Does Fat Grafting Influence Postoperative Edema in Orthognathic Surgery?

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Purpose: Autologous fat grafting is a useful adjunctive procedure to orthognathic surgery and may also confer anti-inflammatory properties. The purpose of this study is to answer the clinical question: among patients undergoing orthognathic operations, what are the effects of fat grafting on facial edema (magnitude, duration, and rate of decrease)?

Methods: A retrospective cohort study was performed. Three-dimensional photos (Canfield, Fairfield, NJ) from preoperative and a series of postprocedure time-points were analyzed. The data set was divided into a fat-grafted cohort and a non-fat-grafted cohort and later analyzed using paired and unpaired *t* tests and linear regressions to determine significant correlations.

Results: One hundred sixteen pre- and postoperative three-dimensional photo data sets were included. The sample included 29 subjects. The facial volume was analyzed both overall and comparing each subgroup (orthognathic vs. orthognathic + fat grafting group). Postoperative facial volume increase averaged 23.7% for the entire cohort (FG and nFG). By week 12, the swelling decreased about 62% from baseline. In all patients, there was a statistically significant decrease in facial volume with time. In the fat-grafted group, despite adding volume, the facial volume was equal to the non-fat-grafted group at week 1, yet the rate of decrease was faster through week 12.

Conclusion: The majority of postoperative facial edema decreases by 12 weeks following orthognathic surgery. In this cohort of patients, despite the addition of volume, concurrent fat grafting lessened postoperative edema, and led to a greater magnitude and speed of resolution.

Key Words: 3-dimensional (3D) volume, adiposederived stem cells, fat grafting, Lefort 1, postoperative edema

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Postoperative edema can be a lingering nuisance following orthognathic surgery.[1] Postorthognathic swelling has been previously analyzed using 3-dimensional (3D) volume data over time.[2–4] Other methods that have been used include magnetic resonance imaging and cone beam computed tomography, but they are costly and associated with unnecessary radiation.[5] Advances in 3D surface imaging technology have provided a safe and quick tool to generate volume data following surgery.[6]

Autologous fat grafting has been used in facial reconstruction, especially for facial asymmetry and atrophy (ie, hemifacial microsomia, Parry–Romberg syndrome), to add volume and improve contours.[7–9] Fat grafting has also been used to enhance aesthetic results in facelift.[10] We, and others, have used facial lipofilling as an aesthetic adjunct to orthognathic surgery to add volume and camouflage irregularities.[8,11,12] Though some resorption is expected, what remains will persist with time, as documented on magnetic resonance imaging.[13,14] Histopathology of fat-grafted sites also confirms the biologic influence, demonstrating fat globules, adipocytes, and neovascularization.[15] In plastic surgery, structural fat grafting was reported by Coleman, demonstrating stability at the nasolabial folds (without fat resorption) after 3 months to over 6 years.[16] More recently, it is recognized that fat grafting may exhibit anti-inflammatory properties, due to cytokines and adipose-derived stem cells (ADSCs).[17,18] Studies have demonstrated that grafted fat affects neighboring tissue to repair nearby tissues through angiogenesis/vasculogenesis.[19,20] There is plasticity between preadipocytes and macrophages and enhanced immune response leading to permanent tissue remodeling.[21–23] This activity has been suggested to modulate scarring and may mitigate edema and swelling.[17,18,24,25] Clinically, fat grafting has been used in breast reconstruction after resection of tumors, vocal cord augmentation, velopharyngeal insufficiency, and ulcers in the lower extremities.[26–29] Structural fat grafting has been shown to be a safe procedure with low rate of complications in a cohort with ages of 15 to 71 years.[30] Structural fat grafting has been used in conjunction with orthognathic surgery to improve outcomes.[31]

The purpose of this study was to investigate the effect of fat grafting, on facial edema (magnitude, duration, and rate of decrease), when performed in concurrent with orthognathic surgery. The investigators hypothesize that fat grafting will not increase edema, and lead to an equal reduction in swelling with time as if no fat grafting was done. The specific aims of the study were to measure the preoperative and postoperative volumes at 1, 12, and 36 weeks.

