When I want to inject at multiple tissue levels including superficially, I use Belotero Balance. For minimal swelling post-injection—even though this depends on some non-controllable factors such as whether you happen to hit a blood vessel—I use Prevelle Silk, and I see the corrective effect last up to nine months with supraperiosteal implantation. For lips, I combine Perlane and Restylane for volumizing and shaping with contour stability. I use Belotero Balance, Juvéderm Ultra, or Juvéderm Ultra Plus when I want spread and a bit more of a tumesced look to the lips. When I want minimal swelling and sharp definition as we used to achieve with collagens, I use Prevelle Silk (Figure 9).

NS: HAs with a higher G prime do a better job at allowing me to volumize a face. I can get more lift with higher G prime products like Perlane and Voluma than I could with other HAs.

FIGURE 9. Volumetry with non-Tyndall HA. **a)** Before and **b)** immediately after 1.5 cc cohesive polydensified matrix HA submucosally to lips, superficially to vermilion borders, and intradermally to perioral region and oral commissures. Note lack of Tyndall Effect with intradermal implantation.



Courtesy of Hema Sundaram MD

CM: My clinical impression is that Juvéderm seems to be more hydrophilic than does Restylane. I think that's a benefit in some areas. It gives the impression of great correction in areas like the nasolabial fold early on, and that can be persistent for some time. For me, it's a little bit of a disadvantage in areas like the nasojugal fold, where you don't want it to be water laden because it looks puffy. So I prefer Restylane in the nasojugal folds. In the marionette lines, I like the softness that Juvéderm provides, and the fact that it distributes a little more evenly. In the lips, I like a little more stiffness, and I like the product to stay right where I put it. Creating a lip border, a lip roll, is a little easier in my hands with Restylane, and it stays right where I want it.

MG: My experience over the last seven or eight years with the HA fillers has been a little different. Although I thought theoretically that Juvéderm should be better in certain locations than others, I found no difference between Juvéderm and Restylane in the lips or in the nasolabial folds. The only place where I have found a difference is in the nasojugal folds. What we really need is a side-by-side comparative study of one filler on one side of the face and one on the other.

GM: I like to use Restylane on the supraorbital ridge in order to raise the brow. This is another supraperiosteal injection. It doesn't swell, and it is also going to stay where you're putting it.

HS: I use Perlane or Restylane supraperiosteally in the supraorbital ridge with anterograde serial puncture followed by massage. Contour stability—the tendency of these products to stay where they are put—is a function of their having high viscosity and therefore less tendency to spread.

GM: We are looking toward using each of the fillers based on their characteristics and where we put them. The volumizing fillers, the softer ones, the more robust, firmer ones, and the superficial filler, are all part of our toolbox. We need to educate our patients that we don't have one magic bullet. We need to mix and match and use different things in different places.

HS: Science can help us individualize the palette of fillers for each patient to meet his or her objectives. Each product has distinct benefits and disadvantages. Leveraging the strong points of each is key to the advanced use of fillers.

HS: ***Are there any challenges inherent to using HA fillers, and how can we diminish or overcome these challenges?***

CLINICAL CHALLENGES AND SAFETY CONSIDERATIONS

Periocular Swelling

GM: One way that you can get puffiness of the eyes is if you overcorrect the nasojugal fold at the periosteum; you will essentially block the lymphatics along the eyelids that would drain the eyes. And I've seen some patients who came to see me three or four months after injection (not necessarily mine), with persistent puffiness because they were overfilled and injected heavily. Some are older patients, who have less drainage and probably have really too much of a problem to really correct, and a clinician may try to correct it with a big volume of robust HA at the periosteum. The beauty of hyaluronic acid, though, is that we can salvage this by using hyaluronidase to dissolve what we need to remove when that problem occurs.

CM: I agree with the concept that it's lymphatic outflow obstruction. I don't know that anyone has proven whether it's just simply water retention due to the hydrophilic nature of HAs or whether it has something to do with lymphatic outflow. No one has demonstrated that, to my knowledge, in any kind of trial or study looking at lymphatic outflow.

HS: We've talked about two types of puffiness and swelling. There's short term swelling, and we identified specific products that we felt anecdotally were a little bit more likely to produce that. And now we're talking about more long-term puffiness, which may be a sequela of partial lymphatic obstruction. Do you think there is any correlation with the hydration of a product?

GM: We definitely would see less swelling with fully hydrated products, and ones with lower concentration, because they have less of an ability to absorb water. Clinically, Prevelle Silk has very little swelling. That's one of its real big advantages, though the compromise is definitely in longevity, which was about three to four months on the original nasolabial fold study.[6]

MG: The problem is that whenever you put a needle into the skin of a patient, you can get a bruise. I find that the incidence of bruising is not reflective of the type of filler but of the mere chance of hitting a blood vessel. So I cannot reassure any patient 100% that she or he will not get swollen or bruised from a filler.

CM: I completely agree. I think that the swelling phenomenon is much more related to trauma than it is to product characteristics.

GM: I think that you can tell the difference between this phenomenon of a filler being water-hungry and the kind of swelling you get from that, as opposed the swelling you get from trauma. When I inject the nasolabial folds and the lips, I tell my patients that by tomorrow it's going to look better than it does the day of injection. It looks better even four hours later. And that's not necessarily because of inflammation, trauma, or bruising. It is that phenomenon of water absorption occurring around or in the filler itself.

HS: I agree that there's a difference. The trauma-related swelling is going to happen if you hit a blood vessel. As Dr. Goldman said, you can't predict that. We can try to minimize swelling due to trauma by employing controlled injection technique. I find that slow, careful serial micro-aliquot injections minimize trauma-related bruising and swelling with high G prime and viscosity products.[16] I also agree that swelling can be product-related to some extent—that partially hydrated HA products may be inherently more likely to cause swelling, all other things being equal. And, as discussed before, it can be related to the individual patient, too.

CM: Where we don't want a lot of swelling, we can use the products that don't "absorb water very much" to our advantage.

Vascular Infarction

GM: A challenge that I'd like to bring out is something we're learning as we're putting more volume into areas, and using HAs everywhere: HAs may do the same thing that we learned Zyplast (bovine collagen) did in the glabella, which is to cause infarction. And this can also occur in that soft triangle at the very upper nasolabial fold where the angular artery comes through. I think we all should be aware of it, how to try to prevent it, and what to do to treat it.

HS: I certainly include both the glabella and the nasolabial angle in my checklist of danger zones, where I'm watching very closely for any signs of vascular occlusion, including blanching, since I do not add epinephrine to my fillers when mixing them with lidocaine. I try to inject very slowly and carefully. Hyaluronidase can be used to dissolve misplaced HA filler, and it is advisable for some clinicians to also keep Nitropaste (topical nitroglycerin) in their offices to produce vasodilitation with the aim of aborting vascular occlusion if they have noted the early signs.

Over-Correction

NS: Compared to other products, I think HAs have fewer challenges. They are very user-friendly and can be adjusted easily by adding or removing product. One issue is that because HAs are so safe and easy to use, novice injectors can make mistakes. They are so motivated to add volume (as this is the new hype) that they over-inject their patients. This creates a negative image of the product and people begin to think that all fillers create this look, not realizing that most patients look natural and that they can't notice the product when it is injected correctly. One should not be able to tell someone had volume restoration, if it's done correctly.

CLINICAL CHALLENGES AND SAFETY CONSIDERATIONS

HS: ***What are the specific techniques that we find useful for HA fillers?***

GM: Especially in the tear trough (nasojugal fold), I like an anterograde injection. I'll advance the needle down to just above the periosteum, walking along the inferior orbital ridge. And I'll push the filler in front of my needle. And I can watch the rise and control it as I advance. I think I'm creating less trauma by doing that—less shearing and cutting and less possibility of severing vessels than with retrograde injection, where I'm going to make my needle incision and then bring the filler out afterward. For nasolabial folds I do both anterograde and retrograde injections and a bit of fanning and what we used to call the bridging technique—coming in from the cheek at the side, and filling in the volume.

MG: I agree, but the only difference is that when injecting superficially, I use an injection technique very similar to with the collagens, where I'm doing small superficial injections instead of the linear injections.

CM: I agree; I do serial point injections for finer lines. In the nasojugal area, I feel it is safer to go retrograde because there's less chance of piercing a vessel and cannulating it and causing a periocular embolic phenomenon. That's theoretical; I don't know that it's ever happened. But to me it just seems a little safer.

NS: I use a multitude of techniques when injecting HAs. I believe that slower injection will result in less adverse events. I like to inject vertically, or perpendicular to the skin, in areas where I am trying to get elevation, like the cheek and small lips. I like to dilute HA in areas that have very superficial lines, and I like to gently massage the area with ultrasound gel to make sure the final result is smooth and consistent.

HS: ***Dr. Maas, this retrograde technique is something you employ for all HA products?***

CM: Yes. My thinking is that if you're injecting anterograde, in theory you could be pushing the vessels out of the way. But if you don't do it enough, you could actually cannulate a vessel. The chance of doing that is smaller if you're going retrograde: if you go across a vessel when you're inserting a needle you're going to immediately see some bruising, and you know you want to avoid injecting in that area. No one's studied this, but that's the way I feel about it, so that's how I do it.

HS: I usually use anterograde technique when injecting HAs below the dermis, except in the philtral column and labiomental crease where I inject retrograde to optimize definition. I use serial threading technique in these areas and also in the nasolabial folds, nasojugal folds, and pre-jowl sulci. I like to crosshatch in the nasolabial folds, especially when layering Restylane over Perlane or Juvéderm Ultra over Ultra Plus. I've moved more towards serial puncture with gentle post-injection massage in the midface, temples, and even for defining the vermilion borders. I find that slow injection of microaliquots with serial puncture is an especially useful technique to use with the higher G prime and viscosity HAs, Restylane and Perlane, to lift the midface efficiently with minimal tissue trauma.

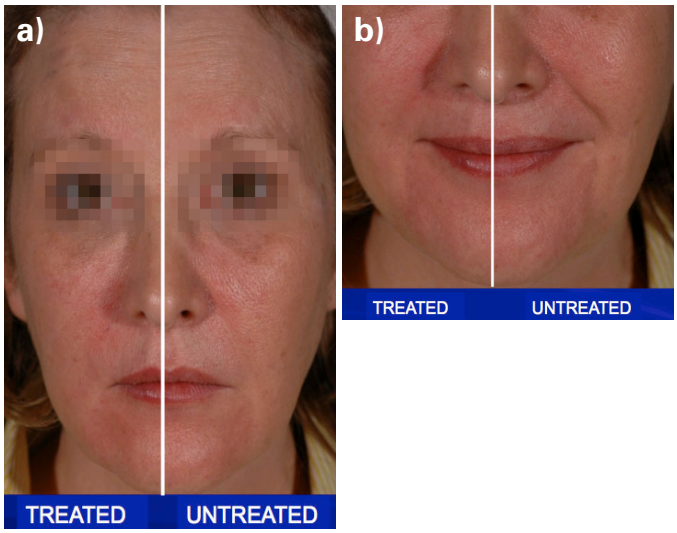
When I use Juvéderm Ultra Plus in the midface, I inject larger volumes at each point with anterograde serial puncture or threading to get some lift despite this product's lower G prime and viscosity. The water that the Juvéderm pulls in augments the lift. There are some differences in how I inject partially hydrated versus fully hydrated HAs. I inject just inside the vermilion border with Restylane, which is partially hydrated, as I find this produces better lip eversion than injecting directly into the vermilion border, which can then get blurred after water is absorbed. I inject directly into the vermilion border with Prevelle Silk, just as I used to with Cosmoplast or Zyplast collagen fillers. If using Juvéderm for the lips, I will add Prevelle Silk to define the vermilion border since it won't pull in water and thus gives a more precise line (Figure 10).

When injecting intradermally with Belotero Balance or Prevelle Silk, I inject retrograde for precise placement in the desired tissue plane, with serial threading or serial puncture "blanch" technique.[17]

NEW INDICATION FOR AN HA FILLER

HS: ***In 2011, an HA filler received U.S. FDA approval for the first time for submucosal implantation for lip augmentation in patients over the age of 21. How do you feel that this new***

FIGURE 10. a-b) Volumetry with non water-absorbing fillers. The left side shows the patient before injection. The right side shows results immediately after injection of 2 cc fully hydrated HA (Prevelle Silk) supraperiosteally to nasojugal fold, intradermally to nasolabial fold, submucosally to lips and superficially to vermilion border plus 2 cc crosslinked collagen (Evolence) subdermally to nasolabial folds, mid and lower face. Patient also received abobotulinumtoxin A (Dysport) to upper and lower face. Note lack of tissue edema with two fillers that do not absorb water after implantation.



Courtesy of Hema Sundaram MD

approval, for small particle HA (Restylane), will impact the use of HA fillers in the US?

NS: For years these products have been used off label. I believe that most patients know this, yet with FDA approval comes the ability for the companies that supply these products to market and promote the new indication. This will increase the overall market and improve awareness of these products.

MG: I know I speak for many, if not all physicians, who want more direct-to-consumer information regarding HA fillers and appreciate the studies that were conducted to gain this indication.

GM: An FDA indication for facial fillers beyond the nasolabial folds was long in coming. Direct-to-consumer information concerning HA usage for lip rejuvenation, based on real objective studies, will benefit both physicians and patients in understanding our use of fillers for the aging face.

FUTURE NEEDS

HS: ***Are there enough HAs in our toolbox, or are there specific demands for others?***

GM: The first thing is whether we have a need for products that are not yet in the United States, such as Juvéderm Voluma or Restylane SubQ, in addition to the fillers we already have?

