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The association of the sebum excretion rate with melasma, erythematotelangiectatic rosacea, and rhytides

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Abstract

Background: Rosacea and melasma are two common skin conditions in dermatology. Both conditions have a predilection for the centrofacial region where the sebaceous gland density is the highest. However it is not known if sebaceous function has an association with these conditions.

Aims and Objectives: We aimed to assess the relationship between facial glabellar wrinkle severity and facial sebum excretion rate for individuals with rosacea, melasma, both conditions, and in those with rhytides. Secondly, the purpose of this study was to utilize high resolution 3D facial modeling and measurement technology to obtain information regarding glabellar rhytid count and severity.

Materials and Methods: A total of 21 subjects participated in the study. Subjects were divided into four groups based on facial features: rosacea-only, melasma-only, rosacea and melasma, rhytides-only. A high resolution facial photograph was taken followed by measurement of facial sebum excretion rate (SER).

Results: The SER was found to decline with age and with the presence of melasma. The SER negatively correlated with increasing Wrinkle Severity Rating Scale. Through the use of 3D facial modeling and skin analysis technology, we found a positive correlation between clinically based grading scores and computer generated glabellar rhytid count and severity.

Conclusion: Continuing research with facial modeling and measurement systems will allow for development of more objective facial assessments. Future studies need to assess the role of technology in stratifying the severity and subtypes of rosacea and melasma. Furthermore, the role of sebaceous regulation may have important implications in photoaging.

Keywords: photoimaging, rosacea, melasma, rhytid, sebum

Introduction

The development of facial rhytides is a universal finding in the aging population [1]. Rosacea and melasma are two common facial dermatologic skin conditions [2,3]. Rosacea is a chronic remitting-relapsing inflammatory skin condition with four subtypes: erythematotelangiectatic, papulopustular, ocular, and phymatous; the first two are the most common. Erythematotelangiectatic rosacea (ETR) is characterized by prominent erythema and blood vessels, whereas papulopustular rosacea is characterized by perifollicular inflammatory papules and pustules. Both subtypes have a predilection for the centrofacial region. Melasma is a chronic skin disorder that results in symmetrical, blotchy, hyperpigmented facial pigmentation. Rosacea is more prevalent in light skin adults (Fitzpatrick type I-II), whereas melasma is more common in adults with darker skin types (Fitzpatrick type III-IV) [4,5]. Both conditions have a predilection for the centrofacial region, where the sebaceous gland density is the highest, suggesting a possible association between sebaceous function and pathogenesis.

Recent studies have reported a difference in the sebum profile of patients with rosacea compared to healthy controls [6]. Specifically, among patients with rosacea, there was a greater concentration of myristic acid and a lower concentration of long chain saturated fatty acids (arachidic acid, behenic acid, tricosanoic acid, lignoceric acid) and cis-11-eicosanoic acid- a monounsaturated fatty acid. Among patients with melasma, the sebum content and excretion rate was similar between lesional and non-lesional skin [7].

Sebaceous glands have been shown to deliver antioxidants to the stratum corneum in the form of squalene, coenzyme Q10, and vitamin E, possibly enhancing resistance to oxidative stress and reducing skin aging [8-10]. Therefore, understanding the relationship between sebaceous activity and rhytid formation may have important implications in the prevention and treatment of photoaging.

Current evaluations of rhytides and facial features such as redness and pigmentation are based on subjective grading rather than an objective measurement. One goal of this study was to understand how skin feature detection from high resolution 3D modeling technology may allow for more accurate and objective tracking and analysis of facial features. This may be especially helpful for studying facial rhytides characteristics because precise measurements of surface area and skin contouring are required. Therefore, two aims of this study were to investigate the association between facial sebum excretion rate (SER) and glabellar rhytid severity, and to assess how computerized grading correlates with subjective grading of rhytides.

Materials and Methods

A total of 21 subjects were recruited in the study with an average age of 51.8 years ± 12.1 standard deviation (SD), and a median age of 53 years. Subjects with melasma and/or ETR were included as diagnosed by a board-certified dermatologist. Prior to participation, each subject was allowed to acclimatize in a climate-controlled room for 15 minutes. Then each subject's face was cleansed with alcohol and high resolution facial photographs and skin biometrics were obtained with the 3D BTBP Clarity Pro® Facial Modeling & Measurement System from Brigh-Tex BioPhotonics (BTBP, San Jose, CA). This clinical study was approved by the Institutional Review Board at the University of California, Davis. Each subject provided written informed consent prior to participation.

BTBP's technology integrates the use of multi-spectral light with skin mapping technology to create a surface and subsurface map of the subject's face (skin), utilizing facial detection parameters and biometrics. The surface and subsurface skin maps are compiled using trained algorithms that identify, track, and measure various skin conditions and facial features, such as rhytid count and severity.

