

Development of a Single Indicator of Facial Skin Aging and Youthful Plump Appearance; Ageless-U and Its Use for Evaluating the Efficacy of Treatment with *Galactomyces* Ferment Filtrate-Containing Anti-Aging Skin Care Formula

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Abstract

Background/Objective: Wrinkles, nasolabial folds, pigmented spots, and roughness are representative parameters reflecting facial skin aging. Among them, nasolabial folds are a particular concern associated with aging. However, changes in the skin surface topography on the cheek above these folds remain unclear. This research aimed to develop a dynamic multi-angle imaging method and a single indicator of skin aging to quantify both the aged and youthful plump appearance of the skin. **Methods:** A facial imaging system was used in two separate studies to capture images from multiple angles. An image analysis algorithm quantified facial lines and two diagonal facial lines from the outer and inner cheek regions, forming a U-shaped line. Block analysis computed the average slope and intercept of line segments, and an excircle with its center coordinate was calculated from the U-shaped line. The elevation of this coordinate on the cheek, termed “Ageless-U,” served as a single indicator representing the severity of sagging of aging-related facial lines and the youthful appearance in a wide angle of view of the facial skin. Eighty-five East Asian women aged 22 - 57 participated in Study 1 to examine relationships between Ageless-U, age, skin elasticity, and visual signs of aging. In Study 2, 35 East Asian women aged 32 - 54 applied a *Galactomyces* ferment filtrate-containing anti-aging skincare product twice daily for 4 weeks, with measurements at

baseline, week 2, and week 4 to determine this product's efficacy against facial aging. **Results:** In Study 1, Ageless-U significantly descended with increasing age and was associated with reduced skin elasticity and hydration, with notable declines in the 20s and 40s and its position was significantly lowered from the upper cheek to lower cheek. In Study 2, daily treatment elevated Ageless-U at both 2 and 4 weeks. **Conclusion:** Ageless-U is an early indicator representing topographic features of the skin aging on the face, and the youthful plump skin appearance at the same time. Ageless-U descent can be prevented and reversed by the appropriate treatment of anti-aging skincare products.

Keywords

Facial Skin Aging, Youthful Plump Skin Appearance, Ageless-U, Skin Elasticity, *Galactomyces* Ferment Filtrate (Pitera™)

1. Introduction

Aging is the natural fate of all living organisms. Facial skin aging is a major human concern, especially among women. Moreover, because the face is constantly exposed to environmental stressors such as ultraviolet radiation, pollutants, and mechanical friction, it tends to show accelerated and more visible signs of aging. Deterioration of surface topography and tonal attributes of facial skin are the most prominent visible features associated with skin aging. Topographical and color information of the face can be classified in terms of several specific features, such as wrinkles-facial lines, hyperpigmented spots, surface roughness, texture, and pores, which have been measured and quantified by a variety of imaging techniques [1]-[5]. The intensity and speed of the aging process differ markedly between individuals and ethnicities [5] [6]. For example, wrinkles are known to increase more rapidly and more conspicuously in Caucasian than in East Asian women. Meanwhile, hyperpigmented spots are more apparent in East Asian women than in Caucasian women [6]. Among various skin aging parameters, wrinkles, hyperpigmented spots, and skin roughness are considered to be particularly representative of an older appearance of the female face [5]. Facial skin aging is also associated with dehydration [5] [7], while nasolabial folds are a notable concern associated with aging [8] [9]. Nasolabial folds are reported to become apparent in Asians in their 30 s or 40 s; however, changes in the skin surface topography on the cheek above these folds remain unclear [8].

SK-II Pitera™ contains *Galactomyces* ferment filtrate (GFF), which works as a potent antioxidative agonist for aryl hydrocarbon receptor [10] [11]. GFF is known to increase the expression of filaggrin, caspase-14, and claudin-1, which may facilitate the production of natural moisturizing factors and strengthen the tight junction structure [10] [12] [13]. GFF also inhibits oxidative stress due to

proinflammatory cytokines via activation of the antioxidative system [11] [14]. Several efficacy evaluation studies have revealed that the daily application of Pitera™ indeed increases the hydration of facial skin [7] [15] [16]. It also alleviates mask-induced skin damage [16] and can effectively reverse facial skin aging after twice-daily application for 12 months [7].

Visual examination of the condition of facial skin generally involves evaluation of its overall condition across large regions of the face [17] [18]. Such examinations include assessments of features such as facial lines, which are associated with perceptions of visible skin firmness and plumpness [19] [20]. Skin-moisturizing cosmetics are expected to maintain and improve the appearance of the firmness of facial skin. However, few methods or systems have been developed for objectively evaluating the visual appearances of both skin aging and youthfulness, while there is also a lack of visible indicators for performing such evaluation in a convenient and quantitative manner. As such, we developed a novel imaging method and system capable of capturing images of a large area of the face from multiple angles to comprehensively quantify facial lines and their shape and direction as a representation of skin aging. We also used this approach to measure improvements in the youthful, plump appearance of the skin by identifying elevation or descent on the cheek of the central coordinate of an excircle based on those facial lines associated with treatments with an anti-aging skincare formula. We report here the design, capabilities, and applications of our method and the associated system.