HS: Restylane SubQ and Juvéderm Voluma are available outside the U.S. Voluma is currently undergoing phase 3 (pre-approval) FDA studies in the U.S. The G prime and viscosity differ for these two products, although their clinical purpose is similar—they are implanted subdermally to provide tissue contouring with greater lift and longevity.

GM: One problem we have is that when we really volumize the face, it becomes a very expensive enterprise. If we're using 6 to 8 cc of filler, we're up at several thousand dollars. Many of my patients just can't afford that. It would be nice to have a filling agent that is a bit more robust and packs more into a syringe with a little bit less expense and less need to keep changing syringes back and forth. So is that Voluma, is that Restylane SubQ?

NS: When you get Voluma you will find that it helps fill a void in the U.S. In Canada I would just like some HAs that are finer like the ones I create with diluted product.

MG: I would like an HA filler with more lift. I totally agree with Dr. Monheit about volume. I would like a filler that came in a multi-use bottle, where we could extract the amount of filler that we needed for each patient.

CM: Those are areas where there's some opportunity for sure. At the end of the day, it's going to be a very interesting paradigm for the average doctor to figure out which products he's going to use. A lot of this is going to come down to price, unless there's some tremendous advantage that's offered by one product over another.

HS: It's worth noting that U.S. FDA studies for approval of fillers are done solely with implantation into the mid to deep dermis of nasolabial folds. So when a product comes to market, anything outside is relatively uncharted territory. Products may behave the same way within these narrow study confines even though they have quite different physicochemical characteristics that give them unique clinical profiles as a result of variations in lift, tissue spread, and tissue distribution. We have to put products through their paces post-FDA approval to truly understand how best to use them.

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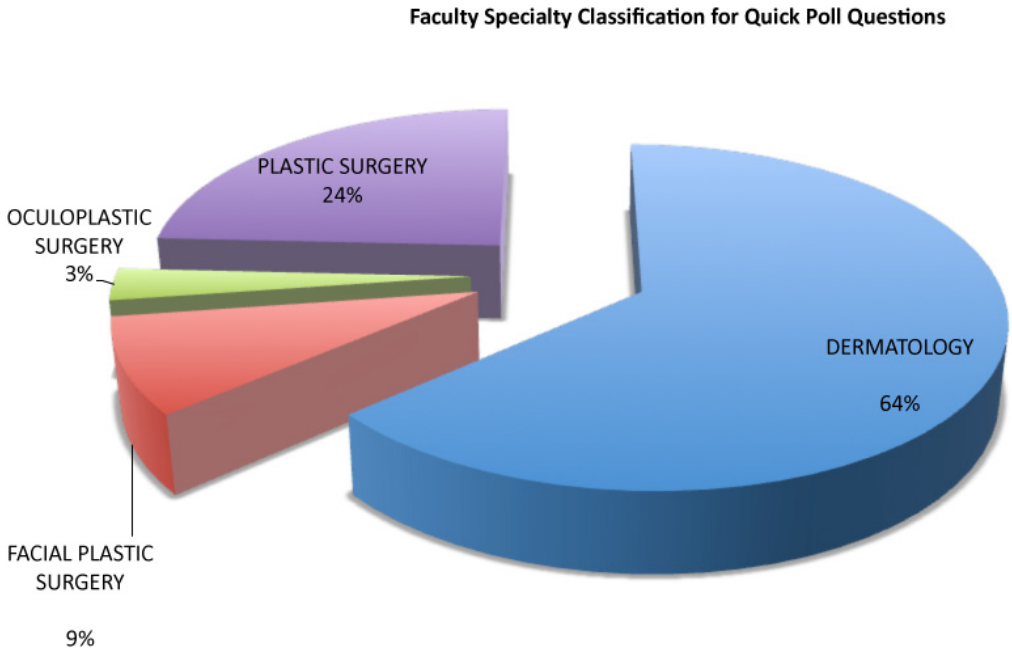
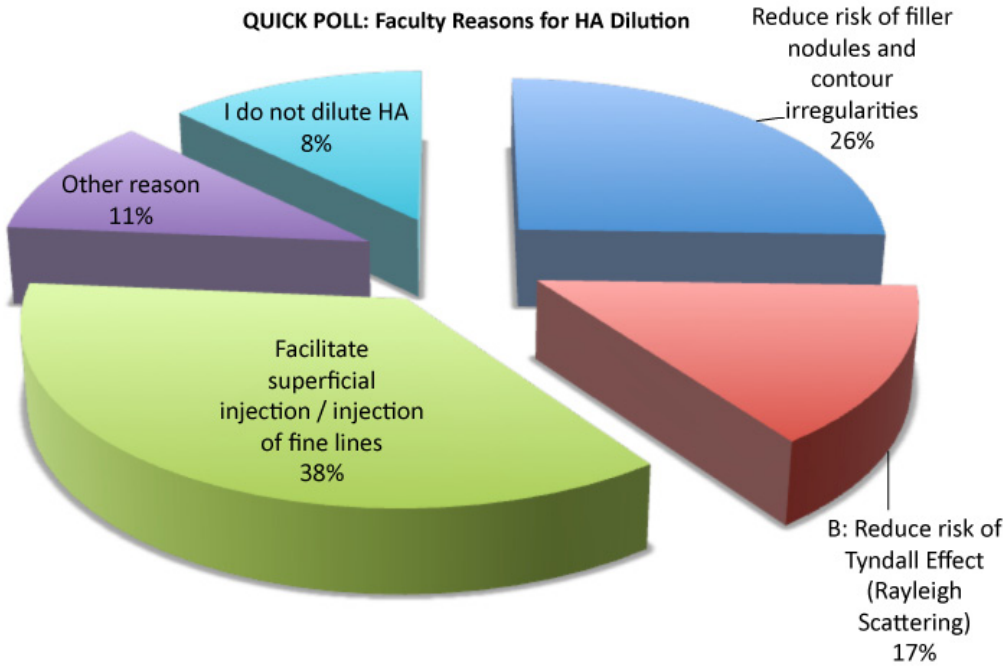
ADDRESS FOR CORRESPONDENCE

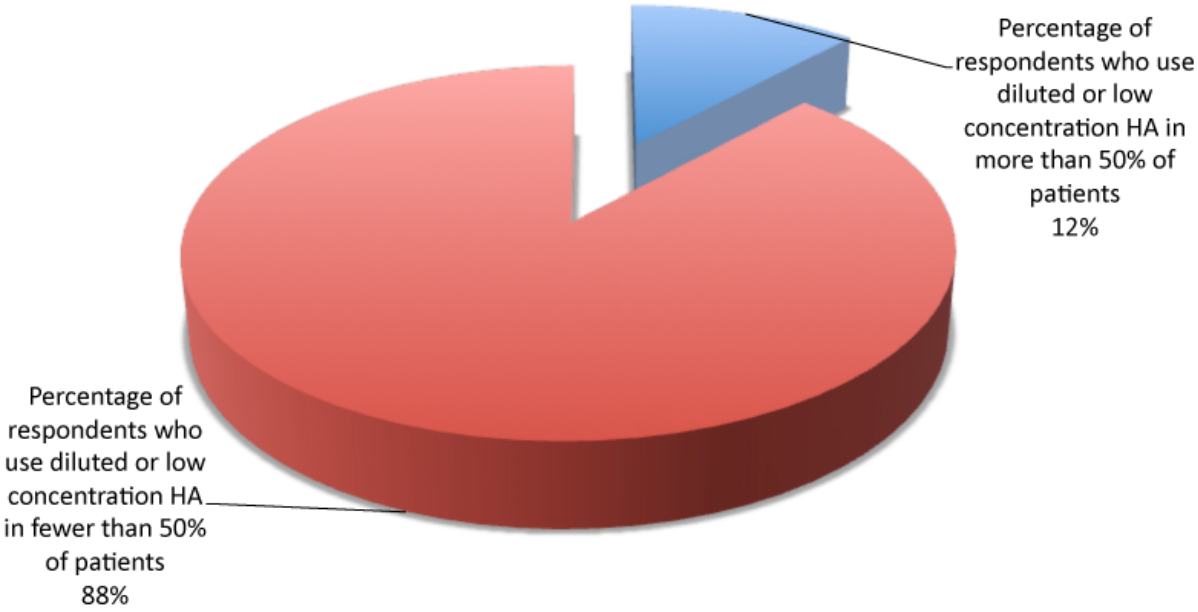
Hema Sundaram MD
11119 Rockville Pike, Ste 205
Rockville, MD 20852
Phone:.....(301) 984-3376
E-mail:.....hemasundaram@gmail.com

Quick Polls

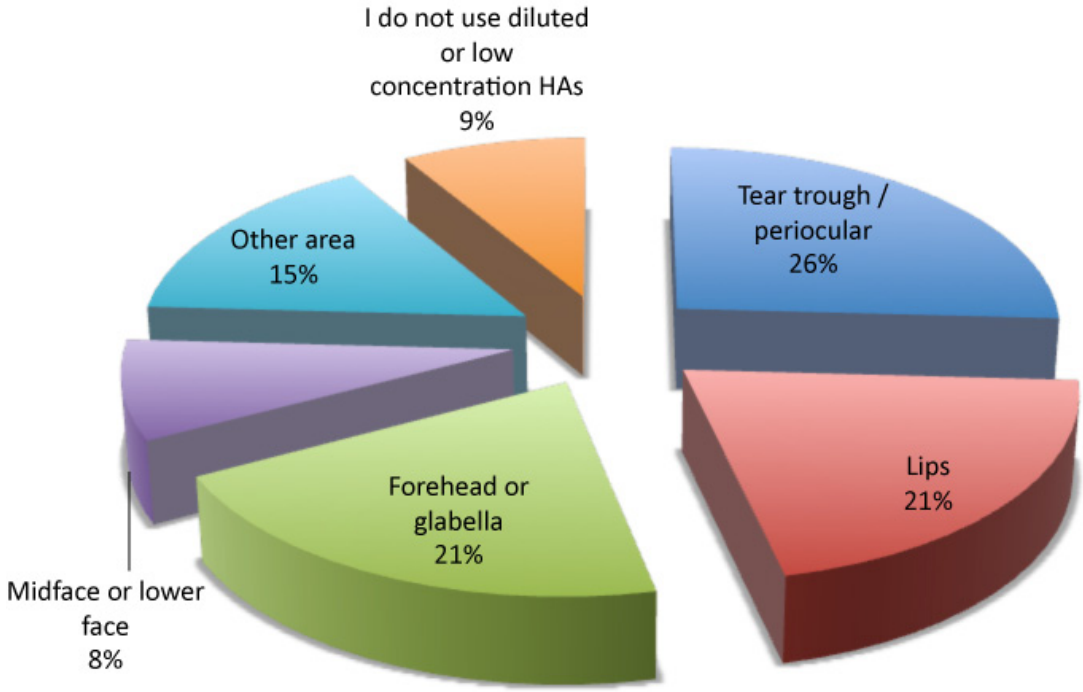




QUICK POLL: Faculty Usage Percentage of Diluted HA or Low Concentration HA in Patients

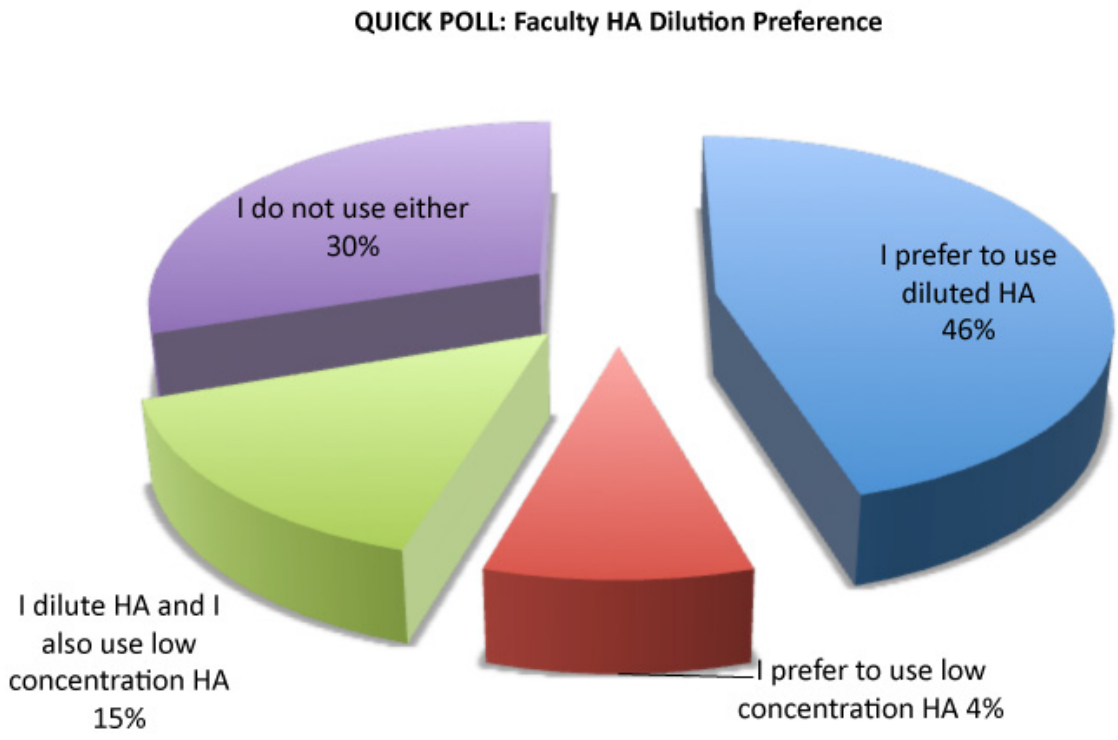


QUICK POLL: Faculty Usage Frequency of Diluted HA or Low Concentration HA



Diluted HA = Juvéderm or Restylane

Low Concentration HA = Prevelle Silk



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 (D), 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)

Midface Volumizing With Calcium Hydroxylapatite

Derek H. Jones MD
University of California at Los Angeles, Los Angeles, CA
Skin Care and Laser Physicians of Beverly Hills, Beverly Hills, CA

ABSTRACT

Injectable volumizing of the cheeks to correct age-related lipoatrophy is commonly performed off-label with hyaluronic acid, poly-L-lactic acid, and calcium hydroxylapatite. A case of a 72-year-old male with age-related cheek lipoatrophy treated with calcium hydroxylapatite is presented.