Glabellar rhytid count and average glabellar rhytid severity were analyzed with facial feature detection software in the 3D BTBP Clarity Pro® Facial Modeling & Measurement System. The glabellar rhytid count was calculated through detecting distinct rhytides that met a minimal depth threshold; the glabellar severity was determined through the measurement of the depth of the rhytides. Following the photographs, sebum excretion rates (SER) of four facial zones (right and left forehead, and right and left cheeks) were measured using a Sebumeter® (Courage and Khazaka, Cologne, Germany). The SER was obtained by taking an average of the four measured areas. Glabellar rhytid severity was blindly assessed clinically by four physician graders using the Wrinkle Severity Rating Scale (WSRS) [11]. All of the physician graders participated in a training session with standardized photographs prior to engaging in grading of the experimental subject photographs. The WSRS utilized a five-point scale for rhytides: none (0), very mild (1), mild (2), moderate (3), or severe (4).

Statistical Analysis

Statistical analysis was conducted using t-test, a one-way ANOVA, and Pearson correlation coefficients were calculated. In cases of non-parametric measures, a Spearman rank-order correlation coefficient was calculated. In this study, $p < 0.05$ was considered statistically significant.

Results

Subject demographics

A total of 21 subjects were enrolled in this study and divided into four cohorts: rosacea-only, melasma-only, rosacea and melasma, and rhytides-only. The rhytides-only group was defined as subjects that did not have any other facial dermatological diagnosis. Six subjects were diagnosed with rosacea, with an average age of 50.2 years ± 9.7 (SD) and a median age of 51.5 years. Five subjects were diagnosed with melasma, with an average age of 58.6 years ± 14.8 (SD) and a median age of 62 years. Three subjects presented with both rosacea and melasma, with an average age of 45 years ± 4.0 (SD) and a median age of 45 years. There were seven subjects with rhytides-only, an average age of 51.14 years ± 13.9 (SD), and a median age of 53 years. The demographic data is summarized in Table 1.

Average facial sebum excretion rate

The average facial SER was evaluated for each subject using a Sebumeter®. The average facial SER negatively correlated with increasing age (Figure 1) and increasing WSRS score (Figure 2). The rosacea-only group had an average facial SER of 51.42 μg/cm^2 ± 36.6 (SD), p=0.154 (Table 1). The average facial SER for subjects with melasma-only was 44.15 μg/cm^2 ± 13.7 (SD), p=0.025. Among subjects with rosacea and melasma, the average facial SER was 34.92 μg/cm^2 ± 26.6 (SD), p=0.044. In the rhytides-only cohort, the average facial SER was 78.04 μg/cm^2 ± 26.0 (SD). The average SER for all 21 subjects was 56.20 μg/cm^2 ± 30.4 (SD) (Table 1, Figure 3).

