

Reliable Soft Tissue Augmentation

A Clinical Comparison of Injectable Soft-Tissue Fillers for Facial-Volume Augmentation

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Abstract: While injectable fillers for facial-volume augmentation have been extensively marketed, there are few published reports comparing the clinical efficacy and cost-effectiveness of multiple injectable agents for soft-tissue augmentation in the face. We present our experience in 976 patients with the use of 4 common injectable agents: autologous fat, Hylaform, Restylane, and Radiesse. We analyzed the injection characteristics of each filler, including injection volume, complication rate, revision rate, and longevity, across 3 commonly treated anatomic regions: the nasolabial fold, glabella, and lips. We subsequently performed a detailed cost-effectiveness analysis of each filler in each anatomic region.

Our results demonstrate that autologous fat transplantation is ideally suited for the treatment of the nasolabial fold and glabella, particularly in combination with other procedures. Fat grafting to the lips is limited to use as an adjunct to other facial surgery due to the prolonged recovery time required. We prefer Radiesse for the isolated treatment of the nasolabial folds and glabella. However, Radiesse is not recommended in the lips due to the increased incidence of complications. Last, the hyaluronic fillers Restylane and Hylaform have an excellent safety profile and are our first choice for isolated lip augmentation procedures.

Key Words: fat grafting, injectable filler, Restylane, Hylaform, Radiesse

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The recognition of the importance of soft-tissue volume loss as a component in facial aging has led to a renewed interest in reliable soft-tissue augmentation. Historically, injectable options for soft-tissue augmentation of the face were limited to fat

transplantation, collagen, and off-label materials, which were plagued with variable success and numerous complications. In 2005, plastic surgeons and the public have been inundated with numerous “new” injectable fillers, which have been introduced for facial-volume enhancement and have been extensively marketed, with various claims of clinical efficacy.^{1,2} Our practice has had significant experience with the use of 4 injectable fillers for volume augmentation of the face, namely, autologous fat, Restylane, Hylaform, and Radiesse.

Our largest experience is with the use of autologous fat transplantation. Facial fat grafting has had a resurgence of interest due to technical improvements in the harvesting and purification of fat, which have significantly diminished the variability often associated with this procedure. Our technique of harvesting and purifying fat has been previously described.^{3,4} Autologous fat grafting has many advantages over other injectable fillers due to its excellent safety profile, flexibility, and proven track record.⁵ Nevertheless, the need for a donor site, as well as variable resorption of fat transplants, remains the largest drawback for facial fat grafting.

The alloplastic materials we evaluated fall into 2 categories: those derived from hyaluronic acid (HA) and those derived from calcium hydroxylapatite. Restylane and Hylaform are both HA derivatives that have been extensively marketed for soft-tissue augmentation. Hylaform is avian based, while Restylane is purified from HA generated by bacterial fermentation. The principal differences between these HA products are in their respective particle size, cross-linking, and concentration of HA. Restylane has greater cross-linking between strands of HA and thus has an improved longevity profile.^{6–8} We additionally studied Radiesse, a calcium hydroxylapatite-based product that has been studied in diverse applications (ie, radiopaque tumor marker, bladder neck augmentation, and vocal cord injection) and has been marketed for off-label use in facial-volume augmentation.⁹ Because of its biochemical properties, Radiesse is the longest-lasting alloplastic filler we studied, though it has significant limitations in certain anatomic areas.

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The purpose of our study is to present our clinical experience with the use of autologous fat, Restylane, Hylaform, and Radiesse for facial soft-tissue augmentation. We present an anatomic site-by-site comparison evaluating the longevity, morbidity and recovery, cost, and complications associated with the use of these filler materials.

METHODS

We performed a detailed retrospective chart review of 976 consecutive patients who were treated for facial-volume augmentation and wrinkle reduction. All patients were treated by a single surgeon between the years of 1996 and 2004. We assessed each patient for the following: type and amount of product used, anatomic region injected, infection rate, touchup/revision rate, and last, overall longevity. Standardized patient photos were obtained preprocedure and 3, 6, 9, and 12 months postprocedure. These photographs were reviewed by a single blinded observer who rated the degree of persistence at each time point. Only patients who completed 1 year of follow-up were included in this study, although many were followed with excellent results for even longer.

After compiling our clinical results, we examined the economic costs associated with the use of each filler by anatomic region of injection for a typical patient in our practice. In this analysis, we examined cost per treatment and cost per year across each anatomic region for each material. While factors such as the cost of physician time, revisions, and complications are important economic variables, we excluded these costs in our simplified analysis.

