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Patterns of Superficial Midfacial Fat Volume Distribution Differ by Age and Body Mass Index

Jacob I. Tower[1] · **Kimberly Seifert**[2] · **Boris Paskhover**[3]

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Abstract

Background The changes that occur to midfacial fat with increasing age and BMI are poorly understood. The aim of this study was to determine how superficial cheek fat volume and distribution are differentially predicted by changes in BMI versus age.

Methods We conducted a retrospective observational study of patients with facial computed tomography scans. Superficial cheek fat volumes were measured, and multiple linear regression analysis was performed to model the relationships between cheek fat and corresponding sex, age, and BMI data.

Results A total of 109 patients were included in our analysis (51 male, 58 female). The subjects' ages ranged from 21.7 to 91.1 years with a mean (SD) age of 59.7 (15.0) years. The mean (SD) superficial cheek volume of the subjects was 10.46 (2.57) cc. Female subjects had a significantly greater mean total superficial cheek fat volume compared to male subjects (11.18 cc vs. 9.64 cc; $P < 0.001$). The results of multiple linear regression analysis indicated that together, age, sex, and BMI explained 50.8% of the variance in cheek fat volumes ($R^2 = 0.51$, $P < 0.001$). BMI significantly predicted total cheek fat volume ($\beta = 0.239$, $P < 0.001$), in addition to age ($\beta = 0.029$, $P < 0.017$) and sex ($\beta = -1.183$, $P = 0.001$; female = 0, male = 1). Age predicted the greatest gain of fat in the caudal subdivision of cheek ($\beta = 0.015$, $P < 0.001$), whereas BMI predicted the greatest gain in the cephalad subdivision ($\beta = 0.106$, $P < 0.001$).

Conclusions Age, sex, and BMI are important predictors of midfacial fat volume. This study shows that increases in age and BMI differentially predict the distribution of superficial cheek fat.

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Keywords Aging · Cheek · Fat · Face · Facial rejuvenation · Computed tomography

Introduction

To reverse the aesthetic changes of the aging face, surgeons need to understand their causes. In the midface, aging is associated with loss of cheek projection and the development of prominent nasolabial folds and tear troughs. These morphologic changes have been attributed to theories of insidious processes related to the malar fat pad including attenuation of ligamentous support and volume loss [1, 2]. There is still disagreement about which of these processes is the dominant force behind midfacial aging. In addition, although a more nuanced understanding of facial fat compartmentalization has developed, the distinct roles that these compartments may be playing in midfacial aging are still being elucidated [3–6]. There is a

✉ Jacob I. Tower
jacob.tower@yale.edu

[1] Department of Surgery, Section of Otolaryngology, Yale School of Medicine, 800 Howard Avenue, 4th Floor, ENT Office, New Haven, CT, USA

[2] Department of Radiology and Biomedical Imaging, Yale School of Medicine, New Haven, CT, USA

[3] Department of Otolaryngology – Head and Neck Surgery, Rutgers New Jersey Medical School, Newark, NJ, USA

paucity of objective data to support the volume loss and gravitational descent theories of facial aging, and the contradictions within existing data are difficult to reconcile [7]. The majority of radiographic studies of midfacial fat and aging do not take into account the compartmentalization of facial fat which may account for some of the inconsistency in this field of research.

Facial aging is a multifactorial process and dependent on changes to skin, fat, muscle, and bone. A comprehensive model of facial aging that accounts for the contributions of each of these tissues will allow a more nuanced understanding of aesthetic phenomena and how to address them with facial rejuvenation procedures from deep-plane rhytidectomy to dermal fillers. In the context of recent discoveries regarding facial skeletal aging, it seems that summarily explaining midfacial aging as global "gravitational descent" or "volume loss" of the soft tissue envelope is no longer adequate. For example, as a result of imaging studies we now understand that significant bone resorption and retrusion of the maxilla occur with aging, which undoubtedly has an impact on midfacial aesthetics [8–12]. Similarly, by using advanced imaging to study the fat compartments of the soft tissue envelope, we will gain insight into their individual contributions to the aesthetics of facial aging and come closer to a comprehensive model which takes into account all tissue types.

