DERMACLAIM
Test & Trust

Project Reference

DC.288.36.077

Sponsor and Test Product

DEAD SEA & ARAVA SCIENCE CENTER

Bracelet Tanka T-Collagen

Title of Study

CLINICAL ASSESSMENT OF THE ANTIAGING EFFECTS IN 24 VOLUNTEERS DURING 12 WEEKS

Dermaclaim Lab S.L. ® || VAT: B16909699 || www.dermaclaim.com

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1. EXECUTIVE SUMMARY

OBJECTIVE: To evaluate the antiaging effects of "Bracelet Tanka T-Collagen", after topical use for 12 weeks. Additionally, to gather information of the volunteers' perception of the product's efficacy.

PROCEDURE: A clinical evaluation with the test product was initially carried out on 26 volunteers, aged from 39 to 61 years (mean 52.0 ± 6.3). The volunteers were required to be female between 40 and 65 years of age, presenting moderate to very severe signs of facial ageing (grades 2-4 in Eiben-Nielson photonumeric scale for wrinkles), and a willingness to comply with instructions. All the subjects participating in the study gave their informed consent signed before the start of the treatment. The study was in compliance with the tenets of the Declaration of Helsinki. The selected volunteers were ordered according to the date of recruitment and use the test product for 12 weeks, according to client's needs. 24 out of the 26 initially recruited volunteers completed the study. Before the start of the treatment (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84), subjects attended Dermaclaim's facilities for the corresponding measurements. Upon arrival, volunteers were allowed to acclimatize to environmental conditions (23 ± 1 ºC, 45 ± 10 % humidity) for 15 minutes. Then, facial wrinkles were evaluated in crow's feet (2 sides) and forehead by 3D skin topography analysis using AEVA-HE V4 (FoV, S). Skin firmness (1/R0), elasticity (R2), elastic recovery (R7), and skin fatigue (R9) were also evaluated in the cheek using Cutometer MPA Dual 580. After that, high resolution macroscopic pictures were also obtained using camera Nikon D8400 installed in the HeadScan Bench Light Face, including complete professional photographic setup. Data recorded from every individual at each of the timepoints were normalized versus baseline values (D0) for the whole group and statistically analyzed for each parameter. In addition, participant's subjective perception of the product efficacy was assessed with an individual questionnaire answered at each of the timepoints.

RESULTS: The topical use of Bracelet T-Collagen provoked a reduction of crow's feet area, number, and perimeter by 1.8 %, 8.1 %, and 3.7 %, respectively, after 12 weeks of application (D84), even though results were not statistically significant ($p > 0.05$), compared to baseline values before the start of the treatment (D0). No significant neither relevant effects were observed for the depth or volume, neither after 6 weeks of use (D42) (Figure 1, Table S1).

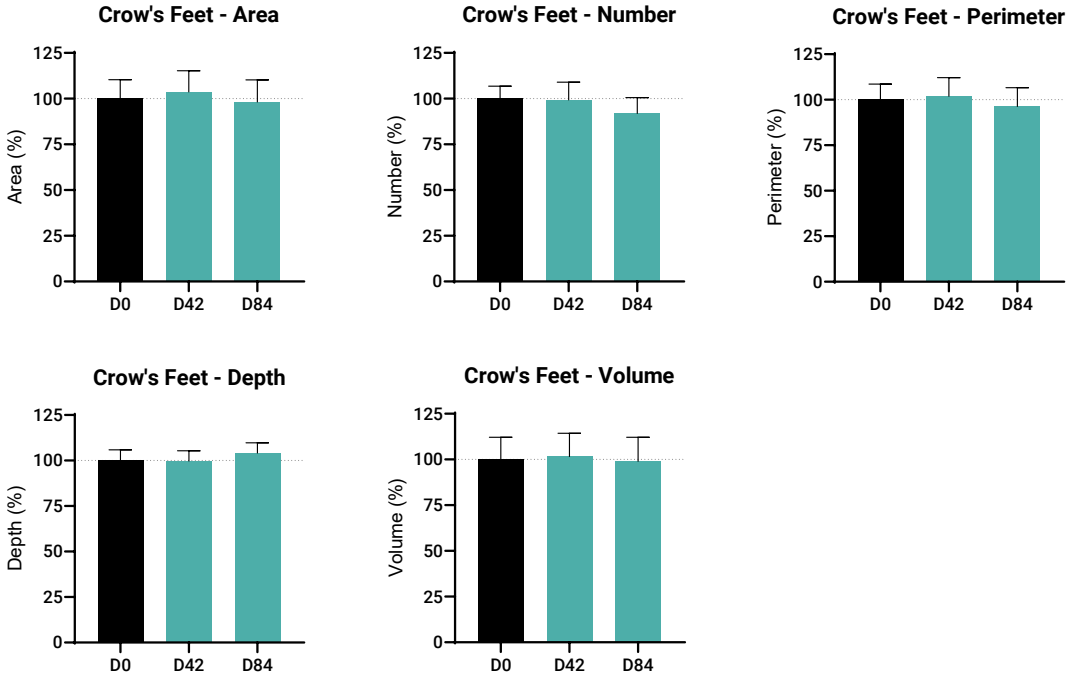
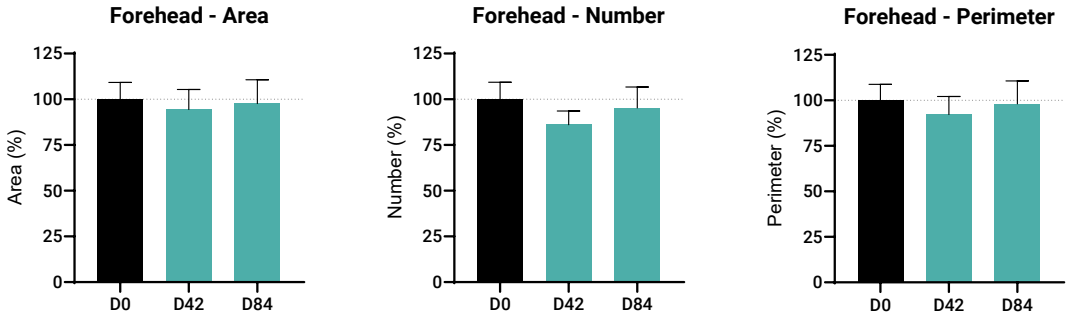


Figure 1. Effects of the application of Bracelet T-Collagen on crow's feet wrinkles*. Graphical representation of the area, number, perimeter, depth, and volume of crow's feet wrinkles (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

With regard to forehead wrinkles, results indicated the application of the bracelet during 12 weeks (D84) provoked a non-significant reduction of the area (2.3 %), number (4.8 %), perimeter (1.9 %), depth (1.0 %), and volume (1.4 %), compared to D0. When the effects were assessed after 6 weeks of application, results indicated reductions by 5.6 % (area), 14.0 % (number), 7.8 % (perimeter), 0.7 % (depth), and 4.2 % (volume), compared to baseline values before the start of the treatment (D0) (Figure 2, Table S2).



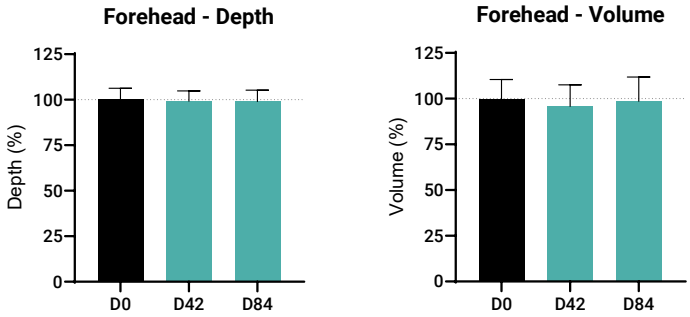
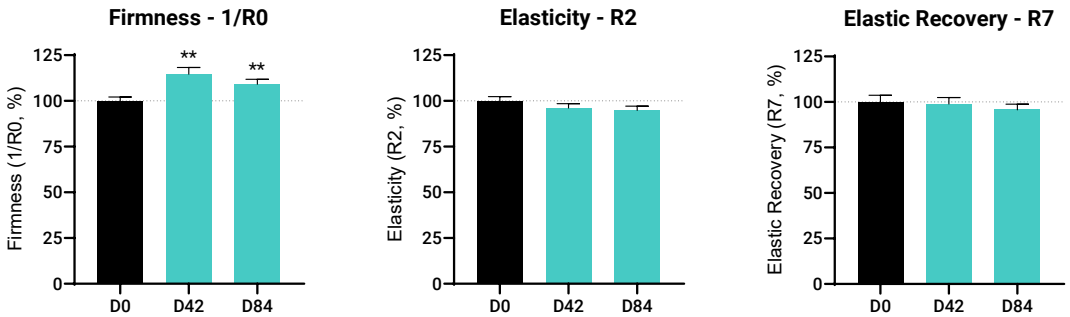


Figure 2. Effects of the application of Bracelet T-Collagen on forehead wrinkles*. Graphical representation of the area, number, perimeter, depth, and volume of forehead wrinkles (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

With regard to skin biomechanical properties, results indicated the application of T-collagen significant increased skin firmness by 14.7 % and 9.2 %, after 6 weeks (D42) and 12 weeks (D84) of application, respectively, compared to baseline values before the start of the treatment. No statistically significant effects were observed for skin elasticity nor elastic recovery, whereas skin fatigue was significantly reduced by 9.7 % after 6 weeks (D42) of use and non-statistically reduced by 3.3 % after 12 weeks (D84) (Figure 3, Table S3).



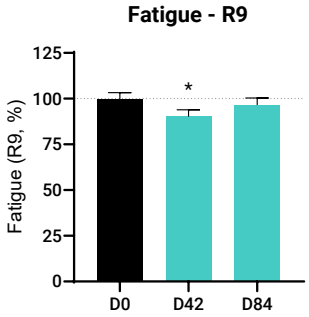


Figure 3. Effects of the application of Bracelet T-Collagen on skin biomechanical properties. *Graphical representation of the skin firmness (1/R0), skin elasticity (R2), elastic recovery (R7), and skin fatigue (R9) parameters on the cheek (ROI) (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

On the other hand, results from the individual questionnaire showed an overall acceptance of 52.0 after 6 weeks of application (D42) and 53.5 after 12 weeks of treatment (D84). Specifically, 3 out of 20 parameters yielded a significant result over 80 % at D42, whereas 4 out of 20 items yielded a significant result at D84.

Regarding cutaneous compatibility and acceptability, participants showed no Serious Undesirable Effects (SUE) and declared neither discomfort nor Undesirable Effects (UE) throughout the period of treatment or the following 7 days.

CONCLUSION: The **topical treatment with "Bracelet Tanka T-Collagen" displays antiaging and firming capabilities**, substantiated in **non-statistically significant reductions of crow's feet and forehead wrinkles** parameters, together with a **significant increase of skin firmness**, compared to baseline values before the start of the treatment.

These results were partially subjectively confirmed with the volunteers' perception through the self-assessment questionnaire, reporting an overall acceptance of 52.0 after 6 weeks of application and 53.5 after 12 weeks of application.

Regarding skin acceptability and surveillance, the treatment showed good cutaneous compatibility and may claim "**Dermatologically tested**", "**Clinically tested**", and "**Tolerance tested**".