METHODS

Study Design

This retrospective cohort study was performed in concordance with the Yale University Institutional Review Board (Protocol number: HIC# 1101007932). To address the research purpose, the investigators designed and implemented a case-control study.

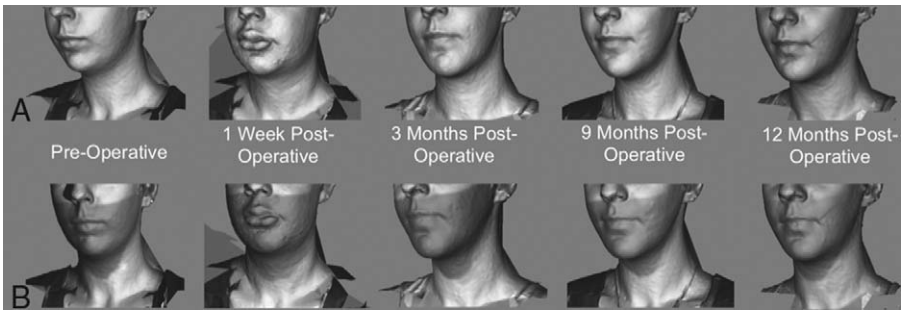

FIGURE 1. (A) Patient preoperative, patient postoperative 1 week, patient postoperative 12 weeks, patient postoperative 36 weeks, patient postoperative 52 weeks, received fat grafting. (B) Volume measured (shaded in darker gray) of (A).

The study population was composed of all patients who underwent orthognathic surgery (Le Fort I, +/− bilateral sagittal split osteotomies [BSSO]) with or without fat grafting (FG, nFG) between May 2012 and August 2014. To be included in the study sample, patients had to have longitudinal follow-up with 3D photos at various time points (preoperative photos within 4 weeks of the surgery, 1, 12, and 36 weeks), not have other surgeries on the face within that time period, and have all the required demographic data recorded (BMI, Lefort advancements, BSSO advancements, and genioplasty advancements). Patients were excluded as study subjects if they were syndromic.

Fat Grafting

Sites of injection include labiomental, nasolabial, cheeks, parasymphysis, and lips, in multiple planes deep to superficial. It should be noted that all patients received the same regimen of perioperative steroids, and intraoperative hypotensive anesthesia. Blood transfusions were not required in any patient.

Fat was harvested and injected at the end of the orthognathic procedures. Donor site was either the medial thigh or lower abdomen. Fat was aspirated using manual suction on a 10 cc syringe with a Coleman cannula. The aspirate was later strained, using the telfa rolling technique, and processed in standard fashion. Small aliquots were injected, using a sharp 19-gauge needle, into each site (in 1 mL intervals), including labiomental sulcus, parasymphysis, lips, cheeks, nasiolabial folds, and piriform region.[32,33] Local anesthesia with epinephrine is injected in the face before for vasoconstriction, which lessens bruising, hematomas, and intravascular infiltration of the fat. The volume of fat injected ranged from 3.5 to 25 mL.

Study Sample

Demographic and operative data were tabulated, including orthognathic procedures undertaken, and the volume and sites of fat grafting when performed. Three-dimensional photos were taken preoperatively, and 1, 12, and 36 weeks postoperatively. Images were captured using the Vectra M3 Imaging System and analyzed using Mirror Software (Canfield Scientific, Fairfield, NJ).[34–37] The facial mask region was demarcated from tragus to tragus horizontally, excluding the nose, and inferiorly to the level of the thyroid cartilage (Figs. 1 and 2), and volumetric analysis performed. Percentages and absolute value of difference were calculated in reference to the baseline preoperative 3D photo. The postoperative edema was calculated using the baseline to compare the volume, duration, and rate of reduction in facial swelling. Additionally, we examined the relationship between postoperative edema and the presence/absence of fat grafting used. Statistical analysis included paired and unpaired t tests as well as linear regression ($P < 0.05$ being significant).