Superficial cheek fat is of particular interest because it lies immediately under the skin, and therefore, minor volumetric or positional changes can result in obvious aesthetic changes. This architectural component of the soft tissue envelope is a target of procedures including rhytidectomy and injectable fillers that address midfacial ptosis and volume loss, respectively. Measuring compartmental fat volumes radiographically is inherently challenging because the septal barriers and ligamentous attachments that divide the facial fat compartments are not easily visualized with any imaging modality and cannot be identified with the precision of surgical dissection [13, 14]. However, consistent, easily identifiable radiographical landmarks can be used to approximate the divisions of facial fat compartments [14]. In this study of midfacial aging, we focused on a radiographically defined zone of superficial cheek fat which corresponds to superficial nasolabial and medial cheek fat compartments, as described in anatomical studies [3–5].

The goal of this study was to investigate whether patient factors including age, sex, and BMI can predict the volume distribution of the superficial cheek fat compartment. Our primary aim was to determine whether superficial cheek fat volume declines with aging. Our secondary aim was to determine whether any changes in volume occur uniformly throughout the superficial cheek, or whether the upper and lower cheek evolves differently in response to gains in BMI versus aging. In this observational study of computed tomography radiographical data, we demonstrate that superficial cheek fat volume increases with age, BMI, and female sex. Moreover, chronological aging is associated with a disproportionate volumetric gain of fat in the caudal aspect of the superficial cheek compartment at the level of the nasolabial fold, whereas increasing BMI is associated with disproportionate volume gain in the cephalad aspect of the cheek overlying the malar eminence.

Materials and Methods

This study was approved by the Yale School of Medicine IRB. A retrospective query of our institution's radiology report database from 2/1/2013 to 2/5/2018 was performed to identify adult subjects who underwent inpatient CT studies of the head, including the entire midface, with a slice thickness of 0.63-mm. The query start date parameter was selected because the current university electronic medical record (EMR) system was implemented on 2/1/2013. Subjects were excluded from the study for evidence of prior facial surgery, previous or current facial trauma, pathology that distorted the bony or soft tissue structures of the face, or the presence of an endotracheal tube, cervical collar, or other appliance which could distort the facial fat. Each subject's age, sex, and BMI data were collected from the EMR's hospital inpatient encounter that corresponded with the date that the CT scan was performed.

CT scans were analyzed in the axial plane to obtain volumetric measurements of superficial cheek fat as previously described [14]. The deep boundary of superficial cheek fat was a linear plane between the zygomaticus major and levator labii superioris muscles; the superficial boundary was the skin. The anteromedial boundary was defined by the convergence of skin and levator labii superioris. The posterolateral boundary was marked by the posterior border of zygomaticus major.

The axial slice that contained the most prominent anterior projection of the nasal spine was identified as a reference point. Bilateral cross-sectional measurements of superficial cheek fat were taken at every third axial slice from 9.45-mm caudal to the reference point, to 11.34-mm cephalad to the reference point. There were 12 measured slices over a vertical distance of 20.79-mm for each scan. Volumetric measurements were calculated by taking the sum of the cross-sectional areas multiplied by their interval distances to the next measured slice in the CT scan (1.89-mm).

For further analysis, the total superficial cheek fat volume was subdivided into cephalad, middle, and caudal thirds by applying the volume formula to the cross-sectional areas of the cephalad, middle, or caudal 4 slices. For each patient, the superficial cheek fat volumes were measured bilaterally. The average volume of the left and right side was used for all statistical analyses. Three-dimensional reconstructions were created for select subjects using Vitrea Software (Vital Images Inc, Minnetonka, MN).

Statistical analysis was performed using Microsoft Excel. The mean, range, and standard deviation were calculated for age, BMI, and cheek volume measurements for the total study population. The same descriptive statistics were also calculated separately for the male and female subjects. Unpaired two-tailed t tests were used to evaluate the null hypothesis that the means were equal between male and female subjects. Multiple linear regression analyses were performed to model the relationships between age, sex, BMI (independent variables) and the total, cephalad, middle, and caudal superficial cheek fat volumes (dependent variables). Sex was coded as a binary variable with values of 1 for male subjects and 0 for female subjects. $P < 0.05$ was considered statistically significant.