RESULTS

Patient Characteristics

Autologous fat was used in 697 (72%) patients, Radiesse was used in 141 (14%) patients, Restylane was used in 86 (8.1%) patients, and Hylaform was used in 52 (5.1%) patients. Soft-tissue augmentation was most commonly performed in the following anatomic locations: nasolabial folds ($n = 547$), lips ($n = 128$), and glabella ($n = 301$). The median age of each patient was 43 (range = 27–68). The average length of follow-up for each patient was 14 months (range 12–31 months).

Nasolabial Folds (NLF)

Of the 547 patients who received treatment of the NLF, 378 received autologous fat grafting, 26 received Hylaform, 41 received Restylane, and 102 received Radiesse injections.

The typical injection volume for patients receiving autologous fat to the NLF was approximately 5 mL (2.5 mL per side). The injection procedure takes on average 45 minutes (harvesting, processing, injection) and was well tolerated in the majority of patients. Patients typically experienced ecchymosis and swelling 2–3 days following injection; how-

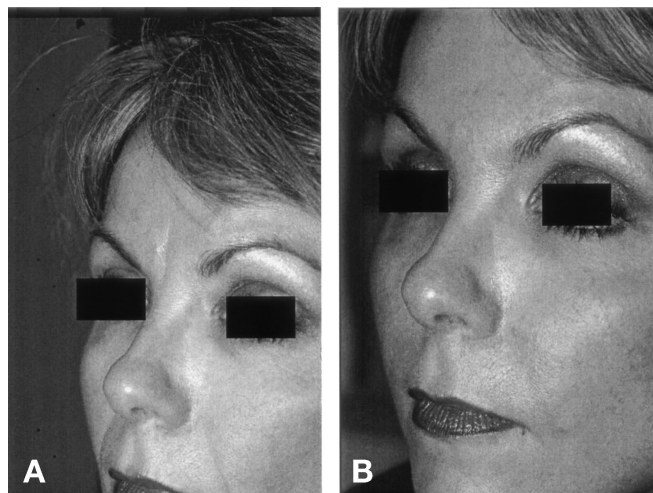


FIGURE 1. Autologous fat grafting, glabella and NLF. A, Pre-operative photo. B, Nine months after Botox injection and 1 mL fat to the glabella + 2 mL fat to the nasolabia I fold.

ever, these reactions were always self-limited. Approximately 10% of patients required one touchup, which was defined as a repeat injection for the same anatomic area between 6 and 12 months of the initial injection. The average longevity for autologous fat in the NLF was greater than 12 months (Fig. 1).

Restylane and Hylaform in the NLF have very similar injection characteristics. A typical volume of injection is approximately 3 mL (1.5 mL per side). The procedure typically takes 10–15 minutes. Complications and adverse reactions to Restylane or Hylaform injection were minimal, and there was no incidence of infection. The principal difference between Restylane and Hylaform in the NLF is longevity. We found that Hylaform lasts 3 months in the NLF, while Restylane typically lasts 4.5 months (Fig. 2).

Lastly, Radiesse injection to the NLF was performed with 2 mL (1 mL per side). Patients typically recovered within 24 hours from mild to moderate swelling at the injection site. Approximately 20% of patients receiving Radiesse injections

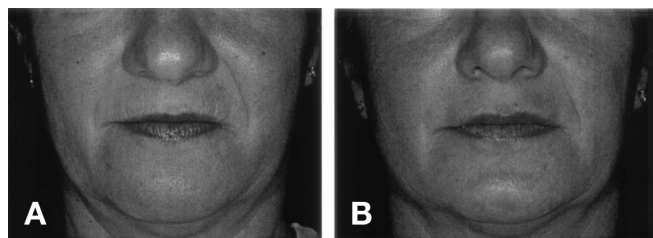


FIGURE 2. Nasolabial folds. A, Preoperative photo. B, Four months after 2 mL injection of Restylane on the R NLF and 2.2 mL Hylaform to the L NLF. Note the persistence of Resytlane on the right and decreased persistence of Hylaform on the left NLF.

required a touchup within 3 months (typically <1 mL). The longevity of Radiesse in the NLF was excellent, averaging 11 months.