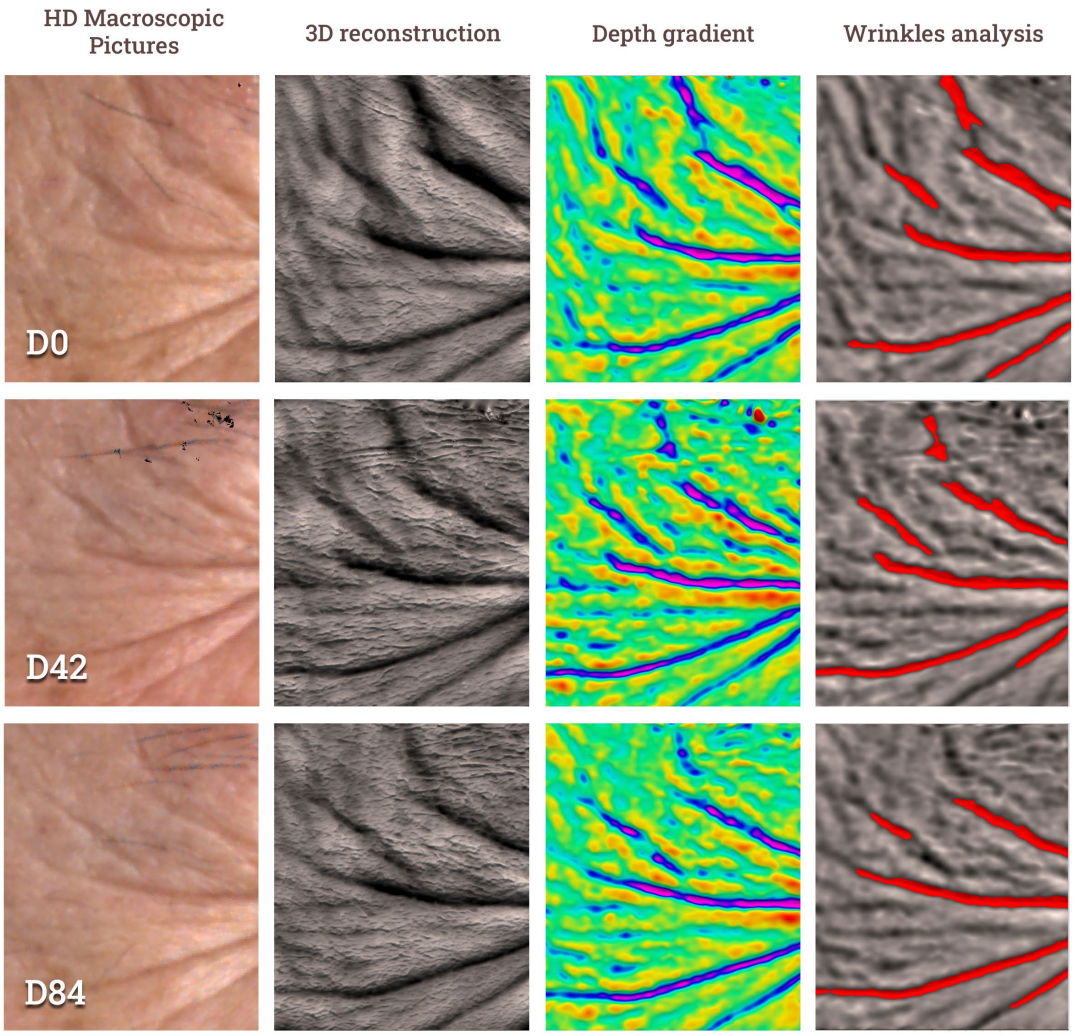


Figure 4. Effects of Bracelet T-Collagen in crow's feet wrinkles for Volunteer 13 (right eye). *From left to right, Region of Interest (ROI) from macroscopic HD picture obtained, 3D extraction of ROI, 3D extraction of wrinkles colored according to depth gradient, wrinkles analysis from the ROI using object detection with threshold value.*

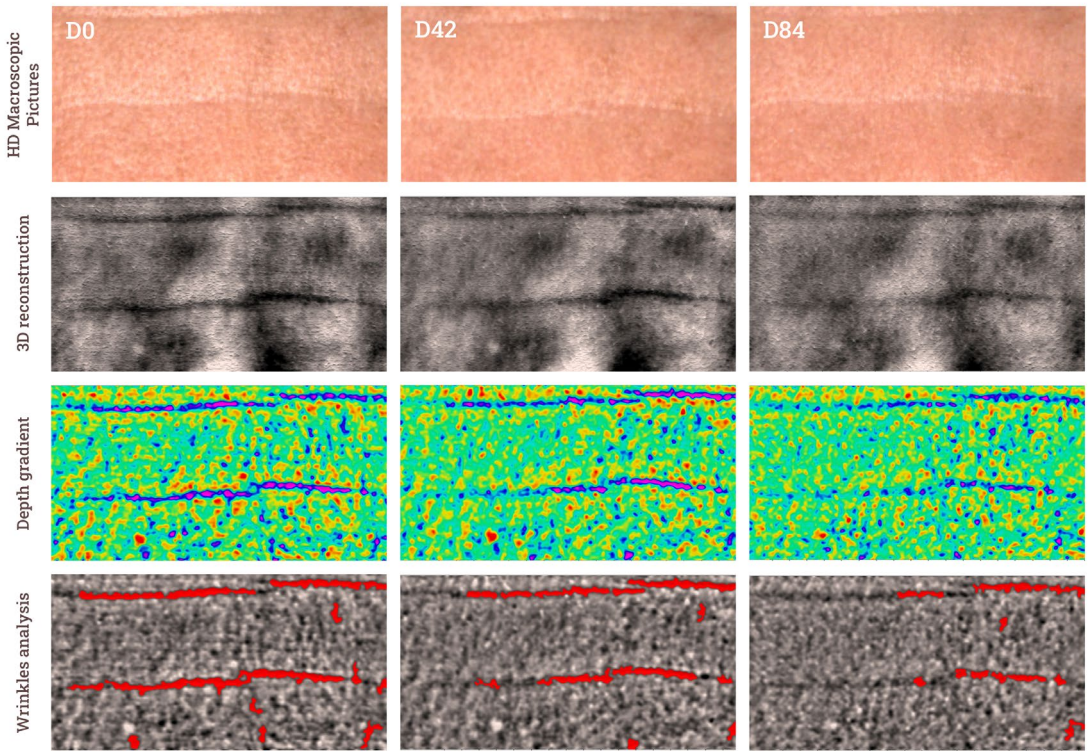


Figure 5. Effects of Bracelet T-Collagen in forehead wrinkles for Volunteer 04. *From above to below, Region of Interest (ROI) from macroscopic HD picture obtained, 3D extraction of ROI, 3D extraction of wrinkles colored according to depth gradient, wrinkles analysis from the ROI using object detection with threshold value.*

Figure 6. Effects of Bracelet T-Collagen for Volunteer 13 (left side). *HD macroscopic pictures obtained using Nikon D5600 + HeadScan Bench Face Light including official colorchart at the different timepoints.*

2. IDENTIFICATION OF STUDY

PROJECT REFERENCE: DC.288.36.077

SPONSOR: Dead Sea & Arava Science Center

TEST PRODUCT: Bracelet Tanka T-Collagen

TITLE: Clinical assessment of the antiaging effects in 24 volunteers during 12 weeks.

CLINICAL PROJECT MANAGER: Lucía Fernández Gómez, MSc

STUDY DIRECTOR: Alejandro Pérez Fernández, PhD

DERMATOLOGICAL SURVEILLANCE: Eduardo Bernía Petit, MD **License No**.: 464624840

3. PROVIDER AND EXPERIMENTAL CENTRE

COMPANY: Dermaclaim Lab S.L.

VAT NUMBER: B16909699

ADDRESS: Parc Cientific Universitat de Valencia (PCUV). Calle Agustín Escardino Benlloch, 9. 46980, Paterna (Valencia), España

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TESTING FACILITIES: Calle Doctor Vicente Zaragozà, 38 Bajo. 46020, Valencia (Valencia), España

EMAIL: clinica@dermaclaim.com **PHONE**: +34 644 03 50 20

4. SPONSOR

COMPANY: Dead Sea & Arava Science Center

ID TAX: 580458776

ADDRESS: Masada National Park. M.P. Dead Sea, 8691000. Israel

PROJECT RESPONSIBLE: Nimrod Vardi, CEO

EMAIL: amnonvardi@gmail.com

5. TEST PRODUCT

PRODUCT NAME: Bracelet T-Collagen

REFERENCE & BATCH: Not provided

INCI: Not provided

DERMACLAIM REFERENCE: DC.0397

GALENIC: Plastic bracelet.

NUMBER AND TYPE OF SAMPLES: 53 units

CONTENT:

STORAGE CONDITIONS: Room temperature (23 ± 1 ºC), protected from direct sunlight.

Figure 7. Test sample. *Image showing the Bracelet T-Collagen in its original plastic container, used by the volunteers during the clinical study.*

Sun cream "Crema protección solar facial antiedad Deliplus FPS 50+ con color resistente al agua" from Deliplus, was provided by the laboratory to the volunteers, to be applied each morning, in parallel to the bracelet wearing, during the full period of study.

Upon arrival at Dermaclaim Lab S.L. facilities, the test material was assigned a unique laboratory code number and registered into a daily log identifying sponsor, product name, batch number, number of units and quantity received, date of reception, status of the reception, storage conditions and reference of the project in which the sample is being analyzed.

Samples are kept for a period of 12 months, beyond submission of final report, unless otherwise specified by the sponsor.

6. DATES OF STUDY

STUDY START DATE: 10/07/2023

DATE OF SAMPLES' RECEPTION: 19/07/2023

PROCEDURE'S START DATE: 06/09/2023

PROCEDURE'S END DATE: 30/11/2023

FINAL REPORT DATE: 11/11/2023

REPORT REVIEWED DATE: 12/12/2023

REPORT DELIVERY DATE: 12/12/2023

7. ETHICAL RELEVANCE

This study was performed under clinical surveillance at the testing facilities. Experimental controls are the same participants whose parameters are evaluated upon product application, prior to initiate the treatment. This study has been conducted according to the general conditions of Dermaclaim Lab S.L., established for research studies involving human volunteers.

Before the beginning of the study, Dermaclaim internally assessed and approved its suitability for the product type and the methodology to be used. The study aimed at a better knowledge of the efficacy of the test product and the foreseeable risk incurred by the volunteers who took part in the study were minor, thus, there was a suitability between the aim of the study and its possible risks.

The experimental conditions adopted (areas of treatment, quantity of product, frequency, duration, etc.) reproduced the normal conditions of use of the test product, and the test performed on a "small scale" reflected the application by the future consumers.

The study protocol is in accordance with the Scientific Committee on Consumer Safety (SCCS) guidance. It meets all international standards for research studies involving human subjects, Structure and Content of Clinical Study Reports from ICH Harmonised Tripartite Guideline; International Recommendations ICH Topic E6, European Parliament and Council Guideline 2001/20/CE, the Good Clinical Practices (ICH-GCP), and the World Medical Association. It has been conducted pursuant to the Declaration of Helsinki (1964), with the amendments of Tokyo (1975), Venice (1983), Hong Kong (1989), South Africa (1996), Edinburgh (2000), Seoul (2008), and Fortaleza (2013).

8. INTRODUCTION

One of the major challenges of the 21st century is the fight against aging, defined as a set of both physiological mechanisms altering the physical and intellectual capacities of human beings. Aging of the skin is only one visible part of this process and one of the most prevalent cosmetic concerns to women [*Boismal et al., 2020*]. The many noticeable manifestations such as wrinkles, sagging, uneven skin tone, and dull and dry skin can significantly impact self-esteem and social relations [*Rattanawiwatpong et al., 2020*].

The skin has three layers: The epidermis, dermis, and subcutaneous tissue. With the aging process of the skin, these three components undergo degenerative changes, and changes to the dermis are the most obvious. The main components of the skin are collagen and elastin, which form and maintain its 3D structure, and glycosaminoglycans (GAG), among which the most relevant is hyaluronic acid (HA), a major component of the extracellular matrix (ECM), which due to its high hydrophilic properties, preserves moisturization and firmness of the ECM [*Tanaka et ak., 2016*]. The collagen and elastin content decreases with age, and the skin gradually loses its mechanical tension. The HA content of the skin also decreases with aging: the HA amount in the skin of a 75-year-old person is less than one-quarter of that in the skin of a 19-year-old subject [*Genovese et al., 2017*].

Skin aging can be classified into two categories: Intrinsic and extrinsic [*Farage et al., 2008*]. Intrinsic aging occurs with advancing age and is characterized by fine wrinkles and a thinning epidermis [*Zeng et al., 2014*]. In contrast, extrinsic aging is characterized by deep wrinkles, skin laxity, and hyperpigmentation, and is mainly caused by chronic sun exposure [*Xia et al., 2015*]. Both intrinsic and extrinsic factors, especially ultraviolet light-induced oxidative radicals, contribute to the etiology of aging.

Skin aging has many manifestations such as wrinkles, sagging, uneven skin tone due to hyperpigmentation spots, dryness, etc. Obsession with a youthful appearance has become commonplace in modern society and has resulted in an upswing in cosmetic treatments trying to reverse the aging process [*Honigman and Castle, 2006*].

9. PANEL OF VOLUNTEERS

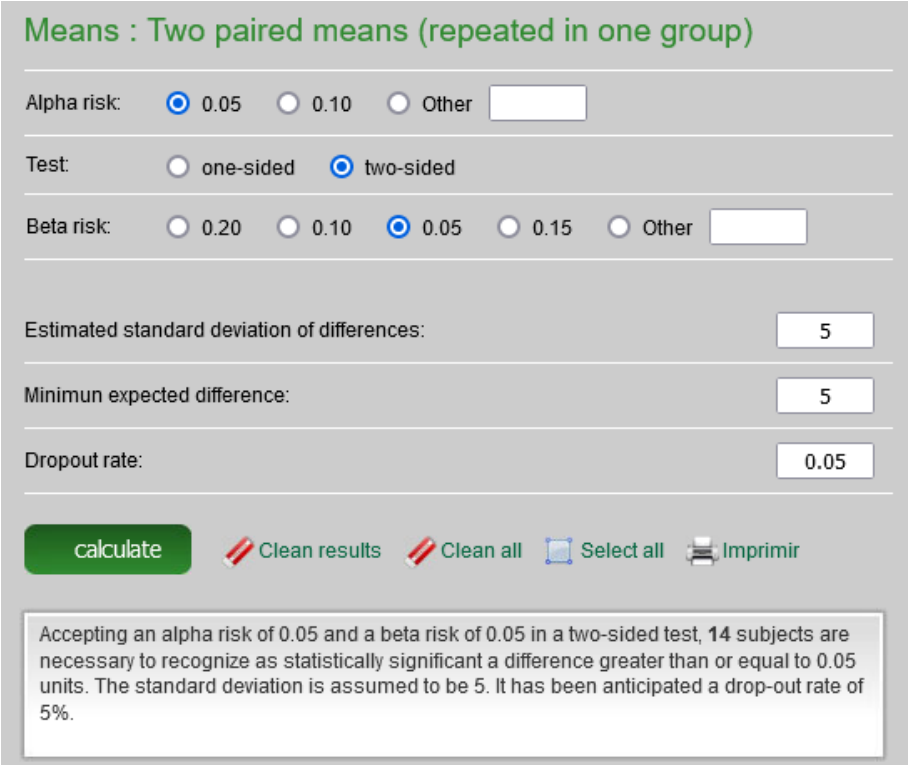
9.1 Number

The number of volunteers initially recruited for the study was 26 (Attachment 1), meeting with all the inclusion criteria. Volunteer 10 withdrew from the study after the intermediate visit at D42, referring absence of effects. Volunteer 16 was removed from the study by the researcher at D42 after referring to have remove the bracelet several times during the first period of treatment. The remaining 24 volunteers completed the treatment and corresponding data was included in the analysis.

