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Making the Right Choices: Attaining Predictable Aesthetic Results With Dermal Fillers

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ABSTRACT

The types and number of dermal fillers have evolved, allowing clinicians to select the most appropriate agent for each specific use. Filler properties differ both between and among classes, so clinicians must have a thorough understanding of these properties and the best techniques to use to provide the most satisfactory outcomes. This article reviews and highlights the key properties of different types of fillers, technical aspects of their use, safety considerations and the importance of patient factors in treatment selection. Making the right treatment choices must involve all of these issues to optimize aesthetic outcomes and patient satisfaction. The authors illustrate how to make the best choices through a series of case examples using a variety of filler types. Although most fillers can provide acceptable outcomes when used appropriately, the hyaluronic acids have become the most frequently used products because of their physicochemical properties and clinical benefits.

INTRODUCTION

An increasing array of dermal fillers and volumizers is now available to aesthetic clinicians. Their basic properties, similarities, differences, and aesthetic uses have been reviewed extensively.¹⁻¹⁴ From a practical, clinical standpoint, this expanding palette of options allows clinicians to offer their patients many more minimally invasive options for facial rejuvenation than ever before. At the same time, clinicians must be able to help their patients select among these options to achieve optimal and predictable outcomes. This is best accomplished by knowing how to tailor the selection to the patient's needs, goals and specific aspects of their presentation. To a certain extent, this ability embodies the art of aesthetic medicine, but this art must be grounded in a thorough knowledge of the fundamentals: the multiple variables that must be taken into account in clinical decision-making. This article will provide the authors' practical perspectives on the factors they consider when formulating treatment plans for their patients, treatment strategies based on these factors and case examples illustrating their strategies' practical applications.

Maximizing Predictability of Outcomes—Products, Proficiency and Patients

Along with safety, patient satisfaction is a top priority. A key consideration in achieving high levels of patient satisfaction is the ability to provide predictable outcomes. Experience demonstrates that although all fillers can provide satisfactory results when used properly, a large number of interacting factors influence the predictability of these outcomes. These include product variables, clinician proficiency and patient-related factors (Table 1).

Products and Proficiency

Filler materials range from autologous fat and biologically derived substances to synthetic compounds as well as combina-

tions of biologic and synthetic compounds. These materials differ, at least to some extent, by their physical and chemical properties, which have important consequences for their versatility, durability, ease of use and specific clinical applications.

TABLE 1.

Variables Contributing to Predictable Outcomes With Dermal Fillers

Filler Factors and Technical Considerations	Patient Variables
Duration	Age
Source	Sex
Amount of downtime	Skin color (Fitzpatrick skin type)
Level of required skill	Skin thickness
Ease of injecting	Aesthetic presentation
Formulation properties (e.g., smoothness, viscosity, cohesivity, malleability)	Wrinkle/fold thickness
Types of potential complications (e.g., short-term, procedure-related, technique-related, delayed and long-term material- and technique-associated)	Presence of telangiectasias
Reversibility (i.e., ability to reverse complications or to correct overtreatment noninvasively)	Treatment history
Versatility (i.e., ability to be used for a range of indications)	Aesthetic goals and expectations; psychological factors
Correction goal (i.e., undercorrection, overcorrection, optimal correction, need for touch-ups or multiple sessions)	Budgetary considerations

Collagens

Collagens were the leading soft tissue fillers until the advent of the hyaluronic acids (HAs), and since have largely been supplanted by them.¹⁵ Bovine collagens are no longer commercially available in the United States (U.S.), and the collagens currently used are either human or porcine in origin. In addition, the use of human derived collagens such as Cosmoderm and Cosmoplast has decreased and these products are no longer marketed by their manufacturer. Thus, they are largely irrelevant to physicians with active esthetic practices. Depending on their formulation, some collagens were useful for some clinicians because they can be used to treat crow's feet and very fine papillary defects, and can be layered over other fillers that are intended for mid-to-deep dermal or subcutaneous injection.^{1,12,16} This was very useful for treating patients with etched lines overlying deep folds, such as the nasolabial folds. Generally, collagens vary in their degree of cross-linking and concentration, and in their specific indications. For collagens, a primary disadvantage is their rather short duration of effect, with some lasting two to four months on average, and occasionally up to approximately six months.^{1,7,17} The relative brevity of their effects may have made the human and bovine derived collagens suitable for treatment-naïve patients who have trepidations about soft tissue augmentation and wish to begin treatment with a more temporary agent.¹ Also, collagens are typically associated with lower rates of bruising, providing an option for patients who require an immediate result with virtually no downtime.

Understandably, patients are particularly interested in the duration of the correction achieved. Although many collagens have been considered very versatile fillers because of their variable concentrations, their brevity of effect (with the exception of Evolence) is, in general, a major limitation.¹² The availability of cross-linked, longer-acting HAs has undoubtedly played an important role in the rapid growth of minimally invasive aesthetic procedures.