J Drugs Dermatol. 2012;11(suppl 3): s31-s32.

CASE VIGNETTE

A 72-year-old Caucasian male with a history of pituitary tumor resection 20 years prior and prostatectomy 12 years prior presented with a desire to treat facial lipoatrophy of long standing duration related to advancing age and lean body mass. Other than well-controlled hypertension, he was in good health with no related comorbidities.

Patient Management

Treatment options for midface volumizing[1,2] were thoroughly reviewed with the patient, and risks, benefits, and indications for each option were reviewed. After electing for injectable volumizing with calcium hydroxylapatite, areas to be injected were cleansed with alcohol and demarcated with a surgical marker. Treated areas included the atrophic mid-malar area, the lateral sub-malar area, and the nasolabial folds. Four 1.5 cc syringes of calcium hydroxylapatite were each admixed with 0.2 cc of 2% lidocaine with epinephrine 1:100,000. Each syringe was injected through a 28G thin-walled 3/4-inch needle, using a slow injection with linear anterograde and retrograde techniques strictly in a subdermal plane. Care was taken in the areas around the angular artery in the superior nasolabial fold area and the around the parotid gland in the inferior sub-malar area to avoid damage. Six cc total were injected. No significant adverse events were noted and the patient reported high satisfaction at one week follow-up (Figure 1).

DISCUSSION

Options for midface volumizing include hyaluronic acid, poly-l-lactic acid and calcium hydroxylapatite.[1,2] Much of the initial research with these fillers was conducted on patients with human immunodeficiency virus (HIV)-related facial lipoatrophy, often requiring volumes of 12 cc or more. Using this model, it became quickly apparent that lipoatrophy related to age and lean body mass was also an excellent indication. Calcium hydroxylapatite is an excellent option for this indication, with durability of correction that lasts for about one year. In the authors experience, average volume requirements for age or lean body mass lipoatrophy such as presented here are in the range of 6 cc. While none of these fillers carry a specific FDA-indication for midface volumizing in the non-HIV infected individual, newer forms of hyaluronic acid are currently undergoing study for this indication.[1] It is notable that hyaluronic acids are reversible with hyaluronidase in rare instances of adverse events or misplaced product.

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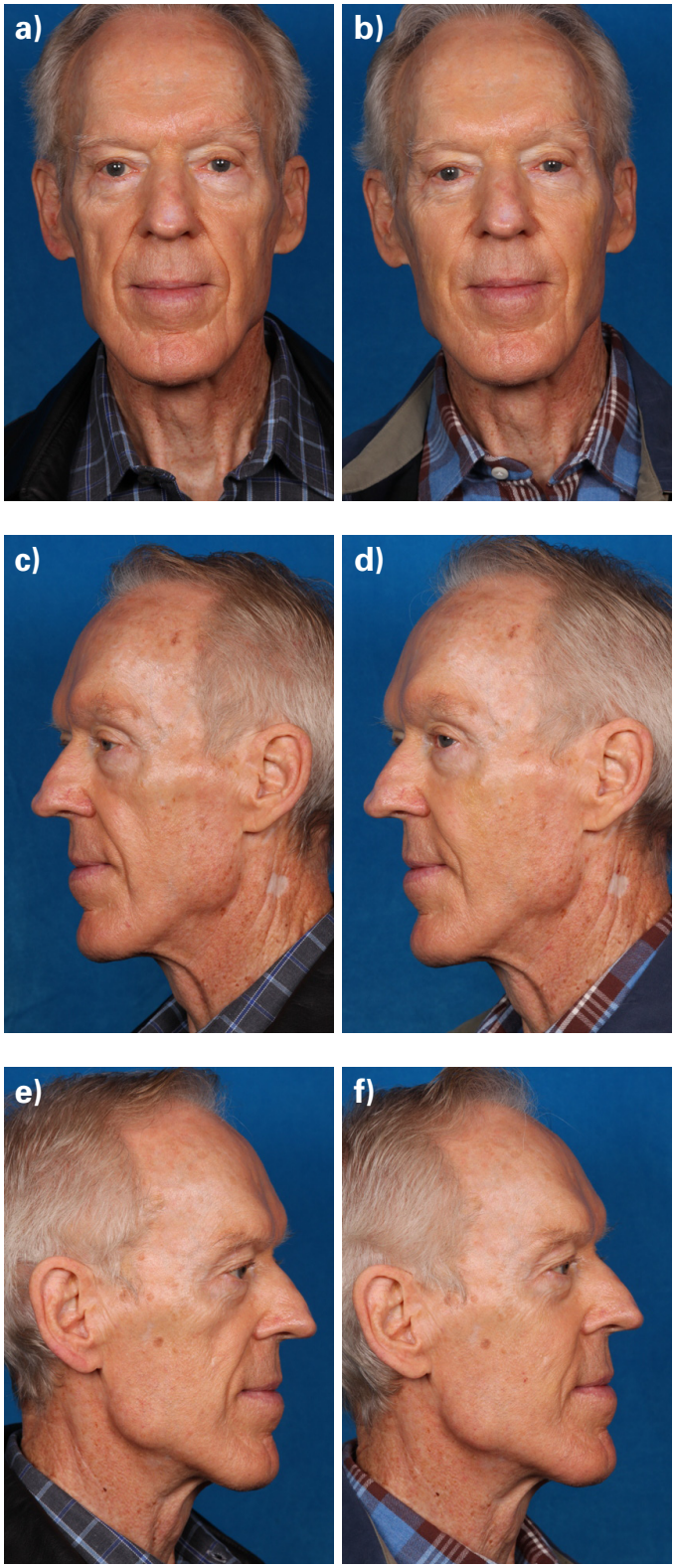
2. Jones D. Volumizing the face with soft tissue fillers. *Clin Plast Surg.* 2010;38(3):379-390.

FIGURE 1. Frontal views of the patient **a)** before and **b)** one-week after volumizing for facial lipoatrophy related to age and lean body mass with 6 cc of calcium hydroxylapatite. **c-d)** Right and **e-f)** left lateral views.



ADDRESS FOR CORRESPONDENCE

Derek H. Jones MD
9201 West Sunset Blvd. Suite 602
Los Angeles, CA, 90069
Phone:.....(310) 246-0495
Fax:.....(310) 246-0496
E-mail:.....derekjonesmd@gmail.com

COMMENTARY

I agree with Dr. Derek Jones' choices of approved agents. For a novice injector, I think both of us would be happier if the product used was reversible, and so the use of a hyaluronic acid filler that can be reversed with hyaluronidase would be most appropriate. Poly–L–lactic acid would create a new subcutaneous connective tissue scaffold gradually over several injection sessions and would be a wonderful alternative product to use. It is also particularly useful when the overlying skin has become very thin due to photodamage as it can be most helpful in the dermal repair process. Calcium hydroxlapatite is a completely synthetic filler. The smooth round polished beads of calcium hydroxyl apatite are suspended in a carboxymethylcellulose carrier medium. (When my patients look puzzled, I tell them it is like "liquid lettuce"). This product is injected subcutaneously and will mold and sculpt very nicely on the first day, especially if—as Dr. Jones does—the product is mixed with some local anesthetic to make things more comfortable for the patient and less viscous for the injector.

In our practice, we ask the subjects to return in follow-up in about two weeks. At this point any swelling that had occurred as a result of the treatment needle intrusions has settled, and it is not uncommon for the individual to request some further augmentation. As with any cosmetic procedure, excellent photos as seen here are a must throughout the treatment process. Patients often like to have copies too to show to their friends. They also help the patient to know when a re-treatment would be appropriate.

FURTHER READING

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Jean Carruthers MD
University of British Columbia, Vancouver, BC, Canada

Full-Face Rejuvenation With a New Range of Customized Hyaluronic Acid Fillers

Hugues Cartier MD[a] and Hema Sundaram MD[b]
[a]Centre Medical Saint Jean, Arras, France
[b]Sundaram Dermatology, Cosmetic & Laser Surgery, Rockville, MD

ABSTRACT

A patient presenting with multiple facial indications received a full-face rejuvenation with a new range of hyaluronic acid fillers, including five different products with distinct physical properties. Choice of filler and the injection volume were provided for each indication, as well as various injection techniques for lip enhancement. Aesthetic improvements and high patient satisfaction were observed nine months after the injections.

J Drugs Dermatol. 2012;11(suppl 3):s33-s34.

CASE VIGNETTE

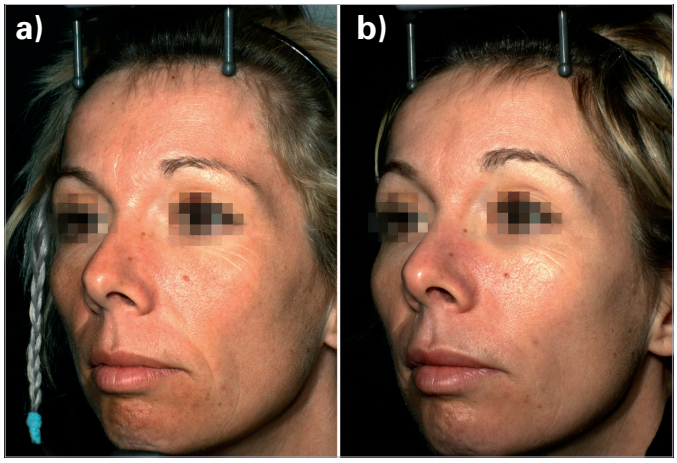
A 42-year-old Caucasian woman presented with the complaints of deepening nasolabial folds and loss of cheek volume (Figure 1). She also wished to have a better defined Cupid's bow on her upper lip. The morphology of her face was examined at rest, lying down and sitting up, and upon various facial movements (smiling, puckering of the lips, puffing out of the cheeks). To achieve best results, one needs to think three-dimensionally, considering not only the defect itself but also the nearby structures. Specifically for this patient, cheek enhancement should be performed first, which smoothes the cheek folds and improves the adjacent nasolabial folds so that less filler product is required. After discussion with the patient, it was agreed to treat her cheek folds, tear troughs and crow's feet as well, in order to achieve a more natural looking result.

A new, customized range of hyaluronic acid gel fillers (Emervel®, [hereafter referred to as HA_E]) was selected by the treating physician. The aim of the manufacturing process for these fillers is to facilitate their tissue integration after implantation. The rheologic properties of these fillers have been discussed in a recent publication. The five products of the range have the same total HA concentration (20 mg/mL) and well-differentiated physical properties due to varying degrees of cross-linking and gel calibration.[1] One of these products (HA_E Touch) is currently available without lidocaine, while the other four are available with or without lidocaine.

DISCUSSION

All the HA products were injected via sharp needles. Malar enhancement was performed with supraperiosteal and subcutaneous injections of the most volumizing product in the range (HA_E Volume) with retrograde fanning technique; 0.6 mL was injected on each side at the first visit and 0.9 mL on each side at touch-up three weeks later.[2] The firmest product of the range, (HA_E Deep), was injected during the first session into the deep dermis of the nasolabial folds with retrograde linear threading and fanning technique, in order to achieve a long-lasting result despite the frequent movement of the perioral region.[3] During the second, touch-up session, this product was injected into the mid dermis perpendicular to the direction of the nasolabial folds to create a firm support against the mid face. Tear troughs were corrected with a small volume of the firmest product (HA_E Deep), to avoid over-correction. The needle was inserted inferior to the orbital rim and then, after advancement to the orbital rim at the supraperiosteal level, 0.1 mL was injected in microdroplets deep to orbicularis oculi on each side, followed by tissue massage. As an alternative, a product with a smaller gel calibration (e.g., HA_E Classic) would also have been appropriate.[4] To smooth the periorbital and cheek areas, the gel of the smallest calibration (HA_E Touch) was injected superficially with retrograde crosshatching and fanning technique. Lips were both contoured and enhanced using the product specifically intended for this indication (HA_E Lips), injected submucosally with retrograde technique via the supplied 30 G ultra-thin-wall needle for treatment precision, which is essential for lip rejuvenation.[5] A series of side-by-side serial puncture injections perpendicular to the vermilion border was performed to enhance the upper and lower lips. Retrograde linear threading injection along the upper vermilion border and in the philtrum projected the upper lip forward. The total volume injected at baseline and touch-up three weeks after was 6.7 mL. At nine months, the patient remained improved compared to baseline and was very satisfied with the durability of the results. No specific side effects were reported other than expected injection site reactions.

FIGURE 1. a) Before injection. **b)** Nine months after injection.



A full-face approach to treating several indications simultaneously has been increasingly used to achieve well-balanced and natural looking results. Soft tissue fillers of different physical properties allow adaptation to individual facial indications. The range of HA fillers used for this patient by the treating physician [Cartier] contains five distinct products, and provided effective, safe, and satisfactory results in full face rejuvenation.

Editor's note: Higher HA crosslinking produces a firmer product, and larger gel calibration (a measure of the solid phase of the HA gel) produces more volumizing capability.

