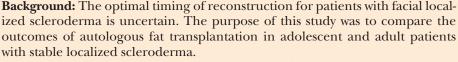
# Tracking Fat Grafts by Magnetic Resonance Imaging: A Comparative Study of Adolescent and Adult Patients with Stable Localized Scleroderma

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**Methods:** Adolescent (age 10 to 19 years) and adult (age >19 years) patients with no previous surgery were enrolled (n = 10, each group). Preoperative magnetic resonance imaging, blood tests, and dermatological assessments were used to assess disease activity. All patients underwent autologous fat transplantation for anatomic facial fat restoration with preoperative magnetic resonance imaging planning. Preoperative, immediate, and 1-year postoperative 3-dimensional Dixon magnetic resonance imaging scans, with image registration and fusion techniques, were used to track fat grafts. Patient satisfaction was assessed with a 5-point Likert scale.

**Results:** There was no significant difference in sex, body mass index, disease severity, or volume of injected fat between the 2 groups (P > 0.05), except for age (P < 0.05). The 1-year postoperative fat graft retention rate was not significantly different, with  $36.6\% \pm 2.4\%$  (range, 25.3% to 49.3%) in the adolescent group and  $32.9\% \pm 1.7\%$  (range, 27.3% to 40.1%) in the adult group (P > 0.05). Surgical outcomes were favorable in all patients, with satisfaction scores of  $3.8 \pm 0.2$  points in the adolescent group and  $3.6 \pm 0.2$  points in the adult group (P > 0.05).

**Conclusion:** In patients with stable localized scleroderma, the initial autologous fat transplantation was equally effective in improving facial contour deformity, with no significant difference in fat graft retention or patient satisfaction. (*Plast. Reconstr. Surg.* 155: 171e, 2025.)





ocalized scleroderma (LoS) is a rare autoimmune disease. Craniofacial LoS usually manifests as unilateral skin tissue fibrosis, subcutaneous soft-tissue atrophy, and even deep tissue involvement, including bone and brain involvement. By the end of disease progression,

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the atrophic deformity caused by LoS is irreversible, and reconstructive surgery for facial lesions can reestablish facial symmetry.<sup>3-6</sup> Autologous fat transplantation (AFT), which is less invasive and more rapidly restorative than traditional free tissue flaps, has become the main means of soft-tissue reconstruction for craniofacial contour deformities.<sup>7</sup> However, the efficacy of AFT in patients with LoS is poor and characterized mainly by high absorption rates, especially in the initial procedure,<sup>8,9</sup> which may be caused by the inflammatory

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microenvironment and adipose-derived stem cell impairment.  $^{10}$ 

The optimal timing of surgery for juvenile LoS patients is not clear. It is recommended that medication, such as immunosuppressants, be administered during the active phase and reconstructive surgery be performed after stabilization.<sup>11-13</sup> However, the disease develops gradually at an early age, and even if the disease has stabilized before adulthood, there is still concern that the surgical outcome will be unpredictable because of growth. 14,15 There is still a lack of comparative studies of surgical outcomes between adolescents and adults with stable LoS. Although previous facial reconstruction AFT studies have emphasized the importance of multilevel and multiregional injections, 16,17 no previous study has focused on reconstruction of the superficial and deep fat compartments in patients with LoS. In this article, we present a new AFT approach suitable for LoS patients that is based on the disease characteristics of atrophy and the anatomic facial fat restoration (AFFR) principle with superficial and deep fat compartment reconstruction. We compared the initial surgical outcomes of adolescent patients with those of adult patients by means of serial magnetic resonance imaging (MRI) examinations and satisfaction assessment.

## PATIENTS AND METHODS

This was a preliminary prospective observational study of patients with LoS who underwent initial AFT between March of 2022 and September of 2022 in our department. Patient information, including age, sex, body mass index (BMI), LoS damage index<sup>18</sup> (LoSDI), degree of atrophy,<sup>19</sup> and operation time, was collected from medical records. Preoperative and postoperative MRI data and photographs were collected as well. Patients between the ages of 10 and 19 years old were defined as the adolescent group, and those older than 19 years were defined as the adult group<sup>20</sup> (World Health Organization standard). Results of facial fat-grafting procedures stabilize between 6 months and 1 year postoperatively.21 Therefore, at 1 year postoperatively, the patients returned to the outpatient clinic to undergo repeated MRI examinations and to complete satisfaction surveys.