According to the date of recruitment, the subjects were ordinally assigned a permanent identification number within the study, from 1 to 26.

The number of volunteers recruited for the study is enough to determine statistically significant differences, based on Granmo Calculator software, developed and owned by Institut Municipal d'Investigació Mèdica, Barcelona, Spain – Program of Research in Inflammatory and Cardiovascular Disorders.

Alpha-risk: 0.05 | Beta risk: 0.10 | Test: Two-sided | Estimated SD: 7.5 % Minimum expected difference: 5 % (wrinkles) | Drop-out rate: 5 % of panel (0.05)



9.2 Inclusion criteria

The specific inclusion criteria, defined in the protocol, were as follows:

- ✓ Gender: Female
- ✓ Age: 40 - 65 years.
- ✓ Presenting moderate to very severe facial wrinkles (grades 2-4 Eiben-Nielson photonumeric scale for wrinkles) [*Eiben-Nielson and Kerscher, 2021*].
- ✓ Last participation in a clinical study, ending at least one month before the start of this experiment.
- ✓ Wash-out period of 15 days before the start of the treatment with no application on the area of study.
- ✓ Individuals with overall good health status and free of relevant health problems, including neurological, dermatological, or systemic disorders that could interfere with the results, under the Clinical Project Manager and the Study Director criteria.
- ✓ Individuals who understand the instructions of use and are willing to cooperate with the study, as stated.
- ✓ Reading, understanding, and signature of the Protection of Personal Data and Communication consent.
- ✓ Reading, understanding, and signature of the Informed Consent for the study DC.288.36.077.

Figure 8. *Images showing the Scientific Assessment Scale of Skin Quality (SASSQ) for wrinkles, described in Eiben-Nielson and Kerscher, 2021.*

9.3 Exclusion criteria

- Subjects with a history of any form of skin cancer, melanoma, lupus, psoriasis, connective tissue disease, diabetes, or any disease that would increase risk associated with study participation.
- Relevant cutaneous marks in the experimental area, which could interfere with the instrumental measurements or the clinical pictures (surgeries, scars, sunburns, etc.).
- Allergy or reactivity to any of the components of the test product, or a product within the same or similar category than the tested one.
- Individuals currently undergoing medical treatment that may mask or interfere with the test results, under the Clinical Project Manager and the Study Director criteria.
- Relevant aesthetic treatments (cleansing and exfoliation, mesotherapy, led-light therapy, carboxytherapy, microneedling, etc.), on the experimental area finishing less than 6 months before the start of the study.
- Females who are pregnant or lactating or have been pregnant or given birth within the six-month period immediately preceding the start of the study.
- Forecast of change of routine or relevant way of life, during the period of study.

9.4 Recruitment tools and panel management

Panel recruitment is accomplished through advertisements in social media (Facebook, Instagram, or LinkedIn), direct communication (WhatsApp or SMS), any other electronic media, or any combination thereof.

Panel management is conducted by using Clinic Cloud v20220215.1 premium application (DOCTORALIA INTERNET SL, B62834981).

9.5 Constraints of the study

The constraints imposed on the volunteers were as follows:

- Full respect of the test products conditions of use.
- No application or intake of other products intended to improve the status of the experimental areas during the period of study.

- ❖ No changes in hygiene and/or make-up habits.
- ❖ No intense sun exposure during the period of treatment.

9.6 Panel features

Number of subjects initially recruited | completing the study Drop-outs (N, % of total)	26 | 24 2 (8 %)
Age range (Mean ± SD)	39 – 61 (52.0 ± 6.3)
Gender	Male: 0 | Female: 26
Ethnicity (race)	Caucasian: 21 | Latin: 5
Skin type (according to sebum levels)	Dry: 11 | Combination: 15 Oily: 0
Skin phototype (according to Fitzpatrick)	II (white): 9 | III (light brown): 16 IV (moderate brown): 1

Skin phototype is classified according to *Fitzpatrick, 1988*; whereas skin type is classified according to *Kim et al., 2006* (Table 1):

Type	U-zone (cheek, chin)	T-Zone (forehead, nose)
Dry	< 70 µg/cm^2	< 100 µg/cm^2
Normal	70 – 170 µg/cm^2	100 – 210 µg/cm^2
Oily	> 170 µg/cm^2	> 210 µg/cm^2

Table 1. *Classification of the objective facial skin type by reference values of sebum casual levels measured with Sebumeter SM 815 (µg/cm^2).*

9.7 Informed consents

Informed consent forms describing reasons for the study, possible adverse effects, associated risks and potential benefits, and their limits of liability were obtained from volunteers prior to initiating the study. The participants read, signed, and dated the informed consent document to indicate their authorization to proceed and acknowledge their understanding of the contents (Attachment 9).

Additionally, all the volunteers included in this study had previously read, understood, and signed the Protection of Personal Data and Communication consent.

9.8 Transfer of image rights and use by the sponsor

All the volunteers were requested to read, understand, and sign or reject the Informed Consent for Clinical Photographies for the study DC.288.36.077, before the start (Attachment 10).

Images from all the volunteers included in the study may be used by the sponsor for internal discussion of the results. However, the sponsor can only make commercial use of the images from the volunteers who accepted the transfer of image rights for this study DC.288.36.077 by signing the Informed Consent for Clinical Photographies.

In the event that the sponsor wants to make use of the images from volunteers who rejected the Informed Consent for Clinical Photographies, it is responsibility of the sponsor to avoid full personal recognition, meaning the face of the specific volunteer will not be recognized, for example, by using a black bar to cover the complete area of eyes.

10. METHODOLOGY

10.1 Experimental conditions of use of the test product

The experimental conditions, defined in the protocol, were the following:

- Experimental areas: Wrist / Arm.
- Guidelines of use for the test product: To wear 1 bracelet in the same wrist / arm for 12 weeks (bracelet at D42 is substituted for 1 new bracelet).
- Application at research center: Plastic bag containing the bracelet was open in the clinical facilities and placed into volunteers' wrist.
- Application at home: 1 bracelet per month, in the same wrist / arm. Sun protector cream must be used each morning, to avoid sun-related interferences on the results.

10.2 Verification of the panel

On the first day of attendance to the experimental center, the Clinical Project Manager verified the inclusion and exclusion criteria previously defined for this study. In case of non-compliance with any of the criteria, the volunteer was excluded prior to the start of the study.

10.3 Environmental conditions

Fifteen minutes before every measurement, the volunteers were subjected to an acclimatization period under the following environmental conditions:

- Controlled temperature: 23 ± 1 ºC
- Controlled relative humidity: 45 ± 10 %

During the acclimatization period, the test area must not be covered by clothes, as far as possible.

Measurements were conducted on dry and clean face, without make-up.

10.4 Measurement site and frequency of measurements

The 3D skin topography parameters (wrinkles) were recorded from crow's feet and forehead (wrinkles), using AEVA-HE V4 (FoV, S) system (Eotech). The volunteers were

installed on the VisioTOP-500 bench for accurate and stable positioning and re-positioning between the different measuring times.

Skin biomechanical properties were recorded in the cheek using Cutometer MPA Dual 580 (Courage + Khazaka Electronic GmbH).

Instrumental measurements were performed before the start of the treatment (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84).

The measurements were conducted by the Clinical Project Manager of the research center, who has an appropriate experience, or by a qualified and experienced technician under their supervision.

10.5 Instrumental assessment of the efficacy

10.5.1 AEVA-HE V4 system (Eotech)

10.5.1.1 Active stereometry combined with fringe projection

Photogrammetry is the science and technology of obtaining reliable information about physical objects and the environment through the process of recording, measuring, and interpreting photographic images and patterns of electromagnetic radiant imagery [*ASPRS, 2015*]. There are many variants of photogrammetry.

Stereophotogrammetry involves estimating the three-dimensional coordinates of points on an object employing measurements made in two or more photographic images taken from different positions (see stereoscopy). Common points are identified on each image. A line of sight (or ray) can be constructed from the camera location to the point on the object. It is the intersection of these rays (triangulation) that determines the three-dimensional location of the point. Stereophotogrammetry is emerging as a robust non-contacting measurement technique to determine dynamic characteristics and mode shapes of non-rotating [*Sužiedelytė-Visockienė, 2013*] and rotating structures [*Lundstrom et al., 2012*].

Active stereometry also uses 2 cameras with an additional projection unit which projects patterns on the object, used to find coincident points on surfaces which may not have specific structure. The pattern used in AEVA-HE system is a combination of known contrast lines (grey code) and sinusoidal fringes shifted on the object. The

specific and unique algorithm does not need correlation of points and still uses phase shifting technique to get pixels resolution.

Fringe projection technique consists to project contrast line pattern (grey code) for the optical triangulation and fringe projection shifted for phase unwrapping. The camera detects the pattern contrast and deformation, as well as fringe deformation. The algorithm calculates absolute points on the contrast line and relative depth from the phase difference between points. Both are combined to produce high resolution depth map.

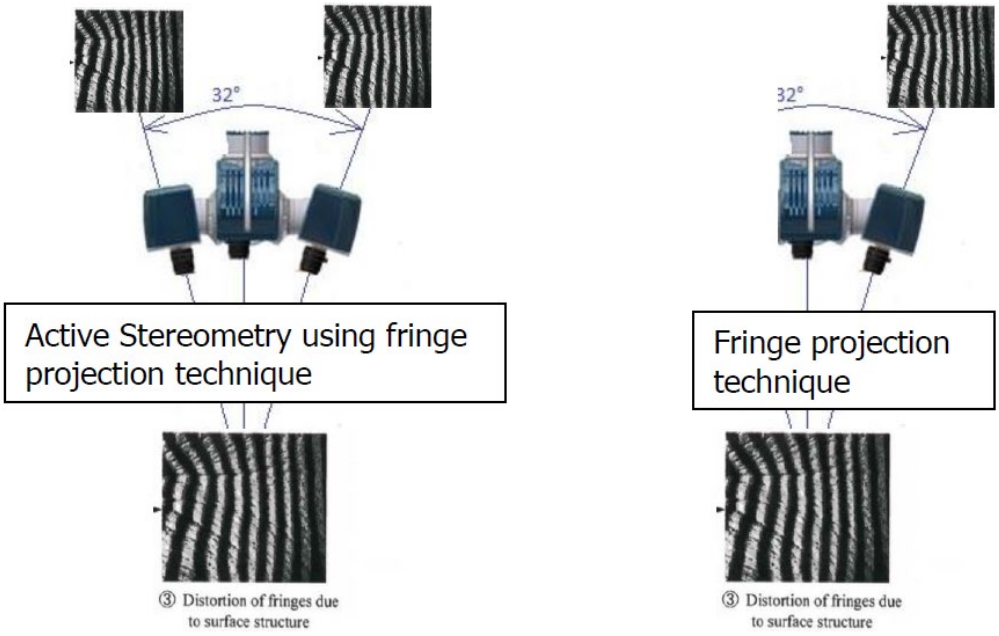


Figure 9. *Schematic representation of active stereometry technique combined or not with fringe projection.*

The main limitation of the fringe projection technique was that the camera resolution was limited to the fringe spacing, thus, increasing fringes would cause less contrast and more sensitivity to movement. Stereometry does not depend on the projected fringes anymore, being limited to the pixel spacing resolution. Therefore, it becomes possible to increase camera resolution to have larger field of view and still get higher resolution in the 3D data map.

Sensitivity of only fringe projection technique is given by the fringe interval projected on the object (about 1 mm), while stereometry combined with fringe projection is limited to pixel interval (about 0.5 mm). Both techniques are limited by the camera

noise, which is the only real limit of the stereometry nowadays. Active stereometry is also less sensitive to movement because both cameras “see” the same movement at the same time. Both cameras can also process auto-calibration because a known pattern can define which pixels from the left camera correspond to which pixels from the right camera and correct any shift between both cameras.