Results

Overall, 109 subjects were included in our analysis (Table 1). There were 51 male subjects and 58 female subjects. The mean (SD) age of the total subjects was 59.7 (15.0) years. There was no significant difference between the mean age of male and female subjects (57.9 vs. 61.4 years old, respectively; $P = 0.23$). The mean (SD) BMI of the total subjects was 28.1 (6.7) kg/m^2. There was no significant difference between the mean BMI of male and female subjects (27.5 kg/m^2 vs. 28.6 kg/m^2; $P = 0.40$).

The superficial cheek fat was measured bilaterally for all subjects. There was no significant difference between the total volumes of the left and right superficial cheek (D.N.S.). The mean (SD) superficial cheek volume of the total subjects was 10.46 (2.57) cc. Female subjects had a significantly greater mean total cheek fat volume compared to male subjects (11.18 cc vs. 9.64 cc; $P < 0.001$). When the cheek volume was divided into cephalad, middle, and caudal portions, female subjects were found to have significantly greater mean fat volumes in each subdivision compared to male subjects. For all subjects, the mean cephalad, middle and caudal cheek fat volumes accounted for 39%, 35%, and 26% of the total volume, respectively.

Superficial cheek fat volumes were scatter-plotted by BMI (Fig. 1) and age (Fig. 2), and multiple regression analysis was performed to test if age, sex, and BMI predicted subjects' total superficial cheek fat volumes (Table 2). The results of the regression indicated that the three predictors explained 50.8% of the variance ($R^2 = 0.51$, $P < 0.001$). It was found that BMI significantly predicted total cheek fat volume ($\beta = 0.239$, $P < 0.001$), in addition to age ($\beta = 0.029$, $P = 0.017$) and sex ($\beta = -1.183$, $P = 0.001$). With particular attention to age, this result suggests that for each additional year the model predicts an increase in total superficial cheek fat by 0.029 cc.

Additional multiple regression analyses were performed to test if age, sex, and BMI predicted subjects' cephalad, middle, and caudal superficial cheek fat volumes. The results of the cephalad fat regression indicated that the three predictors explained 54.8% of the variance ($R^2 = 0.55$, $P < 0.001$). BMI significantly predicted cephalad cheek fat volume ($\beta = 0.106$, $P < 0.001$), as did sex ($\beta = -0.477$, $P < 0.001$); age was not a significant predictor ($P = 0.43$). The middle cheek fat regression indicated that the three predictors explained 47.9% of the variance ($R^2 = 0.48$, $P < 0.001$). BMI significantly predicted middle cheek fat volume ($\beta = 0.078$, $P < 0.001$), as did age ($\beta = 0.010$, $P = 0.013$) and sex ($\beta = -0.406$, $P = 0.002$). The caudal cheek fat regression indicated that the three predictors explained 38.9% of the variance ($R^2 = 0.39$, $P < 0.001$). BMI significantly predicted caudal cheek fat volume ($\beta = 0.055$, $P < 0.001$), as did age ($\beta = 0.015$, $P < 0.001$) and sex ($\beta = -0.300$, $P = 0.011$).

Discussion

The data in this study show that age, sex, and BMI are all important, independent predictors of superficial cheek fat volume. We show that with increasing age, there is an incremental gain in superficial cheek fat volume by approximately 0.03 cc per year. Such a small trend would take decades to shape the contours of the midface, which seems consistent with our perceptions of aging. (i.e., it would take over three decades for 1 cc of fat to be deposited in the superficial cheek as a function of chronological aging alone). By subdividing the cheek into cephalad, middle, and caudal divisions, we further show that the majority of this age-associated volume gain occurs in caudal aspect of the superficial cheek which is approximately at the level of the nasolabial fold.

According to our data, despite the caudal division of the cheek containing only 26% of the total fat volume, this is where 52% of age-related volume gain occurs. In contrast, the fat gains associated with an increase in BMI occur disproportionately in the cephalad cheek at the level of the malar eminence. Volume differences between the sexes occur proportionately among the cheek subdivisions. These findings suggest that volume changes associated with age, BMI, and sex shape the contours of the face differently, and explain why facial volume changes that occur with changes in body weight appear different from volume changes that occur with chronological aging. With