The detailed inclusion and exclusion criteria are listed in Table 1. The enrolled patients were in a healthy and stable condition and had maintained a stable weight during the 1-year follow-up period. This study was approved by the ethics committee of Peking Union Medical College Hospital (identification no. K2393) and

**Table 1. Inclusion and Exclusion Criteria** 

|           | Criteria  |  |  |
|-----------|---|--|--|
| Inclusion | Confirmed diagnosis of facial LoS by the dermatology department of our hospital and a strong desire for facial reconstruction   |  |  |
|           | Under long-term follow-up in the dermatology<br>clinic of our hospital and no disease progression<br>for at least 1 year, as confirmed by a dermatologis  |  |  |
|           | Preoperative blood inflammatory markers within<br>normal range, including C-reactive protein, pro<br>calcitonin, and erythrocyte sedimentation rate   |  |  |
|           | Preoperative MRI scan showing no sign of brain<br>abnormality or disease activity, as assessed by a<br>radiologist specializing in craniofacial MRI   |  |  |
|           | Adults: BMI between 18.5 and 28; adolescents:<br>BMI within the normal reference range (no<br>underweight or obesity) according to the stan-<br>dardized growth charts for Chinese adolescents <sup>2</sup> |  |  |
| Exclusion | Presence of risk factors, such as smoking, vascular disease, hypertension, diabetes mellitus, or infectious diseases <sup>9</sup>   |  |  |
|           | History of facial surgery   |  |  |
|           | Treatment with glucocorticoids, methotrexate, or other immunosuppressive agents from 1 year before surgery to the end of the follow-up period   |  |  |
|           | Contraindications to MRI examination  |  |  |
|           | Underweight or obese; or BMI changes signifi-<br>cantly during follow-up (>2 points) <sup>23</sup>  |  |  |
|           | Unable to complete follow-up visits on time   |  |  |
|           |   |  |  |

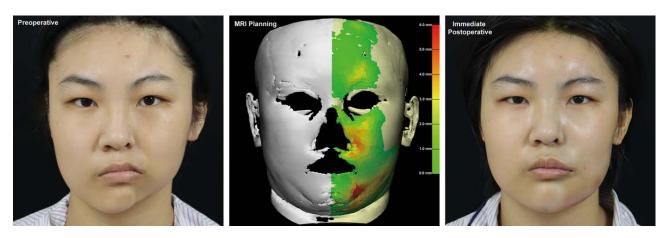
conducted in accordance with the Declaration of Helsinki (2013). Patients or their parents provided written informed consent.

#### **Preoperative Planning**

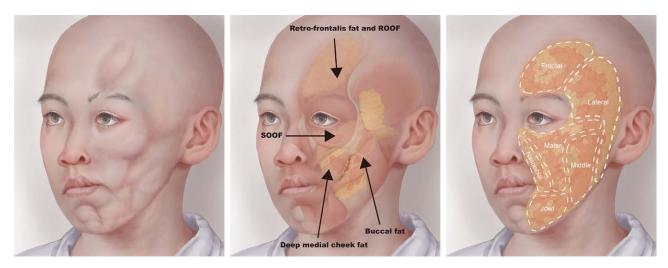
All patients underwent AFT under general anesthesia in the day care ward of our hospital. For a precise AFT procedure using the AFFR principle, preoperative MRI was used to assess the extent of defects at different levels. By comparing fat signals on both the healthy and affected sides, the region and the thickness of the AFT could be estimated and further visualized with wall thickness analysis (Fig. 1) using 3-Matic Research software (version 13.0 for Windows; Materialise, Leuven, Belgium). With the aim of matching the structure, thickness, and shape of the postoperative fat tissue on the affected side with those of the normal side as closely as possible, only fat signals from both sides were compared, not the overall contour, as in previous studies based on mirror images.24

#### Liposuction

Liposuction was performed mainly on the lower abdomen and supplemented by the inner thigh when there was insufficient fat.<sup>8,25,26</sup> The donor area was infiltrated with tumescent solution



**Fig. 1.** MRI-assisted preoperative planning was performed by comparing the thickness of fat tissue (*center*) on the affected and healthy sides (patient 10). There was moderate overcorrection immediately postoperatively (*right*) compared with preoperatively (*left*).