Hyaluronic Acids

Currently, HAs are the most widely used dermal filling agents in the United States and worldwide.^{15,19} HAs are generally considered less technique-sensitive, and are thus more forgiving than semipermanent or permanent fillers. Moreover, they are reversible, resorbable, and have excellent safety profiles.^{1,11,20-23} Permanent products, such as silicone, are very technique-dependent. More viscous products, such as calcium hydroxylapatite (Radiesse[®], BioForm Medical, San Mateo, CA), are also technique-dependent.

Certain fillers, whether HA (such as Radiesse) or poly-L-lactic acid (such as Sculptra[®]), do not contain collagen but stimulate the body's production of new collagen.

Radiesse must be injected into the correct plane and the injection site must then be massaged. Bolus injections and failure to

massage can result in lumps and undulations of the surface architecture. Sculptra (Dermik Laboratories, Bridgewater, NJ) has recently been approved for cosmetic indications in the U.S.

With these collagen-stimulating fillers, improper reconstitution or improper placement can result in nodules if it is injected in excess or too superficially. Results are also dependent on the patient's ability to synthesize collagen. In general, results with any product depend on the depth of placement and the interaction with the patient's unique anatomy. Viscous products placed against thin skin do poorly and reflect poor technique and poor judgment.

Although individual HAs share many class properties, they differ considerably among themselves. HA fillers that are approved by the FDA and are available in the U.S. are the Prevelle[™] (Mentor Corporation, Santa Barbara, CA), Restylane[®] (Medicis Aesthetics Inc, Scottsdale, AZ) and Juvéderm[®] (Allergan, Inc., Irvine, CA) families of products. These products differ considerably in their proprietary manufacturing processes and consequently in many of their physicochemical properties.^{4-6,24-31} The science behind these differences and their clinical relevance has recently been explored in detail.³¹

Some of the important properties that affect clinical performance of HAs are the extent of cross-linking, gel hardness (G'), gel consistency, viscosity and extrusion force, HA concentration and extent of hydration.³¹ Once HAs are cross-linked to reduce their naturally rapid biodegradation in tissue, the resulting gel must be processed or sized to permit its injection through a fine-gauge needle.³¹ Restylane products are sized into particles of an approximately average size.³¹ Thus, Restylane has approximately 100,000 gel particles per mL, whereas Perlane[®] (Medicis Aesthetics Inc, Scottsdale, AZ) is composed of about 10,000 gel particles per mL. The larger Perlane particles are larger and intended for deeper injections.^{5,32} In contrast, Juvéderm products are smooth consistency gels produced by homogenization of the gel mass.³¹ This process results in softer gels (i.e., lower G' values) that extrude readily through the needle. One other factor that influences the extrusion force (but has no influence on tissue correction or duration) is the amount of free hyaluronic acid which helps to lubricate the product as it is pushed out of a syringe. It was recently reported that Juvéderm products can be injected more easily than Restylane products with a consistent, slow rate of pressure on the syringe plunger.²⁵ However, the relevance of this report needs to be corroborated with more data.

Synthetic Fillers

Synthetic fillers were developed, in part, to attempt to extend the clinical duration of benefit over that of biologically based products. These products, however, differ considerably in their clinical performance and intended use. For example, poly-L-lactic acid is indicated for treating human immunodeficiency virus (HIV)-associated lipoatrophy, although it is also used for panfacial rejuvenation.

nation in patients with congenital volume deficiencies or aging-related lipoatrophy.³³ Calcium hydroxylapatite (Radiesse) also is indicated for HIV-associated lipoatrophy as well as for treating moderate-to-severe wrinkles and folds.³⁴ Sometimes classed as a semipermanent agent, calcium hydroxylapatite has a rather variable reported duration of effect, typically ranging from six to 18 months.^{2,7,10,35} The longer-duration HAs, such as Juvéderm, provide clinical benefits lasting approximately nine months to one year (Juvéderm® Ultra, Allergan, Inc., Irvine, CA) or one year or more (Juvéderm® Ultra Plus, Allergan, Inc., Irvine, CA), which is reflected in their FDA-approved product label.^{29,30,36} Restylane has also achieved a long duration approval that lasts up to one year. However, both the Restylane and Juvéderm duration claims rely on "touch up" injections that require patients to return to get filled at intervals that may or may not be relevant to real world experiences by clinicians.

Yet another synthetic product combines polymethylmethacrylate (PMMA; Artefill®, Suneva Medical, San Diego, CA) with a bovine collagen carrier, which means that skin-testing is required.³⁷ Artefill is indicated for the treatment of nasolabial folds and is considered a permanent filler; however, the continued distribution of this product is in doubt.