Table 1 Demographic statistics and superficial cheek fat volumes

	Total	%	Men	%	Women	%	Difference	*P* value
N	109		51	47	58	53		
Age (years)								
Mean	59.7		57.9		61.4		3.5	0.23
Range	21.7–91.1		25.1–84.2		21.7–91.1			
SD	15.0		15.2		14.8			
BMI (kg/m^2)								
Mean	28.1		27.5		28.6		1.1	0.40
Range	16–50.22		17.65–49.5		16–50.22			
SD	6.74		6.27		7.15			
Superficial cheek fat volume (cc)								
Total fat								
Mean	10.46		9.64		11.18		1.54	0.001
Range	5.21–17.07		5.21–17.07		6.39–16.07			
SD	2.57		2.69		2.24			
Cephalad fat								
Mean	4.08	39	3.77	39	4.37	39	0.60	0.002
Range	1.92–6.74		1.92–6.74		2.46–6.58			
SD	1.05		1.08		0.95			
Middle fat								
Mean	3.64	35	3.37	35	3.89	35	0.52	0.002
Range	1.81–5.83		1.81–5.83		2.32–5.64			
SD	0.88		0.91		0.77			
Caudal fat								
Mean	2.74	26	2.53	26	2.93	26	0.40	0.005
Range	1.25–4.50		1.25–4.50		1.55–4.37			
SD	0.76		0.79		0.68			

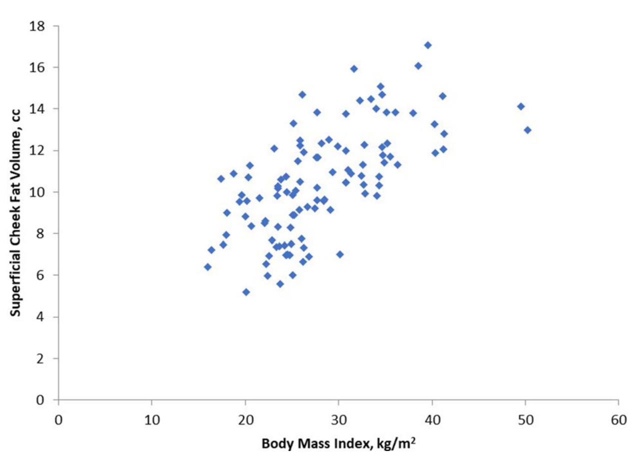

Fig. 1 Scatterplot displaying total superficial cheek fat volume versus BMI

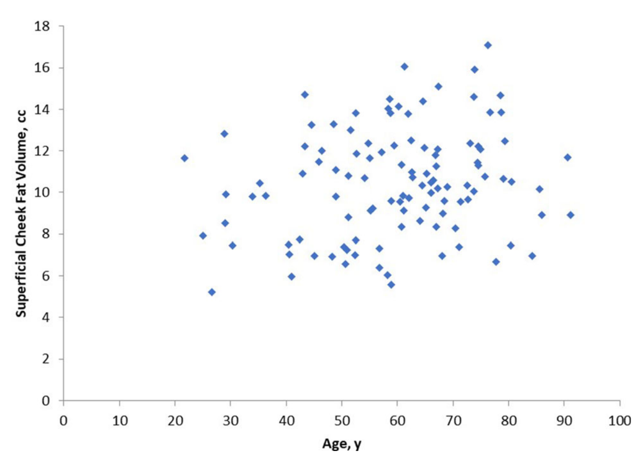

Fig. 2 Scatterplot displaying total superficial cheek fat volume versus age

chronological aging, fat seems to slowly accumulate disproportionately in the superficial caudal cheek over a period of decades. This finding could explain how gradual fat deposition in this area—either by attenuation of ligamentous support and gradual sinking of the medial cheek fat, or a localized metabolic phenomenon leading to volume gain—can produce a more aesthetically prominent nasolabial crease with aging.