Lips

Due to the greater degree of motion, lip augmentation with injectable fillers is not as forgiving when compared with the NLF region. Of the 128 patients who received treatment of the lips, 87 received autologous fat, 17 received Hylaform, and 24 received Restylane. Due to the high incidence of mucosal nodules associated with the use of Radiesse for lip augmentation we did not inject any patients with Radiesse in this region (Fig. 4).

Autologous fat grafting has been extensively used in the lips but is plagued by a significant degree of swelling and ecchymosis, which requires a prolonged recovery period of nearly 1–2 weeks (Fig. 3). Fat grafting to the lips is also associated with significant variability of resorption due to the motion in this region. Nearly 30% of our patients required a touchup procedure within the first 6 months. Despite this variability, the average longevity of autologous fat in the lips was greater than 12 months, with some patients experiencing results lasting longer than 2 years.

Restylane and Hylaform have similar characteristics when used for lip augmentation. In this region, we found Restylane to last 4.5 months, while hylaform typically lasts 3 months. Both materials are well tolerated when injected in the lips and have minimal patient recovery time. Restylane injections were associated with slightly more swelling (typically 1–3 days) when compared with Hylaform. The average injection volume of restylane was 1.5–2 mL, while that for Hylaform was 2–3 mL. Touchups associated with the use of Restylane and Hylaform were required in 20% of patients at 3 months.



FIGURE 3. Autologous fat grafting lips. A, Preoperative photo. B, One week after 2-mL fat injection to upper and lower lips (note ecchymosis). C, Nine months postoperative result.

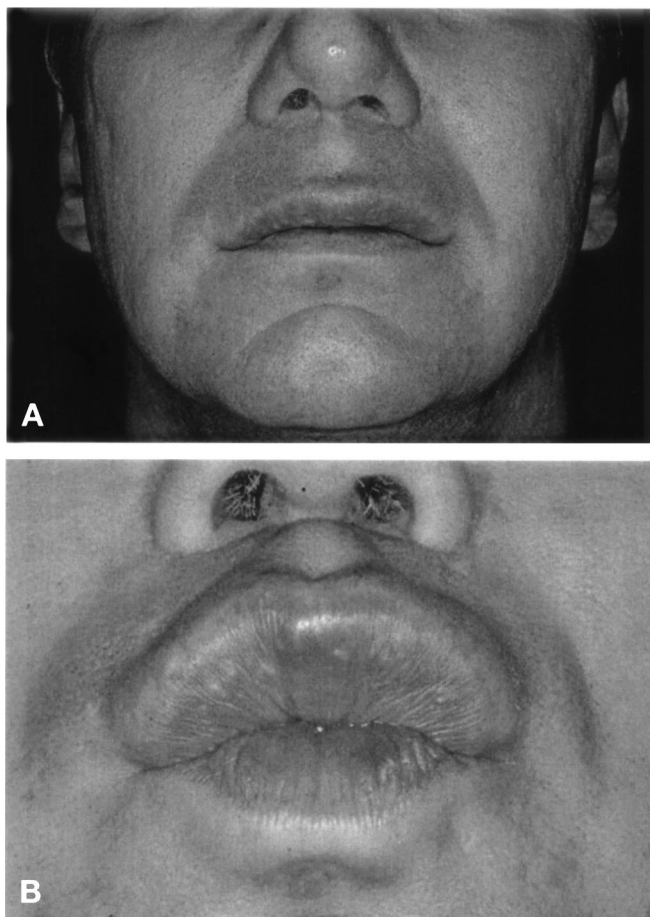


FIGURE 4. Prominent mucosal lip nodules 6 months after Radiesse injection to the upper and lower lips performed by another physician.

Glabella

Of the 301 patients who received treatment of the glabella, 232 received autologous fat grafting, 9 received Hylaform, 21 received Restylane, and 39 received Radiesse injections.

The glabella is an excellent area for volume augmentation in the face. Nearly all fillers work well in the glabellar region but require preoperative Botox injections to decrease motion.^{10,11} Therefore, we used preoperative Botox approximately 5 days to 1 week prior to treatment of the glabella for all patients. Botox was not given simultaneously due to the concerns of intraoperative spread and potential eyelid ptosis. We found a typical injection volume in the glabella to be 1 mL, regardless of the type of filler used. Complications and touchups for this region were minimal, regardless of the type of filler used.