Permanent fillers have been associated with more serious, delayed-onset adverse events. The problems, as with the correction, tend to be permanent. Also, the synthetic fillers—both semipermanent fillers such as Radiesse and Sculptra, and permanent fillers such as Artefill—are less forgiving with respect to injection techniques, are less versatile in their uses, and are not reversible, and unwanted effects can last for a significant period of time. In a recent study, 35.7% patients reported irregularities following injection with Radiesse. Half of these patients noted that these irregularities persisted for more than three months.³⁸ Some of the complications with semipermanent and permanent fillers require aggressive management including surgical excision.²³

Safety

Overall, fillers have excellent safety profiles, but any filler can result in complications. Therefore, the probability, predictability and types of complications associated with various fillers need to be considered when selecting a product. Many adverse events are related to the procedure and the experience and skill of the injector, rather than the product. Transient bruising and swelling are common, but proper technique such as injecting slowly and gently; avoiding an improper injection plane or excessive volume; or injecting in an inappropriate facial area can help minimize or prevent these complications.^{17,39-41} Techniques for preventing or managing complications have been reviewed extensively and the reader is referred to these articles.^{1,23,39,40,42} One of the important advantages of HAs is their reversibility. In the case of overcorrection or misplacement,

hyaluronidase is highly effective in preventing or reversing the complications.^{20-22,43}

Of greatest concern are the relatively rare, delayed-onset, potentially serious complications such as true granulomatous reactions.^{23,42,44} The exact causes of these reactions, which can occur months or years after filler implantation, are unknown, but may be linked to tissue trauma, filler degradation, the presence of a biofilm, or a combination of these factors.^{45,46} It appears that the highest risks of these complications are with the so-called permanent products such as silicone gels and polyacrylamides, and with longer-lasting products such as Sculptra.^{39,46-48}

Other Technical Considerations

A comprehensive knowledge and appreciation of facial anatomy is the foundation of good technique.^{16,39} Skin thickness varies between different portions of the face, for example, and fillers differ in their intended planes of injection.³⁹ Improper placement of a filler can lead to lumps, beading, and nodules.⁴⁴ Clinicians also must be aware of the optimal degree of correction recommended when initiating treatment with fillers. Inadequate volumes can result in unsatisfactory outcomes, whereas excessive volumes can lead to complications.

Older collagens, for example, required overcorrection because of their dilution with resorbable agents.^{7,44} Newer collagens do not require overcorrection and thus, offer a greater degree of predictability. Published recommendations and product labeling instructions for HA fillers and HA-stimulators, such as Radiesse, suggest correcting to 100% of the desired volume effect and recommend against overcorrecting.^{27-30,34,44} Clinical experience with HAs suggests that treating to full correction (including touch-ups) may prolong the ultimate duration of clinical effect. Among HAs, differences in the propensity for initial swelling²⁵ may result in greater need for touch-ups. Products such as ArteFill and Sculptra are best used by scheduling several visits to treat to optimal correction.^{32,33}

Because of differences in each formulation's consistency, clinicians may find that fillers vary somewhat in their malleability after injection. Although most dermal fillers are malleable after injection, the clinical experience of some clinicians suggests that the newer collagens must be molded rather soon after injection because of the rapidity in which it solidifies (although if injected properly, little massage is needed).

The aforementioned considerations indicate that it is a filler's full spectrum of properties that contribute to the predictability or consistency of its clinical performance and overall benefit:risk profile. It is incumbent upon clinicians to understand these properties and to be able to evaluate them in the context of an individual patient's needs, goals and aesthetic presentation, to maximize benefits and minimize risks.

Patient Factors and Their Impact on Soft-Tissue Augmentation

Patients seek minimally invasive aesthetic treatments for various reasons, which encompass a broad and complex range of psychosocial considerations and motivations involving body image and self-perceptions.⁴⁹ Patients also vary widely in their aesthetic presentations, degree of deficit, anatomy and physiology, and even in behaviors that affect facial appearance (e.g., muscle activity and facial mobility). Treatment selection can be influenced by these and other patient variables, including age, sex, budgetary considerations, skin color and thickness, and the extent and type of facial aging (Table 1).⁴⁹⁻⁵²

For example, as aging progresses, volume deficits become increasingly apparent. Therefore, older patients tend to require deeper injections of more cohesive and/or viscous products to provide greater lift. In addition, they require more volume for a cosmetic improvement that do younger patients. Patients with thicker skin need thicker, more robust products, whereas those with thinner skin require less viscous fillers. Individuals with deeper wrinkles and folds also require a more robust filling and volumizing agent, and layering of products is often successful with these patients. Clinicians have noted that patients with skin of color often require volumizing in the midfacial area because of sagging skin, but are unlikely to have suffered the photodamage associated with lighter skin color.⁴⁹ Patients with lighter skin and the presence of telangiectasias require deeper filling agents because more superficial fillers are likely to be visible and their skin is more likely to bruise. In addition, the use of opaque products may cause visible nodules in patients with transparent skin. Thus, the use of clear products, such as the HA gels, may be warranted in this population.