2. Materials and Methods

2.1. Subjects in Studies 1 and 2

Skin evaluation was performed in 2024 on 85 healthy East Asian females in Study 1, and on 35 East Asian females in Study 2.

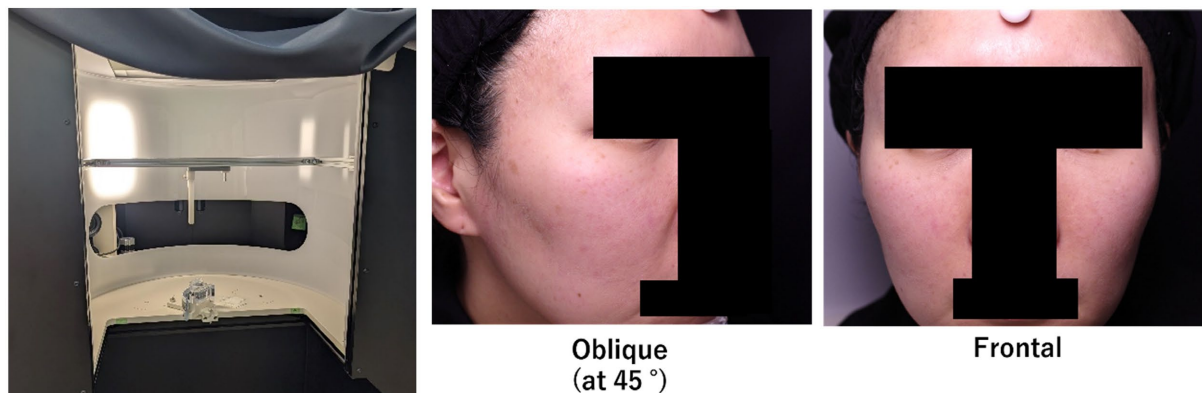
In Study 1, the age of the subjects ranged from 22 to 57 years old [mean \pm standard deviation (SD), 43.2 ± 9.3]. The number of subjects in Study 1 by age group was as follows: 9 in their 20s (25.9 ± 2.0), 22 in their 30 s (34.8 ± 2.3), 26 in their 40s (46.2 ± 2.9), and 28 in their 50s (52.5 ± 1.5). In Study 2, the subjects were aged from 32 to 54 years old (45.9 ± 7.5). Prior to commencing the studies, written informed consent was obtained from all subjects and we obtained approval for the study protocols from the Ethical Committee of Global Product Stewardship at P&G Innovation Godo Kaisha (ethical approval numbers ES24-008 and CT24-013).

2.2. Facial Optical Imaging

The subjects washed their faces using the prescribed cleansing foam and then spent 15 min becoming accustomed to the environment of the measurement room. The measurement room was maintained at a constant temperature and humidity (room temperature $20 \pm 2^\circ\text{C}$, relative humidity $50 \pm 5\%$). None of the subjects underwent any type of esthetic treatment, such as laser cosmetic procedures

during the study period.

Each subject's face was photographed using a multi-angle dynamic imaging system illuminated by light-emitting diodes (Color Temperature: 5600 K) mounted on top of a camera (**Figure 1**). A high-resolution digital camera, capable of generating 2160 (vertical) \times 3840 (horizontal) pixels, was also mounted in the imaging module. This enabled the capture of images from multiple angles, with these images extracted from the recorded video using a Python script that leveraged OpenCV to obtain individual frames, ensuring consistent sampling for subsequent analysis.



Each subject's face was photographed using the multi-angle dynamic imaging system. Images were taken from the front and obliquely (at 45°) to capture the inner and outer cheek regions.

Figure 1. Picture of the multi-angle dynamic imaging system and images obtained by it.

2.3. Objective Image Analysis for Ageless-U and Other Skin Aging Parameters

Ageless-U, defined as the Y-coordinate of the center of an excircle based on the cheek's U-shaped line, was employed as a single indicator of age-related changes in facial topography. To calculate Ageless U, a facial imaging system was developed to capture facial skin images (from the front and obliquely) as described above.

Using an image analysis algorithm, we quantified the total area, average angle, and height of the topographical facial lines on the inner and outer cheek regions separately. From these measurements, tangent lines were estimated from two distinct diagonal lines derived from the facial line data, collectively termed the U-shaped line (**Figure 2**).

A block analysis on the regions of interest (ROIs) for the inner and outer cheeks was then employed to detect line segments, and the average slope and intercept of these segments were computed. For the outer cheek measurements, images were taken obliquely at a 45° angle, while frontal images were used for the inner cheek measurements. The coordinates between frontal and oblique images were aligned using mouth landmarks detected by Mediapipe Face Mesh [21], and the intersection of the average lines from the inner and outer regions was calculated to determine the U-shaped line variables.

Next, an excircle was fitted to the U-shaped line, and the Y-coordinate (reflecting height on the cheek) of its center was calculated. This coordinate, termed Ageless-U, was employed as a single indicator that represents the severity of sagging and area of these U-shape facial lines caused by skin aging. The calculation of the U-shaped line and Ageless-U is performed via the following steps.