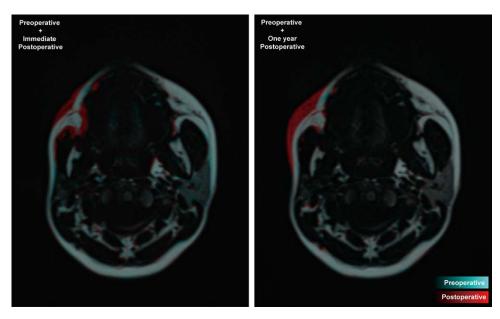
**Fig. 2.** Illustration of a patient with LoS (*left*) undergoing reconstruction of the deep fat compartments (*center*), and the subcutaneous fat (*right*) following AFFR. *Dark brown* areas indicate the preoperative fat; the postoperative fat is indicated by the *yellow* areas.

(0.06%) lidocaine with 1:1,000,000 epinephrine), and subcutaneous fat was manually aspirated with a 2.5-mm, multihole blunt cannula. After centrifugation at  $3000 \times g$  for 3 minutes, the upper oil layer and the lower sediment were removed, and the middle layer of fat was transferred to 1-ml syringes for transplantation (Coleman technique). The incisions were mostly made in hidden areas, such as the scalp, with an 18-G needle, and an incision at the modiolus covered most of the cheek and chin region. Fat was slowly injected in a retrograde manner using a 1.0-mm blunt cannula through a single side hole.

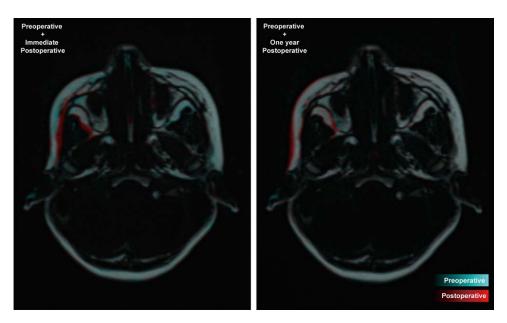
# **Anatomic Facial Fat Restoration**

The principle of AFFR is that fat is transplanted as closely as possible to normal anatomic structures to aid conformation (Fig. 2). The characteristics

of fat distribution in an anatomic region and the characteristics of atrophy should be considered simultaneously. In the temporal, cheek, and chin regions, there was a large amount of subcutaneous fat, and subcutaneous injections were planned preoperatively. In addition, the atrophy caused by lesions in the lower middle face was usually not limited to subcutaneous fat; therefore, deeper tissue loss could be augmented by lipofilling in the deep facial fat pads. As a natural gap existed between these deep fat pads and the surrounding tissue, even in patients with severe atrophy (Figs. 3 and 4), the fat grafts would spread along these gaps after lipofilling to achieve physiological structural restoration<sup>28</sup> (Fig. 2). The sensation of breakthrough as the needle advances deeper and the sensation of superficial tissue thickness at the tip of the cannula could help to confirm that



**Fig. 3.** Fused MRI scans (patient 16, lower face) show restoration of fat at different levels after AFT using the AFFR principle. In addition, the overall postoperative contour was close to normal (fat images in 3-dimensional Dixon sequence: preoperative, *cyan*; postoperative, *red*).