The active stereometry is a real breakthrough in the 3D measurement technology, and it is proposed as high-end system, when maximum accuracy and high resolution are required.

10.5.1.2 VIsioTOP-500 bench

The volunteers were located in the VisioTOP-500 bench for accurate and steady positioning and re-positioning between the different measuring times.

Figure 10. VisioTOP-500 bench. *Image showing the VisioTOP-500 bench, where the volunteers are installed for the acquisitions of the images with AEVA-HE system.*

Volunteers are installed in the bench, according to the following steps:

- Rotate the black plate at 90º, release the head block, and set the earplug in open position.
- Put the finger coats on the earplugs or clean with antiseptic product (ethanol).
- Lift the motorized table to maximum height.
- Welcome the volunteer and get them seat down, with the bottom well against the seat back, well centered in the seat and the back as much in contact with the seat back as possible.
- When the volunteer is correctly installed, move the table down until the earplugs are at the same height as the ears.
- The volunteer should now take the earplugs in hands and put them into their ears, in a comfortable manner.
- Lock the head block and rotate the back plate down.
- The volunteer must look to the mirror and check their head is correctly centered. The volunteer will see a vertical line going through the center of each eye.
- Using the lips laser line, please, the volunteer is asked to adjust her/his head orientation up and down, in order to get the laser line matching both lips corners.
- Apply the rest plate against the back of the volunteer's head and check the laser line is still matching the lips corners.
- Lock the head rest plate using the know located on the top of the bench.

10.5.1.3 Wrinkles evaluation using object detection with threshold value

Object detection is performed based on a previously established threshold (plane). Objects above or below this plane are detected and quantified (Valley object detection).

The following parameters are calculated:

- Area (mm^2): Sum of the surface of all the objects detected.
- Number (N): Indicates the number of wrinkles detected in the ROI analysis.

- Circumference (mm): Average length of the contour of the detected objects (wrinkles) = perimeter.
- Depth (mm): Average depth of the wrinkles detected below the threshold.
- Volume (mm^3): Wrinkles below the threshold are detected and shown in red. The volume of the depression in the detected objects is automatically calculated.

A Z threshold is applied to the topography. This threshold is a plane parallel to the mean plane of the topography (the mean plane is the zero level of the heights of the topography points). All the points below are valley objects (folds, wrinkles, fine lines, pores, etc.) and those above are bump objects (acne, pimple, scars, etc.).

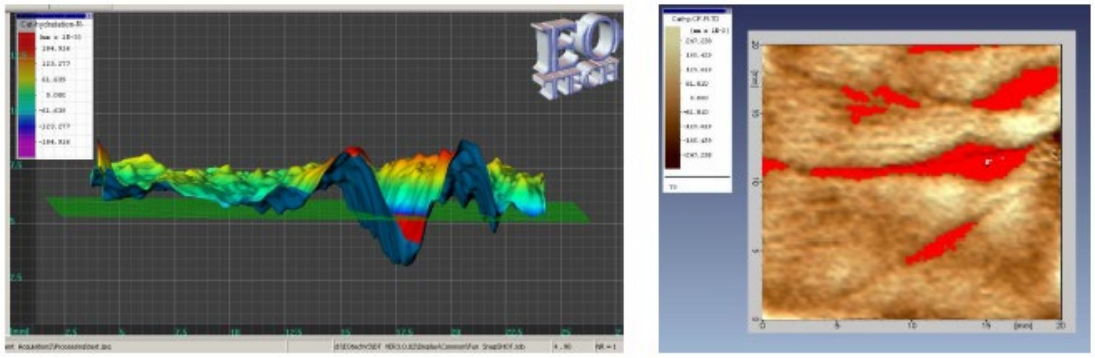


Figure 11. Z threshold plane. *Left. Three-dimensional representation of the Z threshold plane used by the AEVA-HE system and software, to determine objects below and above the corresponding plane. Right. Representation of the wrinkles (in red) identified by the software using the Z threshold plane.*

The position of the Z threshold is defined using the histogram of the topography heights, or in other words, the height distribution curve of the topography points. A percentage of points is set, and the corresponding Z threshold position is found.

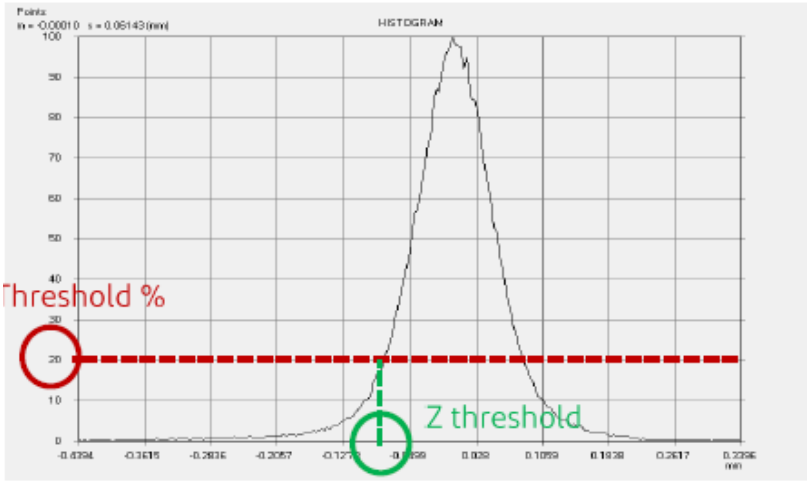


Figure 12. Histogram of the topography heights. *Histogram showing the height distribution curve of the topography points detected by the AEVA-HE system using Z threshold plane.*

The Z threshold is defined for baseline measurements at D0. For all the other times, the value of the threshold calculated at D0 is automatically applied.

The technical specifications established for this analysis are described as follows:

- Zone definition:
  - Crow's feet: Width 15 mm / Height 18 mm | Leveling order: 7
  - Forehead: Width 50 mm / Height 20 mm | Leveling order: 7
- Threshold: 10-50% Scan mode | Step Threshold 10
- Zone filtering:
  - Crow's feet: HF Cutoff, 0.8 mm | LF Cutoff, 3.5 mm
  - Forehead: HF Cutoff, 0.8 mm | LF Cutoff, 3.5 mm
- Maximum number of objects detected: 200
- Minimum object area detected: 0.85 mm^2

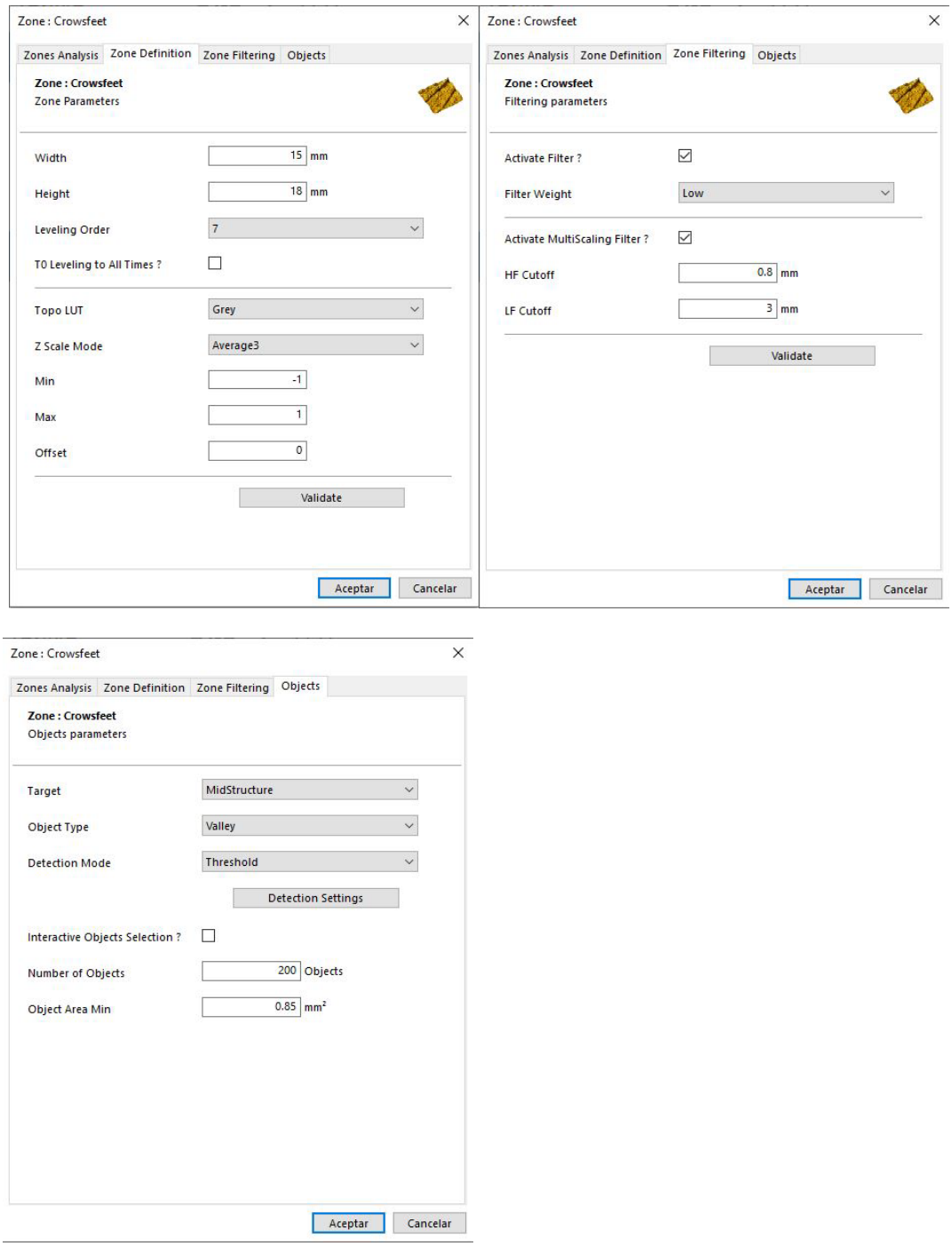


Figure 13. Wrinkles evaluation parameters from AEVA-HE. *Example of images from AEVA-HE software parameters used for the evaluation of wrinkles during the study.*

10.5.2 CameraScan software analysis (Orion Concept)

High resolution macroscopic pictures were analyzed, if required, using CameraScan software (Orion), after being obtained using a professional photography studio setup, including the following equipment:

- Camera Nikon D8400 24 Mpx and objective 40 mm macro-2.8.
- HeadScan Bench Light Face (Orion Concept)
- Vinsetto Table with automatic adjustable height
- Flash Leds 2x2 white led spots 4000ºK, IRC95
- Flashes Xenon 2 Elinchrom 400, drived by the camera
- Support of flash for bench
- Automatic polarization gelatin filter wheel of flashes for camera.
- OrionTechnoLab color checker

10.5.3 Cutometer® MPA Dual 580 (Courage + Khazaka Electronic GmbH)

The measuring principle of the Cutometer® is based on the suction method, where negative pressure deforms the skin mechanically. The pressure is created in the device and draws the skin into the aperture of the probe and after a defined time, releases it again.

Inside the probe, the penetration depth is determined Cutometer principle by a non-contact optical measuring system. This optical measuring system consists of a light source and a light receptor, as well as two prisms facing each other, which project the light from transmitter to receptor. The light intensity varies due to the penetration depth of the skin. The resistance of the skin to the negative pressure (firmness) and its ability to return into its original position (elasticity) are displayed as curves (penetration depth in mm/time) in real time during the measurement. From these curves a variety of interesting measurement parameters can be calculated related to elastic and visco-elastic properties of skin surface and skin aging [*Nikolis et al., 2022*].

The typical shape of a curve of human skin is based on the different forces of elastin and collagen in the skin. Elastin is responsible for the flexibility of the skin whereas collagen's main task is to keep the skin in shape.

The first, very straight part of the curve is shaped by the proportion of elastin in the skin as it easy to displace and very flexible. When skin starts to "creep" inside the probe, the collagen has taken over. It is stronger and resists the mechanical force better. Immediately after the pressure of the device has ceased, the collagen starts to bring skin back to its original shape. Therefore, in young skin with fresh collagen, the skin instantly returns more closely to its original position than in aged skin. In the end, eventually the elastin sees to the complete recovery of the skin [*Henning et al., 2022*].

The software of the Cutometer® MPA 580 allows to calculate a lot of interesting parameters from the different portions of the measurement curve. The following parameters were measured in this project:

- 1/R0: Firmness (mm). Inverse of the amplitude at the end of the suction phase.
- R2: Visco-elasticity (%). Resistance to the mechanical force versus ability of returning.
- R7: Elastic recovery (%). Proportion of the immediate recovery compared to the amplitude after suction.
- R9: Skin fatigue (mm). Tiring effects, visible for repeated suction/recovery circles.

A clear correlation with ageing has been demonstrated for R2 and R7 parameters [*Krueger et al., 2011; Ahn et al., 2007; Ryu et al., 2008*].

