Aging of the midface is characterized by a combination of two important changes in the facial architecture. The first change is an increase in skin laxity and the gravitational descent of the soft-tissue envelope. The second change, which has been only recognized more recently, is loss of volume from atrophy of the maxillary skeleton, facial musculature, and subcutaneous tissues. It is this recognition of volume loss that has led to an increasing use of various dermal fillers. The types of injectable dermal fillers used with some success in midface restoration include hyaluronic acid derivatives, calcium hydroxyapatite products, and lipotransfer techniques. However, the duration of the effect of these fillers is limited to 6 to 12 months. Therefore, there is a desire to identify injectable materials for soft-tissue augmentation that have a duration of effect that extends beyond the aforementioned products. One such category of injectable agents consists of poly-L-lactic acid (PLLA).

Injectable PLLA (Sculptra/Sculptra Aesthetic; Valeant) is a resorbable soft-tissue augmentation device of nonanimal origin. It has been used as a cosmetic volume enhancer since 1999. In Europe, it was first marketed as New-Fill (Biotech Industry SA). By 2004, Sculptra was introduced to the American market by Dermik Laboratories for use in HIV associated facial lipoatrophy. In 2009, the US Food and Drug Administration (FDA) approved an aesthetic indication for Sculptra, marketed under the name Sculptra Aesthetic.

OBJECTIVE To demonstrate the efficacy and longevity of injectable poly-L-lactic acid as a volumizing injectable in the midface region quantitatively using 3-dimensional (3-D) imaging.

DESIGN, SETTING, AND PARTICIPANTS Prospective study assessing changes in midfacial volume in 15 women aged between 40 and 60 years using a 3-D imaging system at 12, 24, 36, and 48 weeks after 3 treatments with poly-L-lactic acid. Three-dimensional imaging was acquired using the 3-D camera and software.

INTERVENTION Patients were treated with poly-L-lactic acid. The first 2 treatments were 6 weeks apart. The third treatment was performed 12 weeks after the second treatment.

MAIN OUTCOMES AND MEASURES Changes in midfacial volume following 3 treatments of poly-L-lactic acid were measured quantitatively using the 3-D imaging system. A paired t test was used to analyze the difference between pretreatment and posttreatment values at each study time point.

RESULTS Of the 15 patients, 1 only received 2 treatments and was therefore excluded from the statistical analysis. There was a statistically significant increase in mean midfacial volume at all study time points, 12 weeks (mean [range], 7.2 [1.6-20.7] mL; P < .001), 24 weeks (mean [range], 7.2 [1.9-19.4] mL; P < .001), 36 weeks (mean [range], 4.6 [1.1-9.2] mL; P = .002), and 48 weeks (mean [range], 4.1 [0.8-6.4] mL; P < .001), compared with pretreatment volume. There was no significant change in volume between each of the follow-up time points.

CONCLUSIONS AND RELEVANCE Our prospective investigation quantitatively demonstrates the efficacy of poly-L-lactic acid as a long-acting volumizing agent, with an increase in midfacial volume from baseline sustained at least 1 year after treatment.

LEVEL OF EVIDENCE 2.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01307865

Sculptra® Aesthetic is a synthetic biodegradable polymer that is resorbable and biocompatible. It is in the same family as aliphatic polyesters such as glycolic acid and citric acid. Polymers of lactic acid have been widely used for many years in different types of medical devices, such as resorbable sutures, intrabone implants, and soft-tissue implants, as well as a carrier for prolonged delivery of several therapeutic agents. The mechanism of action is thought to be a gradual process of neocollagenesis. Increased levels of collagen type I have been shown in the skin samples of patients treated with Sculptra® at 8 and 24 months. The majority of reports on the longevity of Sculptra® are based on physician observation, either directly or by means of examination of 2-dimensional photographs and patient satisfaction surveys. Using these methods, duration of effect has been demonstrated for at least 2 years. However, no quantitative data exists regarding the amount of volume change expected with Sculptra® or the duration of the treatment effect.

Our aim was to use 3-dimensional (3-D) imaging to objectively quantify the results of soft-tissue augmentation with Sculptra® Aesthetic in the midface region in a prospective manner. The 3-D imaging system used in this study was Canfield Scientific’s VECTRA® 3-D system combined with Mirror imaging software (Canfield Scientific). Studies by the National Institutes of Health (NIH) as well as others have demonstrated the accuracy and reproducibility of results obtained using this system. This system has also been used with great efficacy to analyze volumetric changes after fillers as well as fat grafting.

Methods

Patient Selection

Fifteen patients meeting the inclusion criteria were enrolled from the New York State capital district in the northeastern United States. Inclusion criteria included male and female patients aged between 40 and 60 years, normal body mass index (BMI, >18.5 and <24.9 [calculated as weight in kilograms divided by height in meters squared]), and no prior surgical or nonsurgical treatment (ie, prior dermal fillers) to the midface within the past 2 years. Exclusion criteria included patients younger than 40 years or older than 60 years, a BMI lower than 18.5 or greater than 24.9, prior surgical or nonsurgical treatment to the midface within the past 2 years, hypersensitivity to PLLA, immunosuppressed state, or history of autoimmune disease.