Table 2 Multiple regression summary for age, sex, and BMI as predictors of volume

	Coefficient	% Total	LL 95% CI	UL 95% CI	*P* value
Total cheek fat					
Sex	− 1.183[a]		− 1.886	− 0.48	0.001
Age	0.029		0.005	0.052	0.017
BMI	0.239		0.187	0.291	< 0.001
Cephalad cheek fat					
Sex	− 0.477[a]	40.3	− 0.753	− 0.201	< 0.001
Age	0.004	13.8	− 0.006	0.013	0.43
BMI	0.106	44.4	0.086	0.127	< 0.001
Middle cheek fat					
Sex	− 0.406[a]	34.3	− 0.653	− 0.158	0.002
Age	0.010	34.5	0.002	0.019	0.013
BMI	0.078	32.6	0.06	0.096	< 0.001
Caudal cheek fat					
Sex	− 0.300[a]	25.4	− 0.531	− 0.069	0.011
Age	0.015	51.7	0.007	0.022	< 0.001
BMI	0.055	23.0	0.037	0.072	< 0.001

[a] 1 = male, 0 = female

Our findings are comparable to other radiographic analyses of cheek fat aging. Similar to our results, in an MRI study of 20 female subjects, Gosain et al. [15] found age-related volumetric increases in the superficial cheek fat pads. However, in contrast to our findings, they noted selective hypertrophy in the upper cheek with age. By comparison, Gierloff et al. [13] in a CT study of cadaveric facial fat compartments found that older subjects had an increase in the sagittal diameter of the lower cheek, which is more in line with our results. In another CT study of 80 male subjects, Jang et al. [16] also found thickening of the midfacial fat with aging. Finally, Wysong et al. [17, 18] in MRI studies of men and women measured the thickness of medial cheek fat at a single location and found that cheek thickness diminishes between young and middle-aged subjects, but not middle-aged and older patients. Importantly, among this research, the only prior study to utilize the concept of fat compartments was Gierloff et al. This distinction is critical because it is likely that fat compartments age independently—viewing the face as a mass of shifting soft tissue overlooks and trivializes the complexity of facial architecture.

One major advantage of the present study is the use of volumetric measurements to compare cheek fat across individuals. Volumetric measurements capture three-dimensional information about the facial anatomy, rather than a one-dimensional tool such as simply measuring fat "thickness" at arbitrarily selected anatomical locations [16–18]. By measuring volumes, we can take into account fat content at levels of the cheek relative to bony landmarks. This is important considering that the shapes of the individual fat compartments seem to shift with changes to BMI and age as we have shown. A second major advantage of the present study is the use of linear regression to compare for volume trends over time as a function of age, rather than arbitrarily designating patients into categories of "young," "middle-aged," and "old" for comparison, which differ dramatically and overlap across the literature [13, 15, 17, 18]. To our knowledge, this has not been performed before, but it is the most natural and useful statistical method for looking at a trend such as volume change with age. Finally, a major advantage of this study is that, to our knowledge, the number of subjects included exceeds that of any comparable prior publication.

Overall, our data suggest that facial aging is more complex than a global process such as "volume loss." Facial aging involves multiple tissues, and with regard to fat it is more appropriately conceptualized as a compartmentalized process. If there is relative loss of fat volume in a compartment, the concept of facial fillers to restore a youthful contour makes sense; however, a significant *gain* of soft tissue cannot be corrected with this approach (though it can sometimes be masked). The mechanisms of the changes in superficial facial fat distribution are unclear, but as others have speculated are probably multifactorial and may be related to ligamentous attenuation (fat "sinking" into place in the lower cheek with age), or compartmentalized differences in fat metabolism [7].

The changes that occur to superficial cheek fat with aging clearly do not completely account for all of the midfacial features associated with age, but they can be viewed in the context of other tissue aging processes. The midfacial skeleton also undergoes significant changes that contribute to the aesthetics of aging with widening of the orbital and piriform apertures, decreasing maxillary angles and loss of maxillary projection [8–12]. The soft tissue envelope is draped over this bony framework, and thus, any comprehensive model of facial aging must take bone and soft tissue into account. One example of an application of this research becomes obvious when viewing it from a surgical perspective. The superficial soft tissue envelope which includes medial superficial cheek fat is repositioned superiorly and laterally in a deep-plane rhytidectomy. This maneuver is in harmony with our research findings which show that fat increases in the inferior superficial cheek with age—rhytidectomy reverses this change. On the other hand, the deep fat compartments are not typically addressed during rhytidectomy, but along with the adjacent Ristow space, they are accessible by injection of volumizing agents which may be necessary in the loss of bony maxillary projection [4]. By understanding the various anatomical changes that are happening in concert with aging, we can see how the roles of various rejuvenation techniques come into play. Having an accurate model of aging of each tissue component and fat compartment of the face will allow for surgeons to approach the face in a systematic way, approaching each individual aspect as needed and obtaining more consistent results.