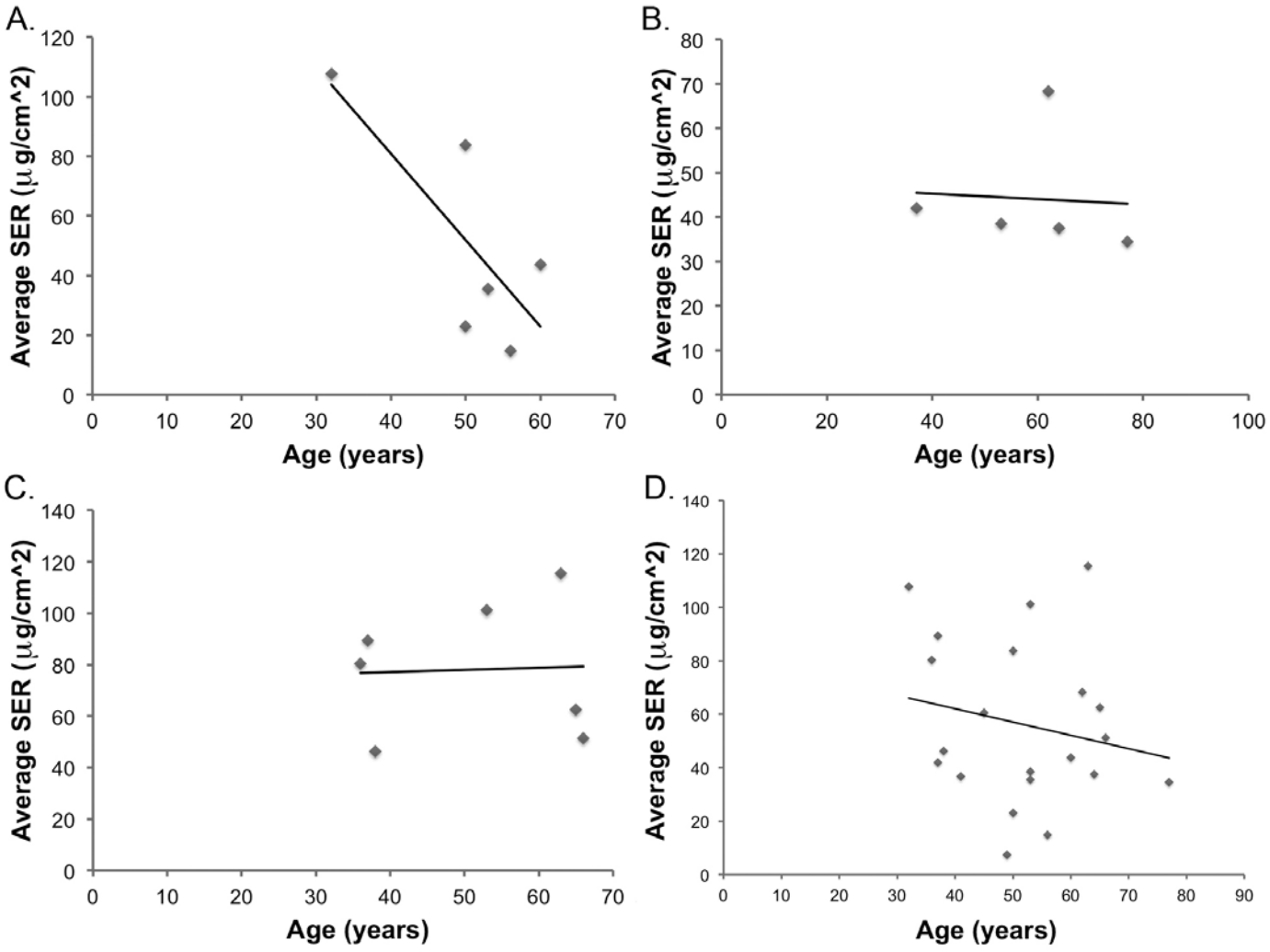

Figure 1. Correlation of average sebum excretion rate and age for subjects with (A) rosacea-only, correlation= -0.7674, p=0.94; (B) melasma-only, correlation= -0.0657, p=0.15; (C) rhytides-only, correlation=0.0461, p=0.03; and (D) all subjects, correlation= -0.2839, p=0.54.