The volumes postoperatively were made relative to the postoperative 36 weeks volume in all analyses due to extensive literature search, subgroup analysis, and the data available. Previous studies have chosen between 24 and 52 weeks as the point of edema resolution. Twelve months was chosen in 1 study, subjectively assuming that 100% of postoperative edema should resolve by that time. Objectively, this study revealed that the bulk swelling occurred during the first 3 weeks, and by 12 weeks 80% of edema remitted compared with postoperative week 1.[2] Another report chose 6 months as baseline, and concluded that facial volume reduced 90% by 12 weeks (and 100% by 6 months).[38] A subgroup analysis of the difference between postoperative 36 and 52 weeks showed no statistical difference for either the non-fat-grafted group ($P = 0.8$) and the fat-grafted group ($P = 0.7$). Final resolution of edema was determined at 36 weeks, compared with baseline volumetric measurements in this analysis. Edema was defined as the volume increase after surgery not including bony differences by using the baseline as 36 weeks. The demographic variables are age, gender, BMI, LeFort advancement, and summation of forward advancements (the summation of the forward maxillary advancement of the LeFort + the forward mandibular advancement of the BSSO + forward advancement of the genioplasty). The predictor

FIGURE 2. (A) Patient preoperative, patient postoperative 1 week, patient postoperative 12 weeks, patient postoperative 36 weeks, patient postoperative 52 weeks, received fat grafting. (B) Volume measured (shaded in darker gray) of (A).

TABLE 1. Demographic Variables per Fat Grafting and Nonfat Grafting (Ranges in Parenthesis)

	Nonfat Grafting (%)	Fat Grafting (%)	*P* Value
Age (y)	32 (20–64)	23 (17–54)	0.05
Gender (% female)	0.7	0.9	0.06
BMI (kg/m^2)	22.5 (15.5–28.8)	20.3 (16–25.7)	0.11
LeFort advancement (mm)	4.4 (2–10)	5.1 (2–12)	0.55
Summation of forward advancements (mm) (Lefort + BSSO + genioplasty)	9.3 (2–28)	9.6 (2–18)	0.93

BSSO, bilateral sagittal split osteotomies.

variable is the presence or lack of fat grafting and the outcome variables are the postoperative volume at 1, 12, and 36 weeks. In terms of operative variables, the surgeon is the same for all operations, the fat grafting technique is the same, all done at the same hospital with the same intraoperative fluid management, postsurgical management protocols and the volume fat grafted ranged from 3.5 to 25 mL.

RESULTS

The data includes 116 photographic datasets (from 29 patients) that met the inclusion criteria and were analyzed in our study. The patients were divided into 2 groups: non-fat-grafted group and the fat-grafted group. The non-fat-grafted group consisted of 12 patients, 70% female, average age 32 years (range 20–64), BMI of 22.5 (range 15.5–28.8) with 58% of the patients having LeFort osteotomies, BSSO, and genioplasty, while the remainder had only LeFort osteotomies. The fat-grafted cohort consisted of 17 patients, 90% female average age 23 years (range 17–54), BMI of 20.3 with 88% of patients having combined LeFort osteotomies, BSSO, and genioplasty with the remained having LeFort osteotomies. There was no statistical difference between 2 groups (FG and nFG) in demographic variables: BMI, LeFort advancement, and summation of forward advancements (the summation of the forward maxillary advancement of the LeFort + the forward mandibular advancement of the BSSO + forward advancement of the genioplasty) (Table 1). The total amount of fat grafting was an average of 10 mL (3.5–25 mL).

In the entire cohort, volumetric measurements revealed an initial postoperative increase in facial volume of 49 cm^3 (a 36% increase) at postoperative week 1 (Table 2). The volume decreased to a 14% increase at postoperative week 12. The difference between the different time points was shown to be statistically significant ($P < 0.01$). By 12 weeks postoperative edema was down to 62% compared with week 1.