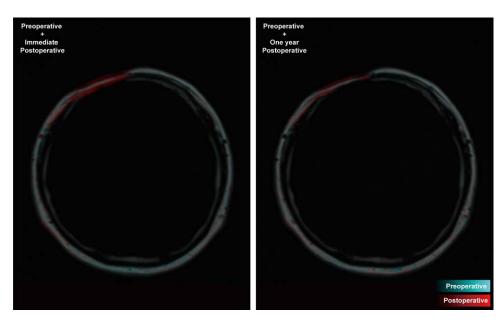
**Fig. 4.** Fused MRI scans (patient 16, middle face) show the reconstruction of the deep fat compartments with long-term stable results.

the cannula is entering the deep fat pads. There is less subcutaneous fat in the forehead and scalp than in the cheek, and lesions in this area tend to be generalized atrophy of the skin, subcutaneous fat, and bone; therefore, only a small amount of fat needs to be injected subcutaneously to achieve a natural-looking apperance<sup>29,30</sup> (Fig. 5). Most of the fat should be injected underneath the frontalis and aponeurosis to compensate for the bony atrophy in this region. After intraoperative

visualization of facial symmetry, moderate overcorrection (no more than 10%) was performed to compensate for absorption (Fig. 1).

# **Outcome Assessment with MRI**

Due to the slightly different positions of the patients during the examination, all images were adjusted so that all axial images were parallel to the Frankfurt plane. As the patient's position during different examinations could not be



**Fig. 5.** Fused MRI scans (patient 14, upper face) show that forehead injections were supplemented primarily underneath the frontalis (or aponeurosis), with small amounts subcutaneously.

maintained, the Elastix medical image registration toolbox was used for registration of postoperative and preoperative images.<sup>31</sup> For a direct illustration of the changes, we stained the grayscale fat images with pseudocolor and fused the preoperative (cyan) and postoperative (red) images (Figs. 3 through 5). In this way, the changed fat in the fusion images appeared in red, while the unchanged fat remained white on the scans. After manual labeling of fat in preoperative and postoperative images within the operative area, fat graft volume retention was calculated using the following formula:

 $Volume\ retenion\ =\ \frac{Immediate\ postperative\ volume-Preoperative\ volume}{One\ year\ postoperative\ volume-Preoperative\ volume}\times 100\%$ 

The Digital Imaging and Communications in Medicine data were standardized, registered, labeled, and analyzed using 3-dimensional Slicer software (version 5.0.3 for Windows; www.slicer.org).

## **Clinical Assessment**

Standardized facial photographs were taken preoperatively and 1 year postoperatively. Patients were asked to rate their satisfaction with the surgery by comparing their preoperative and postoperative photographs. Adolescent patients were evaluated by their parents. A Likert scale was used for rating, with scores ranging from 1 to 5, with 1 being the least satisfied and 5 being the most satisfied.

#### **MRI Scan Protocols**

Fat graft remodeling was assessed by comparing preoperative, immediate postoperative (within 6 hours after surgery), and 1-year postoperative MRI scans. (See Video 1 [online], which shows 3dimensional schematics of 2 patients based on fat images collected preoperatively, immediately postoperatively [<6 hours], and 1 year postoperatively [above]. Fat tissue in potentially affected areas is shaded *light blue* [preoperative], *green* [immediate postoperative], and *yellow* [1-year postoperative] [below].) Patients were asked to maintain a standardized position during the examination. For optimal assessment of fat, a 3-dimensional Dixon sequence with a gradient echo sequence was performed using a 3.0-T scanner (Magnetom Vida; Siemens Healthineers), as previously described. 32,33 The acquisition and reconstruction voxels were 1.14 mm, 1.14 mm, and 1.00 mm. Four sets of images were obtained with 3-dimensional Dixon T1-weighted sequences: in-phase images, opposed-phase images, fat images, and water images. In fat images, only fat signals were displayed, without interference from other tissues. Transverse, sagittal, and coronal images were reconstructed and exported as Digital Imaging and Communications in Medicine data.