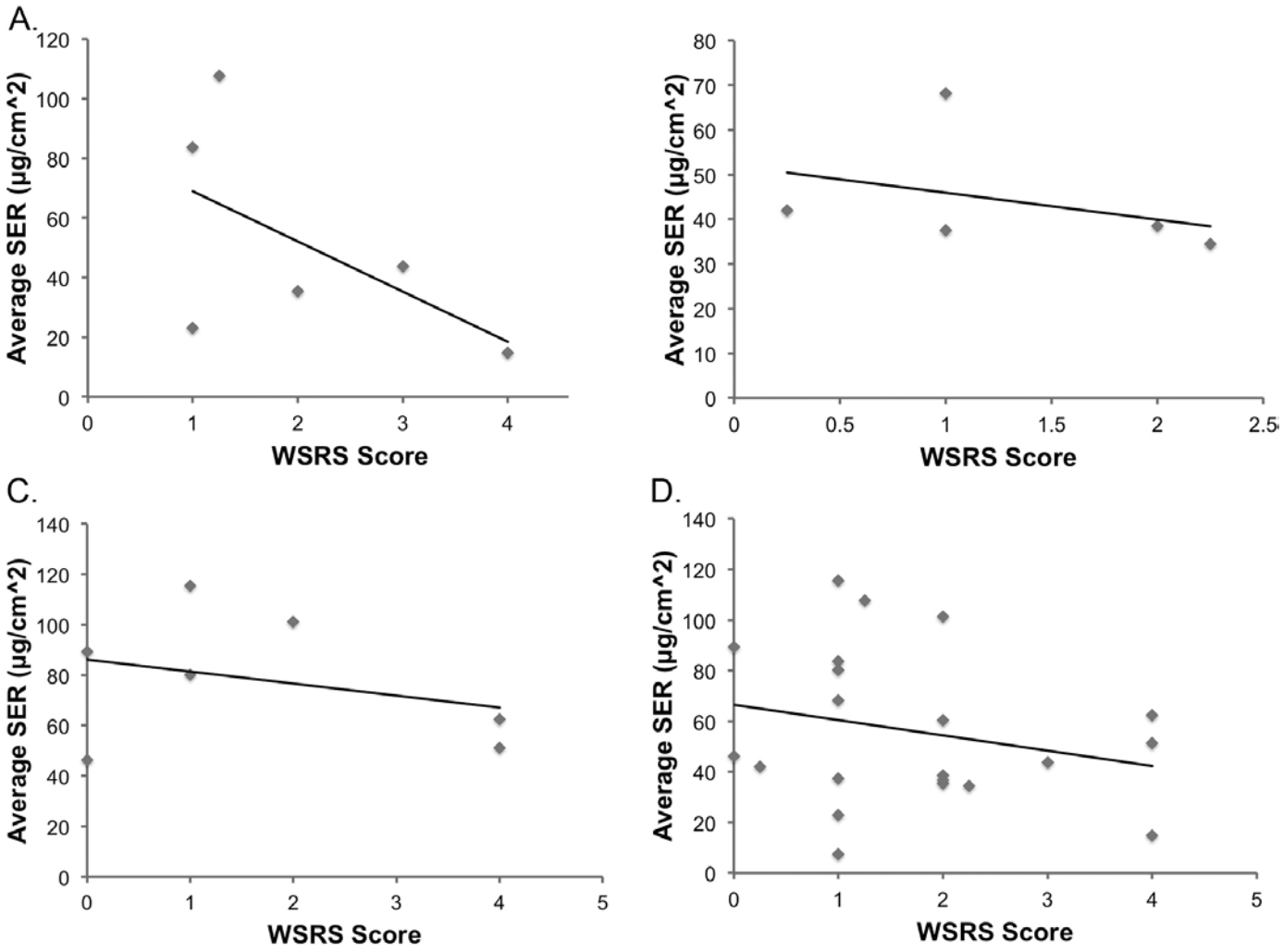

Figure 2. Correlation between average sebum excretion rate and wrinkle severity score for subjects with (A) rosacea-only, correlation= -0.5661, p=0.008; (B) melasma-only, correlation= -0.3583, p=0.00012; (C) rhytides-only, correlation= -0.3134, p=5.11 x 10-6; and (D) all subjects, correlation= -0.2432, p=4.03 x 10-10.

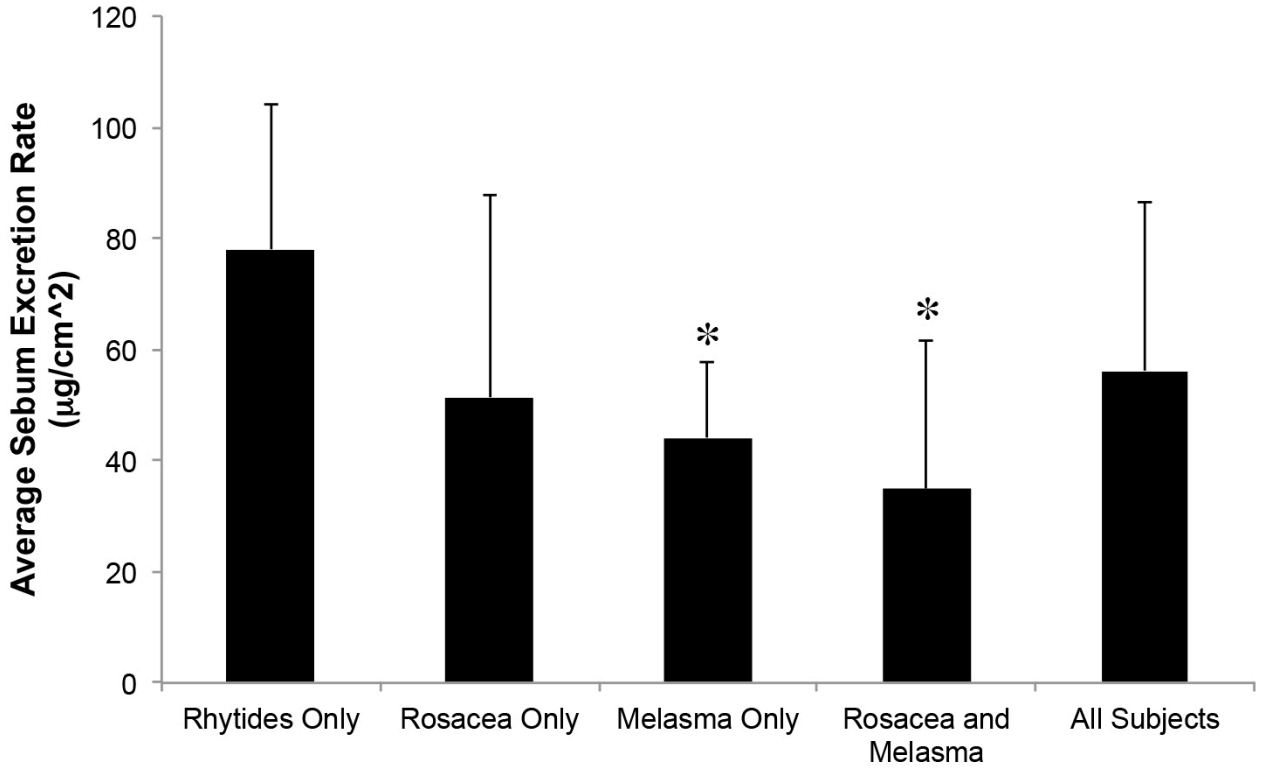

Figure 3. Average sebum excretion rate of subjects in each cohort. * = $p < 0.05$.