Fat grafting in the glabella can have quite long-lasting results, with the average patient experiencing a longevity of greater than 12 months.^{12,13} Patients who received autologous

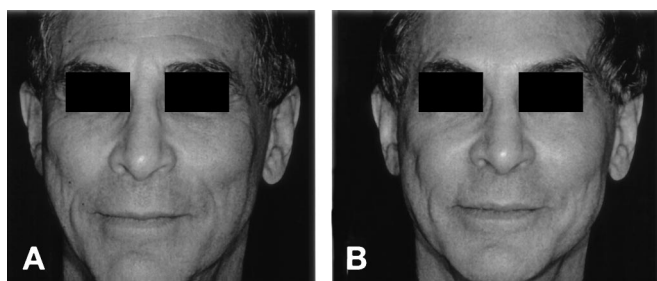


FIGURE 5. Radiesse to the nasolabial folds and glabella. A, Preop photo. B, Twelve months s/p 2 mL Radiesse to NLF and 1 mL Radiesse + Botox to the glabella.

fat to the glabella recovered within 24–48 hours (see Fig. 1). Restylane and Hylaform also work well in this region. In the glabella, we found Restylane to last an average of 5 months compared with Hylaform, which lasts nearly 4 months. Additionally, Radiesse was also quite effective due to its increased longevity of 13 months in this region (Fig. 5).

Economic Analysis

We performed a simplified cost-effectiveness analysis for the use of these filler materials for facial augmentation.

We calculated the cost of the material per injection and labeled this value “material cost.” Our typical fee for each injection was labeled “surgeon’s fee.” The total patient cost represents the material cost plus the surgeon’s fee.

On a per-treatment basis (Table 1), fat grafting and Radiesse injection to the NLF appear to be costly when compared with the HA derivatives. However, when the longevity of each product is taken into account (see Table 2), one will note that fat and Radiesse are more cost-effective. This phenomenon is due to the fact that the HA derivatives (Restylane and Hylaform) require multiple injections to maintain the same efficacy as Fat and Radiesse at 1 year. In addition, fat grafting has no material cost, although there is an unaccounted cost of increased physician time and handling.

Similarly, in the lips, autologous fat grafting is relatively expensive on a per treatment basis when compared with the HA fillers (Table 3). When examined on a yearly basis, however, the overall cost of all fillers used in this region are much closer (Table 4). Restylane is marginally more cost-effective on a yearly basis when compared with Hylaform due to its greater persistence and therefore fewer average injections per year. Due