Performing intergroup analysis (comparing fat-grafted and non-fat-grafted patients) there was no difference in facial edema ($P > 0.5$) when measured at postop week 1 (Table 3). However, compared with the 36 weeks steady-state mark (in order to take into account postsurgery bone changes), the non-fat-grafted group maintained 10.2% persistent edema, while the fat-grafted group was only 0.1% (nearly 0 cm^3), at 12 weeks. The difference between these 2 groups was statistically significant ($P < 0.05$). Regression analysis revealed there was no linear correlation between the amount of fat grafting and the postoperative decrease of facial edema (Table 4).

TABLE 2. Overall (FG + nFG) Average Increase in Volume Over Time Relative to Preoperative Baseline

Time (wk)	Change in Volume (cm^3) (FG + nFG)	Change in Volume (%) (FG + nFG)	Significance (*P* Value)
1	48.5	36.4	—
12	31.2	14.4	<0.01
36	6.1	11.7	<0.01

FG, fat grafting.

DISCUSSION

The purpose of this study was to determine the effect of fat grafting on postoperative edema following orthognathic surgery. Our hypothesis was that the anti-inflammatory components of fat grafting would counteract the increase in volume conferred by adding fat leading to a similar extent and rate of resolution as if no fat was added. The overall cohort (FG + nFG) showed nearly 62% of swelling resolved by postoperative week 12 (Table 2). In other studies, about 80% of postoperative volume was seen to resolve by week 12.[2] Comparing the nFG and FG groups, the nFG patients held onto more edema with time, with 10.2% persistent swelling compared with only 0.1% (nearly 0 cm^3) FG, at 12 weeks. The results demonstrated that despite fat grafting, the augmentation of volume and the trauma induced by multiple injection sites, the overall initial postoperative volume was similar between the groups and reduced at 12 weeks in the fat-grafted cohort.

These results suggest that fat grafting may be providing a mechanism to mitigate development of and quicken resolution of postoperative edema. In fat harvest and injections, adipose-derived stem cells (ADSCs) are a component of the aspirate and injection. Adipose-derived stem cells have been shown to exhibit paracrine activity and anti-inflammatory properties, including the suppression of IL-1β, IL6, and NO in mouse models and action through cyclooxygenase 2/prostaglandin E2 pathway in vitro studies, decreasing diapedesis and leading to less inflammatory fluid and cells.[39,40] There is also extensive literature of using ADSCs to reduce inflammatory response and oxidative stress in kidney transplants to prevent ischemia-reperfusion injury.[39,41]

Past reports have suggested the aesthetic benefits, and improved patient satisfaction, when using fat grafting with orthognathic surgery.[12,31] This unrecognized improvement in facial swelling in the fat-grafted group may be a contributing factor to the overall satisfaction score. Facial fat grafting in this setting is intended to provide volumetric enhancement, and smooth contours, but the regional administration does not appear to correlate with global volume increase (Table 4). As a result, it appears that fat grafting (at

TABLE 3. Average Increase in Volume (Edema) With or Without Fat Grafting Relative to Week 36

Time (wk)	No Fat Grafting (%)	Fat Grafting (%)	Significance (*P* Values)
1	26.7	21.5	0.51
12	10.2	0.1	0.04

TABLE 4. Overall (FG + nFG) Linear Correlation Between Volume Decrease and Fat Grafting

Time (wk)	R^2
1	0.014
12	0.047

least 3.5 mL) not only brings about cosmetic improvement, but also leads to faster resolution of facial edema, which may improve postoperative course, and time to final aesthetic orthognathic outcome. Future efforts will include longer follow-up, increasing the cohort number, and better defining the aesthetic optimization when performing concurrent fat grafting and orthognathic surgery.