# **Statistical Analysis**

Comparisons of quantitative data (BMI, volume, LoSDI, retention, and satisfaction) with normal distributions were performed using independent 2-sample *t* tests (2-sided). Data are presented as mean



**Fig. 6.** (*Left*) Preoperative and (*right*) 1-year postoperative photographs of an LoS patient (patient 16) after a single AFT reconstruction using AFFR. The patient shows improved facial symmetry.



**Fig. 7.** (*Left*) Preoperative and (*right*) 1-year postoperative photographs of an LoS patient (patient 14) after a single AFT reconstruction using AFFR. The patient shows improved facial symmetry.

 $\pm$  SEM; data (age) with nonnormal distributions were compared using Mann-Whitney U tests. The Fisher exact test was used for comparison between categorical variables (sex, side, donor/recipient site, and degree of atrophy). A P value less than 0.05 was considered significant. All analyses were performed using GraphPad Prism software (version 9.3.1 for Windows; GraphPad Software, Boston, MA).

#### **RESULTS**

Between March and September of 2022, a total of 47 patients with LoS underwent AFT in

our department. One patient had lesions located on the trunk; 1 had a metallic brace that prevented MRI; 8 patients had previously undergone surgery; and 8 patients refused to participate. All procedures were performed by a single senior specialist (X.L.) within 1 or 2 hours. Thirty patients were enrolled initially; during follow-up, 9 patients did not complete follow-up on time, and 1 patient had a significant BMI change. A total of 81 MRI examinations were performed. Twenty patients (10 adults and 10 adolescents) who completed their follow-up at 1 year postoperatively were

Table 2. Demographic Characteristics and Clinical Information of Enrolled Patients

| Group  | Adolescent Group<br>(n = 10)<br>15 (13, 16.3) | Adult Group<br>(n = 10)<br>22.5 (20, 31.3) | <i>P</i> <0.01 <sup>a</sup> |
|--|---|--|-----------------------------|
| Median age (25th percentile, 75th percentile)    |   |  |                             |
| Sex, no. (%)                                     |   |  |                             |
| Female   | 4 (40)  | 5 (50)                                     | >0.05 <sup>b</sup>          |
| Male   | 6 (60)  | 5 (50)                                     |                             |
| BMI, mean ± SEM                                  |   |  |                             |
| Preoperative                                     | $22.1 \pm 0.8$                                | $23.2 \pm 1.0$                             | >0.05°                      |
| Postoperative (1 year)                           | $22.3 \pm 0.8$                                | $23.3 \pm 1.0$                             | >0.05°                      |
| Side, no. (%)                                    |   |  |                             |
| Right  | 5 (50)  | 5 (50)                                     | >0.05 <sup>b</sup>          |
| Left   | 5 (50)  | 5 (50)                                     |                             |
| Donor site, no. (%)                              |   |  |                             |
| Lower abdomen                                    | 6 (60)  | 7 (70)                                     | >0.05 <sup>b</sup>          |
| Abdomen and inner thigh                          | 4 (40)  | 3 (30)                                     |                             |
| Predominant recipient site, no. (%) <sup>d</sup> |   |  |                             |
| Upper face                                       | 5 (50)  | 6 (60)                                     | >0.05 <sup>b</sup>          |
| Lower face                                       | 5 (50)  | 4 (40)                                     |                             |
| Injection volume, mean ± SEM, mL                 | $38.6 \pm 5.2$                                | $39.1 \pm 7.5$                             | >0.05°                      |
| LoSDI, mean ± SEM <sup>e</sup>                   | $5.5 \pm 0.4$                                 | $5.7 \pm 0.4$                              | >0.05°                      |
| Degree of atrophy, no. (%) <sup>19</sup>         |   |  |                             |
| Mild   | 2 (20)  | 3 (30)                                     | >0.051                      |
| Moderate   | 6 (60)  | 4 (40)                                     |                             |
| Severe   | 2 (20)  | 3 (30)                                     |                             |
|  |   |  |                             |

<sup>&</sup>lt;sup>a</sup>Mann-Whitney U test.