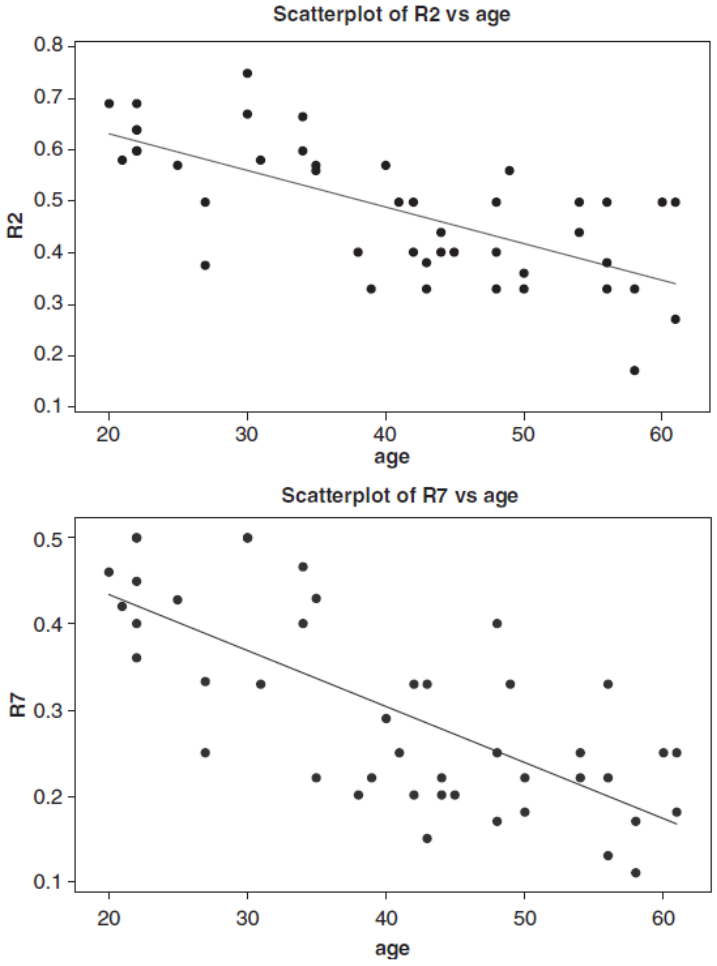


Figure 14. *Scatter plots of Cutometer parameters R2 or R7 vs age.*

10.6 Calibration of the instrumental equipment

Calibration complete report for AEVA-HE system is shown in Attachment 12.

Calibration report of CameraScan picture acquisition software installed in the HeadScan Bench Light Face, using an official colorchart provided by Orion TechnoLab, is shown in (Attachment 13).

Calibration report for the instrumental probe (Cutometer MPA Dual 580) are shown in Attachment 14.

10.7 Subjective evaluation of the efficacy

The efficacy of the treatment was subjectively assessed by participants via an individual questionnaire, filled in at different timepoints, which covered items concerning sensory experience, treatment effectiveness, and consumer behavior, previously defined with the Sponsor. Volunteers' opinion was considered since it could reflect that of the potential consumer.

All the volunteers included in the study were considered to assess the cosmetic efficacy via questionnaire. For each item, the volunteers had to express their satisfaction according to an ordinal scale (1 = Strongly disagree | 2 = Disagree | 3 = Agree | 4 = Strongly agree), and the results were expressed in percentage of satisfied volunteers (scores 3 and 4).

10.8 Checking of the acceptability

A visual examination of the experimental area was performed by the responsible technician before and after the application of the test product. The protocol and complete data were supervised, approved, and signed by the dermatologist.

The volunteers were requested to highlight any reaction observed and sensation of discomfort felt after the use of the test product, to the responsible technician conducting the study.

In case of reactivity or discomfort, the main sensations were described as heating, stinging, pruritus (itching), pulling, burning, or watering. The intensity of the sensations of discomfort was assessed according to an ordinal scale (slight, moderate, severe). The

main visible signs that might be noted could be erythema, oedema, vesicle, bulla, papule, sab, dryness, coloration, or macula.

According to the specific information reported by the volunteer and the definitions provided by The European Cosmetic and Perfumery Association (Colipa), the reaction is classified as undesirable event, undesirable effect (UE), or serious undesirable effect (SUE) (Table 2, Attachment 15.3).

Undesirable event	Undesirable effect (UE)	Serious undesirable effect (SUE)
0	0	0

Table 2. Undesirable events table*. Table showing undesirable events, undesirable effects (UE), and serious undesirable effects (SUE), taken place during the period of treatment.*

Participants showed no Serious Undesirable Effects (SUE) and declared neither discomfort nor Undesirable Effects (UE) throughout the period of treatment or the following 7 days.

10.9 Checking of the acceptability

10.9.1 Statistical analysis of the instrumental efficacy

All the 24 volunteers completing the study were considered to assess the efficacy of the test products.

For instrumental measurements, parameter values in the experimental area of an individual at a given timepoint are normalized versus baseline measurements of the same experimental area for the whole panel. This way, the inter-individual random variation is corrected, and the statistical power of the result is increased [*Guo et al., 2017*].

The individual results were expressed in percentage relative to baseline values (D0) for all the parameters studied. Mean ± Standard Error of the Mean (SEM) were calculated and shown in the graphs. * denotes statistical significance with p-value < 0.05. ** denotes statistical significance with p-value < 0.01. *** denotes statistical significance with p-value < 0.001. **** denotes statistical significance with p-value < 0.0001.

GraphPad Prism V10 software was used for the statistical analysis. Data were statistically analyzed applying ordinary one-way ANOVA with Dunnett's multiple

comparison tests. One-way ANOVA is a technique that can be used to compare whether more than two sample's means are significantly different or not (using the F distribution). The ANOVA tests the null hypothesis, which states that samples in all groups are drawn from populations with the same mean values. The ANOVA produces an F-statistic, the ratio of the variance calculated among the means to the variance within the samples. If the group means are drawn from populations with the same mean values, the variance between the group means should be lower than the variance of the samples, following the central limit theorem. A higher ratio therefore implies that the samples were drawn from populations with different mean values [*David, 2002*; *Mishra et al., 2019*].

ROUT (Robust regression and Outlier removal) method was used to identify outliers in the raw data, with a coefficient Q of 1 %. The value of Q determined how aggressively the method defines the outlier and unless specific elsewhere, it is recommended to stick to 1 % in this type of research experiments [*Motulsky and Brown, 2006*].

10.9.2 Statistical analysis of the panelist self-assessment

For each item, the volunteers had to express their satisfaction according to an ordinal scale (1 = Strongly disagree | 2 = Disagree | 3 = Agree | 4 = Strongly agree).

Satisfaction was considered for scores 3 and 4, and the threshold to consider a remarkable satisfaction percentage was set at 80 % by Dermaclaim scientific staff.

10.10 Consumption control

Product samples assigned to volunteers were weighed before the start of the treatment and at the timepoints set for measurements (D84 / D42) and the applied amount was calculated by subtraction (D84/D42 – D0) (Attachment 3).

N Vol	WRIST	QUANTITY OF SAMPLES USED (g)					
		D42		D84		Bracelet	SPF
		Bracelet	SPF	Bracelet	SPF	Per day	Per day
	MEAN	0,0	25,3	0,1	50,8	0,001	0,605
	SD	0,1	16,1	0,2	27,6	0,002	0,329

Table 3. Consumption control results*. Mean average and standard deviation with regard to the quantity of sample used during the study after 6 weeks (D42) and 12 weeks (D84) of treatment, and the average quantity used per day (in grams).*

10.11 Volunteers' diary

Not applicable.

10.12 Follow-up of volunteers during the period of treatment

In order to keep all the volunteers involved in the study, reduce the possibilities of abandonment, and assure the correct application of the corresponding treatment, Dermaclaim is in direct contact with the volunteers through the following:

- Reminder email for each appointment.
- Reminder WhatsApp before each specific appointment.
- Individual contact with each volunteer every 2 weeks.

10.13 Protocol deviations

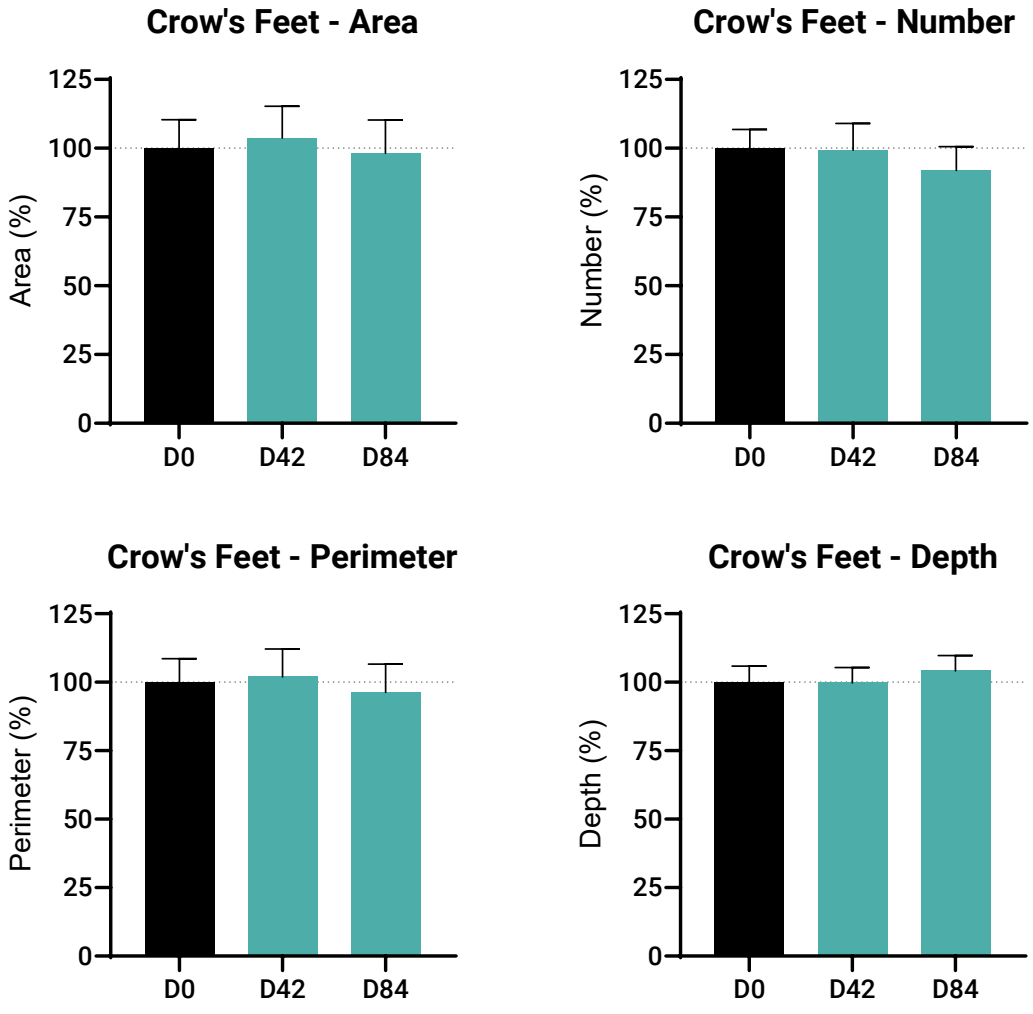
Volunteers 04, 07, 09, 14, 17, 19, 20, and 21, forgot to bring the SPF sample at D42 visit and their consumption control could not be conducted for this timepoint.

Volunteer 21 used another different SPF sample during the study, due to a personal misunderstanding with the technical team, and consumption control was not conduced on sun cream for this specific volunteer.

11. RESULTS

11.1 Crow's feet wrinkles

The topical use of Bracelet T-Collagen provoked a reduction of crow's feet area, number, and perimeter by 1.8 %, 8.1 %, and 3.7 %, respectively, after 12 weeks of application (D84), even though results were not statistically significant ($p > 0.05$), compared to baseline values before the start of the treatment (D0). No significant neither relevant effects were observed for the depth or volume, neither after 6 weeks of use (D42) (Figure 15, Table S1).