Table 1. Study demographics, facial SER, and median wrinkle score

Cohort	Average Age **Median Age (years)**	Gender	Average Facial SER (μg/cm^2)	**Median WSRS Score**[1]
Rosacea	50.2 ± 9.68 (SD) 51.5	6 Female 0 Male	51.42± 36.56 (SD), p=0.154	1.625 p=0.704
Melasma	58.6 ± 14.81 (SD) 62.0	4 Female 1 Male	44.15 ± 13.74 (SD), p=0.025*	1.0 p=0.629
Rosacea and Melasma	45.0 ± 4.0 (SD) 45.0	3 Female 0 Male	34.92 ± 26.55 (SD), p= 0.044*	2.0 p= 0.965
Rhytides only (Control)	51.14 ± 13.90 (SD) 53.0	3 Female 4 Male	78.04 ± 25.96 (SD)	1.0
All subjects	51.76 ± 12.10 (SD) 53.0	16 Female 5 Male	56.20 ± 30.37 (SD)	1.25

[1]Median WSRS score was based on blinded grading using the Wrinkle Severity Rating Scale, p values obtained for comparison against rhytides only cohort, *indicates significant outcome

Wrinkle Severity Rating Scale (WSRS) Score

As expected, the WSRS scores correlated with age (Figure 4). Subjects with rosacea-only had a median glabellar WSRS score of 1.625, (p= 0.704). In the melasma-only cohort, the median glabellar WSRS score was 1.0, p= 0.629. The median glabellar WSRS score for subjects with both rosacea and melasma was 2.0, p= 0.965. Among subjects in the rhytides-only cohort, their median glabellar WSRS score was 1.0. The median WSRS score for all 21 subjects was 1.25 (Table 1). There was no significant difference among the different groups.

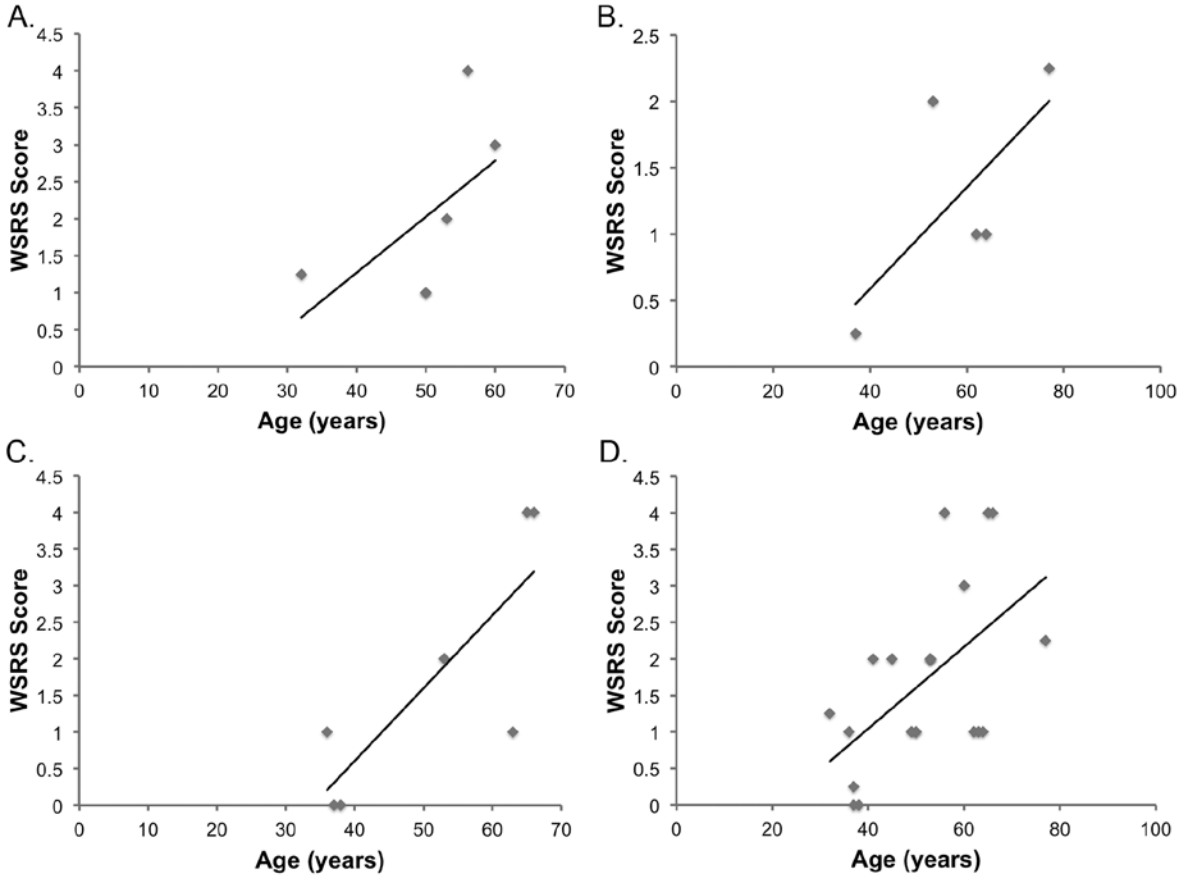

Figure 4. Correlation of wrinkle severity score with age for subjects with (A) rosacea-only, p<0.0001; (B) melasma-only, p<0.0001; (C) rhytides-only, p<0.0001; and (D) all subjects, p<0.0001, correlation = 0.5552.