We envision a comprehensive model of facial aging that takes into account individual fat compartments in the superficial and deep soft tissue planes and the underlying bony changes that act in concert to produce the aesthetics of aging. Such a model could be referenced by surgeons to design optimal treatments for their patients, especially once we understand how each component of the model could be influenced by factors such as specific age, BMI, gender, race, and various disease states and medications.

The complexity of aging-related changes to midfacial fat is illustrated by an example of side-by-side comparison of young and old female patients (Fig. 3). The subject in panels A–C is 49.0 years old, with a BMI of 23.4 and an average superficial cheek fat volume of 9.82 cc. By comparison subject in panels D–F is 85.5 years old with a BMI of 23.5 and an average superficial cheek fat volume of 10.16. The distribution of the fat into cephalad, middle, and caudal subdivision is also similar with only negligible differences. Despite similar BMI's and superficial cheek fat volume distribution, the patients have dramatically different facial contours. The older patient has pronounced tear troughs and nasolabial creases (panel A vs. D) and diminished cheek projection (panel B vs. E). The loss of cheek projection may be a result of bony resorption and retrusion of the maxilla. However, by looking at the cross-sectional views the face through the level of the nasal spine, it is apparent that despite having similar superficial fat content the subjects have dramatically different deep cheek fat thicknesses (panels C vs. F). One could speculate that the diminished deep fat content in the older subject also contributes to the reduced cheek projection. This phenomenon of pseudoptosis has been reported previously and is considered to be a mechanism of midfacial aging related specifically to the deep medial fat compartment [4]. Further radiographic studies are needed to elucidate the role of deep fat in aging. We believe that the methodology described in this article can be adapted to investigate