The presence of the same volume at week 1 was also surprising given that all patients in the fat-grafted group underwent more comprehensive orthognathic procedures (88% had combined Le Fort, BSSO, and genioplasty vs. only 58% of the non-fat-grafted group). It is important to note that the data were analyzed relative to the 36 week postoperative volume state, which would account for these differences. This suggests that fat injections confer a protective effect against edema, despite needle injections, added volume, and more involved bone cuts, likely due to anti-inflammatory properties.[17,39,40]

One potentially confounding question is whether or not concurrent fat resorption influenced measurement of edema resolution. However, if fat resorption continued to occur in a major/appreciable way, this would end up reflecting a continued decrease with time of volume in the fat-grafted subjects. Instead, we saw the data reaching a constant, steady-state facial volume sooner in the fat-grafted subjects (minimal or no decrement following 12 weeks). The volume differences between the postoperative 12 and 36 weeks in non-fat-grafted cohort ($P = 0.2$) were not statistically significant, nor in the fat-grafted cohort ($P = 0.8$). Additionally, if the edema and volume were greater immediately postoperative in the fat-grafted cohort, the resorption could be counted toward measurement of edema resolution (but we actually had a lesser overall volume in the fat-grafted subjects at 1 week postop). Imaging to confirm the contribution of edema versus fat was not performed due to expense, radiation, and logistical reasons. The previous literature demonstrated presence of stable facial volume increase from fat density, confirmed on CT images, by 6 months, which was consistent with our results (as measured on 3D photogrammetry).[13]

The weaknesses of the study are the small sample size and the discrepancy in procedures and age between the 2 cohorts. The small study cohort limits the data analysis. It could explain why there is no correlation between the amount fat grafted and the postoperative volume. There is also a difference in the procedures between the patient cohorts. The nFG has 58% Lefort advancements with BSSO and genioplasty advancements and 42% LeFort only procedures while the FG cohort has a greater amount of Lefort advancements with BSSO and genioplasty advancements (about 88%). The difference in procedures can be accounted for by comparing the distances of advancement, which demonstrates no statistical difference (Table 1), and by comparing all figures to the postoperative 36 weeks picture. The difference in age of the 2 cohorts could be a factor affecting the volumes seen. The nFG group has an average age that is 9 years greater than the FG group, yet statistically this is not significant. The ages between the 2 groups are similar also in seeing the median between the 2 groups: the median of the nFG is 25 years and the median of the FG is 20 years. It has not been reported in detail in the literature how age affects postoperative edema utilizing 3D images. It is important to consider in studying fat grafting because aging redistributes fat compartments throughout face possibly altering the effect of the fat grafting injections, this should be accounted for by using baseline images near to the date of the operation, as in this study.[42,43] Previous mechanical and histological studies have demonstrated a loss of elastin (reduced elastic recovery), decreased amount and structure of collagen fibers, and reduced matrix metalloproteinases.[44,45] How aging affects injected fat grafting and postoperative volume in orthognathic surgery has not been studied. The negative consequences of fat grafting are increased surgery time, increased cost, and risk associated with a fat grafting procedure and injections.

CONCLUSIONS

Following orthognathic surgery the majority of postoperative facial edema (about 62%) resolves by 12 weeks. According to this cohort, limited by number and differences in procedures and age between cohorts, fat grafting concurrent with orthognathic surgery appears to reduce postoperative edema, and hasten the resolution of facial swelling to its steady state. This anti-inflammatory effect is present despite adding volume, creating needle sticks, and performing more comprehensive osteotomies. Future studies are needed to further characterize the possible mechanistic role of fat grafting in orthognathic surgery.