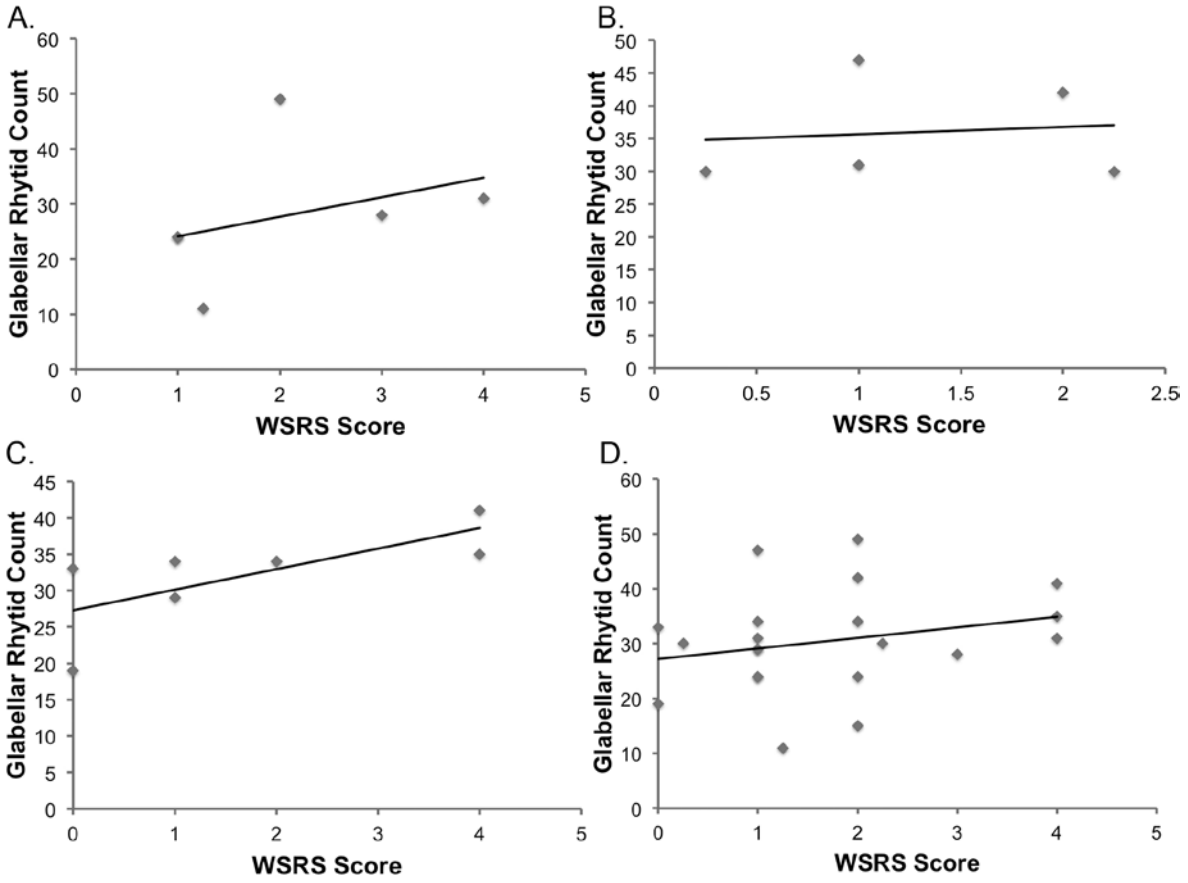

Figure 5. Relationship between glabellar rhytid count and the wrinkle severity score for subjects with (A) rosacea-only, (B) melasma-only, (C) rhytides-only, and (D) all subjects, correlation = 0.2470.