Patients differ in their history, level of knowledge and expectations. They may be treatment-naïve or have a history of successful or unsuccessful treatment. Based on media and other sources of information, they may be misinformed or they may have accurate information. They may be completely comfortable with the decision to seek treatment or may have concerns about the results. They may have a realistic idea of outcomes or have expectations that cannot be met. Regardless, when treating any patient, it is critical to understand their expectations and educate them about their options and the potential outcomes to set the stage for satisfactory results.

Finally, it is critical for the aesthetic practice to be straightforward about cost. It is imperative that physicians help their patients make informed decisions by educating them about evaluating cost in the context of expected longevity and overall safety profiles. Physicians that do not counsel their patients realistically are likely to have unhappy patients. For example, HAs such Juvéderm and Restylane provide long-lasting aesthetic benefits along with excellent safety profiles.

In sum, aesthetic clinicians face unique challenges when selecting optimal soft tissue filling agents for the spectrum of patient presentations and expectations they encounter in practice. This mandates a thorough understanding of the diverse and interacting variables that characterize products and patients to develop the most appropriate overall treatment plan for each individual.

CASE REPORTS

Skin of Color

A 44-year-old African American female presented with deep nasolabial folds (NLFs) resulting from volume loss (Figure 1a). She had no previous treatment history with dermal fillers. She received treatment with two syringes of Juvéderm Ultra Plus into the deep dermis of the NLFs and beneath the muscle of the cheeks. She had excellent diminution of her NLFs, as seen at the follow-up visit four months after treatment (Figure 1b). A combination of antero-grade and retrograde threading and crosshatching (also referred to as "bridging") was used to provide more lift to the skin. No complications were observed or reported by the patient.

Commentary

Juvéderm Ultra Plus, the more viscous of the available Juvéderm products, was selected because of the depth of the patient's NLFs, typical of many patients with skin of color. In addition, the effectiveness, durability of 12 months, and safety of Juvéderm Ultra Plus in severe NLFs and in African American subjects have all been demonstrated in randomized controlled trials.^{29,30,53,54} The injection technique was selected to take advantage of the lifting capacity of this filler.

Given her dark skin and deep fold, other considerations include Radiesse, Evolence, Restylane and Perlane. The thickness of this patient's skin would likely mask the opaque nature of Radiesse and the lifting characteristics of Radiesse, Restylane and Perlane would be appropriate for her.

Treating the Tear Trough and Infraorbital Hollow

A 51-year-old white female (Figure 2a) presented with prominent dark circles resulting from volume loss in her tear troughs. She had been treated two years previously with CosmoDerm® (Inamed Corporation, Santa Barbara, CA) for acne scars (area

FIGURE 1. A 44-year-old African American female presented with deep nasolabial folds (NLFs) resulting from volume loss. She received treatment with two syringes of Juvéderm Ultra Plus into the deep dermis of the NLFs and beneath the muscle of the cheeks.

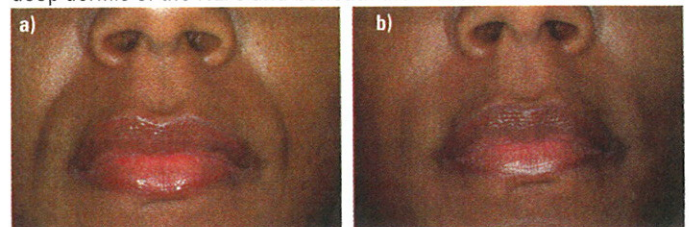
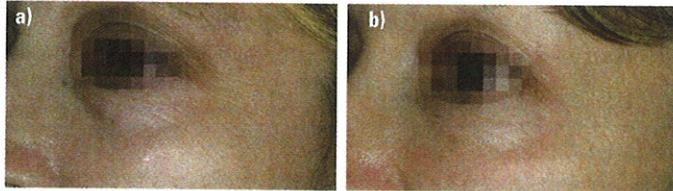


FIGURE 2. A 51-year-old white female **a)** presented with prominent dark circles resulting from volume loss in her tear troughs. She was injected deep in the muscle with a total of 0.6 mL Restylane using the linear threading technique.



not shown in photograph). For her tear troughs, she was injected deep below the muscle (in the periosteal plane) with a total of 0.6 mL Restylane using the linear threading technique.

Commentary

Eight months following treatment, the patient's tear troughs appeared modestly improved and the patient was satisfied with the outcome (Figure 2b). No complications occurred. Restylane was chosen to treat this patient because of its transparent nature. The options for this location would include Juvederm, which is also transparent and Prevelle Silk. This latter product would be useful for someone that is being treated in this location for the first time as it enables both physician and patient to "try out" the correction.

Products that are not appropriate for this location include Artefill and Radiesse, which are likely to be visible. The use of PLLA in this location is controversial but it is likely that when used with dilute amounts of product (e.g., 10–11 mL of diluent) small volume collagen stimulation may be appropriate for certain patients that have deep volume deficits.

Volume Creation in a Younger Patient

A 44-year-old woman had a naturally thin face that became more exaggerated with age (Figure 3). She had not been previously treated with any fillers, and she received a total of 21.4 cc Sculptra in four sessions over seven months.