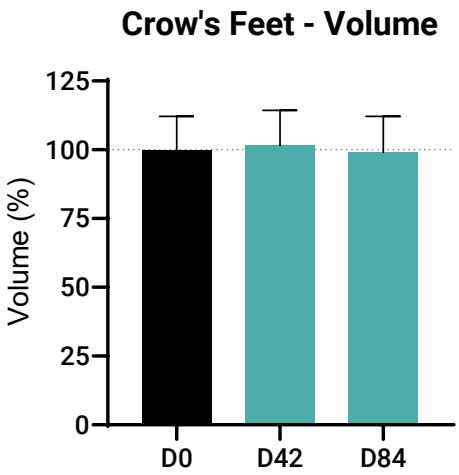
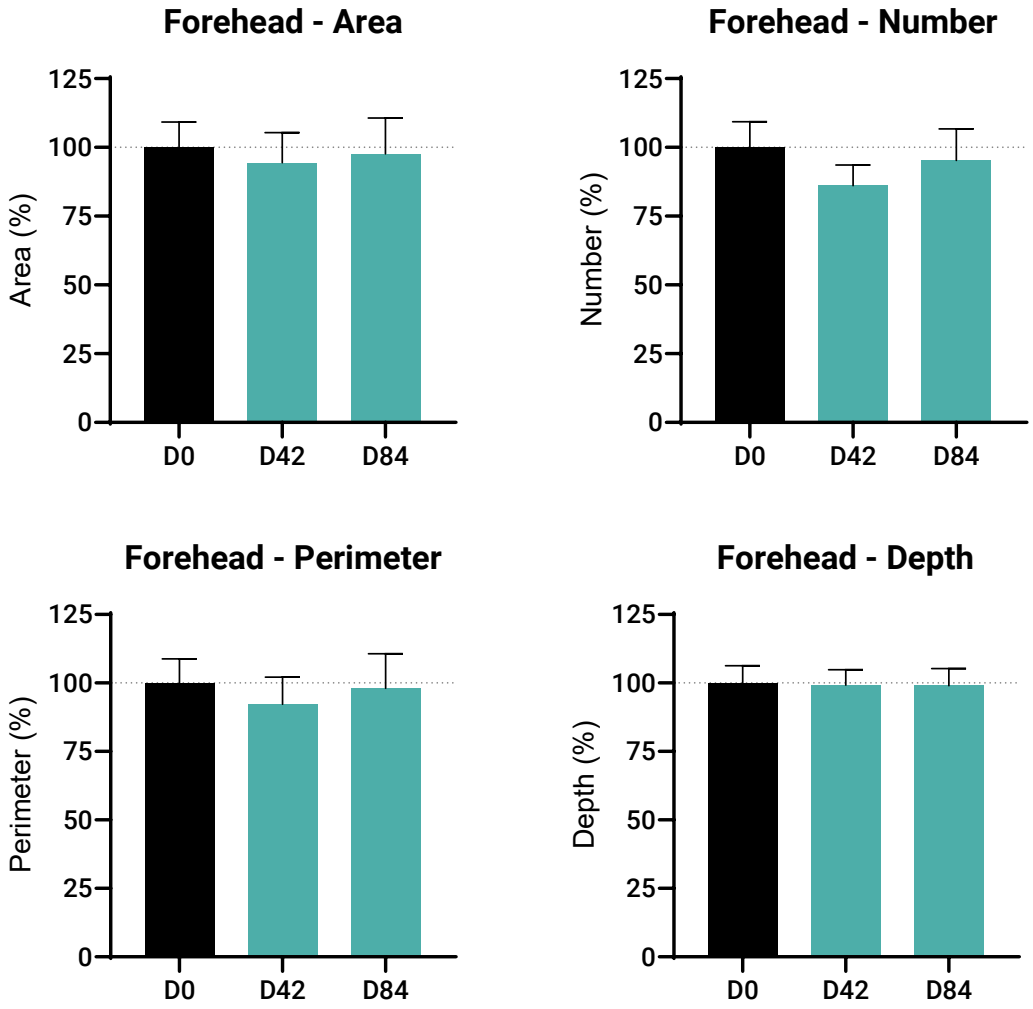


Figure 15. Effects of the application of Bracelet T-Collagen on crow's feet wrinkles*. Graphical representation of the area, number, perimeter, depth, and volume of crow's feet wrinkles (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

11.2 Forehead wrinkles

Results indicated the application of the bracelet during 12 weeks (D84) provoked a non-significant reduction of the area (2.3 %), number (4.8 %), perimeter (1.9 %), depth (1.0 %), and volume (1.4 %), compared to D0. When the effects were assessed after 6 weeks of application, results indicated reductions by 5.6 % (area), 14.0 % (number), 7.8 % (perimeter), 0.7 % (depth), and 4.2 % (volume), compared to baseline values before the start of the treatment (D0) (Figure 16, Table S2).



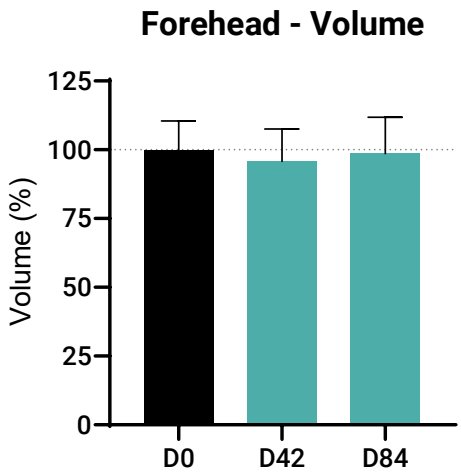


Figure 16. Effects of the application of Bracelet T-Collagen on forehead wrinkles*. Graphical representation of the area, number, perimeter, depth, and volume of forehead wrinkles (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

11.3 Skin biomechanical properties

Results indicated the application of T-collagen significant increased skin firmness by 14.7 % and 9.2 %, after 6 weeks (D42) and 12 weeks (D84) of application, respectively, compared to baseline values before the start of the treatment. No statistically significant effects were observed for skin elasticity nor elastic recovery, whereas skin fatigue was significantly reduced by 9.7 % after 6 weeks (D42) of use and non-statistically reduced by 3.3 % after 12 weeks (D84) (Figure 17, Table S3)

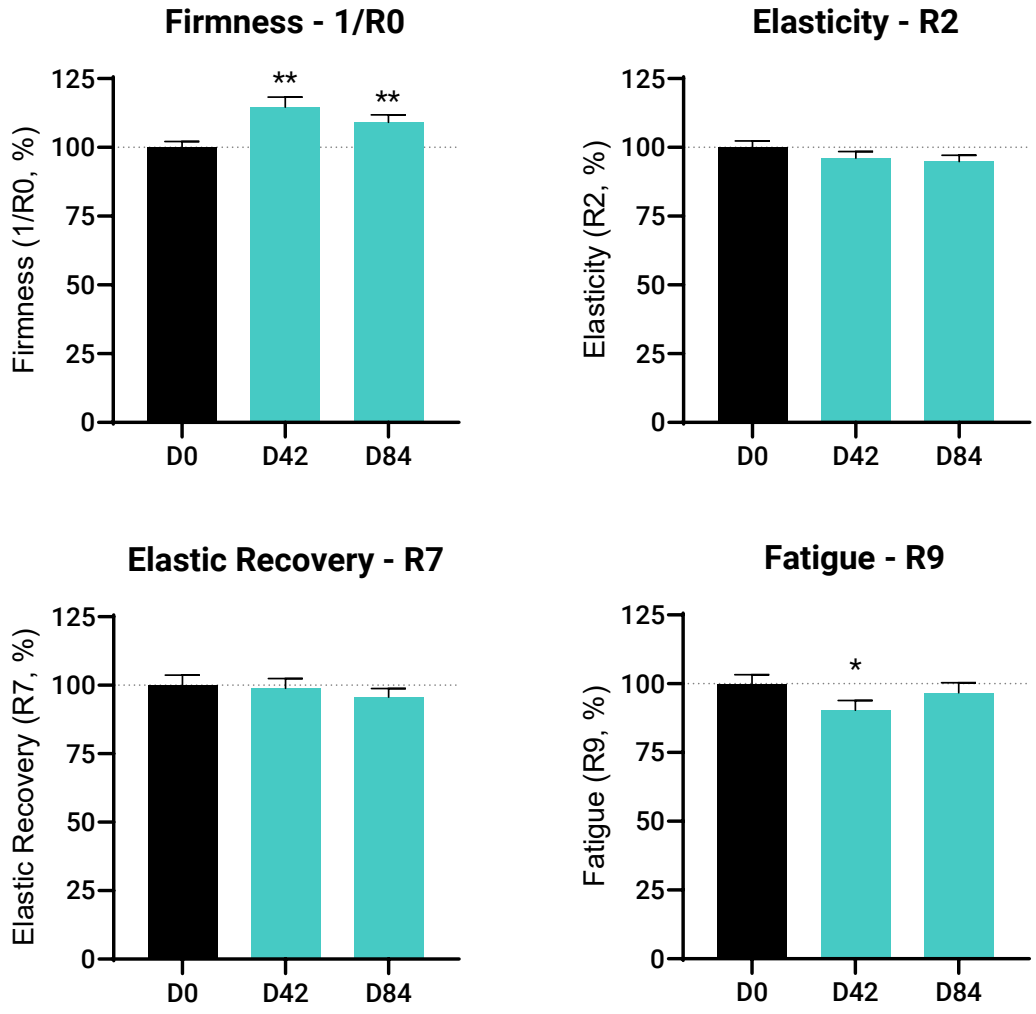


Figure 17. Effects of the application of Bracelet T-Collagen on skin biomechanical properties. *Graphical representation of the skin firmness (1/R0), skin elasticity (R2), elastic recovery (R7), and skin fatigue (R9) parameters on the cheek (ROI) (%), before (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84) with Bracelet T-Collagen, in 24 volunteers. Values obtained at different time points were normalized to the corresponding baseline levels at D0. Mean and Standard Error of the Mean (SEM) are shown. Ordinary one-way ANOVA with Dunnett's multiple comparisons was applied for statistical significance between timepoints.*

12. PANELIST SELF-ASSESSMENT

The number of volunteers that assigned each possible score to the indicated item and the percentage of satisfied volunteers (also indicated as percentage of acceptance), is described below:

QUESTIONNAIRE AFTER 6 WEEKS (D42)					
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**% Satisfaction**
1. How much the application of the Bracelet is simple	1	1	2	21	**92**
2. How much the appearance of the Bracelet is pleasant	2	0	10	13	**92**
3. How much the feeling (texture) of the Bracelet is pleasant	2	0	8	15	**92**
4. How much the odor of the Bracelet is pleasant	2	6	9	8	68
5. How much the design of the Bracelet is attractive	2	4	9	10	76
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**% Satisfaction**
6. My fine lines are smoothed	2	11	9	3	48
7. My crow's feet / forehead wrinkles appear less visible	3	11	8	3	44
8. My skin looks younger	3	9	9	4	52
9. My skin is more hydrated	2	8	10	5	60
10. My skin seems firmer	2	12	6	5	44
11. My skin seems more elastic (flexible)	3	10	8	4	48
12. How much the Bracelet improves your muscle tension	5	12	5	3	32
13. How much the Bracelet improve your joints flexibility	5	11	5	3	32
14. How much the Bracelet relieves the pain in the joints	9	9	6	1	28
15. How much the Bracelet helps you to do your daily tasks	11	6	5	3	32
16. The treatment improve hair appearance	7	13	2	3	20
17. The treatment improve nail appearance	11	8	3	3	24
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**% Satisfaction**
18. I am satisfied with the tested treatment	3	8	8	6	56
19. I would use the treatment again	4	8	6	7	52
20. I would recommend the treatment	5	8	6	6	48
21. I think the price of the tested treatment should be (€)	**19,4 €**				
OVERALL ACCEPTANCE	**52,0**				

QUESTIONNAIRE AFTER 6 WEEKS (D84)					
SENSORY EXPERIENCE	**1**	**2**	**3**	**4**	**% Satisfaction**
1. How much the application of the Bracelet is simple	0	0	2	22	**100**
2. How much the appearance of the Bracelet is pleasant	0	2	6	16	**92**
3. How much the feeling (texture) of the Bracelet is pleasant	0	0	8	16	**100**
4. How much the odor of the Bracelet is pleasant	1	8	8	7	63
5. How much the design of the Bracelet is attractive	1	3	8	12	**83**
TREATMENT EFFECTIVENESS	**1**	**2**	**3**	**4**	**% Satisfaction**
6. My fine lines are smoothed	3	10	8	3	46
7. My crow's feet / forehead wrinkles appear less visible	4	10	7	3	42
8. My skin looks younger	6	7	8	3	46
9. My skin is more hydrated	4	8	9	3	50
10. My skin seems firmer	6	10	4	4	33
11. My skin seems more elastic (flexible)	5	7	9	3	50
12. How much the Bracelet improves your muscle tension	7	8	6	3	38
13. How much the Bracelet improve your joints flexibility	8	7	4	4	33
14. How much the Bracelet relieves the pain in the joints	9	8	4	3	29
15. How much the Bracelet helps you to do your daily tasks	9	4	5	6	46
16. The treatment improve hair appearance	8	8	5	3	33
17. The treatment improve nail appearance	8	9	3	4	29
CONSUMER BEHAVIOUR	**1**	**2**	**3**	**4**	**% Satisfaction**
18. I am satisfied with the tested treatment	4	8	6	6	50
19. I would use the treatment again	5	6	8	5	54
20. I would recommend the treatment	7	4	8	5	54
21. I think the price of the tested treatment should be (€)	**23,2 €**				
OVERALL ACCEPTANCE	**53,5**				

Table 4. *Results for panelists self-assessment via questionnaire after treatment with Bracelet T-Collagen during 6 weeks (D42) and 12 weeks (D84), according to an ordinal scale (1 = Strongly disagree | 2 = Disagree | 3 = Agree | 4 = Strongly agree). Satisfaction was considered for scores 3 and 4, and a remarkable percentage of acceptance was considered when average result is equal or greater than 80 % (in bold).*

Results from the individual questionnaire showed an overall acceptance of 52.0 after 6 weeks of application (D42) and 53.5 after 12 weeks of treatment (D84).