TABLE 1.
Nasolabial Folds Cost/Treatment

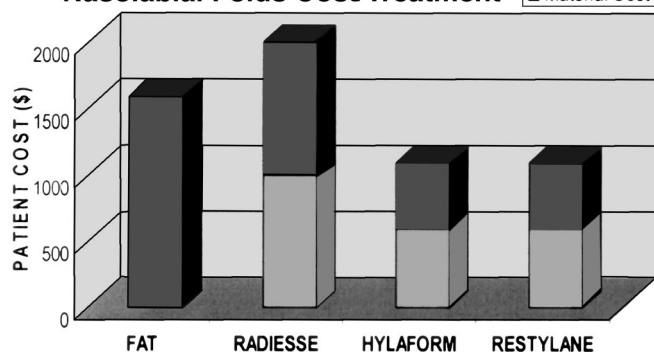


TABLE 2.
Nasolabial Folds Cost/Year

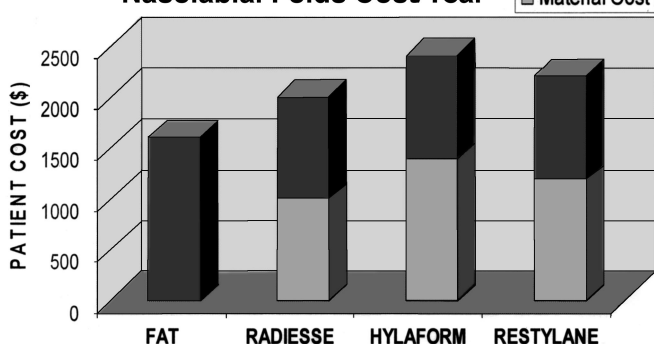


TABLE 3.
Lips Cost/Treatment

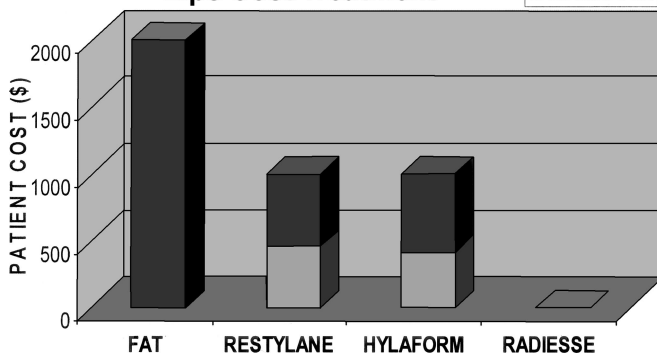


TABLE 4.
Lips Cost/Year

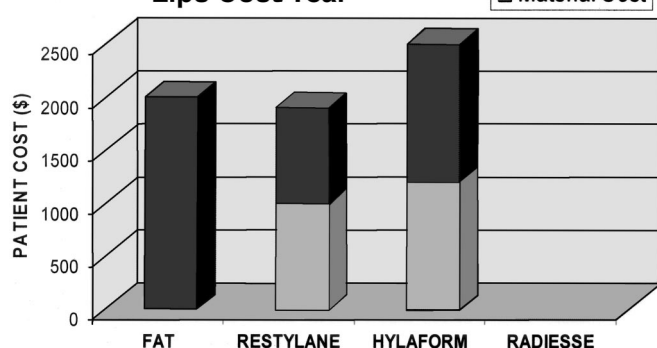


TABLE 5.

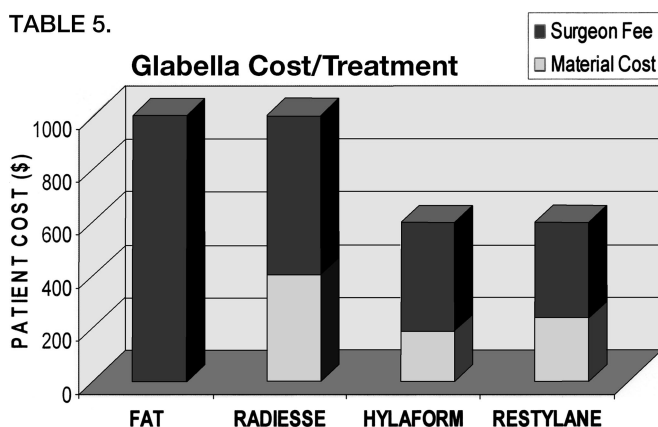
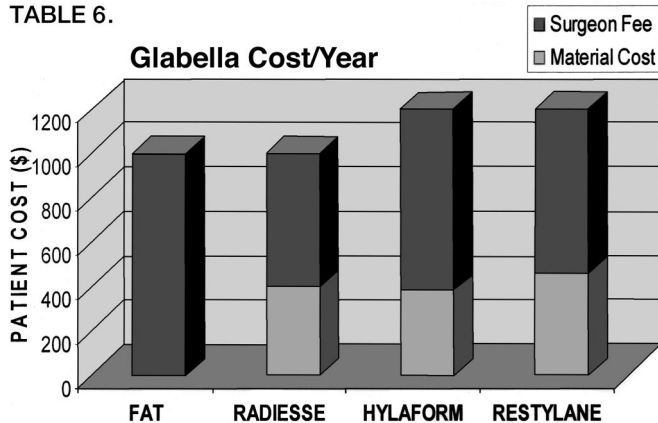


TABLE 6.



to the variability of resorption of fat and the increased recovery associated with fat injection, the cost-effectiveness of fat in this region is questionable.

Last, both Radiesse and Fat have a high cost/treatment in the glabellar region when used with preinjection Botox relative to the HA fillers (Table 5). Nevertheless, the total cost to the patient per year in the glabellar region is approximately the same regardless of the type of filler used (fat and Radiesse are marginally more cost effective due to their increased persistence; Table 6).

DISCUSSION

The number of available injectable fillers for soft-tissue augmentation has increased dramatically in the last several years. The determination of the appropriate filler material is based on multiple variables, including patient safety, ease of injection, longevity, physician preference, cost-effectiveness, and physician profit, among others. We chose to emphasize longevity, safety, patient recovery, and cost-effectiveness to determine the most appropriate filler per anatomic region. We studied those regions commonly treated with fillers for facial-volume augmentation rather than fine-line ablation (ie, peri-

oral rhytids, crow's feet). We found the unique characteristics of each filler made them more appropriate in certain regions when used either in isolation or in combination with other facial procedures. The purpose of our study was to provide a large clinical experience with the use of these fillers in a variety of commonly treated anatomic regions in the face. Additionally, we studied the cost-effectiveness of these fillers across anatomic region, with a particular focus on the cost to the patient for a reliable result lasting 1 year or more.