Commentary

Sculptra is a panfacial volumizing agent that is best suited for patients with substantial degrees of lipoatrophy due to illness, congenital facial structure, or significant weight loss. It is also ideal for patients that have cosmetically significant volume loss or facial descent. This woman was an ideal candidate because of her naturally thin face, which worsened in appearance with age. Alternatives to PLLA would have included large volumes of fillers that would not have been financially viable in this instance.

Perioral Augmentation

A 29-year-old female had been treated previously with Restylane and Captique® (Inamed Corporation, Santa Barbara, CA) in her perioral area (Figure 4a). She reported the dura-

FIGURE 3. A 44-year-old woman had a naturally thin face that became more exaggerated with age. She received a total of 21.4 cc Sculptra in four sessions over seven months.

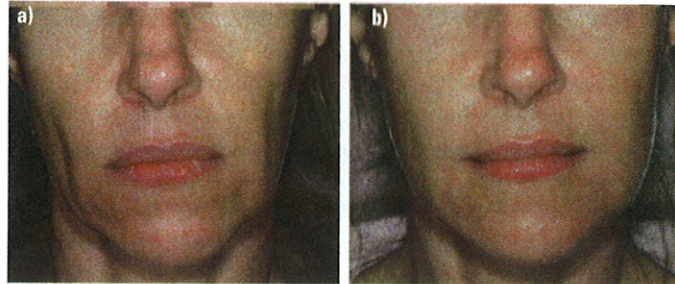
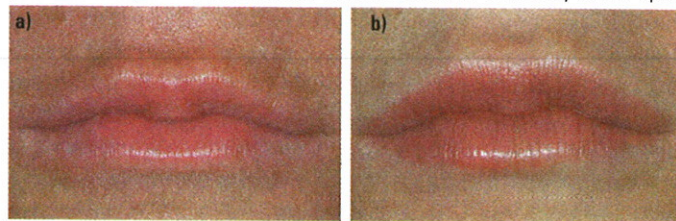


FIGURE 4. A 29-year-old female was treated with 0.8 mL of Juvederm Ultra injected along a scar visible in the upper left quadrant of the perioral area, as well as into the vermilion border and body of the lips.



tion of effect as only two months and was dissatisfied with the outcome. For this treatment, 0.8 mL of Juvederm Ultra was injected along a scar visible in the upper left quadrant of the perioral area, as well as into the vermilion border and body of the lips. A serial-puncture technique was used for the scar. All other treatments were performed using linear anterograde threading.

Commentary

At six months, the patient's perioral area maintained an excellent correction (Figure 4b). Her results lasted longer than six months. Because this patient was dissatisfied with previous HA treatments due to their short-lived results, longer acting hyaluronic acid fillers were appropriate. Juvederm Ultra or Restylane are good choices due to their duration of correction and flow characteristics.

Malar Augmentation Using Layering

A 56-year-old woman presented with moderate midfacial volume loss, NLFs, and perioral rhytids (Figure 5a). Juvederm Ultra Plus was selected to augment the malar area and NLFs. She received 2.4 mL total volume. A combination of fanning and linear threading techniques was used. In addition, 0.8 mL of Juvederm Ultra was injected into the cheeks, NLFs and lip lines.

Commentary

The patient was able to go out to lunch the same day, with no evidence of bruising. Two weeks posttreatment (Figure 5b), the

appearance of the NLFs was greatly diminished. Juvéderm Ultra Plus, a thicker product, was chosen for deeper injections in the malar area and NLFs. Perlane would also be acceptable for this location. Juvéderm Ultra, a less viscous product, was used to superficially complete the correction in these areas and also treat lip lines. Restylane could have been used for the perioral rhytids and its injection with a 32-gauge needle can be especially gratifying for this indication.

Fine Lines in a Younger Female Patient

A female patient is a past and current cigarette smoker (Figure 6a). She presented with fine lines around her mouth and severe glabellar folds. The treatment plan was for combination treatment. She received 20 units of botulinum neurotoxin type A (BoNTA; BOTOX®, Allergan, Inc., Irvine, CA) followed by 0.25 mL of Juvéderm Ultra, both in her glabellar area. In addition, her perioral area was treated with 0.5 mL Juvéderm Ultra. A linear threading technique was used for each area, keeping filler injections superficial in the glabellar area to avoid necrosis.