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ADDRESS FOR CORRESPONDENCE

Hugues Cartier MD
Centre Medical Saint Jean
8 square Saint-Jean
62000 Arras, France
Phone:.....+33 0321713434
Fax:.....+33 0321713226
E-mail:.....hcartier@hotmail.com

COMMENTARY

Facial rejuvenation with injectable fillers is an art. Hugues Cartier, a dermatologist from the north of France, presents a case of a very successful facial rejuvenation, using a new range of customized HA-fillers, which is the first family of HA-fillers that has robust clinical data available. Besides this, two points highlight the level of importance of this vignette: (1) It clearly shows that one or two syringes alone are not sufficient in facial rejuvenation. Even younger women, as Hugues's patient, might need quantities up to 6-7 ml. (2) It also shows that beyond all the present cannula hype, facial rejuvenation using the needles provided by the manufacturer will lead to beautiful results. Summing it up with a good range of products, sufficient volume, appropriate needles and a sense for three-dimensional aesthetics, Hugues allows readers to follow an example for creating similar results in their patients.

Berthold Rzany MD ScM
Charité–Universitätsmediczin Berlin, Germany

Pan-Facial Volumization With Poly-L-Lactic Acid (PLLA)

Laurie Casas MD
Division of Plastic Surgery, University of Chicago Pritzker School of Medicine, Chicago, IL

ABSTRACT

Poly-L-Lactic Acid (PLLA) is a useful dermal stimulatory agent that can be used to correct large volume loss from aging. This illustrative case demonstrates incorporating PLLA injections into a longitudinal plan that can address many aspects of aging.

J Drugs Dermatol. 2012;11(suppl 3): s35-s37.

CASE VIGNETTE

A 66-year-old African-American female presented in 2008 with the chief complaint of facial aging. The patient has had multiple facial procedures since age 50 including upper and lower blepharoplasty (age 50), coronal forehead lift (age 53), and face and neck lift (age 56). She now wished to look more youthful without another surgical procedure but stressed the desire for a natural look. On exam, the patient had significant malar and temporal soft tissue volume loss and loss of mandibular height and thickness which had created a significant prejowl sulcus bilaterally and loss of definition at the mandibular angle (Figure 1).

Patient Management

Since 2008 the patient has been managed with quarterly neurotoxin injections for the corrugator muscles and corners of the brow to maintain brow position and with a skin care regimen that includes daily tretinoin 0.1% and 4% hydroquinone creams to correct uneven skin tone and to stimulate the superficial skin layers. In addition, her pan-facial volume loss was treated with four vials of poly-L-lactic acid (PLLA) (Sculptra Aesthetic) over two months in two sessions. Each vial was hydrated for 48 hours with 5 cc of sterile water. At each session, 2 cc of sterile water and 2 cc of 1% lidocaine were added to each 5 cc vial of hydrated PLLA creating a solution of 9 cc per vial. 9 cc or greater dilutions have allowed for a consistently low rate of nodule formation. 18 cc total PLLA suspension was injected per session. 25-gauge 1.5-inch needles have been used as the author has gained experience, so that for most areas a fanning technique can be used to decrease the number of needle sticks required. Although subdermal, pre-periosteal, and subfacial injections planes are all off label, we have found that the key issue is the even and consistent delivery of the PLLA. The exact plane is chosen based on the tissue characteristics and the desired effect. At each session the volumes used to treat each facial zone were as follows: malar region in the sub-dermal plane (4 cc), temples in the subfacial plane (2 cc), prejowl sulcus in the pre-periosteal plane (1 cc) and mandibular angle in the sub-dermal plane (2 cc). Injection entry points were chosen based on anatomical considerations and treatment areas to be injected. The temple was accessed at the base of the fossa and at the hairline, the malar injection entry sites were inferior to the zygomatic arch medial to the lateral canthus, the mandibular angle was approached along the mandibular border posterior to the facial artery and the prejowl sulcus was injected medial to the sulcus with a triangular depot injection. The two PLLA treatment sessions were performed over a period of two months. The patient's results at two years demonstrate more even skin tone and volume restoration of the malar and temple areas with improvement of the prejowl areas and mandibular angles (Figure 2).

CONCLUSIONS

Pretreatment assessment of this patient was key to developing a longitudinal plan to address her multifaceted aspects of aging. The brow ptosis, although minimal, is treated every 3–4 months with neurotoxin to maintain brow position. The large area of significant bony (mandible) and soft tissue (malar, temples perioral) loss could be treated with either fat injections or PLLA.[1-4] This illustrative patient's uneven skin tones and minimal loss of elasticity are being treated with topical adjuvant therapies. Topical tretinoin is known to improve skin quality and enhance collagen synthesis following resurfacing treatments.[5]

FIGURE 1. Pre-treatment facial views of a 66-year-old female with significant pan-facial volume loss with orbital malar grooves, bilateral prejowl sulcus, marionette lines, and loss of mandibular border definition.

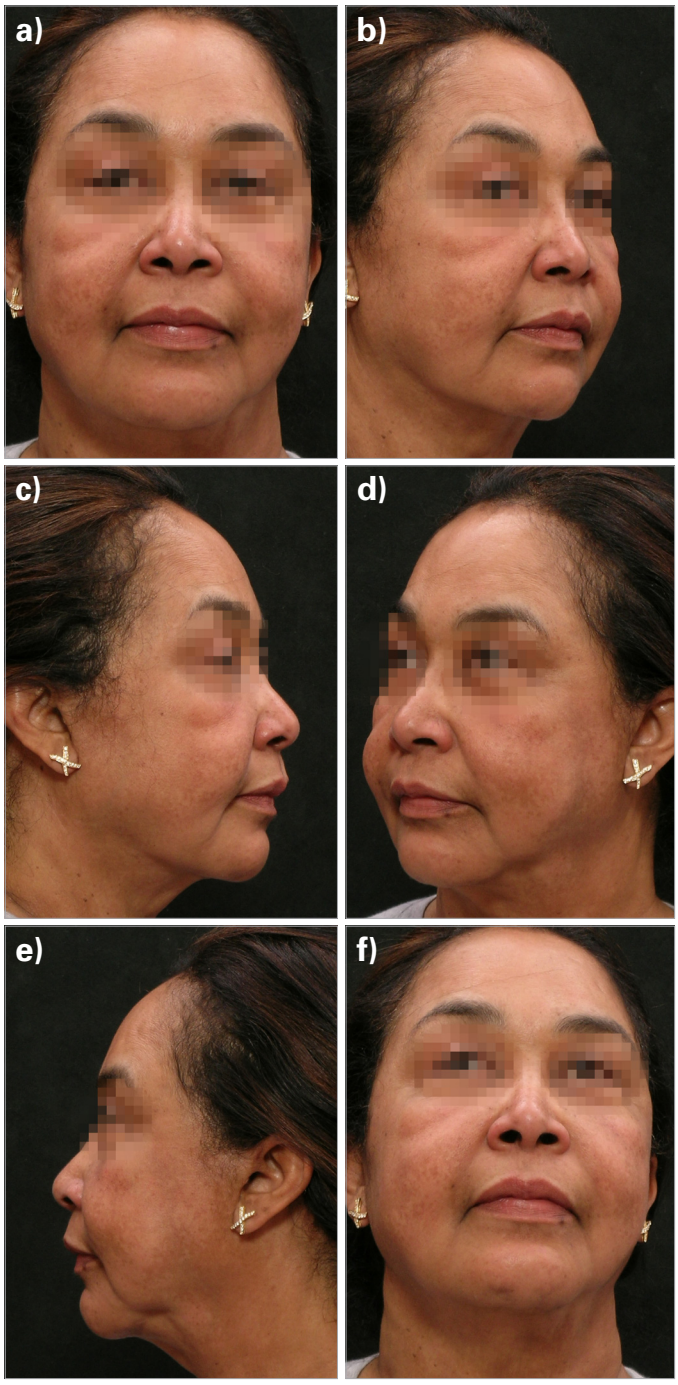
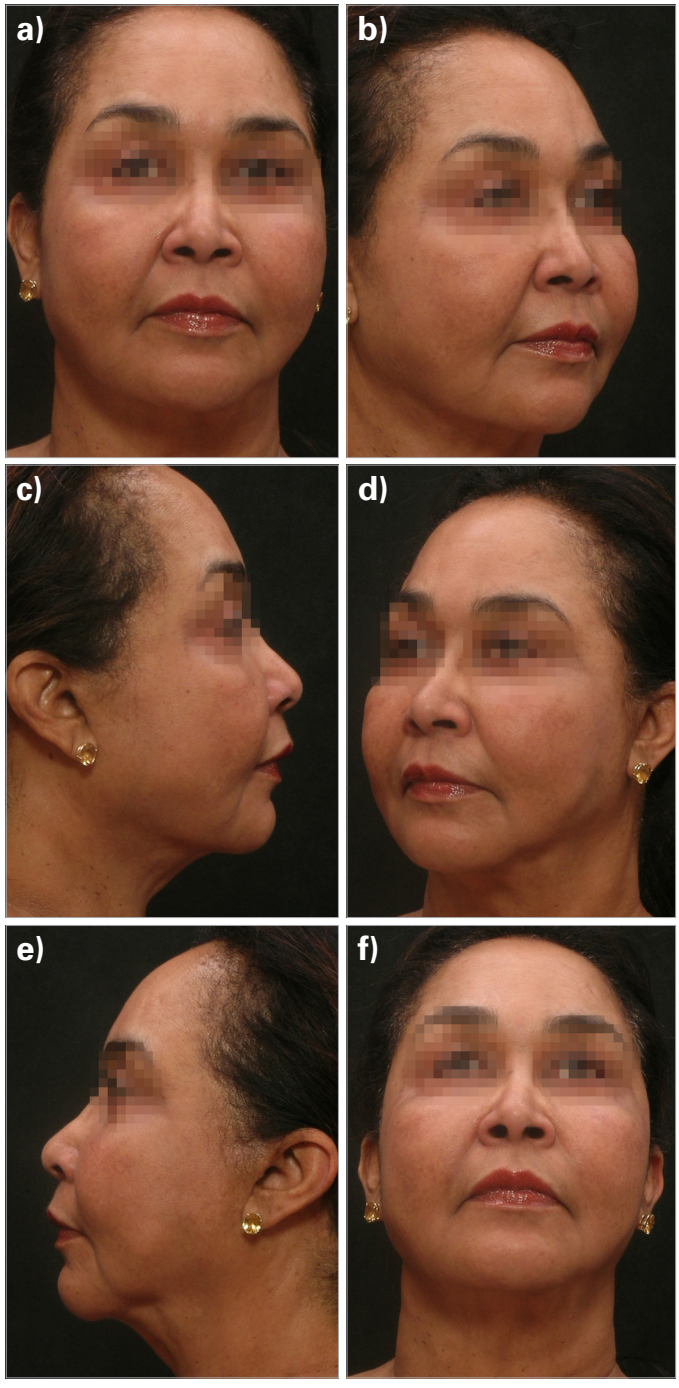


FIGURE 2. Two-year result following combination therapies utilizing a longitudinal plan which included four vials of PLLA over two sessions to malar region (sub-dermal plane), temples (subfascial plane), prejowl sulcus (pre-periosteal plane), and mandibular angle (sub-dermal plane), neurotoxin every three to four months to maintain brow position, and topical daily tretinoin 0.1% and 4% hydroquinone.



In our 106 consecutive patient series, the daily use of topical tretinoin appeared to have a synergistic effect on the collagen formation during PLLA treatments. The anticipated amount of PLLA to achieve full correction was halved in patients who used this daily skincare regimen. In this patient series we found that daily topical use of tretinoin pre and post PLLA treatment was synergistic in optimizing skin quality and the patient's neocollagenesis from PLLA treatment sessions.[6]

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ADDRESS FOR CORRESPONDENCE

Laurie Casas MD
2050 Pfingsten, Suite 270
Glenview, IL 60026
Phone:.....(847) 657-6884
E-mail:.....lcasas@casas.md

COMMENTARY

Dr. Casas describes successful pan-facial volumization with poly-l-lactic acid (PLLA). PLLA, although often included in the category of dermal fillers, is in reality not a filler. PLLA is a biostimulatory agent that leads to fibroblast collagen formation. Thus, unlike the immediate results seen with dermal fillers, delayed "more natural" results may be seen with PLLA. Initial difficulties with PLLA induced nodule formation have been markedly lessened with greater dilution of the injected material.

We have published data showing new collagen formation following injections with calcium hydroxyapatite into human skin. Soon to be published data shows similar electron microscopic evidence of new collagen formation following PLLA injections. Pan-facial volumization with PLLA leads to a natural non-surgical cosmetic enhancement of aging skin.

David J. Goldberg MD JD
Skin Laser & Surgery Specialists of NY/NJ
New York, NY

The Use of Blunt-Tipped Cannulas for Tear Trough Correction

Patrick Trévidic MD
Private Practice, Paris, France

ABSTRACT

A patient presents with skin atrophy and negative vector. The patient's tear troughs and mediojugal grooves were injected with a middle cohesivity hyaluronic acid (HA) filler. Deep implantation of a middle cohesivity HA product minimizes the risk of contour irregularities, and the supraperiosteal plane of the tear trough and eyebrow is anatomically safe for filler implantation. A HA product is preferable for these anatomically unforgiving areas as it can be removed or adjusted if needed by injection of hyaluronidase.

J Drugs Dermatol. 2012;11(suppl 3): s38-40.