Successful fat transplantation still appears to be our preferred approach for the treatment of volume loss to the face. The theoretical benefit of replacing fat loss with autogenous fat is most desirable, while the lack of material cost made the use of fat attractive in most regions. Fat grafting becomes most cost-effective when used as an adjunct to other facial surgery procedures (ie, facelift, eyelid surgery). Specifically, the physician time component is absorbed when performing concomitant surgery. Additionally, the longer patient recovery time associated with fat grafting is less significant when patient's recovery is concurrent with other procedures. This is most evident when examining the use of fat for lip augmentation. We tend to reserve fat grafting for lip augmentation for those patients who are having other surgery and can tolerate the prolonged recovery period required. The potential for greatest longevity still exists with fat transplantation for all areas due to the fact that when fat successfully "takes," it behaves like a patient's natural tissues. Lastly, the instrumentation associated with fat grafting additional flexibility; for example, the v-dissector used for fat grafting in the NLF allows one to subcise this crease for more effective effacement.

Radiesse is a surprisingly effective soft-tissue filler with regards to its overall longevity. However, its off-label use and radiopaque characteristics can be a moderate deterrent. We have seen mucosal nodules when Radiesse is used in the lip and therefore have avoided its use in the lips. Radiesse is best reserved for those regions where deep placement of in the soft tissues can be assured. The longevity profile of Radiesse makes it a cost-effective option for isolated NLF or glabella rejuvenation.

The HA fillers have an excellent safety profile across anatomic regions, and therefore their utilization in all areas is acceptable. However, when evaluating cost-effectiveness and longevity, they seem to be less effective than fat or Radiesse in the NLF and glabella. When evaluating safety and patient recovery, they represent our first choice for treatment of the lips as an isolated procedure. Other excellent uses for these HA fillers include the nasojugal groove and some fine-line ablation that was not specifically studied in our analysis. It appears that Restylane had a greater longevity than Hylaform in all regions. It should be noted that at the time of this publication, Inamed has introduced Hylaform Plus and Cap-

tique as efforts to prolong longevity and introduce a non-avian-derived HA filler.

Lastly, it must be noted that economic analysis is a dynamic evaluation that is based on material cost and market conditions. For example, since the beginning of this study, the unit price of Radiesse has been significantly reduced, thereby improving its cost-effectiveness. Nonetheless, the injection characteristics such as preparation, swelling, longevity, and safety remain critical determinants in the selection of the appropriate facial filler for a given anatomic region.

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OPEN DISCUSSION

W.P. Andrew Lee, MD (Pittsburgh, PA): Because this was a retrospective study, I wonder if there was a basis for the plastic surgeon to choose a certain facial filler for the individual patient and thereby building in a selection bias for your result.

Dr. Kanchwala: That is true. It would be much stronger if it were a prospective study. We are planning to do a similar study. What we did do, however, is to take a look, particularly for a cost-effective analysis, at all patients who came to us for volume augmentation of the face over a period of 1 year in 2004. That mitigates that bias a little bit but not completely.

Charles H. Thorne, MD (New York, NY): I am working on a theory that Restylane is a total farce and that it really doesn't last any longer than collagen. I think you said that it lasts 4 1/2 months. Could you please comment on that?

Dr. Kanchwala: In our experience it lasts 4 1/2 months. We have not used collagen in any significant way in our practice, so I can't give you a head-to-head comparison.

Donald R. Mackay, MD (Hershey, PA): Could you tell us how you evaluated the effectiveness. When you said it lasted longer than a year, what criteria did you apply toward quantifying those results?

Dr. Kanchwala: We basically did it by looking at the patient photographs over time. We assigned a blinded observer and had him essentially rate the results in terms of what he thought the appearance was compared to a preoperative photo. Then whenever he thought it was back to baseline, we called that a negative result.

Dr. Mackay: How did you standardize your photograph?

Dr. Kanchwala: We took all the eyes away and the mouths away and just focused in on the area that we were seeing.

Eugene C. Carroccia, MD (Margate, NJ): Your technique for treatment of your fat?

Dr. Kanchwala: In terms of the harvesting and purification, typically we use a hand-assisted suction device after injection of lidocaine. The fat is then harvested and purified by using a Telfa-rolling technique where we essentially roll it on a Telfa pad. There is no centrifugation. There is no freezing. Then it is loaded into 1-cc syringes and injected with a small-caliber cannula.