Commentary

Post-treatment (Figure 6b), the perioral area achieved a good response without any lumps or bumps, although the potential for such complications is generally elevated around the lips. The combination of BoNTA and HA filler in the glabellar area provided an excellent outcome, and this patient was very satisfied with her treatment overall. With the approval of Dysport, this botulinum toxin is also appropriate for this location. For this individual, 50 units of Dysport would have been appropriate. For proper correction of the severe static and dynamic components of the glabellar lines, a combination of BoNTA and filler was required. The use of Restylane with Dysport or or with Botox would also be an ideal combination for this patient. When injected too superficially, some HA fillers have been known to produce a Tyndall effect which appears as a bluish bump resulting from light scattering effects.²¹

Shorter-Duration Lip Augmentation

This female was interested in having lip augmentation, but was concerned about her potential reactions to the outcome (Figure 7a). It was recommended that she receive conservative treatment with a shorter-acting HA to give her the chance to assess the outcome before deciding on a longer-duration treatment. She received 0.5 mL per lip of Prevelle Silk, which was injected by linear threading.

Commentary

The patient achieved a satisfactory outcome (Figure 7b) without complications. She was pleased with the improved appearance of her lips and decided to pursue additional treatment with a longer lasting HA. For this individual, injections with Restylane, Perlane or Juvederm would be appropriate. Injections with opaque products that are thicker (such as Radiesse) would not be appropriate.

FIGURE 5. A 56-year-old woman presented with moderate midfacial volume loss, NLFs, and perioral rhytids. Juvéderm Ultra Plus was selected to augment the malar area and NLFs. In addition, 0.8 mL of Juvéderm Ultra was injected into the cheeks, NLFs, and lip lines.

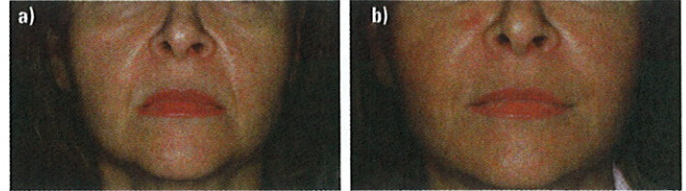


FIGURE 6. A female patient presented with fine lines around her mouth and severe glabellar folds. She received 20 units of botulinum neurotoxin type A (BoNTA; Botox®, Allergan, Inc., Irvine, CA) followed by 0.25 mL of Juvéderm Ultra, both in her glabellar area. Her perioral area was treated with 0.5 mL Juvéderm Ultra.

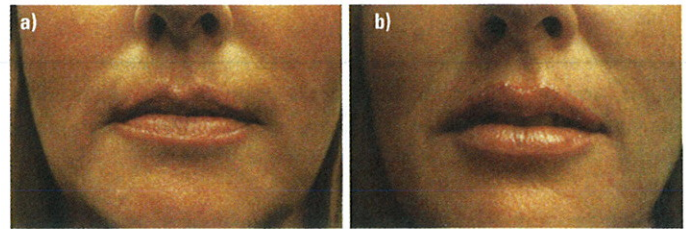
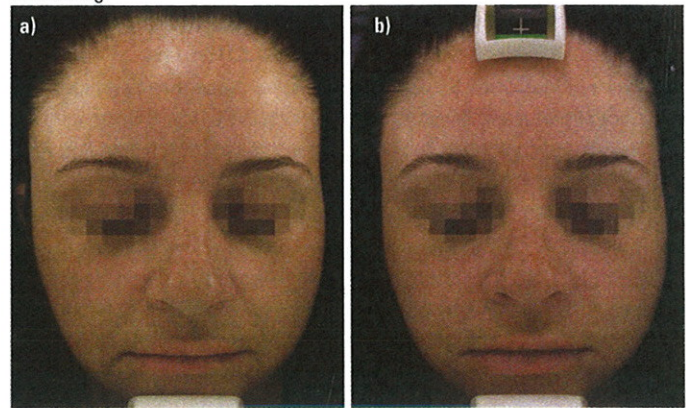


FIGURE 7. A female patient interested in having lip augmentation, received 0.5 mL per lip of Prevelle Silk, which was injected by linear threading.



CONCLUSION

The preceding case examples illustrate several important factors that must be taken into consideration when developing an aesthetic treatment plan and selecting specific products to yield predictable results. The availability of an array of products permits clinicians to select the treatment most likely to lead to optimal outcomes.

In conclusion, most available fillers can lead to satisfactory outcomes when used with the requisite knowledge, skill and understanding of the diverse variables that influence outcomes. It has become apparent; however, that some fillers are easier

to use than others and, all other factors being equal, will have more predictable outcomes in general. In the U.S. and throughout the world, the HAs have become the most frequently used soft tissue filling agents because of their physicochemical properties and clinical benefits. Among these, clinical practice suggests that HAs, and in particular the Juvéderm products, comprise the most versatile and easy-to-inject fillers, which can be used safely in a variety of facial areas to provide a smooth, natural look and feel.

DISCLOSURES

Dr. Lupo is a speaker, investigator, and/or trainer for Allergan, Inc., Dermik Laboratories, Medicis Pharmaceutical Corporation, Johnson & Johnson, Inc., and Bioform Medical, Inc. She is co-founder and shareholder of Cosmetic Boot Camp, LLC.