CASE VIGNETTE

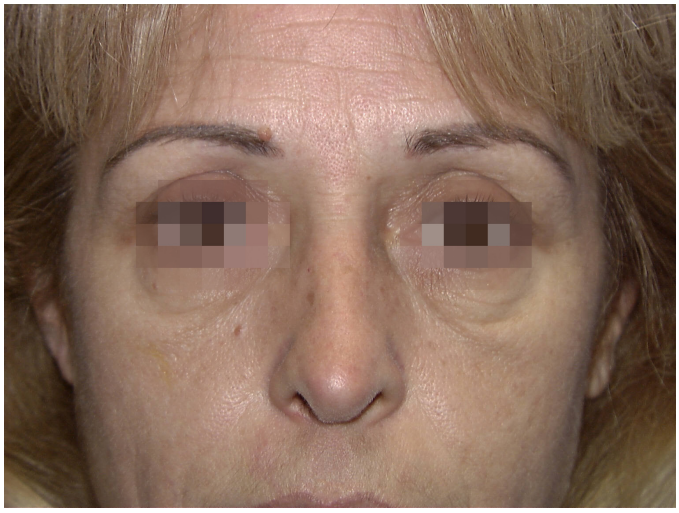
A 42-year-old patient presented complaining that her eyes looked tired and stating that she did not wish to have surgery (Figure 1). She had not had previous surgery or injectables and was in good general health. She was concerned about procedural pain and wanted to avoid a significant change to her face. During examination, the findings included skin atrophy and a negative vector when her face was viewed in profile (Figure 2).

The patient's tear troughs and mediojugal grooves were injected with a middle cohesivity hyaluronic acid (HA) filler. The medial portion of the eyebrow was also injected with the HA filler to correct the sunken eye effect due to volume loss in the upper eyelid.1 To minimize pain and bruising, a rigid 27G 42 mm blunt microcannula was selected for injection (Figure 3).

The injection process was as follows: After local anesthesia of the site selected for insertion of the microcannula, an entry hole was made with a sharp 26 G needle, to obtain the appropriate depth and direction for the microcannula during injection (Figure 4). The microcannula was then passed into the supraperiosteal plane, with the nondominant hand lifting the tissue to keep the cannula in this deep plane, and the microcannula was gently moved on the bone until it reached the inner point of the tear trough. The same process was repeated to move the microcannula along the bone to the head of the eyebrow (Figure 5). The HA filler was deposited with retrograde technique as the microcannula was being withdrawn. On each side, 0.7 mL of HA filler was injected into the tear trough and 0.3 mL into the medial eyebrow. Tissue massage was avoided to prevent displacement of filler from the desired location.

Deep implantation of a middle cohesivity HA product minimizes the risk of contour irregularities (Figure 6), and the supraperiosteal plane of the tear trough and eyebrow is anatomically safe for filler implantation (Figure 7). A HA product is preferable for these anatomically unforgiving areas as it can be removed or adjusted if needed by injection of hyaluronidase. U.S. FDA-approved products that are appropriate for this procedure include cohesive polydensified matrix HA (Belotero Balance), small particle HA (Restylane and "nonparticulate" HA (Juvéderm Ultra). Appropriate products that are currently approved in Europe but not in the U.S. include "single-phase" HA (Teosyal Global Action). The use of a blunt injection microcannula allows a single entry point for each area rather than the several entry points that would be required with a sharp needle. It also decreases patient discomfort and the risk of damage to blood vessels or nerves. It is recommended that periocular injection of fillers should be performed with the patient seated rather than reclining in order to achieve accurate filler placement and help avoid overcorrection.

FIGURE 1.



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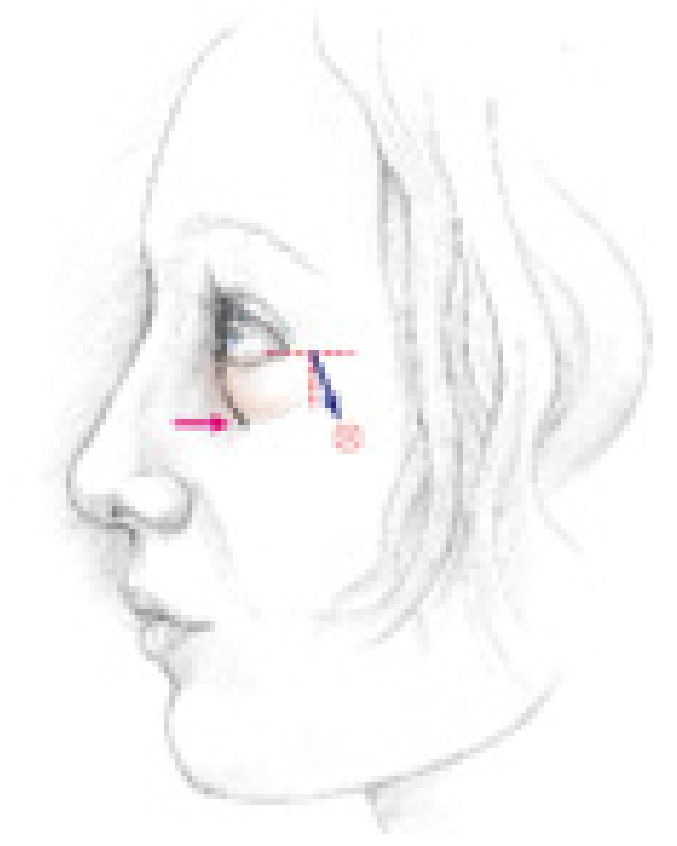

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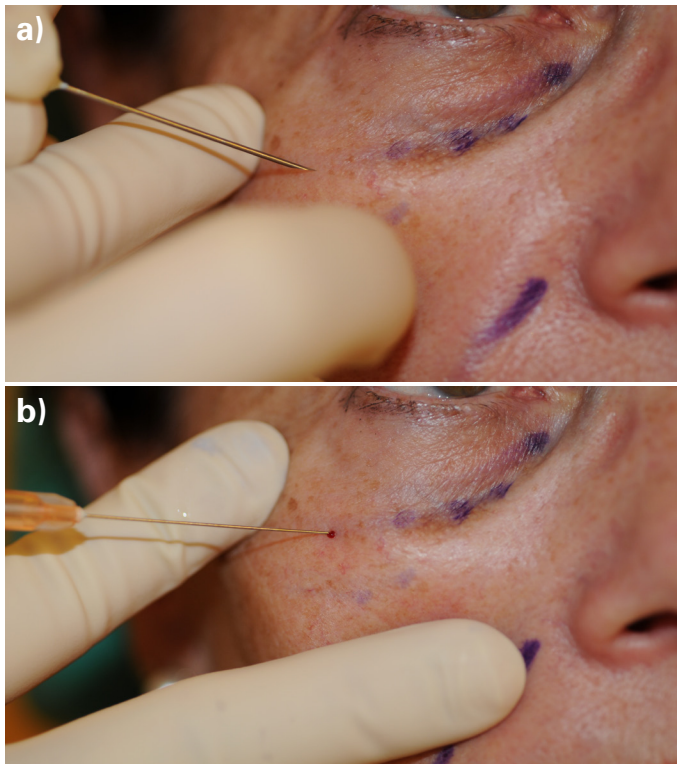

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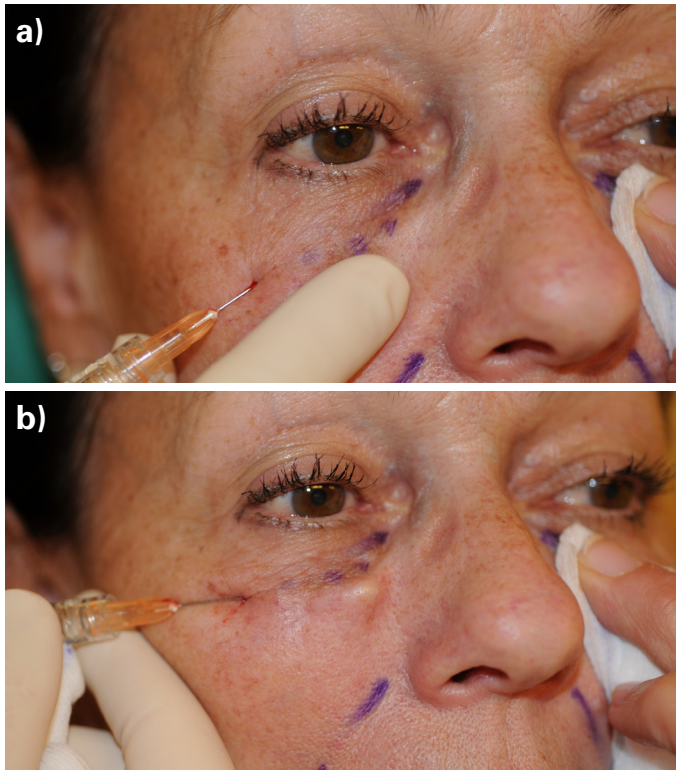

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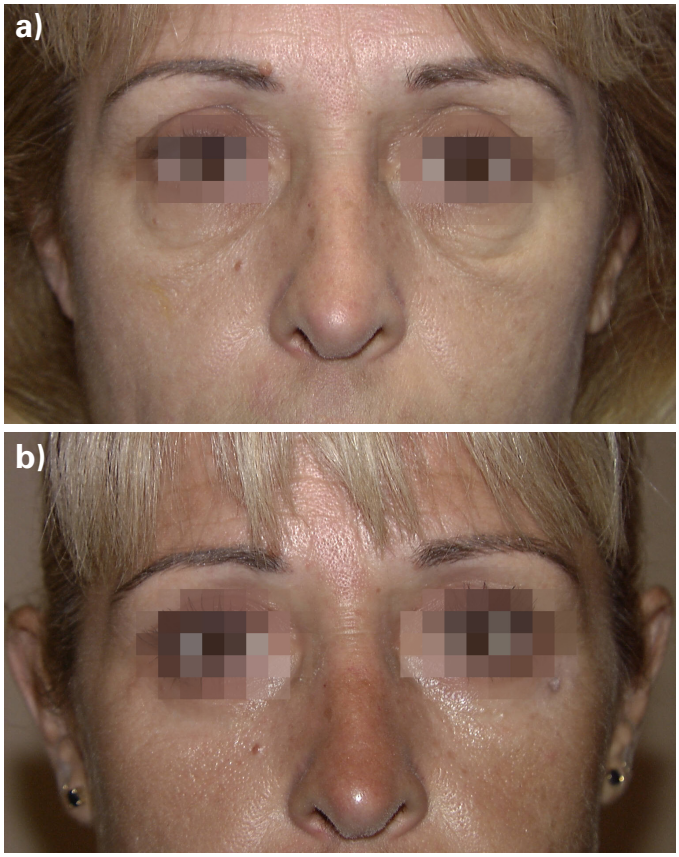

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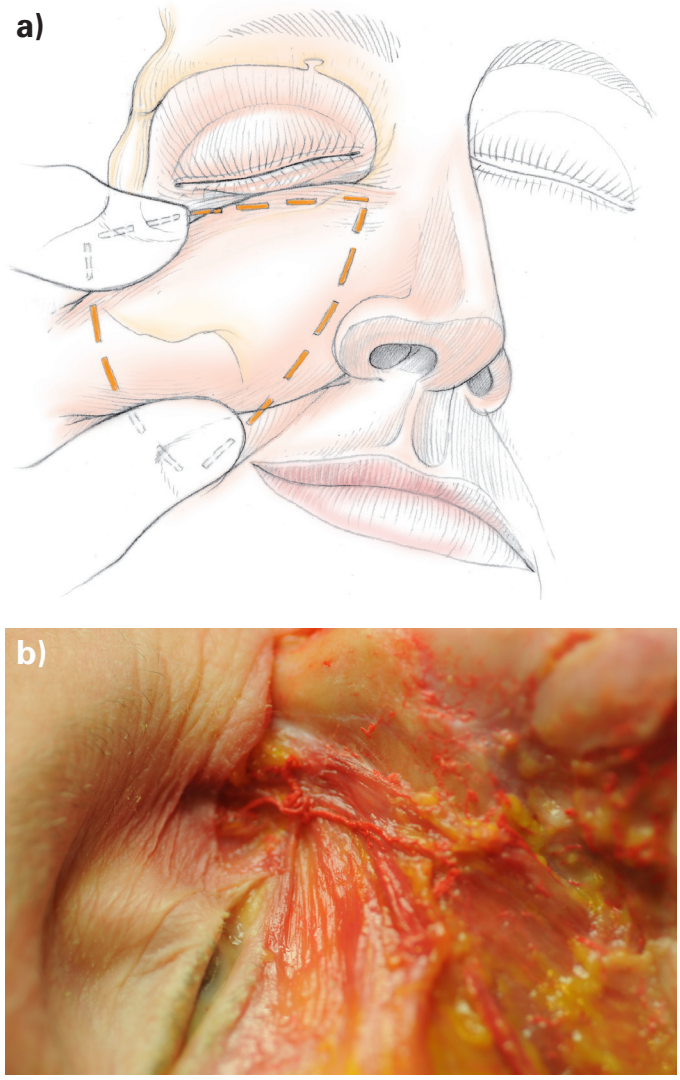

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ADDRESS FOR CORRESPONDENCE

Patrick Trévidic MD
7, rue de Sontay
75116 Paris, France
Phone:.....+01 45 01 64 15
Fax:.....+01 45 00 89 81
E-mail:.....patrick.trevidic@orange.fr

COMMENTARY

It is safe to use a blunt-tipped cannula in the tear trough and eyebrow areas. Unlike needles, the blunt-tipped cannula does not usually injure blood vessels or nerves and thus minimizes bruising. It is also much less painful. An HA is best as it is "erasable" with hyaluronidase. It is not good to massage the area as you want the product to stay where you have injected it with a nice smooth injection technique, as you withdraw the cannula. Never overcorrect the area. It is better to treat over two visits and go slowly. Have the patient sitting up so you can see the full extent of the depression. This technique provides a wonderful rejuvenation of the face.