Product Preparation

Sculptra® Aesthetic is provided as a freeze-dried solid, supplied in a clear glass vial. It is stable at room temperature for up to 2 years in the lyophilized form. In this study, each vial of poly-L-lactic acid was reconstituted using 7 mL of sterile water 24 hours prior to treatment and then stored in the refrigerator. One hour prior to treatment, 1 mL of lidocaine with 1:100 000 epinephrine was added to each vial, for a total of 8 mL.

Injection Technique

Injections were preceded by standard infraorbital nerve block for local anesthetic effect and were administered using Leur lock tuberculin syringes with a 26-gauge needle. The volume was administered using a fan technique to allow for adequate deposition of Sculptra® Aesthetic to the entire midface complex (from lower eyelids superiorly to the upper lip inferiorly, and from the pyriform aperture medially to the zygomatic arch laterally). The total volume injected on each side was evenly distributed across the entire midface complex. In patients with symmetrical volume loss bilaterally, 4 mL of volume was equally distributed on each side. Patients with facial asymmetry received proportionally more on the side with greater volume loss to achieve optimal treatment. The exact distribution of volume delivered to each side was determined by the senior investigator (E.F.W) who also performed all the injections in this study.

Study Protocol

After obtaining approval from the institutional review board of Albany Memorial Hospital and the FDA, as well as written informed consent, patients were enrolled and followed in a prospective manner. Each participant initially received 1 vial (8 mL) of Sculptra® Aesthetic to the midface complex bilaterally for a total of 2 sessions separated by 6 weeks. The third injection was scheduled 12 weeks following the second injection. This allowed the senior investigator to determine which patients would require additional augmentation in order to avoid overcorrection. All study patients were given a diary to record the incidence, severity, and duration of any adverse events that occur during the first 14 days following each injection. This was compared with the incidence of reported adverse events in the literature. A follow-up telephone call was made to all the participants at 72 hours after each injection. Each patient was also evaluated 14 days after each injection to monitor for adverse outcomes. The patients were subsequently followed by means of 3-D photographs at 12, 24, 36, and 48 weeks following the last injection of Sculptra® Aesthetic. A schematic diagram of the study design is presented in Figure 1.

Three-dimensional imaging was completed using the Canfield Scientific VECTRA 3-D system. Care was taken to ensure nonsmiling facial tone in both pretreatment and posttreatment photographs. After registration of each image to the pretreatment image, a circle (150 pixels in diameter) encompassing the entire midface region was marked on each side of the face. Quantitative volume measurements were then made using the 3-D imaging software that compared the volume difference between the pretreatment image and the posttreatment images at each follow-up point in the midface region. The change in midfacial volume of each patient was measured separately on each side. The measurements from each side were then added and averaged to determine the volume change of the entire midface complex in each patient. All volume measurements were recorded in milliliters. An example of 3-D photographs of one our study patients prior to treatment and then at 24 weeks following the last treatment is shown in Figure 2.

A paired t test was used to evaluate the significance of the volume changes observed at each time point compared with baseline. P < .05 was considered significant.
Results

Fifteen patients (30 midface regions) were included in the study. One patient only received 2 injections and was therefore excluded from the final analysis. An additional patient underwent a facelift between her 24- and 36-week follow-up visit, and her data were excluded from the study from that point forward. All study patients were female. The mean age of the participants was 48.7 (range, 40-60 years). The mean BMI of the participants was 20 (range, 18.5-24.7). At each follow-up visit, the patients were questioned regarding any adverse events. A detailed report of the adverse events noted by the participants is given in the Table. All adverse events noted were temporary and resolved without any intervention.

Despite our best efforts to contact each patient prior to their upcoming follow-up appointment, data were not available on every participant at each follow-up time point. The number of participants included in the statistical analysis at each time point is shown in Figure 3. Our findings demonstrate a statistically significant increase in mean (range) midfacial volume at all study time points (12 weeks, 7.2 [1.6-20.7] mL [P < .001]; 24 weeks, 7.2 [1.9-19.4] mL [P < .001]; 36 weeks, 4.6 [1.1-9.2] mL [P = .002]; and 48 weeks, 4.1 [0.8-6.4] mL [P < .001]), compared with pretreatment volumes. There was no statistically significant change in volume between each of the follow-up time points.

The mean midfacial volume change in 5 patients in whom data were available at all follow-up points is demonstrated in Figure 4A. Every participant in this subgroup showed a significant increase in midfacial volume as early as 12 weeks following the last treatment. In 3 of the 5 patients in this subgroup, peak volume increase was seen at 12 weeks following the last treatment of Sculptra Aesthetic. To further evaluate the trend in volume change over time, we plotted the volume changes at

Table. Incidence of Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Incidence, No.*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruising at injection site</td>
<td>14</td>
</tr>
<tr>
<td>Pain at injection site</td>
<td>7</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
</tr>
<tr>
<td>Facial edema</td>
<td>3</td>
</tr>
<tr>
<td>Nodules</td>
<td>1</td>
</tr>
<tr>
<td>Cutaneous eruption</td>
<td>1</td>
</tr>
</tbody>
</table>

* Number of occurrences in all of patients after all the injections.
12 and 48 weeks following the last injection of Sculptra Aesthetic in Figure 4B, which demonstrates that the patients retained a significant portion of their initial gain in midfacial volume at the 48-week follow-up time point. In 3 of the participants, there is a continued increase in midfacial volume at 48 weeks.