Dr. Beer is co-founder and shareholder of Cosmetic Boot Camp, LLC and a shareholder of Theraplex, LLC. He is a speaker, investigator, and/or trainer for Johnson & Johnson, Inc., Lumenis, Allergan, Inc., sanofi-aventis U.S. LLC, Medicis Pharmaceutical Corporation, and Graceway Pharmaceuticals, LLC.

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REFERENCES

- Alam M, Gladstone H, Kramer EM, et al. ASDS guidelines of care: Injectable fillers. *Dermatol Surg*. 2008;34:S115-S148.
- Broder KW, Cohen SR. An overview of permanent and semipermanent fillers. *Plast Reconstr Surg*. 2006;118:7S-14S.
- Brandt FS, Cazzaniga A. Hyaluronic acid fillers: Restylane and Perlane. *Facial Plast Surg Clin North Am*. 2007;15:63-76.
- Coleman SR. Cross-linked hyaluronic acid fillers. *Plast Reconstr Surg*. 2006;117:661-665.
- Carruthers A, Carruthers J. Non-animal-based hyaluronic acid fillers: Scientific and technical considerations. *Plast Reconstr Surg*. 2007;120:33S-40S.
- Clark CP. Animal-based hyaluronic acid fillers: Scientific and technical considerations. *Plast Reconstr Surg*. 2007;120:27S-32S.
- Eppley BL, Dadvand B. Injectable soft-tissue fillers: Clinical overview. *Plast Reconstr Surg*. 2006;118:98e-106e.
- Fagien S, Klein AW. A brief overview and history of temporary fillers: Evolution, advantages and limitations. *Plast Reconstr Surg*. 2007;120:8S-16S.
- Falcone SJ, Berg RA. Crosslinked hyaluronic acid dermal fillers: A comparison of rheological properties. *J Biomed Mater Res A*. 2008;87:264-271.
- Fernandez EM, Mackley CL. Soft tissue augmentation: a review. *J Drugs Dermatol*. 2006;5:630-641.
- Lupo MP. Hyaluronic acid fillers in facial rejuvenation. *Semin Cutan Med Surg*. 2006;25:122-126.
- Matarasso SL. Injectable collagens: Lost but not forgotten—A review of products, indications, and injection techniques. *Plast Reconstr Surg*. 2007;120:17S-26S.
- Monheit GD, Prather CL. Juvéderm: A hyaluronic acid dermal filler. *J Drugs Dermatol*. 2007;6:1091-1095.
- Monstrey SJ, Pitaru S, Hamdi M, et al. A two-stage phase I trial of Evolence³⁰ collagen for soft-tissue contour correction. *Plast Reconstr Surg*. 2007;120:303-311.
- American Society for Aesthetic Plastic Surgery. Cosmetic Surgery National Data Bank: 2007 Statistics. <http://www.surgery.org/download/2007stats.pdf>. Accessed April 9, 2008.
- Carruthers JDA, Glogau RG, Blitzer A, and the Facial Aesthetics Consensus Group Faculty. Advances in facial rejuvenation: Botulinum toxin type A, hyaluronic acid dermal fillers, and combination therapies—consensus recommendations. *Plast Reconstr Surg*. 2008;121(suppl 5):5S-30S.
- Johl SS, Burgett RA. Dermal filler agents: A practical review. *Curr Opin Ophthalmol*. 2006;17:471-479.
- Evolence Instructions for Use. Herzliya, Israel: ColBar LifeScience Ltd.; 2008.
- Fagien S, Stuzin J. Injectable soft-tissue augmentation: The present and the future. *Plast Reconstr Surg*. 2007;120:5S-7S.
- Hirsch RJ, Brody HJ, Carruthers JDA. Hyaluronidase in the office: A necessity for every dermasurgeon that injects hyaluronic acid. *J Cosmet Laser Ther*. 2007;9:182-185.
- Hirsch RJ, Narurkar V, Carruthers J. Management of injected hyaluronic acid induced Tyndall effects. *Lasers Surg Med*. 2006;38:202-204.
- Brody HJ. Use of hyaluronidase in the treatment of granulomatous hyaluronic acid reactions or unwanted hyaluronic acid misplacement. *Dermatol Surg*. 2005;31:893-897.
- Lemperle G, Rullan PP, Gauthier-Hazan N. Avoiding and treating dermal filler complications. *Plast Reconstr Surg*. 2006;118:92S-107S.
- Rohrich RJ, Ghavami A, Crosby MA. The role of hyaluronic acid fillers (Restylane) in facial cosmetic surgery: Review and technical considerations. *Plast Reconstr Surg*. 2007;120:41S-54S.
- Smith KC. Practical use of Juvéderm: Early experience. *Plast Reconstr Surg*. 2007;120 (suppl 6):67S-73S.
- Matarasso SL, Carruthers JD, Jewell ME, and the Restylane Consensus Group. Consensus recommendations for soft-tissue augmentation with nonanimal stabilized hyaluronic acid (Restylane). *Plast Reconstr Surg*. 2006;117(Suppl 3):3S-34S.
- Perlane [package insert]. Scottsdale, AZ: Medicis Aesthetics Inc; 2006.
- Restylane [package insert]. Scottsdale, AZ: Medicis Aesthetics, Inc; 2005.
- Juvéderm Ultra [package insert]. Santa Barbara, CA: Allergan, Inc.; 2008.
- Juvéderm Ultra Plus [package insert]. Santa Barbara, CA: Inamed Aesthetics; 2007.
- Tezel A, Fredrickson GH. The science of hyaluronic acid dermal fillers. *J Cosmet Laser Ther*. 2008;10:45-42.
- Narins RS, Bowman PH. Injectable skin fillers. *Clin Plast Surg*. 2005;32:151-162.