1) Average lines of inner and outer cheek regions.

Calculate the average of the slope product and the length, as well as the intercept of each detected line in the inner and outer cheek regions.

$$\ell_{in} : y = \bar{m}_{in}x + \bar{b}_{in}, \ell_{out} : y = \bar{m}_{out}x + \bar{b}_{out}$$

Adjust the x , y coordinates of the inner cheek tangent line based on the mouth position of the outer cheek.

$$\ell_{in} : y = \bar{m}_{in} (x - \Delta x) + (\bar{b}_{in} + \Delta y)$$

2) Determination of the intersection point of the average lines (A)

Determine the intersection of the average inner and outer cheek lines by solving their linear equations and designate it as point A.

$$x_A = \frac{\bar{b}_{out} - (\bar{b}_{in} + \Delta y) + \bar{m}_{in} \Delta x}{\bar{m}_{in} - \bar{m}_{out}}, y_A = \bar{m}_{in} (x_A - \Delta x) + (\bar{b}_{in} + \Delta y)$$

3) Extending the average lines

Define empirical extension lengths based on the total connected - component counts Σ_{in} and Σ_{out} to apply to average lines to obtain the extended points (B, C).

$$L_{in} = A_{in} + B_{in} (C_{in} - \Sigma_{in}), L_{out} = A_{out} + B_{out} (C_{out} - \Sigma_{out})$$

$$B = \left(\frac{y_A - L_{in} - (\bar{b}_{in} + \Delta y)}{\bar{m}_{in}}, y_A - L_{in} \right), C = \left(\frac{y_A - L_{out} - \bar{b}_{out}}{\bar{m}_{out}}, y_A - L_{out} \right)$$

4) Calculation of the Y-coordinate of the excircle center between A, B and C (IA_y).

Compute the Y-coordinate of the excircle center using the weighted formula on the triangle defined by points A, B, and C, and designate it as IA_y .

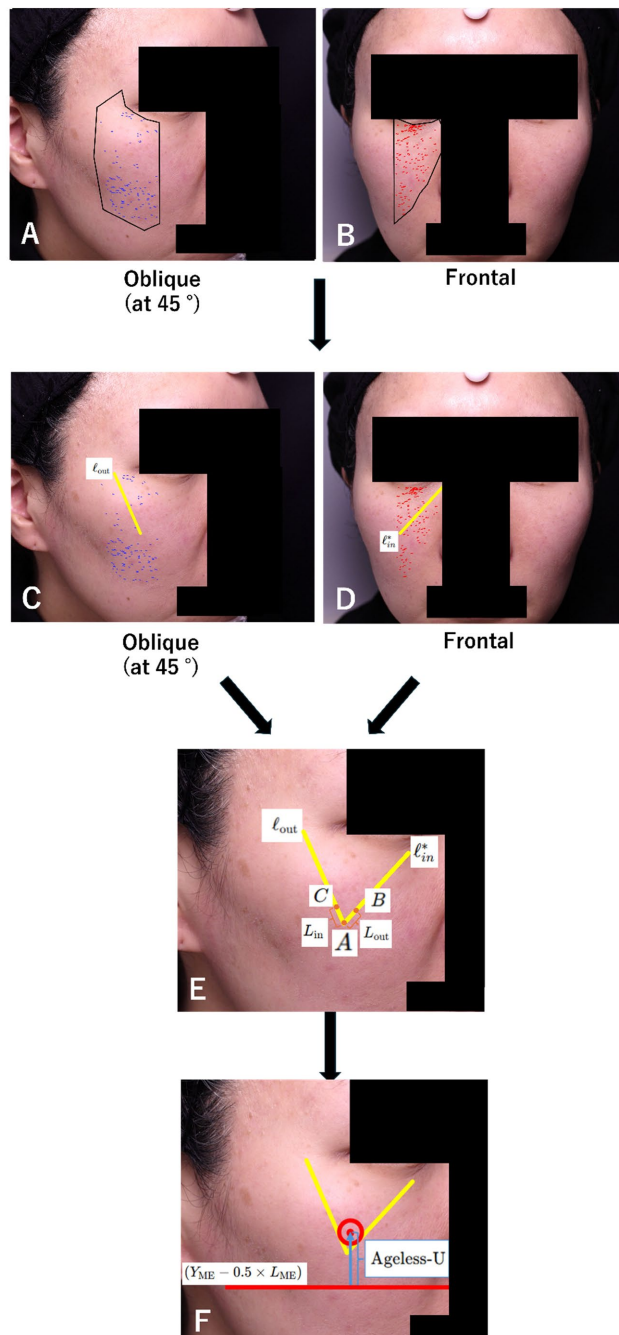
$$a = \|B - C\|, b = \|C - A\|, c = \|A - B\|$$

$$IA_y = \frac{-aA_y + bB_y + cC_y}{-a + b + c}$$

5) Calculation of IA_y with normalized Y-axis (Ageless-U).