Rhoda S. Narins MD
Dermatology Surgery and Laser Center, New York, NY

Hyaluronic Acid "Skinboosters" and Use of Blunt Injection Microcannulas

Marina Landau MD
Dermatology Unit, Wolfson Medical Center, Holon, Israel

ABSTRACT

Skin aging is attributed to a decrease and change in quality of elastic and collagen fibers, as well as ground substance of the skin. Hyaluronic acid "skinboosters" is a novel concept targeting improvement of skin viscoelasticity by placing small amounts of specifically designed HA based products over large areas of dermis or superficial subdermal plane. This serial procedure is performed either by short needle or blunt microcannulas.

J Drugs Dermatol. 2012;11(suppl 3): s41-43.

CASE VIGNETTE

A 37-year-old healthy Caucasian woman was seen for cosmetic consultation. Her main complaint was dissatisfaction with her facial skin quality, smile wrinkles, and acne scars on her cheeks. Her past medical history included acne flare ups in her twenties, successfully treated with oral minocycline, and topical tretinoin. On examination a few medium depth boxcar scars were noted on her cheeks, accompanied by skin "collapse" on smiling, creating cheek wrinkles in motion (Figure 1).

After thorough discussion of possible therapeutic approaches, a series of treatments using a small particle "skinbooster" hyaluronic acid (HA) filler designed to improve skin hydration and elasticity (Restylane® Vital) injected subcutaneously by blunt cannula was started. After three monthly injection sessions (2 ml of product per session), significant improvement in acne scars and skin quality were noted (Figure 2).

Changes in the viscoelastic properties of the skin are among the most striking changes in the aging face. At the molecular level, these changes are attributed to the decrease of elastic and collagen fibers as well as the ground substance content, responsible for hydration of deeper skin compartments in younger skin.[1]

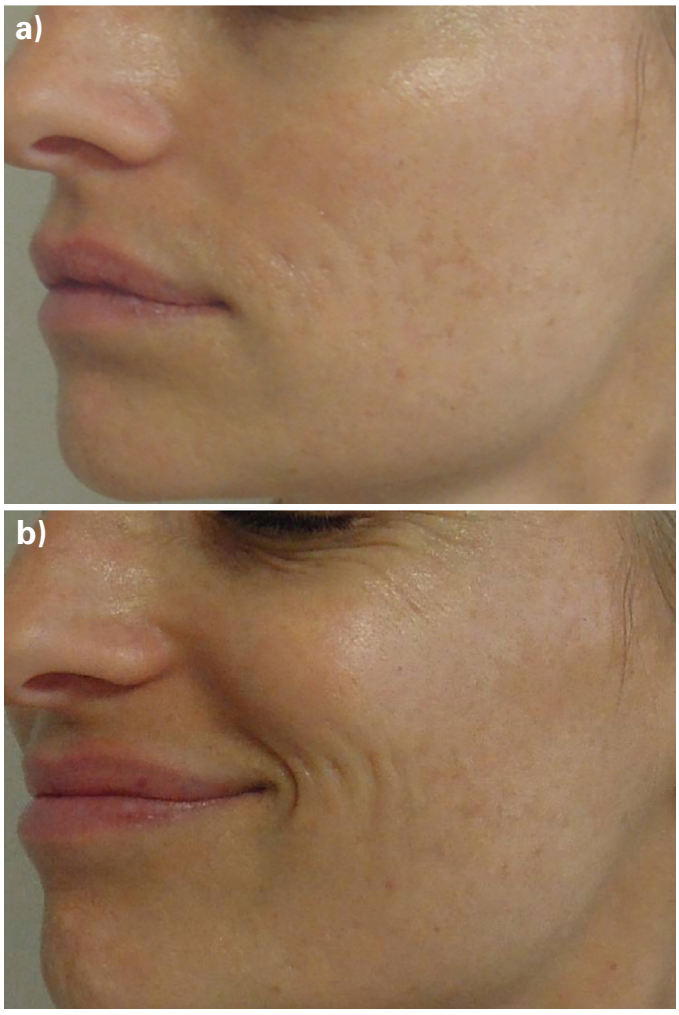
Clinical studies have demonstrated that treatment of facial skin with non-animal stabilized hyaluronic acid (NASHA) small particle gel results in improvement in its elasticity along with clinical improvement in appearance of the skin.[2,3] These results were the basis for the development of the "skinbooster" or revitalization concept.

The product used in this patient for the purpose of "skinboosting" comprises small particles suspended in a smooth and relatively thin non-animal stabilized hyaluronic acid (NASHA) gel (20 mg/ml).

The procedure is performed by either multiple microdroplet injections or more recently by blunt cannula subcutaneous delivery of the product. To place microdroplets repetitively at the same skin depth, we use 32 gauge short (4 mm) mesotherapy needles. During each treatment session, the patient receives about 25 regularly spaced 0.02 ml injections of the "skinboosting" HA filler on each side (Figure 3).

When using a flexible blunt cannula, the injection plan is drawn prior to the treatment. The plan is composed of lines in fan-like fashion placed perpendicular to the direction of the smile wrinkles (Figure 4a). The cannula in inserted through a skin opening parallel to the skin surface to deliver the product superficially (Figure 4b). Usually 2–3 skin openings are sufficient to deliver the product to the whole cheek and perioral area.

FIGURE 1. A 37-year-old patient before treatment: **a)** skin irregularities and acne scars at rest; **b)** smile lines on motion due to decreased skin viscoelasticity.



The aim of both needle- and cannula-assisted techniques is to evenly distribute the product in the dermis or immediate subdermal plane without specifically targeting a wrinkle or scar. Usually a series of three monthly treatments is required.

The advantage of a blunt cannula over the sharp needle is that it is less traumatic and less painful. The risk of bruising from fifty needle injections is significantly higher than from 2–3 cannula insertion holes. In addition, in the case of subdermal scarring, as usually is the case in acne scar patients, the cannula-assisted procedure releases retractions and subdermal fibrotic bands.

This author's experience shows that placing small quantities of "skinbooster" HA over relatively large areas of the dermis and immediate subdermal plane results in improved skin elasticity (disappearance of smile lines) and smoother skin surface. The procedure is effective and well tolerated.

FIGURE 2. After three monthly sessions of "skinbooster" small particle hyaluronic acid (HA) filler with cannula-assisted injections: **a)** improved skin quality and smoothening of acne scars; **b)** elimination of smile lines.

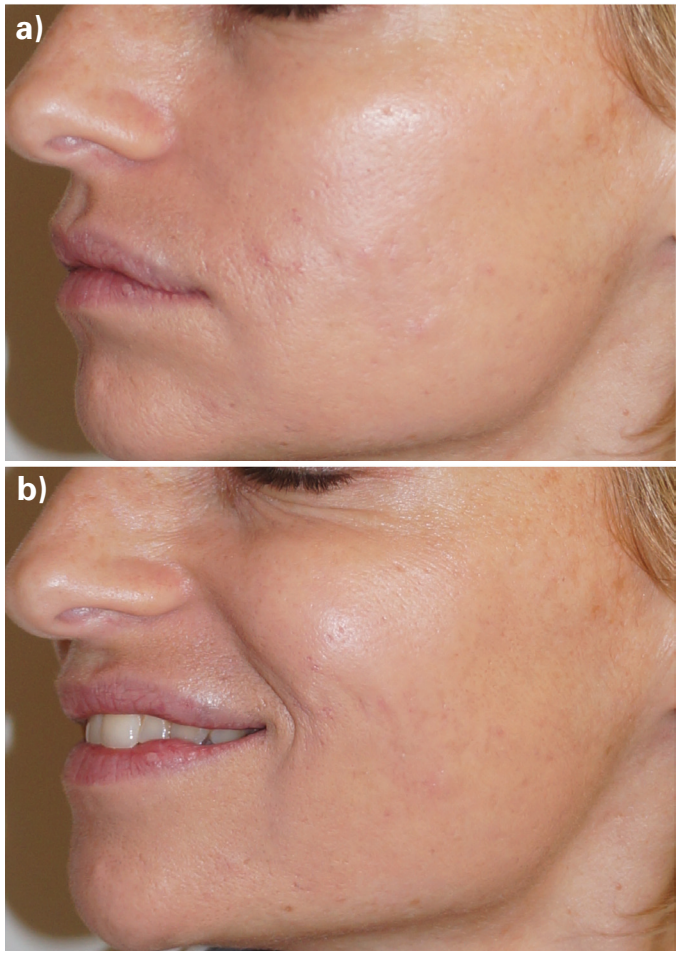


FIGURE 3. Multiple microdroplet injections plan. Each point receives 0.02 ml of "skinbooster" HA.

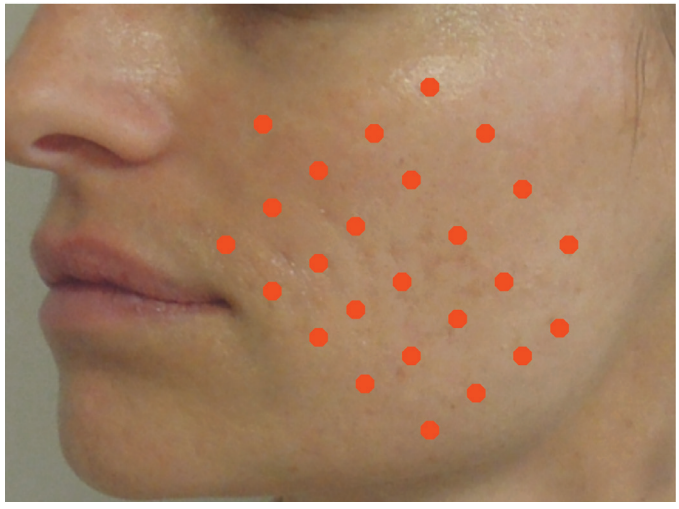
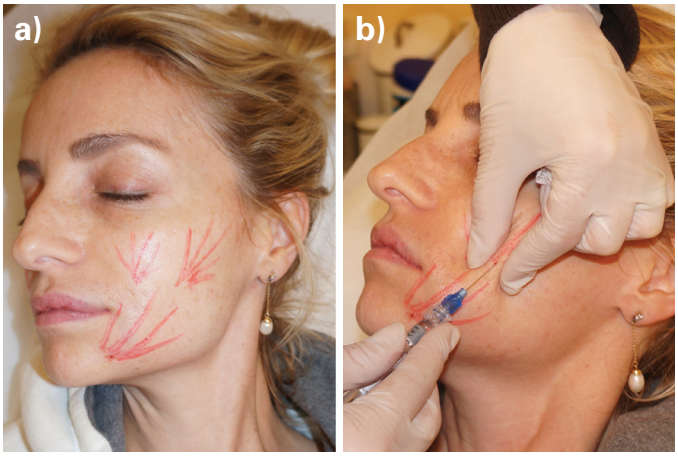


FIGURE 4. a) Injection plan for cannula-assisted procedure: lines in fan-like fashion placed perpendicularly to the direction of the smile wrinkles. **b)** Cannula is inserted through a skin opening parallel to the skin to deliver the product superficially.



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ADDRESS FOR CORRESPONDENCE

Marina Landau MD
56 Joshua Ben Nun Street
Herzlia Pituach, Israel
Phone:.....+972-9-9505151
Fax:.....+972-9-9544579
E-mail:.....dr.marinaclinic@gmail.com

COMMENTARY

In her case vignette, "Hyaluronic Acid 'Skinboosters' and the Use of Blunt Injection Microcannulas," the author describes a novel approach of small particle hyaluronic acid (HA) injection injected subcutaneously by blunt microcannula, with a significant improvement in acne scar and skin quality. For more than two years, many publications have focused on the real improvement in filler techniques provided by the blunt microcannula, which significantly diminishes pain, swelling, bruising, and also recovery time, especially when used for the cheeks, tear troughs, marionette lines, temples and hands. However the blunt tip characteristic of these needles does not allow injection of the superficial dermis, but only the superficial plane of the hypodermis. So the improvement will come from the pharmacologic characteristics of the HA as well as the mechanical stimulation (or micro-needling) of this plane of injection. Moreover the HA needs to be quite thin (low in viscosity) to be adapted to the plane of deposition, and minimal crosslinking seems required.

In regards to the diameter of the microcannula, 27 gauge is preferable to 30 gauge as the thinner cannula is more flexible and could be more traumatic to tissue. The best choice may be a rigid microcannula with a length between 40 to 50 mm and a thin wall that provides a large inner diameter relative to its gauge size to facilitate filler flow and minimize tissue trauma.

To optimize the improvement in rhytides, a very small dose of botulinum neurotoxin (10% of the regular dosing used for treatment of the upper face musculature) can be injected as an adjunct to the HA. In other hands, the technique of superficial volumetry, as described here by Dr. Landau, may also encompass superficial lipofilling in the same plane . The secretion of hormones from the live micro-deposits of fat can also help to optimize aesthetic improvement.

In summary , the author provides a carefully innovative and minimally invasive technique, demonstrating that the present and the future of the injection of fillers will not merely be a simple classic HA injection with a sharp needle.

Benjamin Ascher MD
Paris Academy, Paris, France

FURTHER READING

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Deep Lifting Volumetry With Calcium Hydroxylapatite and Hyaluronic Acid Fillers

Hema Sundaram MD
Sundaram Dermatology, Cosmetic & Laser Surgery, Rockville, MD

ABSTRACT

A 77-year-old woman who complained of a "falling face" and declined surgery was treated with deep implantation of high G prime calcum hydroxylapatite and small particle hyaluronic acid fillers for maximal lifting effect and also with botulinum neurotoxin type A. Combined treatment with soft tissue fillers and neuromodulators can optimize results and potentially improve their longevity.

J Drugs Dermatol. 2012;11(suppl 3): s44-s47.