33. Sculptra [package insert]. Bridgewater, NJ: Dermik Laboratories; 2006.
34. Radiesse injectable implant. Instructions for use. Available at: <http://www.fda.gov/cdrh/pdf5/p050037c.pdf>. Accessed May 18, 2007.
35. Jacovella PF, Peiretti CB, Cunille D, et al. Long-lasting results with hydroxylapatite (Radiesse) facial filler. *Plast Reconstr Surg*. 2006;118:15S-21S.
36. Pinsky MA, Thomas JA, Murphy DK, Walker PS, for the Juvéderm vs. Zyplast Nasolabial Fold Study Group. Juvéderm injectable gel: A multicenter, double-blind, randomized study of safety and effectiveness. *Aesthetic Surg J*. 2008;28:17-23.
37. Artefill [Instructions for Use]. San Diego, CA: Artes Medical Inc.; 2007.
38. Fakhre GP, Perdakis G, Shaddix KK, et al. An evaluation of calcium hydroxylapatite (Radiesse®) for cosmetic nasolabial fold correction: A meta-analysis and patient centric outcomes study [abstract]. *Plast Reconstr Surg*. 2008;22:99.
39. Gladstone HB, Cohen JL. Adverse effects when injecting facial fillers. *Semin Cutan Med Surg*. 2007;26:34-39.
40. Alam M, Dover JS. Management of complications and sequelae with temporary injectable fillers. *Plast Reconstr Surg*. 2007;120:98S-105S.
41. Glogau RG, Kane MC. Effect of injection techniques on the rate of local adverse events in patients implanted with nonanimal hyaluronic acid gel dermal fillers. *Dermatol Surg*. 2008;34:S105-S109.
42. de Bouille K. Management of complications after implantation of fillers. *J Cosmet Dermatol*. 2004;3:2-15.
43. Hirsch RJ, Lupo M, Cohen JL, Duffy D. Delayed presentation of impending necrosis following soft tissue augmentation with hyaluronic acid and successful management with hyaluronidase. *J Drugs Dermatol*. 2007;6:325-328.
44. Lowe NJ, Maxwell CA, Patnaik R. Adverse reactions to dermal fillers: Review. *Dermatol Surg*. 2005;31:1616-1625.
45. Reisberger E-M, Landthaler M, Wiest L, et al. Foreign body granulomas caused by polymethylmethacrylate microspheres: Successful treatment with allopurinol. *Arch Dermatol*. 2003;139:17-20.
46. Christensen L. Normal and pathologic tissue reactions to soft tissue gel fillers. *Dermatol Surg*. 2007;33(suppl 2):S168-S175.
47. Andre P, Lowe NJ, Parc A, et al. Adverse reactions to dermal fillers: A review of European experiences. *J Cosmet Laser Ther*. 2005;7:171-176.
48. Lemperle G, Morhenn V, Charrier U. Human histology and persistence of various injectable filler substances for soft tissue augmentation. *Aesthetic Plast Surg*. 2003;27:354-366.
49. Honigman R, Castle DJ. Aging and cosmetic enhancement. *Clin Interv Aging*. 2006;1:115-119.
50. Burgess CM. Principles of soft tissue augmentation for the aging face. *Clin Interv Aging*. 2006;1:349-355.
51. Tan SR, Glogau RG. Filler esthetics. In: Carruthers A, Carruthers J, eds. *Procedures in Cosmetic Dermatology Series: Soft Tissue Augmentation*. Philadelphia, PA; WB Saunders Company; 2005:8-13.
52. Burgess CM. Soft tissue augmentation in skin of color: Market growth, available fillers, and successful techniques. *J Drugs Dermatol*. 2007;6:51-55.
53. Grimes PE, Thomas JA, Murphy DK, Walker PS. Efficacy and safety of novel hyaluronic acid-based fillers and crosslinked bovine collagen in Caucasians and persons of color. Poster presented at: American Academy of Dermatology Meeting; San Diego, CA. July 26-30, 2006.
54. Lupo MP, Thomas JA, Murphy DK, Walker PS. Effectiveness of next generation hyaluronic acid dermal fillers in the treatment of severe nasolabial folds [abstract]. *J Am Acad Dermatol*. 2007;56:AB199.

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