REFERENCES

1. Phillips C, Blakey G III, Jaskolka M. Recovery after orthognathic surgery: short-term health-related quality of life outcomes. *J Oral Maxillofac Surg* 2008;66:2110–2115
2. Van der Vlis M, Dentino KM, Vervloet B, et al. Postoperative swelling after orthognathic surgery: a prospective volumetric analysis. *J Oral Maxillofac Surg* 2014;72:2241–2247
3. Metzler P, Geiger EJ, Chang CC, et al. Assessment of three-dimensional nasolabial response to Le Fort I advancement. *J Plast Reconstr Aesthetic Surg* 2014;67:756–763
4. Metzler P, Geiger EJ, Chang CC, et al. Surgically assisted maxillary expansion imparts three-dimensional nasal change. *J Oral Maxillofac Surg* 2014;72:2005–2014
5. Maal TJJ, Plooij JM, Rangel FA, et al. The accuracy of matching three-dimensional photographs with skin surfaces derived from cone-beam computed tomography. *Int J Oral Maxillofac Surg* 2008;37:641–646
6. Kau CH, Richmond S, Incrapera A, et al. Three-dimensional surface acquisition systems for the study of facial morphology and their application to maxillofacial surgery. *Int J Med Robot* 2007;3:97–110
7. Clauser LC, Tieghi R, Consorti G. Parry-Romberg syndrome: volumetric regeneration by structural fat grafting technique. *J Craniomaxillofac Surg* 2010;38:605–609
8. Lim AA, Fan K, Allam KA, et al. Autologous fat transplantation in the craniofacial patient: the UCLA experience. *J Craniofac Surg* 2012;23:1061–1066
9. Mazzola RF, Mazzola IC. History of fat grafting: from ram fat to stem cells. *Clin Plast Surg* 2015;42:147–153
10. Marten TJ, Elyassnia D. Fat grafting in facial rejuvenation. *Clin Plast Surg* 2015;42:219–252
11. Clauser L, Polito J, Mandrioli S, et al. Structural fat grafting in complex reconstructive surgery. *J Craniofac Surg* 2008;19:187–191
12. Steinbacher DM. Personal Communication. November 2015.
13. Swanson E. Malar augmentation assessed by magnetic resonance imaging in patients after face lift and fat injection. *Plast Reconstr Surg* 2011;127:2057–2065
14. Coleman SR. Structural fat grafting: more than a permanent filler. *Plast Reconstr Surg* 2006;118(3 suppl):108S–120S
15. Chajchir AMD, Benzaquen IMD. Fat-grafting injection for soft-tissue augmentation. *Plast Reconstr Surg* 1989;84:921–934
16. Coleman SR. Long-term survival of fat transplants: controlled demonstrations. *Aesthetic Plast Surg* 1995;19:421–425
17. Mert T, Kurt AH, Arslan M, et al. Anti-inflammatory and anti-nociceptive actions of systemically or locally treated adipose-derived mesenchymal stem cells in experimental inflammatory model. *Inflammation* 2015;38:1302–1310