ultimately enrolled (Figs. 6 and 7). (See Video 2 [online], which shows a 23-year-old female patient [patient 16] with lesions concentrated mainly in the lower face [Parry-Romberg syndrome]. Fused MRI scans show stable long-term postoperative survival of fat grafts in both the superficial and deep fat compartments after AFFR. See Video 3 [online], which shows a 21-year-old male patient [patient 14] with lesions concentrated mainly in the upper face [en coup de sabre morphea]. Photographs and fusion MRI scans after a single AFT reconstruction using the AFFR principle show improved facial symmetry. See Video 4 [online], which shows postoperative photographs and fusion MRI scans of an 18-year-old female LoS patient [patient 10] after a single AFT reconstruction with AFFR. The patient has improved facial symmetry . See Video 5 [online], which shows postoperative photographs and fusion MRI scans of a 14-year-old female LoS patient [patient 14] after a single AFT reconstruction with AFFR. The patient shows improved facial symmetry. **See** Table, Supplemental Digital Content 1, which

shows detailed clinical information of enrolled patients, <a href="http://links.lww.com/PRS/H284">http://links.lww.com/PRS/H284</a>.)

There was a significant difference in age between the 2 groups (P < 0.01) (Table 2). No significant difference in sex, age, disease severity (LoSDI), degree of atrophy, BMI (both preoperative and postoperative), side, or donor or recipient site was found between the 2 groups (all P > 0.05).

There was also no significant BMI change in either group within 1 year of follow-up (all P > 0.05). The BMI of both patient groups was stable during follow-up (change < 2 points), although patients in the adolescent group were still growing. Despite differences in the severity and extent of disease in each participant, there was no significant difference in the amount of injected fat between the 2 groups (P > 0.05).

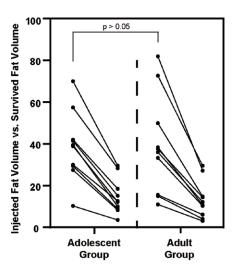
At the 1-year postoperative follow-up, the fat retention rate was  $36.6\% \pm 2.4\%$  in the adolescent group and  $32.9\% \pm 1.7\%$  in the adult group, with no significant difference between the 2 groups (P > 0.05) (Fig. 8). In addition, a more detailed

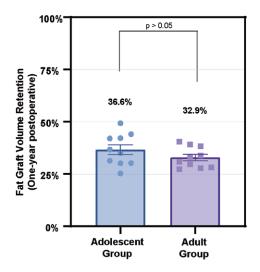
<sup>&</sup>lt;sup>b</sup>Fisher exact test.

ct test

<sup>&</sup>lt;sup>d</sup>There are always multiple facial subunits involved (Denadai R, Buzzo CL, Raposo-Amaral CA, Raposo-Amaral CE. Facial contour symmetry outcomes after site-specific facial fat compartment augmentation with fat grafting in facial deformities. *Plast Reconstr Surg.* 2019;143:544–556), but the lesions were often concentrated on the upper or lower face (ie, en coup de sabre morphea or Parry-Romberg syndrome) (Tollefson MM, Witman PM. En coup de sabre morphea and Parry-Romberg syndrome: a retrospective review of 54 patients. *J Am Acad Dermatol.* 2007;56:257–263).

<sup>&</sup>lt;sup>e</sup>Clinical scores of disease severity were evaluated by dermatologists (Teske NM, Jacobe HT. Using the Localized Scleroderma Cutaneous Assessment Tool (LoSCAT) to classify morphoea by severity and identify clinically significant change. *Br J Dermatol.* 2020;182:398–404).





**Fig. 8.** There was no significant difference in the amount of fat injected between the adolescent and adult groups (*left*). At 1-year follow-up, there was no significant difference in fat retention rate between the 2 groups (*right*). Values are expressed as mean ± SEM.

subgrouping of adolescents also showed no significant difference. There was also no significant difference in retention between different donor sites or among different degrees of atrophy. (See Figure, Supplemental Digital Content 2, which shows that different donor sites [left], more detailed age stratification [center], and different degrees of atrophy [right] did not result in significant retention differences. Values are expressed as mean ± SEM, http://links.lww.com/PRS/H285.)