Discussion

All studies regarding the efficacy and longevity of Sculptra Aesthetic to this point have used subjective measures of evaluation such as patient satisfaction surveys, physician observation, or use of the Wrinkle Assessment Score (WAS). To our knowledge, this is the first study to provide objective data regarding the efficacy and longevity of Sculptra Aesthetic as a volumizing filler. Our data demonstrate a statistically significant increase in facial midfacial volume as early as 12 weeks following the last (third) injection of Sculptra Aesthetic. This is in accordance with a study by Narins et al who demonstrated a significant reduction in the WAS as soon as 3 weeks following the last injection of Sculptra Aesthetic. In our study, midfacial volume was still significantly increased compared with baseline at the 48-week follow-up, which is in accordance with previous studies that demonstrated that the increase in volume was still apparent at 1 year after the last treatment. Our study also demonstrates objectively for the first time that on average, the maximal volumetric enhancement is observed between 12 to 24 weeks following the last of 3 treatments with Sculptra Aesthetic.

Interestingly, we found that most participants demonstrated a gradual decline in midfacial volume at 48 weeks after injection, with the exception of 3 participants who showed a continued increase in volume. In our study, the mean (range) volume increase was 7.2 (1.6-20.7) mL at 12 weeks and 4.1 (0.8-6.4) mL at 48 weeks. The observed wide range of volume changes between different participants and the continued increase in volume at 48 weeks in 2 of the participants is explained by Sculptra’s nature as stimulatory filler. The process of neocollagenesis most likely occurs to various degrees in each individual. None of our patients was noted to have an over-corrected appearance at any point in the study.

In addition to providing objectivity in evaluation of volumetric enhancements, 3-D imaging serves as a novel tool for demonstrating results to patients. In addition, it allows the ability to rotate images on all axes, a distinct advantage over 2-dimensional imaging. When comparing patients’ pretreatment and posttreatment images in 2 dimensions, it is nearly impossible to have exact duplication of head rotation and chin position, particularly in the three-quarters view. This hinders comparisons assessing for the benefits of volumetric enhancement. The ability of image rotation therefore represents an additional advantage in objectively evaluating results that may assist not only in discussions with patients but also in scientific research.

A detailed analysis of the adverse events reported by the patients who participated in this study revealed injection site bruising to be the most common adverse effect of this treatment, followed by pain at the injection site. Other less common adverse effects included headache, facial swelling, and nodule formation. All adverse effects reported in this study were classified as mild and resolved without any intervention. Nodule formation has been a key adverse event associated with Sculptra and Sculptra Aesthetic, with an incidence of 7% to 9% reported in the literature. It is important to note that the formation of nodules appears to be related to the depth of injection. Too shallow of an injection into the superficial dermis appears to predispose to nodule formation. Our low incidence of nod-
ule formation can be attributed to deeper injection into the subcutaneous tissue as well as reconstituting the product in a larger volume to help dilute the injection.

One of the limitations of this study is that currently the quantitative changes are not correlated with qualitative measures of volume change. Future directions of this study include comparison of 3-D volumetric changes with qualitative changes in facial appearance using the Wrinkle Assessment Score. In this scale, the face is assessed using 3 criteria: contour, bony prominence, and visibility of musculature. Photographs are graded on a scale of 1 to 5, with 5 being the most severe. Although all of our patients stated that they were satisfied with the results they saw, their degree of satisfaction was not assessed in detail. In the future, there may be a role for correlating the degree of patient satisfaction to the amount of volume change assessed. One of the other limitations of our study is the small sample size. Future studies with larger number of participants is needed to further validate our findings.

As demonstrated in our study, the individual response to Sculptra Aesthetic is variable but definitive. All patients demonstrated a statistically significant increase in midfacial volume compared with baseline at all follow-up time points. This effect has been demonstrated in previous studies as well. Because each patient responds differently to treatment with injectable PLLA, it is important to allow sufficient time between treatments to avoid overcorrection.

**Conclusions**

To our knowledge, this study is the first to demonstrate the amount of volumetric enhancement as well as the resultant longevity in the midface of Sculptra Aesthetic in a prospective and quantifiable manner. Our study demonstrates that the volumizing effect Sculptra Aesthetic becomes apparent as early as 12 weeks following the last injection and is maintained at the 48-week follow-up (over a year after initial treatment). This study also demonstrates that the maximal volume gain from Sculptra Aesthetic is also noted within 12 to 24 weeks following the last treatment in most participants.

**ARTICLE INFORMATION**

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Study concept and design: Chen, Williams.

Acquisition, analysis, or interpretation of data: Chen, Javadi, Daines.

Drafting of the manuscript: Javadi.

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REFERENCES