Obtain the Y-coordinate of the center point between the mouth and eyes (Y_{ME}) and establish a new reference by shifting this baseline downward by half the difference between the mouth and eyes Y-coordinates (L_{ME}). Recalculate IA_y relative to this new reference to yield Ageless-U.

$$\text{Ageless-U} = IA_y - (Y_{ME} - 0.5 \times L_{ME})$$



(A, B) Line segments within ROIs on the inner and outer cheeks were detected using block analysis. (C, D) Average lines of inner and outer cheek regions are calculated by regressed parameters from line segments on the inner cheek (l_{in}) and the outer cheek (l_{out}) shifted by Δ using mouth landmark to produce the aligned line l_{in}^* . (E) Point A is the intersection of l_{in}^* and l_{out} . By extending these lines downward by fixed lengths L_{in} and L_{out} , points B and C are obtained. (F) Treating A, B, and C as vertices of a triangle, the A-excenter (IA_y) is computed by the weighted formula above. In the final step, the Y-coordinate is normalized by obtaining the center point between the mouth and eyes (Y_{ME}) and establishing a new reference by subtracting half the difference between the mouth and eyes Y-coordinates (L_{ME}). IA_y is recalculated relative to this new reference to yield Ageless-U.

Figure 2. Measurement process of U-shaped line to determine the coordinate Ageless-U.

The ROI of the images was determined from the lower edge of the eyes to the cheek, and the following characteristic objects were detected by measuring the contrast in the shape and pixels using an image analysis algorithm for wrinkles, pores and texture with reference to the literatures [22] [23].

2.4. Biophysical Measurements

Mechanical elasticity of the skin was measured using a Cutometer® (Courage + Khazaka Electronic GmbH, Cologne, Germany) [24] [25] Water content in the stratum corneum of the cheek was measured using Corneometer® (Courage + Khazaka Electronic GmbH).

2.5. Subjective Visual Assessment for Skin Aging and Youthful Plumpness

The subjective impression of facial skin on the cheek region was visually evaluated by five expert skin examiners using a color-calibrated monitor (ColorEdge CG2420, EIZO Corporation, Hakusan, Japan). The examiners assessed perceived skin age subjectively and rated skin plumpness as representative of a youthful plump appearance of the skin on a 5-point scale (0 indicating low plumpness and 4 indicating high plumpness). The relationships between these subjective scores and Ageless U were subsequently analyzed.

2.6. Statistical Analysis

All statistical analyses were conducted using Python 3.8 and Python script. Stats module [26]. Both descriptive and inferential statistical methods were applied as appropriate for analyzing the study data. In addition, Pearson's correlation coefficients (r) were computed among the variables as described below.

In Study 1, correlations of Ageless-U with chronological age, intersection angle of the two lines making up the U-shaped line, and area of the facial lines on the cheek were examined. In addition, correlations of Ageless-U with five skin optical and physical parameters [image analysis data on wrinkles, roughness, pores, hydration, and elasticity (R2, R5)], in addition to two subjectively evaluated variables (plumpness/firmness and skin aging appearance) were examined.

Quantitative comparisons were also performed as follows. In Study 2, six optical and physical parameters of skin [Ageless-U, wrinkles, roughness, pores, hydration, and elasticity (R2)] measured at 2 and 4 weeks after the initiation of twice-daily treatment with the assigned skin moisturizer containing GFF as the major skin care ingredient (SK-II SKINPOWER RE-NEW CREAM) were compared with their levels at baseline using paired t-tests. A p-value of less than 0.05 was considered to indicate statistical significance.

3. Results

We measured the facial skin parameters Ageless-U, U-shaped line-related parameters (intersection angle, area of the facial lines forming a U-shaped line), wrin-

kles, textures, and pores in Study 1 (N = 85 East Asian females, **Table 1**).

Table 1. Measured facial skin parameters in Study 1 (N = 85 East Asian females).

Age (years)	Ageless-U (mm)	U-Shaped Line: Intersection Angle (°)	U-Shaped Line: Area of the Facial Lines (a.u.)	Wrinkles (a.u.)	Texture (a.u.)	Pores (a.u.)
43.2 ± 9.3	25.6 ± 18.5	148.2 ± 7.5	0.0142 ± 0.0102	0.0257 ± 0.0141	0.0433 ± 0.0127	0.0325 ± 0.0122

In Study 1, a significant lowering of Ageless-U on the cheek was observed with increasing chronological age. (**Figure 3(a)** red solid line) Notably, Ageless-U rapidly descended in the 20 s and 40 s (**Figure 3(b)**). Ageless-U also correlated with the intersection angle and area of the facial lines forming a U-shaped line (**Figure 3(c)**). We next analyzed whether Ageless-U was correlated with changes in other skin aging parameters in the skin aging process. The results showed that Ageless-U was significantly correlated with wrinkles ($r = -0.49$, $P < 0.05$), texture ($r = -0.54$, $P < 0.05$), and pores ($r = -0.38$, $P < 0.05$) in Study 1 (**Figure 3(d)**).