Patient satisfaction scores were not significantly different between the 2 groups, with  $3.8 \pm 0.2$  points in the adolescent group and  $3.6 \pm 0.2$  points in the adult group (P > 0.05). There were no postoperative surgery-related complications (neither donor nor recipient site) in any of the patients.

## **DISCUSSION**

Our results show that the efficacy of AFT in adolescent patients is not significantly different compared with adult patients, as long as they are in a stable phase. Despite laboratory evidence suggesting that retention might be higher in younger individuals,<sup>34</sup> we did not find significant variability, at least in LoS patients (Fig. 8). A major concern regarding AFT in younger patients is the overgrowth of fat grafts as the child grows. 15 However, previous studies, 5,9,23,35,36 as well as our study, have shown that retention in LoS patients is low; longterm (≥6 months) retention rates range from approximately 22% to 59%, and even lower rates are anticipated in the initial AFT procedure.<sup>8,9</sup> Therefore, we believe that overgrowth should not be the reason that adolescent LoS patients

are deemed unsuitable for AFT. Most juvenile patients under the age of 10 years are in an active stage. Between the ages of 10 and 19 years (adolescents), if the disease activity is well controlled, we recommend performing reconstructive surgery as early as possible. As adolescents quickly become self-conscious about their appearance, facial deformities can seriously affect their psychological development.<sup>37</sup> Scheduling minimally invasive procedures such as AFT during summer or winter breaks from school, and supplementary treatments at 6-month or 1-year intervals if needed, is also ideal for adolescents' schedules.

We first proposed the application of the AFFR principle in patients with LoS and achieved satisfactory surgical outcomes. Without severe bony deformities, AFT using the AFFR principle not only improves superficial subcutaneous fat atrophy but also compensates, to a certain extent, for the deep tissue atrophy caused by deep fat pad, bone tissue, and muscle tissue atrophy in LoS patients. Compared with traditional free tissue grafting, AFFR allows for better conformity to the physiologic anatomy and is less invasive, making it easier to achieve a natural appearance. If the grafts do not conform to physiological anatomical structures and overcompensate for volume superficially, they tend to create a bloated postoperative appearance, which is even more noticeable when making facial expressions. In addition, excessive superficial grafts tend to sag over time due to the absence of supporting structures, resulting from preoperative depression to postoperative prolapse and bloating (ie, patients go from one deformity to another). (See Figure,

**Supplemental Digital Content 3,** which shows an LoS patient who underwent excessive overcorrection in the superficial buccal area before use of the AFFR principle in our practice. During followup, it was found that the superficial fat gradually sagged and protruded, and eventually required liposuction for contour refinement. [Left] The morphology of the secondary deformity was documented with a 3-dimensional camera [Vectra H2; Canfield, Parsippany, N]], and the protrusions were marked with color for thickness [analyzed with Materialise 3-Matic software]. [Right] The fat image [2 years postoperatively] suggested an excessive overcorrection of subcutaneous fat on the affected side [red] compared with the normal side [blue], http://links.lww.com/PRS/H286.) Therefore, AFT of the deep fat structures is necessary, in addition to appropriate superficial AFT according to fat compartment anatomy. 17,38,39 As research on facial fat has improved, deep fat structures have received increased attention, mostly in aesthetic studies related to aging. For example, suspension<sup>40</sup> and partial excision<sup>41,42</sup> have been used for aging-induced buccal fat pad drop and elongation. It was not until recent years that aesthetic studies began to show that facial depressions could be minimized by buccal fat pad augmentations with AFT. 43,44 Targeting superficial and deep fat compartments can effectively improve volume loss due to aging. 45,46 However, deep fat augmentation has long received insufficient attention in reconstructive surgery. The principles of AFFR have drawn fully on these aesthetic concepts in reconstruction with AFT.<sup>47</sup> However, it is important to note that aging-induced volume deficits are different from those caused by LoS. Aging leads to symmetrical soft-tissue atrophy and redundant sagging of the skin and craniofacial skeletal remodeling, 48 whereas LoS leads to more severe unilateral soft-tissue atrophy, with varying degrees of skin fibrosis, rather than sagging and varying degrees of unilateral bony atrophy. Instead of simply compensating for volume, the goal is to restore the normal facial anatomy by reconstructing the superficial and deep fat compartments with AFT.