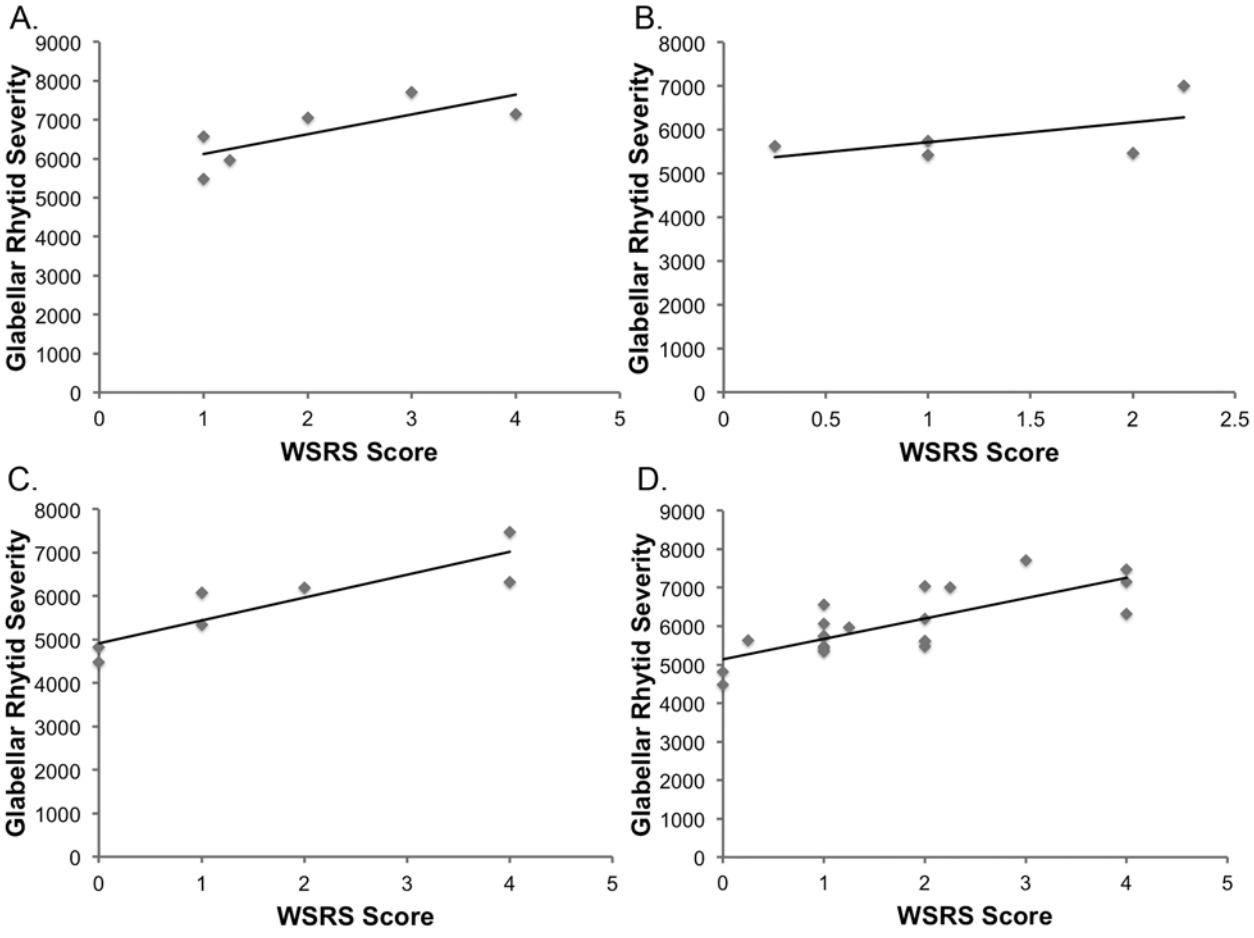

Figure 6. Relationship between glabellar rhytid severity and the wrinkle severity score for subjects with (A) rosacea-only, (B) melasma-only, (C) rhytides-only, and (D) all subjects, correlation = 0.7596.

Rhytid count and severity assessed by facial modeling and measurement

Facial surface analysis was performed on high-resolution photographic images to determine the rhytid severity and count for each subject. Both the rhytid severity and the rhytid count positively correlated with the WSRS scores (Figure 5 and 6). The average glabellar rhytid count and average glabellar rhytid severity for subjects with rosacea-only was 27.8 ± 12.4 and 6651.17 ± 823.6 arbitrary units (AU) (Figure 7), respectively. Among subjects with melasma-only, the average glabellar rhytid count and average glabellar rhytid severity was 36.0 ± 8.0 AU and 5852.45 ± 655.1 AU, respectively. The average glabellar rhytid count and average glabellar rhytid severity for those with rosacea and melasma was 22.67 ± 7.1 AU and 5661.28 ± 72.4 AU, respectively. Among the rhytides-only cohort, the average glabellar rhytid count and average glabellar rhytid severity was 32.14 ± 6.79 AU and 5815.38 ± 1015.31 AU, respectively (Figure 7).