18. Huang S-H, Wu S-H, Lee S-S, et al. Fat grafting in burn scar alleviates neuropathic pain via anti-inflammation effect in scar and spinal cord. *PLoS One* 2015;10:e0137563
19. Neels JG, Thinnes T, Loskutoff DJ. Angiogenesis in an in vivo model of adipose tissue development. *FASEB J* 2004;18:983–985
20. Nakagami H, Maeda K, Morishita R, et al. Novel autologous cell therapy in ischemic limb disease through growth factor secretion by cultured adipose tissue-derived stromal cells. *Arterioscler Thromb Vasc Biol* 2005;25:2542–2547
21. Charrière G, Cousin B, Arnaud E, et al. Preadipocyte conversion to macrophage. Evidence of plasticity. *J Biol Chem* 2003;278:9850–9855
22. Cousin B, André M, Casteilla L, et al. Altered macrophage-like functions of preadipocytes in inflammation and genetic obesity. *J Cell Physiol* 2001;186:380–386
23. Cousin B, Munoz O, Andre M, et al. A role for preadipocytes as macrophage-like cells. *FASEB J* 1999;13:305–312
24. Zellner EG, Pfaff MJ, Steinbacher DM. Fat grafting in primary cleft lip repair. *Plast Reconstr Surg* 2015;135:1449–1453
25. Balkin DM, Samra S, Steinbacher DM. Immediate fat grafting in primary cleft lip repair. *J Plast Reconstr Aesthetic Surg* 2014;67:1644–1650
26. Serra-Renom JM, Muñoz-Olmo JL, Serra-Mestre JM. Fat grafting in postmastectomy breast reconstruction with expanders and prostheses in patients who have received radiotherapy: formation of new subcutaneous tissue. *Plast Reconstr Surg* 2010;125:12–18
27. Cantarella G, Mazzola RF, Domenichini E, et al. Vocal fold augmentation by autologous fat injection with lipostructure procedure. *Otolaryngol Head Neck Surg* 2005;132:239–243
28. Cervelli V, Gentile P, Casciani CU. Use of platelet gel in chronic lower extremity ulcers. *Plast Reconstr Surg* 2009;123:122e–123e
29. Rigotti G, Marchi A, Galiè M, et al. Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: a healing process mediated by adipose-derived adult stem cells. *Plast Reconstr Surg* 2007;119:1409–1422
30. Clauser LC, Tieghi R, Galiè M, et al. Structural fat grafting: facial volumetric restoration in complex reconstructive surgery. *J Craniofac Surg* 2011;22:1695–1701
31. Raffaini M, Pisani C. Orthognathic surgery with or without autologous fat micrograft injection: preliminary report on aesthetic outcomes and patient satisfaction. *Int J Oral Maxillofac Surg* 2015;44:362–370
32. Pfaff M, Wu W, Zellner E, et al. Processing technique for lipofilling influences adipose-derived stem cell concentration and cell viability in lipoaspirate. *Aesthetic Plast Surg* 2014;38:224–229
33. Wu W, Le AV, Mendez JJ, et al. Osteogenic performance of donor-matched human adipose and bone marrow mesenchymal cells under dynamic culture. *Tissue Eng Part A* 2015;21:1621–1632
34. Maal TJJ, van Loon B, Plooij JM, et al. Registration of 3-dimensional facial photographs for clinical use. *J Oral Maxillofac Surg* 2010;68:2391–2401
35. Maal TJJ, Verhamme LM, van Loon B, et al. Variation of the face in rest using 3D stereophotogrammetry. *Int J Oral Maxillofac Surg* 2011;40:1252–1257
36. Heike CL, Upson K, Stuhaug E, et al. 3D digital stereophotogrammetry: a practical guide to facial image acquisition. *Head Face Med* 2010;6:18
37. Metzler P, Sun Y, Zemann W, et al. Validity of the 3D VECTRA photogrammetric surface imaging system for cranio-maxillofacial anthropometric measurements. *Oral Maxillofac Surg* 2014;18:297–304
38. Kau CH, Cronin A, Durning P, et al. A new method for the 3D measurement of postoperative swelling following orthognathic surgery. *Orthod Craniofac Res* 2006;9:31–37
39. Shih Y-C, Lee P-Y, Cheng H, et al. Adipose-derived stem cells exhibit antioxidative and antiapoptotic properties to rescue ischemic acute kidney injury in rats. *Plast Reconstr Surg* 2013; 132:940e–951e
40. Manferdini C, Maumus M, Gabusi E, et al. Adipose-derived mesenchymal stem cells exert antiinflammatory effects on chondrocytes and synoviocytes from osteoarthritis patients through prostaglandin E2. *Arthritis Rheum* 2013;65:1271–1281
41. Chen Y-T, Sun C-K, Lin Y-C, et al. Adipose-derived mesenchymal stem cell protects kidneys against ischemia-reperfusion injury through suppressing oxidative stress and inflammatory reaction. *J Transl Med* 2011;9:51
42. Gierloff M, Stöhring C, Buder T, et al. Aging changes of the midfacial fat compartments: a computed tomographic study. *Plast Reconstr Surg* 2012;129:263–273
43. Rohrich RJ, Pessa JE. The fat compartments of the face: anatomy and clinical implications for cosmetic surgery. *Plast Reconstr Surg* 2007;119:2219–2227
44. Ashcroft GS, Horan MA, Herrick SE, et al. Age-related differences in the temporal and spatial regulation of matrix metalloproteinases (MMPs) in normal skin and acute cutaneous wounds of healthy humans. *Cell Tissue Res* 1997;290:581–591.
45. Daly CH, Odland GF. Age-related changes in the mechanical properties of human skin. *J Invest Dermatol* 1979;73: 84–87