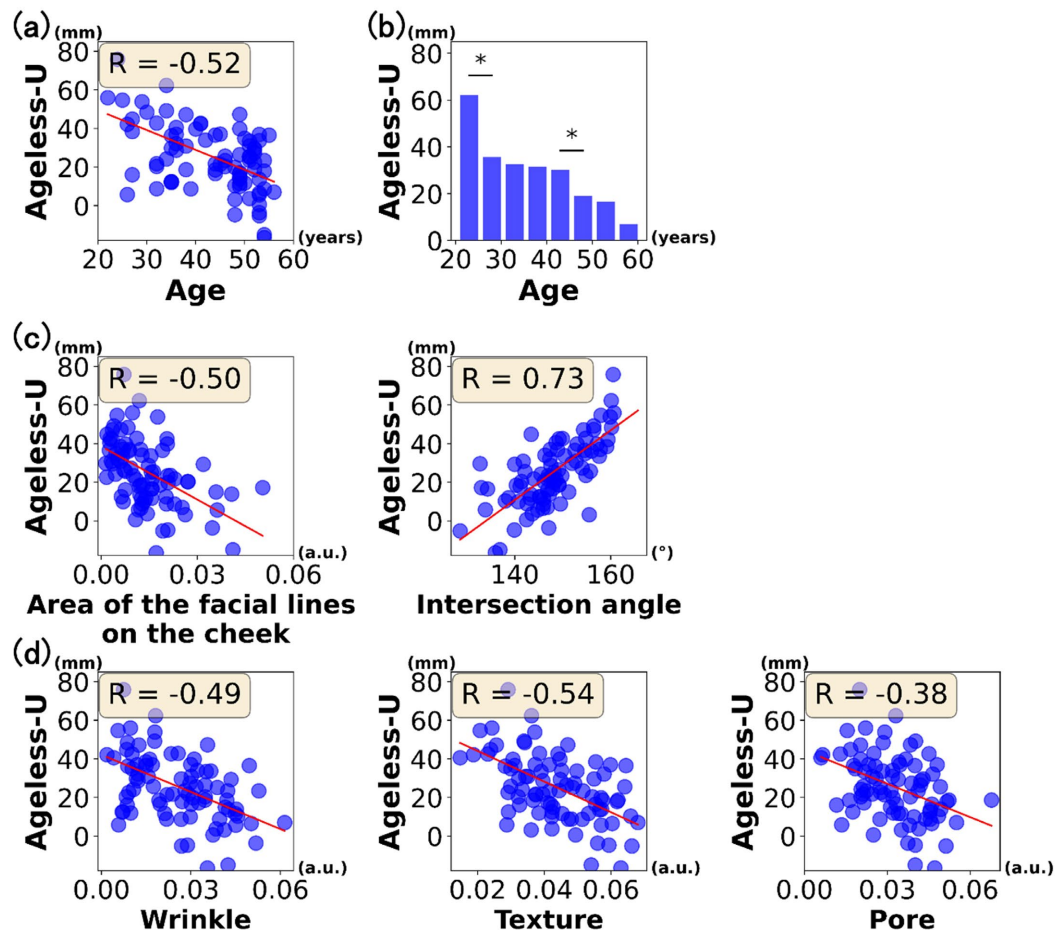


Figure 3. Associations of Ageless-U with Chronological Age and Facial Features. (a) Correlations of Ageless-U with chronological age. (b) Mean Ageless-U values across 5-year age intervals, with a significant decline observed in subjects in their 20s and their 40s. *: $P < 0.05$. (c) Correlations of Ageless-U with intersection angle between U-shaped line and area of the facial lines forming U-shaped line. (d) Correlations of Ageless-U with wrinkles, texture, and pores.

Significant decreases in hydration and elasticity were observed with descending Ageless-U in Study 1 (Figure 4).

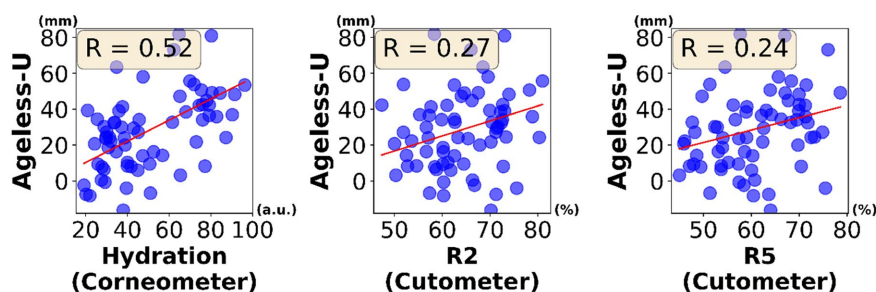


Figure 4. Correlations of Ageless-U with skin hydration (Left) and elasticity (Center and right).

Furthermore, Ageless-U was significantly correlated with subjectively evaluated plumpness/firmness ($r = 0.48$, $P < 0.05$) and skin aging appearance ($r = -0.54$, $P < 0.05$) (Figure 5).