Cadaver-based studies are unsuitable for studying diseases such as LoS, but imaging-based, thin-layer scanning with 3-dimensional reconstruction techniques can reveal lesion anatomy. We applied serial 3-dimensional Dixon MRI for preoperative and AFT outcome assessment, in which the fat image can clearly show facial fat alone, without showing the complexity of facial structures. Unlike previous imaging-based AFT studies, 7,23,32,36,49 we included immediate postoperative MRI images in

the analysis for the first time. This allowed us to achieve in vivo tracking of fat grafts with the help of image registration<sup>31</sup> and fusion techniques.<sup>50</sup> In comparisons of preoperative and postoperative images, it is evident that fat grafts applied with AFFR principles would develop an overall morphology and a parametric structure close to those of the healthy side. One patient who completed the follow-up was excluded due to significant weight loss. (See Video 6 [online], which shows an adolescent male LoS patient who was excluded from the study because of significant weight loss. Fused MRI scans show well-preserved fat in the patient's deep fat compartments.) Intriguingly, the fat grafts transferred to the deep fat compartments in this patient seemed better preserved with significant weight loss, while superficial fat was more vulnerable to weight change, suggesting different tissue environments at different anatomical layers for fat grafts.

Surgical intervention in the active stage is currently controversial.<sup>51</sup> Although some evidence suggests that early microvascular reconstruction might slow down disease progression,<sup>52–54</sup> reconstructive surgery is usually recommended for patients with stable LoS.<sup>13</sup> Therefore, preoperative assessment of disease activity is critical, but it is difficult for plastic surgeons alone to assess disease activity. To maximize benefit to the patient, a multidisciplinary team is necessary for overall management. In clinical practice, preoperative MRI examination of LoS patients not only aids in surgical planning<sup>33</sup> but also screens for potential central nervous system involvement<sup>55</sup> or active deep fascial lesions.<sup>56,57</sup> The long-term dermatologic follow-up also assists in assessment of disease activity. Despite the lack of universally acknowledged diagnostic criteria for disease activity, we integrated a comprehensive dermatological clinical assessment, blood tests, and MRI examinations to ensure that the enrolled patients were in a stable phase. Fat grafts contain active ingredients, such as mesenchymal stem cells and various growth factors, and there is experimental evidence of potential immunomodulatory and tissue regenerative functions. 10,58 Further study is needed to determine whether AFT, cell-assisted AFT, or adipose tissue components can stop or delay LoS during the active phase.<sup>23,59</sup>

A major limitation of this study is that the sample size was small due to the rarity of the disease. Only adolescent LoS patients with a stable BMI were included. It should be noted that growth in adolescence can be rapid, and the outcome of AFT in adolescent LoS patients with a significantly increased postoperative BMI still needs further study, <sup>60,61</sup> with a larger sample size and a longer

follow-up time, especially considering the increasing rate of obesity among adolescents.<sup>62</sup> In addition, differences between superficial and deep fat in different facial subunits were not examined closely in this study. Studies are also needed to determine the differences between surgical modalities, such as AFT and vascularized tissue augmentation, using similar methods.

#### CONCLUSIONS

AFT was equally effective in both stable adolescent and adult patients with LoS, with no significant difference in fat graft retention or satisfaction rates. In addition, we have demonstrated, using serial MRI, that AFFR can effectively improve superficial and deep fat compartment atrophy as well as muscle and bone atrophy, to a certain extent. We hope that future applications can include other facial contour reconstructions.

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## **DISCLOSURE**

The authors have no conflicts of interest to disclose.

## PATIENT CONSENT

Patients or parents or guardians provided written informed consent for use of patients' images.

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#### DATA AVAILABILITY STATEMENT

Data supporting the findings of this article are available from the corresponding author upon reasonable request.

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