CASE VIGNETTE

A 77-year-old woman presented complaining that her face was "falling" and she looked tired and old (Figure 1a). She declined surgery. Examination in repose revealed Fitzpatrick skin phototype I with moderate pan-facial loss of skin elasticity, as determined by skin snap testing. There was volume loss from her mid, lower, and upper face, with prominent nasolabial folds, oral commissures, pre-jowl sulci, and nasojugal folds, and some temporal hollowing. She had bilateral upper eyelid ptosis, which was more pronounced on the right side with partial compensation via eyebrow elevation. There were rhytides in repose, which deepened on animation, in the glabellar, frontal, lateral periocular, and perioral regions, and also some "cobblestoning" of the chin.

Calcium hydroxylapatite (Radiesse®) and small particle hyaluronic acid (Restylane®) fillers were selected for volume restoration. Each was diluted with 2% lidocaine suspension without epinephrine to provide a final concentration of 0.3% lidocaine. CaHA was injected supraperiosteally and subcutaneously in 0.1 to 0.2 mL microaliquots with retrograde serial puncture technique to the midface via a 28G ¾ inch hollow bore needle, with periodic evaluation from above, below and obliquely. CaHA was also injected supraperiosteally into the pre-jowl sulci with retrograde linear threading. Small particle HA was injected via a 29G hollow bore needle 1.) subcutaneously into the nasolabial folds and oral commissures with anterograde serial threading and crosshatching, 2.) submucosally into the lips and the vermilion borders in microaliquots with anterograde serial puncture, 3.) subdermally above and parallel to the superior vermilion border and philtral columns with retrograde serial threading, and 4.) subcutaneously below and parallel to the inferior vermilion border and labiomental crease with retrograde serial threading. A total of 3 cc CaHA and 3 cc small particle HA were injected, with post-injection tissue massage where appropriate (Figure 1b).

The patient was also injected with abobotulinumtoxin A (Dysport®) to the glabella (50 units), frontalis (50 units), superolateral orbicularis oculi for brow lifting (2.5 units each side), lateral periocular region outside the orbital rim (20 units each side), depressor anguli oris (10 units each side), mentalis (5 units at each of two sites), and orbicularis oris (2.5 units at each of two sites superiorly and 2.5 units at each of three sites inferiorly). At follow-up five weeks later, the patient stated that she was very pleased with her results (Figures 2, 3, and 4).

CaHA and small particle HA fillers both have relatively high elastic modulus (G prime) and viscosity.[1] These two rheologic properties respectively confer tissue lifting capacity and contour stability. Particulate fillers with high G prime and viscosity are best suited to implantation subdermally, such as in the subcutaneous or supraperiosteal tissue planes,[2] where their

FIGURE 1. a) The patient in repose before treatment. **b)** The filler injection strategy.
Calcium hydroxylapatite Small particle hyaluronic acid

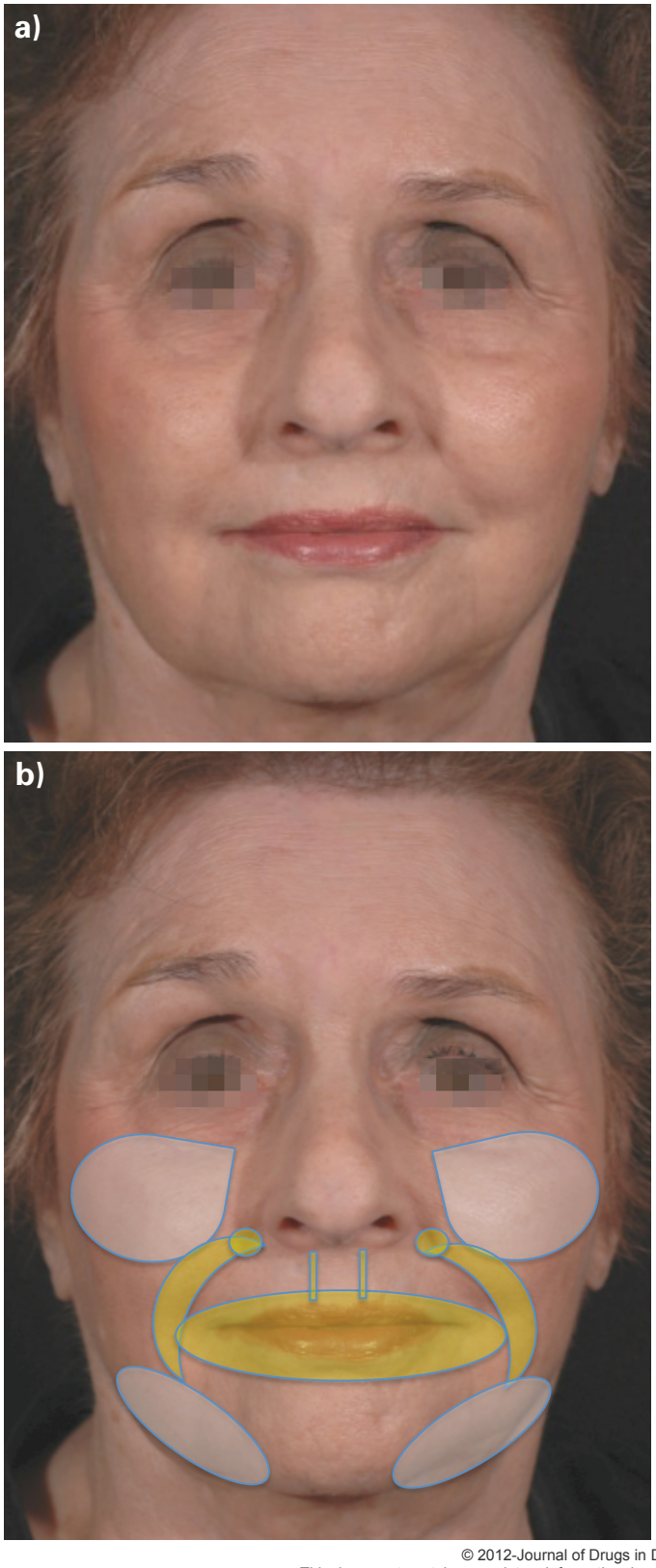
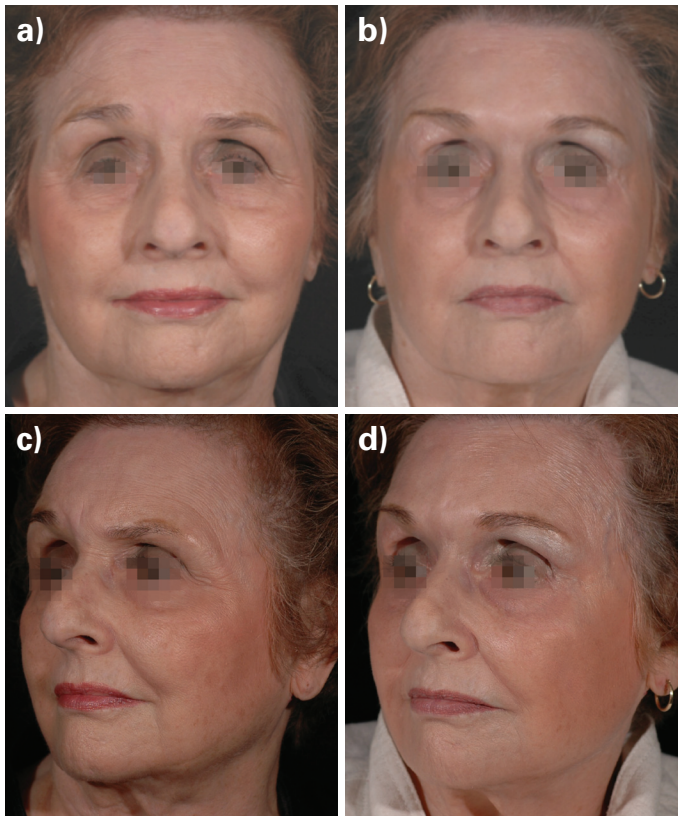


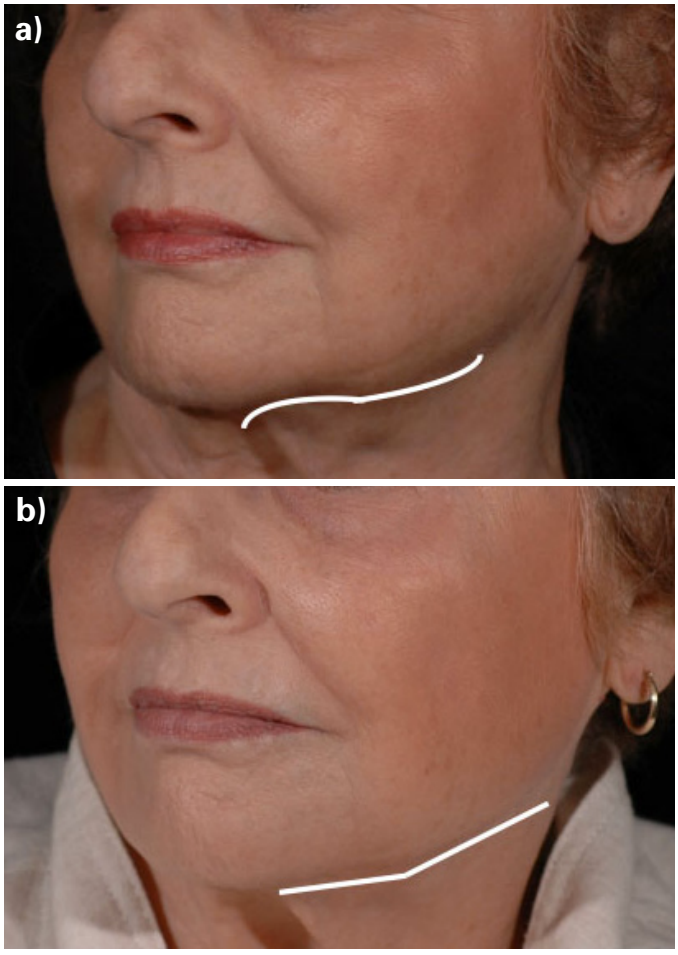
FIGURE 2. The patient in repose **a)** before and **b)** five weeks after CaHA + small particle HA, and BoNT-A injections. The left oblique views **c)** before and **d)** post procedure.



volume efficiency and contour stability enables small volume serial puncture, crosshatching, or threading to provide a vertical vectoring force upon overlying tissue that is upward and perpendicular to the skin surface. Filler dilution with lidocaine or saline somewhat decreases G prime and viscosity, as has been quantified for CaHA.[1] The resultant decrease in extrusion force during injection may decrease tissue trauma, and the increased softness facilitates post-implantation molding. Since these particulate fillers have limited water-binding capacity, resorption of most or all of the diluent would be expected post-implantation. Thus, provided adequate filler is implanted for full correction, there should be no significant impact on filler performance or longevity of results.

The rationale for not adding epinephrine when diluting fillers is that the tissue blanching from epinephrine might obscure blanching due to injection-related vascular compromise. Midface volumetry is key to addressing facial deflation, which is recognized as a cardinal feature of facial aging.[3] Volume-efficient lifting of the midface with a high G prime filler gives secondary improvement in the nasolabial and nasojugal folds due to vertical vectoring. It is noteworthy that this patient's nasolabial folds were still apparent after treatment, yet she ap-

FIGURE 3. The patient in repose **a)** before and **b)** five weeks after CaHA + small particle HA ,and BoNT-A injections. Note improvement in jaw line (white lines).



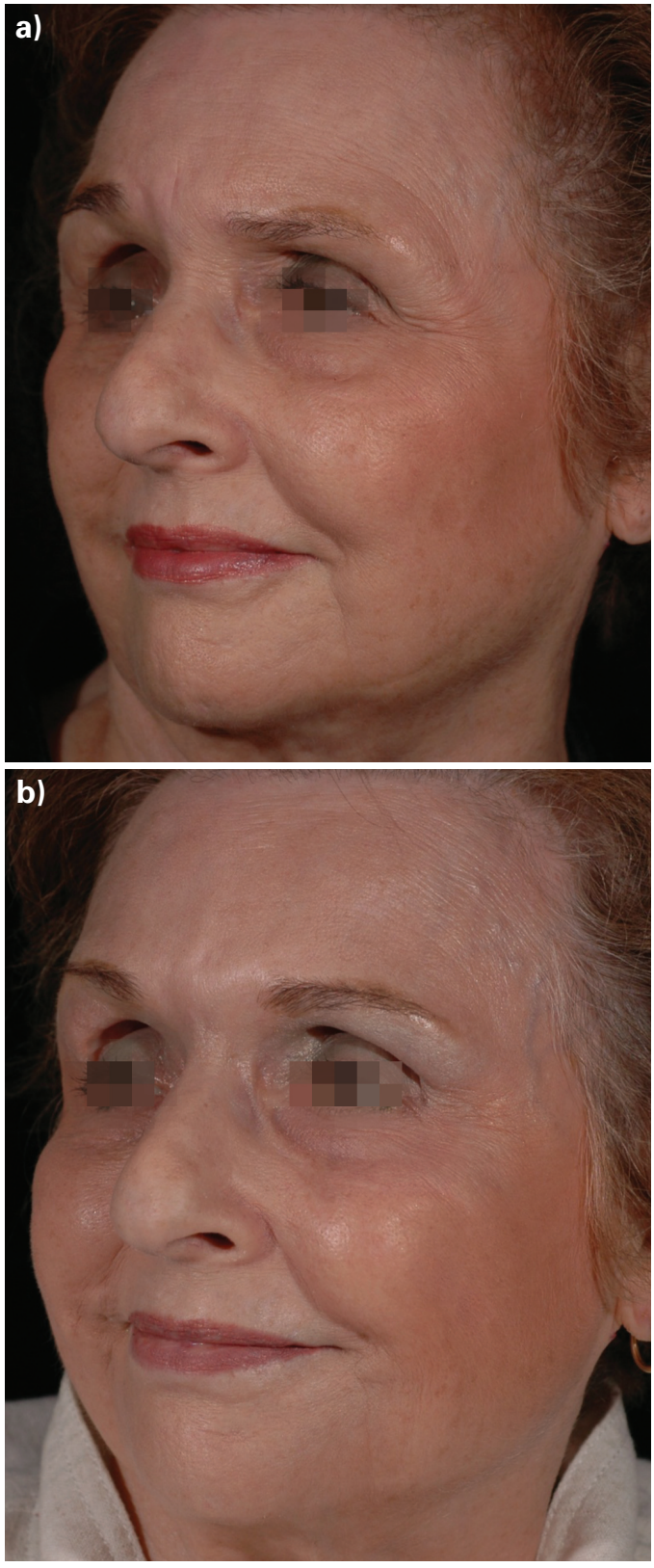
peared significantly rejuvenated. Over-filling of nasolabial folds can result in an aesthetically unappealing, simian appearance.