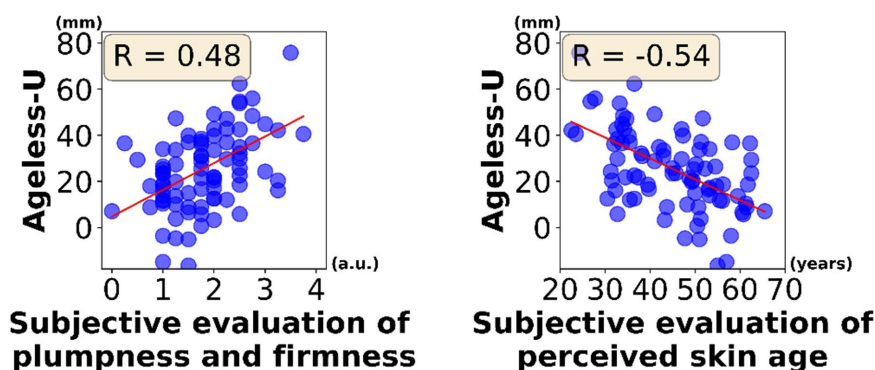


Figure 5. Correlations of Ageless-U with visual evaluation of plumpness and firmness (Left) and perceived skin age (Right).

Table 2. Ageless-U, hydration, elasticity, and skin aging parameters before and after treatment with GFF-containing anti-aging skincare product (N = 35).

	Hydration (a.u.)	Elasticity (R2) (%)	Ageless-U (mm)	Wrinkles (a.u.)
Baseline	53.9 ± 11.5	64.7 ± 7.0	27.0 ± 15.6	0.0244 ± 0.0186
Week 2	60.4 ± 7.9*	63.0 ± 10.5	34.8 ± 15.5 *	0.0238 ± 0.0206
Week 4	59.6 ± 7.3*	68.7 ± 9.9*	36.2 ± 17.6*	0.0196 ± 0.0158*

* $P < 0.05$ compared with the baseline.

As Ageless-U significantly correlated with dehydration, elasticity, and skin aging parameters, we next examined whether appropriate anti-aging skin treatment with a GFF-containing skin aging formula (SK-II SKINPOWER RE-NEW CREAM) can elevate Ageless-U, thereby countering the sagging of the cheeks (Study 2). Thirty-five East Asian females applied the GFF-containing anti-aging skincare product twice daily for 4 weeks, on whom skin measurements were conducted before application (baseline), and after 2 and 4 weeks of application. Application

of the skincare product significantly improved skin hydration and elasticity, and elevated Ageless-U (Table 2, Figure 6). Notably, Ageless-U was significantly improved after both 2 and 4 weeks of application, in association with a significant reduction of wrinkles (Table 2). Images of two representative cases are presented in Figure 7 and Figure 8.

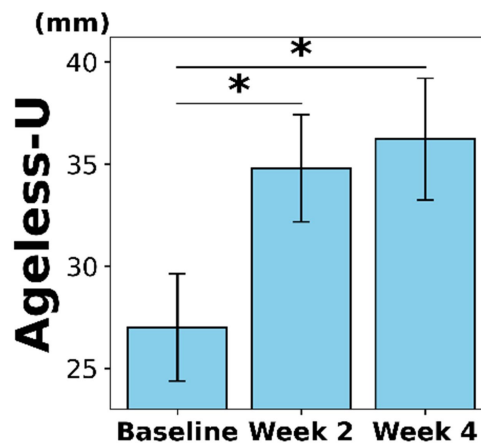
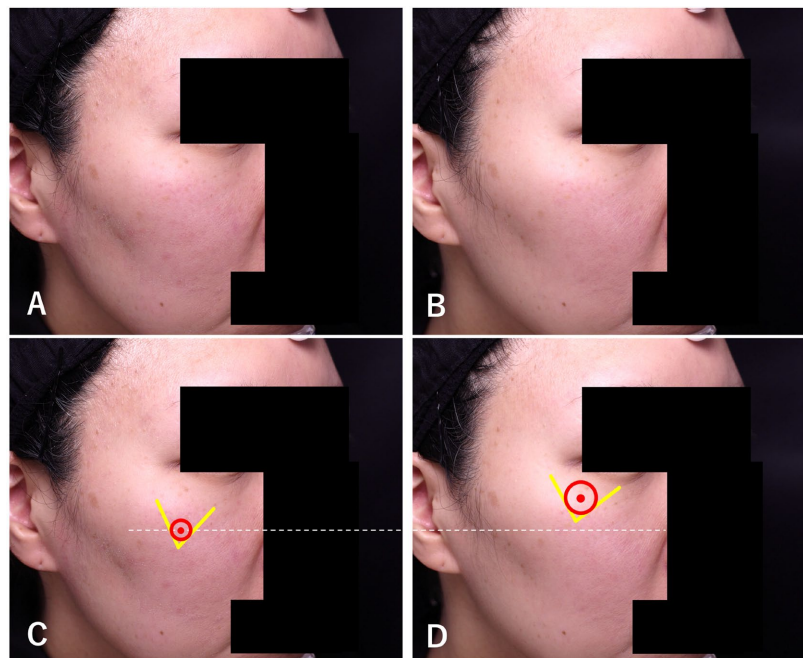
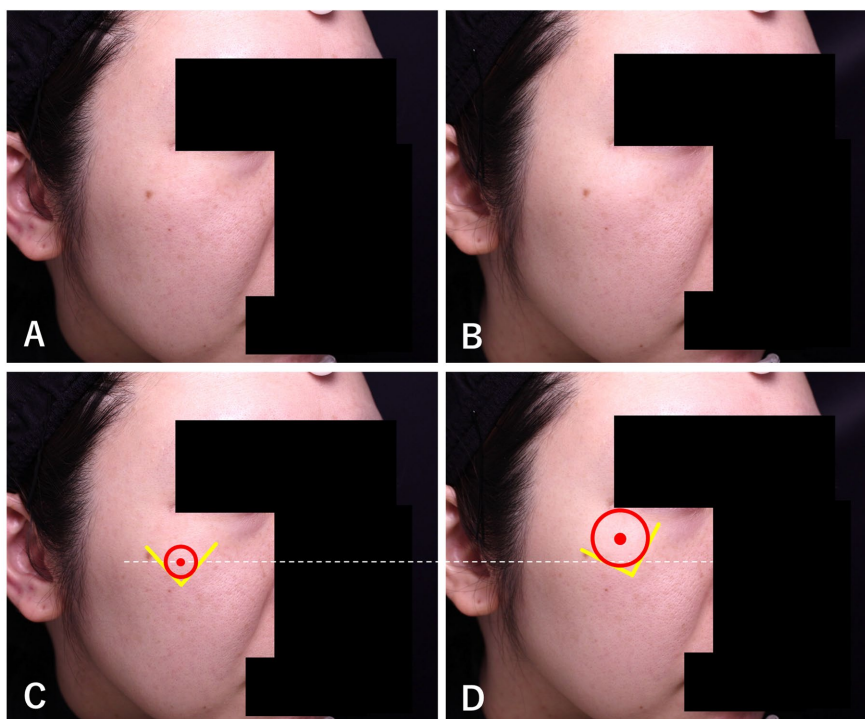