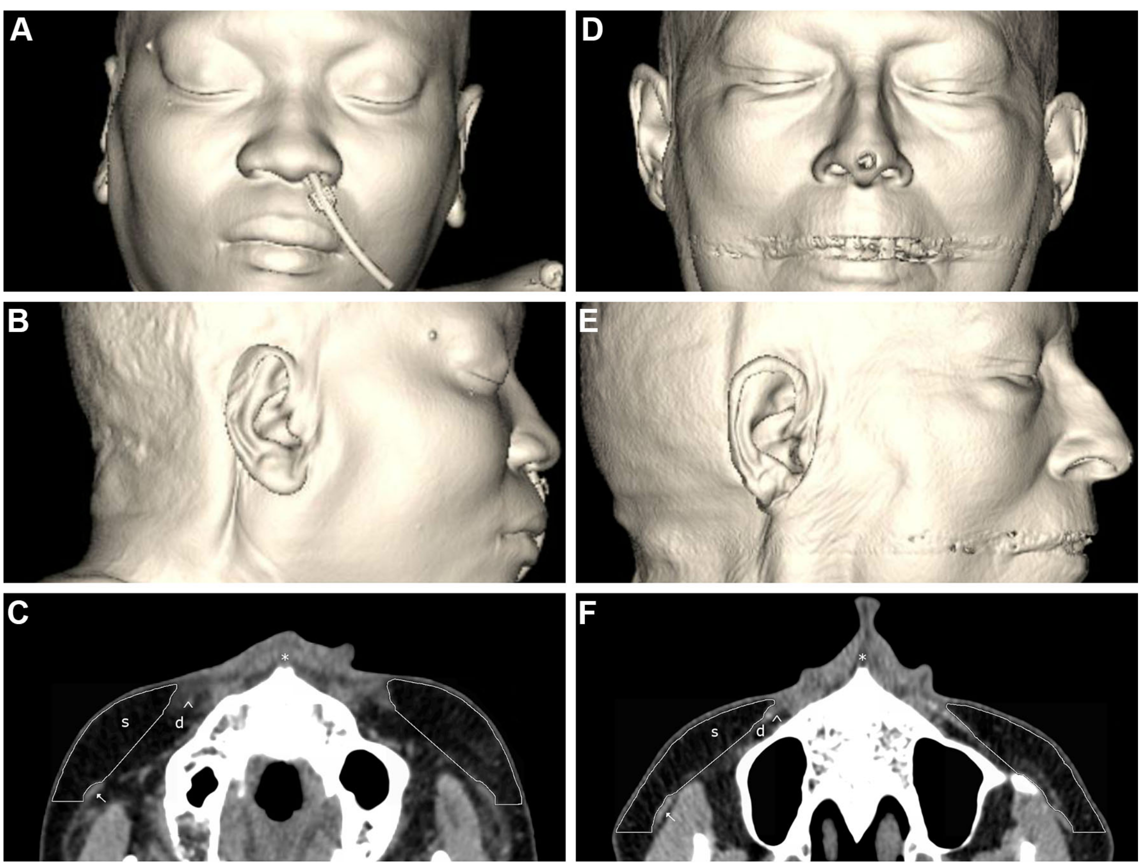

Fig. 3 Three-dimensional reconstructions and corresponding axial views of the face of a young (**a**, **b**, **c**) and old (**d**, **e**, **f**) subject. **c**, **f** Asterisk indicates nasal spine; outlined areas (*s*) circumscribe superficial medial cheek fat; *d*, deep medial cheek fat; arrow, zygomaticus major; caret, levator labii superioris

aging- or disease-related changes of other fat compartments such as buccal fat and deep medial cheek fat.

The current study has important implications for future facial aging studies. First, even when controlling for BMI, male and female subjects have inherently different cheek volumes and comparisons between them must take this into account. Prior quantitative studies by Wysong et al. [17, 18], Jang et al. [16] and Gosain et al. [15] were careful to compare subjects only of the same sex; however, it is unclear whether Gierloff et al. [13] took sex into account in their comparison of compartmental fat volume distribution between old and young subjects. Additionally, BMI or a comparable height–weight index should be taken into account whenever possible when making comparisons across groups for the purposes of studying fat distribution as it relates to facial aging.

Another key difference between the present study and many prior quantitative studies of facial fat is our choice of CT as the imaging modality [15, 17, 18]. Computed tomography imaging is a useful tool for quantifying fat; the ease of distinguishing fat from surrounding muscle, bone, and skin is demonstrated in Fig. 3. Traditionally, MRI is useful for investigating pathological conditions related to soft tissues; however, for the purposes of anatomical, volumetric measurements of fat in a benign setting, computed tomography is a well-established modality with several advantages over MRI [16, 19, 20]. Namely, facial CT typically has higher spatial resolution in comparison with MRI which allows for more accurate volumetric measurements. Furthermore, for the purposes of this study specifically we were able to use precise bony anatomical landmarks (the nasal spine) to standardize our fat measurements for meaningful comparison, and we were able to render very high-fidelity 3D reconstructions of the face. These aspects of the study would have been impossible using MRI without highly specialized image acquisition protocols [21]. In sum, either modality can be used to measure facial fat, but CT offers the advantages of improved spatial resolution, true volume coverage, ease of conversion to 3D reconstructions, and bony detail.

There are limitations to the present study. First, although BMI is a good indicator of total body fat content which can be easily calculated, it can be misleading because of a tendency to overestimate the fat content of individuals with lots of muscle mass. The imperfection of BMI as a proxy measure for body fat content likely accounts for some of the unexplained variance in our regression analysis results. Another limitation to the present study is that the majority of subjects were aged 40–80 years old, with fewer very young or very old adults included in the statistical models. It is unclear whether at extreme ages we would have the same findings, but we believe these data remain relevant because the majority of patients seeking facial rejuvenation coincide with our study population with regard to age. Finally, the present study does not control for various disease states and medications that may have an impact on facial fat distribution; however, even without controlling for such factors age and BMI emerged as significant predictors of cheek fat volume and distribution.