Specifically, 3 out of 20 parameters yielded a significant result over 80 % at D42, whereas 4 out of 20 items yielded a significant result at D84:

- 1. How much the application of the Bracelet is simple (D42 – D84).
- 2. How much the appearance of the Bracelet is pleasant (D42 – D84).
- 3. How much the feeling (texture) of the Bracelet is pleasant (D42 – D84).
- 5. How much the design of the Bracelet is attractive (D84).

13. CONCLUSION AND SIGNATURES

The purpose of this clinical project was to evaluate the antiaging effects of "Bracelet Tanka T-Collagen", after topical use for 12 weeks. Additionally, to gather information of the volunteers' perception of the product's efficacy.

To achieve this goal, a clinical evaluation with the test product was initially carried out on 26 volunteers, aged from 39 to 61 years (mean 52.0 ± 6.3). The volunteers were required to be female between 40 and 65 years of age, presenting moderate to very severe signs of facial ageing (grades 2-4 in Eiben-Nielson photonumeric scale for wrinkles), and a willingness to comply with instructions. All the subjects participating in the study gave their informed consent signed before the start of the treatment. The study was in compliance with the tenets of the Declaration of Helsinki. The selected volunteers were ordered according to the date of recruitment and use the test product for 12 weeks, according to client's needs. 24 out of the 26 initially recruited volunteers completed the study. Before the start of the treatment (D0), after 6 weeks of treatment (D42), and after 12 weeks of treatment (D84), subjects attended Dermaclaim's facilities for the corresponding measurements. Upon arrival, volunteers were allowed to acclimatize to environmental conditions (23 ± 1 ºC, 45 ± 10 % humidity) for 15 minutes. Then, facial wrinkles were evaluated in crow's feet (2 sides) and forehead by 3D skin topography analysis using AEVA-HE V4 (FoV, S). Skin firmness (1/R0), elasticity (R2), elastic recovery (R7), and skin fatigue (R9) were also evaluated in the cheek using Cutometer MPA Dual 580. After that, high resolution macroscopic pictures were also obtained using camera Nikon D8400 installed in the HeadScan Bench Light Face, including complete professional photographic setup. Data recorded from every individual at each of the timepoints were normalized versus baseline values (D0) for the whole group and statistically analyzed for each parameter. In addition, participant's subjective perception of the product efficacy was assessed with an individual questionnaire answered at each of the timepoints.

Results showed the topical use of Bracelet T-Collagen provoked a reduction of crow's feet area, number, and perimeter by 1.8 %, 8.1 %, and 3.7 %, respectively, after 12 weeks of application (D84), even though results were not statistically significant ($p > 0.05$), compared to baseline values before the start of the treatment (D0). No significant neither relevant effects were observed for the depth or volume, neither after 6 weeks of use (D42).

With regard to forehead wrinkles, results indicated the application of the bracelet during 12 weeks (D84) provoked a non-significant reduction of the area (2.3 %), number (4.8 %), perimeter (1.9 %), depth (1.0 %), and volume (1.4 %), compared to D0. When the effects were assessed after 6 weeks of application, results indicated reductions by 5.6 % (area), 14.0 % (number), 7.8 % (perimeter), 0.7 % (depth), and 4.2 % (volume), compared to baseline values before the start of the treatment (D0).

With regard to skin biomechanical properties, results indicated the application of T-collagen significant increased skin firmness by 14.7 % and 9.2 %, after 6 weeks (D42) and 12 weeks (D84) of application, respectively, compared to baseline values before the start of the treatment. No statistically significant effects were observed for skin elasticity nor elastic recovery, whereas skin fatigue was significantly reduced by 9.7 % after 6 weeks (D42) of use and non-statistically reduced by 3.3 % after 12 weeks (D84).

On the other hand, results from the individual questionnaire showed an overall acceptance of 52.0 after 6 weeks of application (D42) and 53.5 after 12 weeks of treatment (D84). Specifically, 3 out of 20 parameters yielded a significant result over 80 % at D42, whereas 4 out of 20 items yielded a significant result at D84.

Regarding cutaneous compatibility and acceptability, participants showed no Serious Undesirable Effects (SUE) and declared neither discomfort nor Undesirable Effects (UE) throughout the period of treatment or the following 7 days.

In conclusion, the **topical treatment with "Bracelet Tanka T-Collagen" displays antiaging and firming capabilities**, substantiated in **non-statistically significant reductions of crow's feet and forehead wrinkles** parameters, together with a **significant increase of skin firmness**, compared to baseline values before the start of the treatment.

These results were partially subjectively confirmed with the volunteers' perception through the self-assessment questionnaire, reporting an overall acceptance of 52.0 after 6 weeks of application and 53.5 after 12 weeks of application.

Regarding skin acceptability and surveillance, the treatment showed good cutaneous compatibility and may claim "**Dermatologically tested**", "**Clinically tested**", and "**Tolerance tested**".

Clinical Project Manager

Lucía Fernández Gómez, MSc **Date:** 04/12/2023

… declares the study was conducted in accordance with the spirit of the Good Clinical Practices (International Recommendations ICH topic E6), and the results reported in this final report accurately and completely reflect the raw data of the study.

Study Director

Alejandro Pérez Fernández, PhD **Date:** 12/12/2023

… declares the study was carried out under my responsibility, the content of the study report is reliable and takes into account the "Guidelines for the evaluation of the efficacy of cosmetics products" (May, 2008) from Colipa. The test product may claim Clinically Tested.

Dermatologist

Eduardo Bernía Petit, MD. College Number 464624840 **Date:** 05/12/2023

… declares the clinical protocol was designed and conducted under my surveillance, in accordance with the Scientific Committee on Consumer Safety (SCSS) guidance. The test product may claim Dermatologically Tested and Tolerance Tested.

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14. ARCHIVING AND DISCLOSURE

All original raw data, including data sheets, clinical protocols, technical procedures, laboratory notebooks, correspondence files, copies of final reports, and remaining samples, are maintained on the premises of Dermaclaim Lab S.L., in limited access marked storage files. Altogether, including the information provided by the sponsor, volunteers' data, information about materials, reagents or methodology, and all the information generated by Dermaclaim Lab S.L. (statistical analysis, graphical representations, etc.) is considered Confidential, and will not be shared with third parties.

To prevent loss of and protect intellectual property, the final report has been electronically signed using the official signature of Dermaclaim Lab S.L. (VAT: B16909699). Any attempt to remove the signature will irreversibly damage the label and leave an immediate trace, thus invalidating the document.

Only reports containing the Dermaclaim Lab S.L. electronic signature intact, will be recognized by Dermaclaim Lab S.L. as a certified original.

Dermaclaim Lab S.L. represents filly independent testing facilities committed to the highest standards of unbiased testing and reporting. Dermaclaim Lab S.L. is not in partnership, affiliation and/or association, in any way, with any other corporation, company, sole proprietorship, partnership, client, laboratory, and/or any other business entity. Dermaclaim Lab S.L. is not legally responsible or bound to any claim(s) provided by a third party claiming any kind of association with Dermaclaim Lab S.L.

The industrial and intellectual property rights that may arise from the contracted services, as well as the ownership of the results, belongs entirely to the Sponsor, unless expressly stated otherwise in the corresponding budget.

15. CERTIFICATIONS AND REGULATIONS

The study protocol is in accordance with the Scientific Committee on Consumer Safety (SCCS) guidance. It meets all international standards for research studies involving human subjects, Structure and Content of Clinical Study Reports from ICH Harmonised Tripartite Guideline; International Recommendations ICH Topic E6, European Parliament and Council Guideline 2001/20/CE, the Good Clinical Practices (ICH-GCP), and the World Medical Association. It has been conducted pursuant to the Declaration of Helsinki (1864), with the amendments of Tokyo (1975), Venice (1983), Hong Kong (1989), and Seoul (2008).

The whole process involving this assay was performed following UNE-EN-ISO 9001/2015 Quality Management System guidelines, certified on August 5th, 2022 (reference code, EC-10984/22) and positively reviewed on July 10th, 2023.

The studies follow the "Guidelines for the Evaluation of the Efficacy of cosmetic Products", COLIPA, May 2008.

15.1 GENERAL PRINCIPLES FOR ALL TESTS (Rev. Efficacy Evaluation Guidelines – May 2008, COLIPA)

Studies must be relevant and comprised of methods which are reliable and reproducible. The studies should follow a well-designed and scientifically valid methodology according to good practices. The criteria used for evaluation of product performances should be defined with accuracy and chosen in compliance with the aim of the test.

Studies conducted on volunteers should naturally respect ethical rules and products tested should have previously undergone a safety investigation. Human studies should be conducted on the target population, when necessary, defined by strict inclusion / exclusion criteria.

Depending on the aim of the study, tests can be open, single- or double-blind.

A study protocol must be drawn up and validated by the parties involved. This is essential to enable the study manager / promoter to monitor the study and the experimenter to carry out the test in order to ensure its quality.

The test laboratories must have standardized operating procedures. The equipment must be the subject of documented maintenance adapted to its use. Whatever the type of study, it is important that the person conducting the study:

- has the appropriate qualifications.

- has the training and experience in the field of the proposed study; and

- is respected for ethical quality and professional integrity.

A study monitoring system must be set up in order to ensure that the protocol and the operating procedures are correctly followed.

Data processing and the interpretation of results must be fair and should not overstep the limits of the test's significance. Data recording, transformations, and representation in tabular or graphical form should be transparent or clearly explained if complex. It should not be designed to overstate the effect(s) measured. Appropriate statistical analysis of the data should be performed.

A critical point for the validity of consumer tests is the wording of the questionnaire. The questions and proposed answers should be clear enough to be unequivocally understood by participants. The answers scale should be well balanced (e.g., same number of positive and negative answers) and not capable of influencing the answer. Special attention should be paid to the wording of questions for which responses will be used to substantiate the claim: the claim should be directly substantiated by the results related to the relevant question without any questionable interpretation.

15.2 SUBSTANTIATION OF CLAIMS (EU Regulation 655/2013)

Cosmetic claims must comply with EU Regulation 655/2013 that provides the Common Criteria to ensure that the information conveyed to the end-users through claims is useful, understandable, and reliable so that consumers can make informed decisions.

Claims for cosmetic products, whether explicit or implicit, shall be supported by adequate and verifiable evidence regardless of the types of evidential support used to substantiate them, including where appropriate expert assessments. Evidence for claim substantiation shall consider the state-of-the-art practices.

Products may bear claims that relate to the nature of experimental studies. Consumer expectations regarding these claims may vary depending upon the presentation of the claim and its specific context. However, in all circumstances, consumers will expect that such claims are made only when the effects tested are favorable.

Use test claims such as tolerance tested, under medical surveillance, clinically tested, dermatologically tested, etc… should be substantiated, according to the following explanation:

TOLERANCE TESTED	CLINICALLY TESTED	DERMATOLOGICALLY TESTED
The product underwent tests under the supervision of a scientifically qualified professional intended to study its tolerance on a target group and that the results of those tests show that the product was well tolerated by this group.	The product was tested on humans under the supervision of a medically qualified professional or another scientifically qualified professional according to a clinical protocol or in a clinical setting.	The product was tested on humans under the supervision of a dermatologist. Depending on the presentation of the claim, it may refer to a specific efficacy or tolerance of the product. Consumer self-perceptions studies are not appropriate to support such claims.

15.3 CLASSIFICATION OF ADVERSE REACTIONS (Colipa, March 2016)

An **undesirable or adverse event** is defined as any human adverse health event which is voluntarily reported by consumers, healthcare professionals, Competent Authorities, and any other individuals to have occurred during or after normal or reasonably foreseeable use (exclude misuse and abuse) of a cosmetic product. It is not necessarily related to the product.

Undesirable effect (UE) means an adverse reaction for human health attributable to the normal or reasonably foreseeable use of a cosmetic product. Undesirable Effects include but are not limited to irritant or allergic reactions that can affect the skin, eyes or mouth. Undesirable effects caused by product misuse and abuse are not included in this definition.

A **serious undesirable effect (SUE)** means an undesirable effect which results in temporary or permanent functional incapacity, disability, hospitalization, congenital anomalies or an immediate vital risk or death.