Figure 6. Effect of GFF-containing anti-aging skincare product on Ageless-U (N = 35). Significant improvements in Ageless-U were observed. *: P < 0.05.



(A) Oblique bare-skin image at baseline. (B) Oblique bare-skin image after 2 weeks of product use. (C) The baseline Ageless-U result, transferred and overlaid onto the oblique image, was calculated as described in Figure 2. (D) The two-week Ageless-U result, transferred and overlaid onto the oblique image, calculated as described in Figure 2. Ageless-U was elevated by 13.2 mm.

Figure 7. Representative case (Case 1) from Study 2 showing elevation of Ageless-U after 2 weeks of treatment with the GFF-containing anti-aging skincare product (SK-II SKINPOWER RE-NEW CREAM).



(A) Oblique bare-skin image at baseline. (B) Oblique bare-skin image after 2 weeks of product use. (C) The baseline Ageless-U result, transferred and overlaid onto the oblique image, calculated as described in [Figure 2](#). (D) The two-week Ageless-U result, transferred and overlaid onto the oblique image, calculated as described in [Figure 2](#). Ageless-U was elevated by 9.8 mm.

Figure 8. Representative case (Case 2) from Study 2 showing elevation of Ageless-U after 2 weeks of treatment with the GFF-containing anti-aging skincare product (SK-II SKIN-POWER RE-NEW CREAM).

4. Discussion

Facial skin aging is an important concern. Physiological or chronological aging starts at birth and is accelerated by various external stresses such as ultraviolet radiation, environmental pollutants, and mechanical stress [27] [28]. Over the course of natural aging, facial skin gradually acquires signs of aging including wrinkles, surface roughness and decreased mechanical elasticity [5] [22]-[24]. Although these parameters well represent facial skin aging, previous research showed the remarkable progression of these features, especially nasolabial folds in those aged 30 or above [5] [8] [19]-[24].

We have validated a novel method for quantifying an early sign of aging that correlates with both aged and youthful plump appearance of the skin, via high-resolution digital imaging. This sign of aging starts as early as their 20 s, which is before any notable aging of the skin has occurred. Importantly, this early sign of aging, termed Ageless-U, observed during the 20 s, suggests that aging occurring during this decade may lead to the more visible aging changes that manifest in the 30s and 40s. Through two separate studies, we confirmed that the imaging methodology using the U-shaped line and the coordinate Ageless-U along with a multi-