DISCUSSION

Recent availability in the U.S. of a high concentration, cohesive polydensified matrix HA with a tissue integration pattern appropriate for intradermal implantation (Belotero Balance®)[4] allows a multi-plane "sandwich" volumetry that can give effective and aesthetically appealing correction of deep nasolabial folds.[5]

When combining fillers and neurotoxin for same-day treatment, injection of fillers first allows precise tissue plane placement, as fluid boluses of neurotoxin could distort the tissue planes. Combined treatment has the potential to optimize the quality and longevity of results.

FIGURE 4. The patient in animation (smiling) **a)** before and **b)** five weeks after CaHA + small particle HA, and BoNT-A injections.



CONCLUSION

This patient's results illustrate the value of rheologic tailoring—the selection of fillers with the appropriate rheologic characteristics to achieve the desired clinical outcome. In this case, the selected fillers, calcium hydroxylapatite, and small particle hyaluronic acid, have good lifting capacity and contour stability by virtue of their relatively high elastic modulus (G prime) and viscosity. While filler rheology and other physicochemical characteristics can significantly influence the results that are achieved with pan-facial volumetry, other important determinants of the ultimate outcome include injection technique, implantation depth, and patient-specific factors such as skin elasticity and the individual tissue response to filler implantation. It was felt that this patient's specific concerns could be well-addressed with deep lifting volumetry alone, whereas other patients may benefit from multi-plane or "sandwich" implantation of fillers both beneath and within the dermis. Combined treatment with fillers plus neuromodulators has the potential to optimize the quality and longevity of these results.

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ADDRESS FOR CORRESPONDENCE

Hema Sundaram MD
11119 Rockville Pike, Ste 205
Rockville, MD 20852
Phone:.....(301) 984-3376
E-mail:.....hemasundaram@gmail.com

COMMENTARY

Dr. Sundaram presents an elegant example of deep, multiplanar combined filler and combination modality non-surgical facial rejuvenation. This case highlights the value of planning optimal planes for each area of the face with the complete rejuvenation picture in mind. Effective volumization of the mid face, jawline, chin and temples calls for deep deposition of filler, including at the supraperiosteal level to achieve the desired effect. Soft tissue augmentation ceases to replace bony angularity or contour at a certain point but, in these areas, augmentation close to the bone better preserves the skeletal contribution to facial shape. Given that aging also involves bone resorption, it stands to reason to "augment" the skeletal contour in addition to augmenting soft tissue/fat loss; in my opinion, this is in effect what is included in deep volumization of some of these areas. The available filler armamentarium allows for the use of multiple fillers for optimal results. I often combine CaHA and different hyaluronic acid fillers to treat different levels and problems. Simultaneous volumization and use of neuromodulators allows for a comprehensive rejuvenation and increases longevity of the filler.

Preserving the anatomy and dynamism of the nasolabial fold is well highlighted. Excessive filler, especially in the superficial plane, leads to an unnatural appearance and blocks the smile, creating dynamic distortion of the face. This often results from too much focus on the fold at the cost of ignoring volume loss in the mid face, where volume repletion lifts the fold effectively.

A very interesting aspect is this patient's lack of interest in surgery. It is important to counsel such patients as to the limits of what can be achieved aesthetically without surgery. I often find that "rejuvenation mishaps" happen when patients seek to inappropriately push the limit with non-surgical modalities. A discussion and understanding will prevent unaesthetic sequelae of this mistaken strategy. Dr. Sundaram has delivered a harmonious and powerful rejuvenation with a well-planned combination approach and meticulous attention to detail.

Haideh Hirmand MD
Cornell Weil Medical College/New York Presbyterian Hospital, New York, NY

CME Post-Test: Please select your best answer for each of the following questions and insert into the Answer Grid found on the Evaluation/Certificate Request Form on page s50. **Return your completed Evaluation/Certificate Request Form to *JDD*** by fax to (212) 213-5435, mail to 377 Park Avenue South, 6th Floor, New York, NY 10016, or to complete this activity online, please visit www.JDDonline.com in the Medical Education Library. Successful completion of the Post-Test is required to earn *AMA PRA Category 1 Credits*™. You must earn a passing score of at least 70% and complete the activity evaluation form in order to complete the course and receive a certificate for *AMA PRA Category 1 Credits*™.

1. Placing fillers in the cheeks and infraorbital regions draws attention to the eyes and deemphasizes which of the following?
   a. Malar fat pads
   b. Forehead and glabellar
   c. Lower one-third
   d. Nose

2. A youthful, feminine appearance is characterized by which of the following?
   a. A square-like jaw
   b. A narrow, petite jaw
   c. Deep hollows around the eyes
   d. A straight nose

3. What is the main difference between skin boosting and wrinkle filling?
   a. Skin layer to which the product is injected
   b. Area "coverage" instead of focal injection
   c. Number of treatments
   d. The effect on secondary collagen production

4. What is the most important advantage of blunt microcannulas?
   a. Decrease of risk of intravascular injection and nerve damage
   b. Ability to inject more difficult area
   c. Simplicity of use
   d. Subcision of subdermal retractions in case of acne scars

5. Which of the following vessels is most likely to be principally affected from direct injection of filler product at the nasal root?
   a. Angular artery
   b. Inferior labial artery
   c. Superior labial artery
   d. Lateral nasal artery
   e. Dorsal nasal artery

6. Which of the following vessels is most likely to be principally affected from direct injection of filler product into the alar groove?
   a. Infra-orbital artery
   b. Inferior labial artery
   c. Superior labial artery
   d. Lateral nasal artery
   e. Dorsal nasal artery

7. Which of the following vessels is most likely to be principally affected from direct injection of filler product into the medial-lateral eyebrow?
   a. Supra-trochlear artery
   b. Supra-orbital artery
   c. Dorsal nasal artery
   d. Angular artery
   e. Facial artery

8. Which of the following factors influences the lifting effect from volumetry with soft tissue fillers?
   a. Depth of implantation
   b. Elastic modulus (G prime) of the filler
   c. Site of implantation
   d. Volume of implanted filler
   e. All of the above

9. Volume restoration to the midface often produces secondary improvement in which of the following?
   a. Perioral rhytides
   b. Pre-jowl sulci
   c. Platysmal bands
   d. Nasolabial folds
   e. All of the above

10. Which of the following statements is true of hyaluronic acid (HA) fillers?
    a. Crosslinking is necessary to confer stability and longevity.
    b. Elastic modulus (G prime) is primarily a measure of degree of filler spread.
    c. Viscosity increases if a HA filler is diluted with lidocaine or saline.
    d. The manufacturing method for all HA fillers is the same.
    e. All of the above

11. Which of the following statements is/are true about different HA products?
    a. All products are crosslinked.
    b. Restylane and Perlane have more bridge-type crosslinking.
    c. Juvéderm Ultra and Ultra Plus have more pendant modification.
    d. Restylane, Juvéderm, and Belotero Balance are all high concentration products.
    e. All of the above.

12. Which of the following is an appropriate injection strategy for deep volumetry with Perlane or Juvéderm Ultra Plus?
    a. Intradermal implantation to the nasojugal fold
    b. Intradermal implantation to the midface
    c. Subcutaneous implantation to the midface
    d. Subepithelial implantation to the vermilion lip borders
    e. Supraperiosteal implantation to perioral lip lines

13. Which of the following strategies may help to decrease the risk of swelling when implanting HA fillers in the nasojugal fold? (Select all that apply)
    a. Avoidance of over-correction
    b. Selection of a fully hydrated HA product
    c. Use of blunt injection microcannulas
    d. Slow careful injection technique
    e. Fanning injection technique

14. Which of the following strategies would NOT be potentially helpful to correct a contour irregularity resulting from implantation of a hyaluronic acid filler?
    a. Extrusion of superficially implanted filler
    b. Injection of hyaluronidase
    c. Tissue massage
    d. Application of nitropaste.

15. "Treat, wait, and assess over 4–8 weeks" is the mantra stated when using which injectable agent?
    a. Hyaluronic acid
    b. Neurotoxins
    c. Tissue massage
    d. Poly-L-lactic acid (PLLA)

16. The biostimulatory agent that has been FDA approved and clinically provides thickening and volumization of the entire face is which of the following?
    a. Calcium hydroxylapatite (CaHa)
    b. Porcine collagen
    c. Polymethymethacrylate (PMMA)
    d. Poly-L-lactic acid (PLLA)
    e. Hyaluronic acid (HA)

17. Which facial injectable agent requires a skin test prior to using it on humans?
    a. Porcine collagen
    b. Calcium hydroxlapatite (CaHa)
    c. Polymethymethacrylate (PMMA)
    d. Poly-L-lactic acid (PLLA)
    e. Neurotoxins

18. Strategies for safe and efficacious volumetry of the periocular region include which of the following?
    a. Injection of the patient in an upright or semi-upright, rather then supine, position.
    b. Use of a blunt injection microcannula when appropriate
    c. Avoidance of over-filling
    d. Selection of a hyaluronic acid filler
    e. All of the above

19. When injecting the periocular region with filler, care must be taken to avoid injury to which of the following?
    a. Temporal branch of facial nerve
    b. Angular artery
    c. Maxillary artery
    d. Zygomatic branch of facial nerve
    e. Lacrimal artery

20. The following are off-label injectable options for facial contouring and volumizing:
    a. Calcium hydroxylapatite (Radiesse)
    b. Poly-l-lactic acid (Sculptra)
    c. Juvéderm Ultra and Ultra-Plus
    d. Restylane/Perlane
    e. All of the above

21. Which of the following injectable products are specifically FDA-approved for midface volumizing in the non-HIV infected normal host?
    a. Calcium hydroxylapatite (Radiesse)
    b. Poly-l-lactic acid (Sculptra)
    c. Hyaluronic acid (Juvéderm Voluma)
    d. Hyaluronic acid (Restylane/Perlane)
    e. None of the above

22. Which of the following injectable products are specifically FDA-approved for midface volumizing in the HIV-infected patient?
    a. Hyaluronic acid (Juvéderm Voluma)
    b. Calcium hydroxylapatite (Radiesse)
    c. Poly-l-lactic acid (Sculptra)
    d. Liquid injectable silicone (Silikon-1000)
    e. B and C

23. Current concepts of pan-facial volumetry include the following:
    a. Primary focus for most patients on filling of the naso-labial folds.
    b. Deep implantation of fillers in the midface.
    c. Waiting period between the first treatment session and a touch-up session of at least three months.
    d. Complete avoidance of sharp needles for filler implantation.
    e. Injection of nasolabial folds before injection of the midface.

24. Which of the following statements about the rheology of fillers is true?
    a. Crosslinking of a filler gel does not affect its firmness.
    b. It is impossible to vary gel calibration and crosslinking with the same HA concentration.
    c. Gel fillers with higher G prime (elastic modulus) are firmer and better able to resist deformation caused by facial movement.
    d. Gel fillers with small gel calibration and low crosslinking are soft and disperse evenly.
    e. All of the above

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

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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

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1 2 3 4 5

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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:

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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.

_____

COMING SOON

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

Look for Part II of this supplement with your April issue of *JDD* and eJDD.

Contributing Faculty

Murad Alam MD (Feinberg School of Medicine, Northwestern University, Chicago, IL), Andrew F. Alexis MD MPH (Skin of Color Center, St. Luke's Roosevelt Hospital, New York, NY), Daniel Cassuto MD (University Hospital [Policlinico] of Modena, Italy), Luc Dewandre MD (Private Practice, Paris, France), Lisa M. Donofrio MD (Yale University School of Medicine, New Haven, CT), Steven Fagien MD (Aesthetic Eyelid Plastic Surgery, Boca Raton, FL), Julius W. Few, Jr. MD (The Few Institute for Aesthetic Plastic Surgery, Chicago, IL), Rebecca Fitzgerald MD (Private Practice, Los Angeles, CA), Timothy C. Flynn MD (Cary Skin Center, Cary, NC), C. William Hanke MD MPH (Indiana University School of Medicine, Indianapolis, IN), Philippe Kestemont MD (CHU Pasteur, Head and Neck Surgery, Nice, France), Z. Paul Lorenc MD (Private Practice, New York, NY), Jason N. Pozner MD (Cleveland Clinic Florida, Boca Raton, FL), Rod J. Rohrich (University of Texas Southwestern Medical Center, Dallas, TX), Mark G. Rubin MD (University California, San Diego, CA), Gerhard Sattler MD (Rosenpark Klinik GmbH, Darmstadt, Germany), Hema Sundaram MD (Sundaram Dermatology, Cosmetic & Laser Surgery, Fairfax, VA), Susan H. Weinkle MD (Private Practice, Bradenton, FL)

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