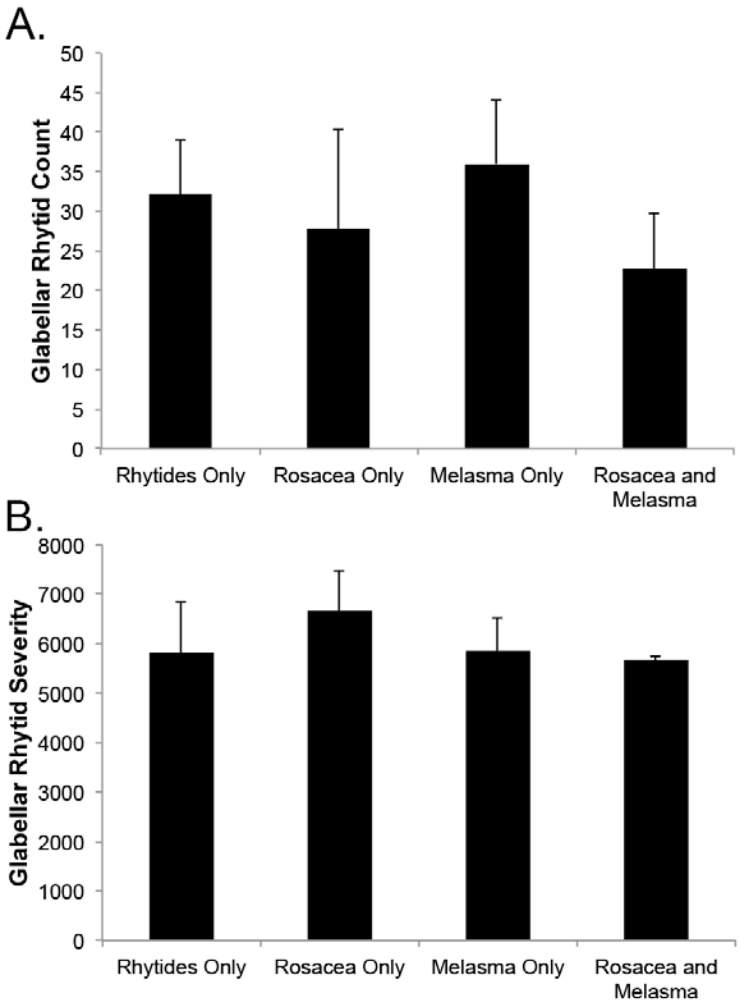

Figure 7. (A) Glabellar rhytid count from computer analysis from BTBP® for all subjects (B) Glabellar rhytid severity based on computer analysis for all cohorts

Discussion

Our study shows several interesting correlations for the facial SER (Table 2). We show that facial SER decreases with age. This is in agreement with a previous study that showed that postmenopausal women had lower sebum secretion when compared to younger and premenopausal women [12-14]. Our study included mostly female participants; however, a similar decline in SER has previously been reported when comparing younger men to older men [14].

We found that the SER is unchanged with the presence of ETR. This is in agreement with a previous study that did not note any association of SER with the presence of rosacea [15] and in agreement with another study of papulopustular rosacea [16]. Our study revealed that the SER was reduced in those with melasma. One previous study evaluated the sebum excretion in lesional and perilesional skin of melasma and reported no difference [7]. Our study differed from the previous study in that we compared the

SER between subjects that did and did not have melasma, whereas the previous study evaluated the SER within the same subject. This suggests that SER may be decreased in those with melasma but the SER does not vary locally on the face in those with melasma.

Sebum is a source of multiple antioxidants including vitamin E and Coenzyme Q10 [10]. The decreased SER noted with melasma may partially contribute to its development because melasma has an etiology in photoexposure. Interestingly, it has been shown that lipids found in the sebum, such as linoleic acid, have been shown to inhibit melanogenesis [17,18]. This raises the possibility that enhancement of sebum secretion may be protective against melasma. However, such a strategy must be balanced against the potential risk for the development of acne. In an older population that is less susceptible to acne, elevating the sebum excretion rate may serve as preventative or therapeutic measure against melasma. A prospective study based on SER and the development of melasma would be needed to better assess for any association.

Current evaluations of rhytides and facial features are mostly based on subjective grading. Herein, we evaluated the utility of a facial surface and skin feature modeling and measurement system to offer a more objective rating system. We found that both the rhytid count and severity correlate with clinical grading. The clinical research community is in the early phases of incorporating this technology for the purpose of tracking facial features and quantifying skin conditions. Continuous research with facial modeling and measurement systems will allow for more precise and standardized analysis of skin features such as rhytides in the dermatological community. Because subjective grading scales are not continuous grades but discrete, this can limit the resolution of ascertaining changes in rhytides. The use of a more objective grading scale would allow for better assessment of both small and large changes in the number and depth of rhytides. Our study was limited to assessment of the glabellar area. Future studies will need to incorporate other anatomical areas typically assessed for therapy such as the entire forehead and the lateral canthi.

This clinical study has some limitations. This study serves as a pilot study and the subject sample size was limited to 21 study participants. The study subjects in the rosacea group were limited to those with erythematotelangiectatic rosacea rather than involving those with other subsets of rosacea. Thirdly, the sebum measurements were limited to assessing overall sebum excretion rates. However, this does not offer information regarding the lipid profiles of the sebum and how individual sebum lipids may have differed with age, presence of rhytides, melasma, or rosacea.

Table 2. Correlation coefficients for cohorts

	Variables Assessed	
Cohort	SER vs average WSRS score[1]	SER vs age
Rosacea	-0.566050951	-0.76743108
Melasma	-0.358324751	-0.065691809
Rosacea and Melasma	0.894378442	-0.55089891
Rhytides Only	-0.313376264	0.046071035
Overall	-0.243216567	-0.283853538

[1]Median WSRS score was based on blinded grading using the Wrinkle Severity Rating Scale [2]; rhytid count was based on facial surface feature analysis [3]; rhytid severity was based on facial surface feature analysis reports of average glabellar rhytid severity

Table 3. Abbreviations

Abbreviation	
BTBP	Brigh-Tex BioPhotonics
ETR	Erythematotelangiectatic rosacea
SD	standard deviation
SER	sebum excretion rate
WSRS	Wrinkle Severity Rating Scale

Conclusion

Our investigation shows that the SER declines with age and with the presence of melasma. Furthermore, we utilized a surface and skin feature modeling and measurement system in order to offer a quantitative and objective method to assess rhytides. Future studies will need to correlate the SER with skin antioxidant measurements to better assess how SER may modulate photoaging. Imaging based facial surface analysis correlated with clinical grading, raising the possibility of incorporating objective rhytid grading into future studies.

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