angle facial imaging system was sufficiently sensitive to enable the measurement of visible skin plumpness. The appearance of skin plumpness, featuring high elasticity and firmness, representing a youthful appearance of the skin, is widely used and communicated among users of skincare cosmetics. However, current methods for evaluating the visible appearance of skin plumpness or firmness usually involve visual assessments by experts, who either examine subjects' faces directly or examine photographs of their faces taken during a study. As such, these approaches involve a certain degree of subjectivity. Several reports have been published on the evaluation of skin sagging using three-dimensional imaging techniques or by measuring the condition of the skin through the application of physical stress [29] [30]. Although these measurements of skin sagging appear to be accurate, they suffer from several disadvantages, such as the measured areas being too small to allow evaluation of the overall condition of the skin and complicated measurement procedures. In the evaluation of cosmetics, the mechanical property of skin firmness (R2, R5) is frequently evaluated using a Cutometer® [31] [32]. This is an important measurement for understanding the physical properties of the skin, but does not incorporate the appearance of plumpness observed on the skin's surface. The imaging method and associated system developed in this study enable the quantitative and automatic measurement of the visual appearance of skin plumpness, thereby overcoming these disadvantages. Our multi-angle imaging system contains a high-resolution digital camera and light-intensity-controlled LEDs. The module has a cover trim that encloses the skin's surface, allowing reproducible imaging of a region of skin of a fixed size under controlled lighting conditions. Our image analysis was therefore developed to quantify the number of facial lines and their direction at inner and outer cheek regions using features called the U-shaped line and Ageless-U, as a coordinate based on that U-shaped line. These parameters can be used to evaluate apparent skin aging and youthful plumpness together in an objective manner. In the present study, we conducted an age-dependent facial skin imaging study on East Asian volunteers. We found that the location of Ageless-U on the cheek was a valuable marker of facial skin aging and also of youthful plumpness of the skin. In this study Ageless-U was calculated using the Y-coordinate of the excircle's center, a value that shows a high correlation with the excircle's radius. Consequently, future investigations may consider representing youthful plumpness using the excircle's radius or through alternative geometric depictions, such as a circle or sphere. For example, excircle area also demonstrated significant correlation with Ageless-U ($r = 0.66$, $P < 0.05$), chronological age ($r = -0.33$, $P < 0.05$) and visible appearance of skin plumpness ($r = 0.31$, $P < 0.05$) (Figure 9).

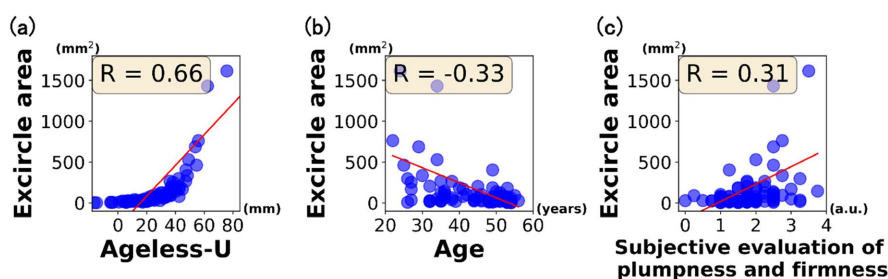
Change of Ageless-U was significantly correlated with changes in wrinkles, texture, and pores as well as mechanical elasticity measured with Cutometer, that is an established skin elasticity measurement method. Ageless-U was found to descend rapidly in the 20 s and 40 s, moving from the upper cheek to lower cheek, despite such decline not being observed for other skin aging parameters. This rapid descent of Ageless-U could lead to sudden morphological changes that pro-

mote wrinkling of the skin in the early 30 s [33].

After 4 weeks of treatment with the GFF-containing anti-aging skincare formulation (SK-II SKINPOWER RE-NEW CREAM), the location of Ageless-U showed a significant improvement by more than 5 mm. Ageless-U is thus a sensitive and useful parameter for evaluating visible skin aging and also plumpness/firmness of the skin. This assessment is useful for dermatologists and plastic surgeons to rapidly and quantitatively understand apparent facial skin aging holistically.

Limitations of this study include a lack of understanding of the precise mechanisms by which the descent of Ageless-U occurs. Further longitudinal prospective placebo-controlled studies are necessary to elucidate whether the GFF-containing skincare product is capable of slowing the long-term aging process. Also, Ageless-U descent may vary by different ethnicities (e.g. Caucasian, African American) or other age groups since Ageless-U is influenced by the severity of topographical aging signs such as wrinkles, fine lines and prolonged pores.

In conclusion, the combination of a digital-imaging system and an image analysis algorithm established in this work appears to provide a reliable single indicator for objectively and quantitatively evaluating the visual appearance of facial skin aging and youthful plumpness. It also appears to be suitable for the objective assessment of responses to skin treatments.



(a) Correlations of excircle area with Ageless-U. (b) Correlations of excircle area with chronological age. (c) Correlations of excircle area with visual evaluation of plumpness and firmness.

Figure 9. Associations of excircle area with Ageless-U, chronological age, and visual facial evaluations.

Author Contributions

Conceptualization and study investigation: K.F., K.M., S.S., S.W., H.T., I.K. Writing - original draft preparation: K.M., K.F. Writing - review and editing: all authors. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement

This study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by P&G Ethics Committee. Data acquisition and analysis were performed in compliance with protocols approved by the Ethical Committee of

Global Product Stewardship in P&G Innovation Godo Kaisha (ethical approval numbers ES24-008 and CT24-013). Written informed consent was obtained from all participants prior to inclusion in the study.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data presented in this paper are available on request from the corresponding author. The data are not publicly available because of privacy restrictions.

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Conflicts of Interest

Hideaki Tanizaki and Izumi Kishimoto are unpaid consultants of P&G Innovation GK. The other authors are employees of P&G Innovation GK.

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