Conclusion

In conclusion, midfacial aging is a complex process that depends on changes to the soft tissue envelope and its underlying bony scaffold. Age, sex, and BMI are all significant predictors of midfacial superficial cheek fat volume. Increasing age is associated with a quantifiable gain of superficial cheek fat volume, distributed mostly in the lower cheek. There does not appear to be any loss of fat volume in the superficial cheek with aging. The mechanisms of the fat gain are unclear, but it is a distinctly different pattern of fat distribution in comparison with that which occurs with gains in BMI. Techniques that eliminate redundancy and reposition the superficial soft tissue envelope in a superolateral vector such as the deep-plane rhytidectomy seem well suited to address this aging-related change. Additional research is needed to determine how the deep midfacial fat compartments change with aging and BMI.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Stuzin JM, Baker TJ, Gordon HL (1992) The relationship of the superficial and deep facial fascias: relevance to rhytidectomy and aging. Plast Reconstr Surg 89:441–449 **(discussion 450-441)**
2. Lambros V (2007) Observations on periorbital and midface aging. Plast Reconstr Surg 120:1367–1376 **(discussion 1377)**
3. Rohrich RJ, Pessa JE (2007) The fat compartments of the face: anatomy and clinical implications for cosmetic surgery. Plast Reconstr Surg 119:2219–2227 **(discussion 2228-2231)**
4. Rohrich RJ, Pessa JE, Ristow B (2008) The youthful cheek and the deep medial fat compartment. Plast Reconstr Surg 121:2107–2112
5. Schaverien MV, Pessa JE, Rohrich RJ (2009) Vascularized membranes determine the anatomical boundaries of the subcutaneous fat compartments. Plast Reconstr Surg 123:695–700
6. Wan D, Amirlak B, Rohrich R, Davis K (2013) The clinical importance of the fat compartments in midfacial aging. Plast Reconstr Surg Glob Open 1:e92
7. Gerth DJ (2015) Structural and volumetric changes in the aging face. Facial Plast Surg 31:3–9
8. Pessa JE (2000) An algorithm of facial aging: verification of Lambros's theory by three-dimensional stereolithography, with reference to the pathogenesis of midfacial aging, scleral show,

and the lateral suborbital trough deformity. Plast Reconstr Surg 106:479–488 **(discussion 489-490)**
9. Paskhover B, Durand D, Kamen E, Gordon NA (2017) Patterns of change in facial skeletal aging. JAMA Facial Plast Surg 19:413–417
10. Mendelson BC, Hartley W, Scott M, McNab A, Granzow JW (2007) Age-related changes of the orbit and midcheek and the implications for facial rejuvenation. Aesthet Plast Surg 31:419–423
11. Shaw RB Jr, Kahn DM (2007) Aging of the midface bony elements: a three-dimensional computed tomographic study. Plast Reconstr Surg 119:675–681 **(discussion 682-673)**
12. Mendelson B, Wong CH (2012) Changes in the facial skeleton with aging: implications and clinical applications in facial rejuvenation. Aesthet Plast Surg 36:753–760
13. Gierloff M, Stohring C, Buder T, Gassling V, Acil Y, Wiltfang J (2012) Aging changes of the midfacial fat compartments: a computed tomographic study. Plast Reconstr Surg 129:263–273
14. Tower J, Seifert K, Paskhover B (2018) Longitudinal analysis of superficial midfacial fat volumes over a 10-year period. Aesthet Plast Surg 42:995–1001
15. Gosain AK, Klein MH, Sudhakar PV, Prost RW (2005) A volumetric analysis of soft-tissue changes in the aging midface using high-resolution MRI: implications for facial rejuvenation. Plast Reconstr Surg 115:1143–1152 **(discussion 1153-1145)**
16. Jang MS, Kim HY, Dhong HJ, Chung SK, Hong SD, Cho HJ (2015) An analysis of Asian midfacial fat thickness according to age group using computed tomography. J Plast Reconstr Aesthet Surg 68:344–350
17. Wysong A, Joseph T, Kim D, Tang JY, Gladstone HB (2013) Quantifying soft tissue loss in facial aging: a study in women using magnetic resonance imaging. Dermatol Surg 39:1895–1902
18. Wysong A, Kim D, Joseph T, MacFarlane DF, Tang JY, Gladstone HB (2014) Quantifying soft tissue loss in the aging male face using magnetic resonance imaging. Dermatol Surg 40:786–793
19. Sarin S, Wenger C, Marwaha A et al (2008) Clinical significance of epicardial fat measured using cardiac multislice computed tomography. Am J Cardiol 102:767–771
20. Marwan M, Achenbach S (2013) Quantification of epicardial fat by computed tomography: why, when and how? J Cardiovasc Comput Tomogr 7:3–10
21. Becker M, Balague N, Montet X et al (2015) Hyaluronic acid filler in HIV-associated facial lipoatrophy: evaluation of tissue distribution and morphology with MRI. Dermatology 230:367–374