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17. ATTACHMENTS

17.1 Attachment 1. Volunteers' data

VOLUNTEERS'S DATA							
Nº Volunteer	**ID Volunteer**	**Gender**	**Age**	**Ethnicity**	**Skin Type**	**Skin Phototype**	**Image consent**
1	1141	Female	45	Caucasian	Combination	III (light brown)	YES
2	1030	Female	55	Latin	Combination	III (light brown)	YES
3	861	Female	45	Caucasian	Dry	II (white)	YES
4	1126	Female	59	Latin	Dry	II (white)	YES
5	2459	Female	39	Caucasian	Combination	III (light brown)	YES
6	517	Female	52	Caucasian	Combination	III (light brown)	YES
7	1431	Female	42	Caucasian	Combination	III (light brown)	YES
8	823	Female	52	Latin	Combination	III (light brown)	YES
9	1343	Female	60	Caucasian	Combination	II (white)	YES
10	866	Female	48	Caucasian	Dry	III (light brown)	YES
11	1787	Female	47	Caucasian	Dry	III (light brown)	YES
12	1584	Female	51	Caucasian	Combination	III (light brown)	YES
13	2537	Female	49	Caucasian	Dry	II (white)	YES
14	1390	Female	61	Latin	Combination	III (light brown)	YES
15	1222	Female	50	Caucasian	Dry	III (light brown)	YES
16	740	Female	56	Latin	Dry	IV (moderate brown)	YES
17	1939	Female	54	Caucasian	Combination	III (light brown)	YES
18	1735	Female	49	Caucasian	Combination	II (white)	YES
19	2435	Female	60	Caucasian	Dry	III (light brown)	YES
20	2437	Female	58	Caucasian	Dry	III (light brown)	YES
21	1813	Female	47	Caucasian	Combination	III (light brown)	YES
22	2661	Female	58	Caucasian	Combination	II (white)	YES
23	2647	Female	45	Caucasian	Combination	III (light brown)	YES
24	729	Female	58	Caucasian	Dry	II (white)	YES
25	549	Female	61	Caucasian	Combination	II (white)	YES
26	1541	Female	50	Caucasian	Dry	II (white)	YES

Table 5. ***Panel data***. *Data (Number of volunteer within the study, Dermaclaim's ID for each volunteer, gender, age, ethnicity, skin type, skin phototype, skin condition, and consent for image rights) of the volunteers included in the study.*

17.2 Attachment 2. Daily visit registration

DAILY REGISTRATION			
Nº Volunteer	**Day 0**	**Day 42**	**Day 84**
1	06/09/2023 8:00	19/10/2023 9:00	29/11/2023 9:45
2	06/09/2023 11:30	18/10/2023 11:00	29/11/2023 11:00
3	06/09/2023 9:15	18/10/2023 9:15	29/11/2023 9:15
4	07/09/2023 11:00	19/10/2023 12:45	29/11/2023 13:30
5	06/09/2023 9:00	18/10/2023 10:00	30/11/2023 10:15
6	06/09/2023 12:00	18/10/2023 15:30	29/11/2023 15:30
7	07/09/2023 15:45	19/10/2023 15:00	30/11/2023 15:15
8	06/09/2023 10:00	18/10/2023 10:15	29/11/2023 10:15
9	06/09/2023 16:25	18/10/2023 15:45	29/11/2023 16:00
10	06/09/2023 13:30	18/10/2023 13:30	29/11/2023 13:30
11	06/09/2023 10:30	18/10/2023 10:30	29/11/2023 10:30
12	06/09/2023 12:00	18/10/2023 11:30	29/11/2023 11:30
13	07/09/2023 16:00	19/10/2023 16:00	30/11/2023 16:00
14	07/09/2023 13:15	19/10/2023 13:00	30/11/2023 13:00
15	08/09/2023 13:00	19/10/2023 15:45	30/11/2023 15:00
16	07/09/2023 10:45	20/10/2023 11:00	
17	06/09/2023 17:00	18/10/2023 17:10	29/11/2023 17:00
18	06/09/2023 15:45	18/10/2023 15:15	29/11/2023 15:30
19	06/09/2023 10:00	18/10/2023 12:00	29/11/2023 12:00
20	06/09/2023 10:15	18/10/2023 12:00	29/11/2023 12:00
21	07/09/2023 8:00	19/10/2023 7:45	30/11/2023 8:15
22	06/09/2023 10:45	18/10/2023 16:30	29/11/2023 15:00
23	06/09/2023 8:15	19/10/2023 8:00	30/11/2023 8:00
24	07/09/2023 15:50	19/10/2023 16:15	30/11/2023 15:45
25	06/09/2023 9:45	18/10/2023 9:30	29/11/2023 9:30
26	08/09/2023 8:00	20/10/2023 7:30	29/11/2023 8:00

Table 6. ***Daily visit registration***. *Date and time for each of the visits conducted for each of the volunteers.*

17.3 Attachment 3. Consumption control

N Vol	WRIST	WEIGHT OF SAMPLES (g)							QUANTITY OF SAMPLES USED (g)					
		D0		D42			D84		D42		D84		Bracelet	SPF
		Bracelet I	SPF	Bracelet I	SPF	Bracelet II	Bracelet II	SPF	Bracelet	SPF	Bracelet	SPF	Per day	Per day
1	RIGHT	8,30	117,90	8,36	93,01	8,13	7,92	79,99	-0,06	24,89	0,15	37,91	0,002	0,45
2	LEFT	7,96	118,02	8,06	93,31	8,20	8,26	65,42	-0,10	24,71	-0,16	52,60	-0,002	0,63
3	LEFT	7,94	116,60	7,84	97,90	8,14	8,02	69,52	0,10	18,70	0,22	47,08	0,003	0,56
4	LEFT	8,07	116,60	8,15		8,05	8,08	23,44	-0,08		-0,11	93,16	-0,001	1,11
5	LEFT	7,93	117,85	7,83	88,10	7,95	7,90	74,31	0,10	29,75	0,15	43,54	0,002	0,52
6	RIGHT	7,94	118,02	7,82	108,15	7,96	7,83	68,40	0,12	9,87	0,25	49,62	0,003	0,59
7	LEFT	7,95	117,82	7,80		8,21	8,04	92,14	0,15		0,32	25,68	0,004	0,31
8	RIGHT	8,11	116,61	8,09	94,75	8,02	7,87	83,51	0,02	21,86	0,17	33,10	0,002	0,39
9	RIGHT	8,17	117,86	7,79		7,94	7,89	74,85	0,38		0,43	43,01	0,005	0,51
10	LEFT	7,94	117,76	7,84					0,10					
11	RIGHT	7,95	116,65	7,80	101,56	7,95	7,86	62,26	0,15	15,09	0,24	54,39	0,003	0,65
12	LEFT	8,02	117,96	8,21	107,41	8,03	8,17	42,50	-0,19	10,55	-0,33	75,46	-0,004	0,90
13	RIGHT	7,95	117,83	7,89	85,29	7,94	7,84	45,13	0,06	32,54	0,16	72,70	0,002	0,87
14	RIGHT	8,22	116,61	8,36		7,96	7,92	93,20	-0,14		-0,10	23,41	-0,001	0,28
15	RIGHT	7,93	116,52	7,85	39,48 | 117,01	8,02	8,11	27,59 | 60,63	0,08	77,04	-0,01	145,31	0,000	1,73
16	RIGHT	7,92	116,61											
17	LEFT	7,93	116,61	7,90		8,12	8,06	96,05	0,03		0,09	20,56	0,001	0,24
18	RIGHT	8,05	117,92	8,10	103,59	8,23	8,18	92,30	-0,05	14,33	0,00	25,62	0,000	0,31
19	LEFT	7,93	117,92	7,97		8,06	8,29	91,37	-0,04		-0,27	26,55	-0,003	0,32
20	LEFT	7,97	116,57	7,91		8,24	8,28	66,36	0,06		0,02	50,21	0,000	0,60
21	LEFT	7,95	116,61	7,91		8,13	8,02		0,04		0,15		0,002	
22	LEFT	8,22	226,63	8,17	194,00	8,17	8,23	170,02	0,05	32,63	-0,01	56,61	0,000	0,67
23	RIGHT	8,23	226,68	8,14	198,34	8,15	8,01	168,93	0,09	28,34	0,23	57,75	0,003	0,69
24	RIGHT	8,05	226,67	8,05	193,56	8,02	8,00	162,75	0,00	33,11	0,02	63,92	0,000	0,76
25	LEFT	7,95	226,54	7,89	218,23	7,92	7,82	197,25	0,06	8,31	0,16	29,29	0,002	0,35
26	RIGHT	8,22	226,30	8,13	203,90	8,21	8,04	185,87	0,09	22,40	0,26	40,43	0,003	0,48
	MEAN	**8,0**	**138,3**	**8,0**	**132,1**	**8,1**	**8,0**	**95,7**	**0,0**	**25,3**	**0,1**	**50,8**	**0,001**	**0,605**

SD	**0,1**	**43,9**	**0,2**	**51,6**	**0,1**	**0,1**	**48,8**	**0,1**	**16,1**	**0,2**	**27,6**	**0,002**	**0,329**

Table 7. Raw data for consumption control*. Raw data (g) regarding the weight of the sample belonging to each volunteer, and calculation of the quantity used at each of the time points, and the mean quantity used per day.*

17.4 Attachment 4. Raw data – Facial wrinkles

Crow's feet wrinkles - AEVA-HE 3D - RAW DATA																		Crow's feet wrinkles - AEVA-HE 3D - RELATIVE DATA TO D0 (%)														
VOL	SIDE	TH	AREA (mm2)			NUMBER (N)			PERIMETER (mm)			DEPTH (mm)			VOLUME (mm3)			AREA (%)			NUMBER (%)			PERIMETER (%)			DEPTH (%)			VOLUME (%)		
			D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84
1	L	30	9,22	5,63	9,37	4,50	2,50	4,50	50,63	32,90	53,30	0,05	0,05	0,05	0,46	0,26	0,47	34,15	20,85	34,71	51,31	28,50	51,31	37,31	24,24	39,28	83,73	82,90	83,73	25,53	14,27	25,96
2	L	10	3,35	0,57	1,59	2,50	0,50	1,00	23,05	4,01	8,26	0,09	0,04	0,09	0,33	0,05	0,14	12,40	2,11	5,89	28,50	5,70	11,40	16,99	2,96	6,09	149,22	70,47	154,20	18,23	2,52	7,92
3	L	30	25,97	30,91	23,30	8,00	8,50	6,00	143,94	161,11	120,75	0,07	0,07	0,07	1,89	2,21	1,78	96,18	114,45	86,29	91,21	96,91	68,41	106,08	118,73	88,99	107,77	112,75	116,06	104,08	121,76	97,89
4	L	10	21,14	21,40	20,26	6,00	6,00	5,50	98,79	99,35	99,88	0,09	0,09	0,08	2,13	2,03	1,74	78,27	79,25	75,02	68,41	68,41	62,71	72,80	73,22	73,60	145,08	144,25	137,62	117,22	111,63	95,88
5	R	50	22,29	27,17	24,21	11,00	11,50	10,00	126,46	152,98	135,35	0,04	0,04	0,04	0,86	1,00	0,90	82,53	100,60	89,65	125,42	131,12	114,01	93,20	112,74	99,75	62,18	63,83	62,18	47,37	54,98	49,74
6	R	50	31,03	45,65	37,97	12,00	14,00	11,50	173,37	220,39	193,43	0,05	0,05	0,05	1,58	2,63	1,95	114,92	169,04	140,60	136,82	159,62	131,12	127,76	162,42	142,55	78,76	84,56	79,59	86,81	144,91	107,36
7	L	40	14,32	20,12	13,47	10,50	13,00	9,50	93,87	132,40	85,03	0,05	0,05	0,05	0,69	0,94	0,66	53,01	74,51	49,86	119,71	148,22	108,31	69,18	97,57	62,67	82,07	81,24	83,73	38,11	51,77	36,34
8	L	50	33,05	31,46	28,41	11,50	14,00	11,00	178,14	184,20	158,07	0,04	0,04	0,04	1,39	1,15	1,24	122,38	116,48	105,19	131,12	159,62	125,42	131,28	135,75	116,49	63,83	59,69	69,64	76,42	63,30	68,01
9	L	50	53,10	58,41	60,01	11,50	11,00	9,00	208,20	220,80	225,69	0,05	0,06	0,06	3,82	4,05	4,25	196,62	216,29	222,20	131,12	125,42	102,61	153,44	162,72	166,33	90,36	94,51	101,14	210,38	222,85	233,74
10																																
11	R	20	11,02	12,83	6,94	5,50	7,00	4,50	68,61	72,98	43,61	0,07	0,07	0,07	0,79	0,88	0,49	40,80	47,50	25,70	62,71	79,81	51,31	50,56	53,78	32,14	111,09	116,89	110,26	43,43	48,56	27,12
12	L	40	21,83	26,56	17,41	10,00	11,00	7,50	124,20	143,51	97,16	0,07	0,07	0,07	1,56	1,81	1,20	80,83	98,36	64,48	114,01	125,42	85,51	91,53	105,76	71,60	107,77	110,26	109,43	86,03	99,46	66,19
13	R	50	54,35	51,37	49,87	11,50	14,50	14,00	246,76	246,87	242,49	0,08	0,08	0,07	4,67	4,47	4,30	201,24	190,24	184,68	131,12	165,32	159,62	181,85	181,94	178,70	127,67	126,84	121,04	257,31	246,27	237,03
14	R	30	33,00	38,08	30,23	11,00	10,50	10,00	167,94	188,60	148,48	0,07	0,07	0,07	2,87	3,24	2,58	122,19	141,00	111,95	125,42	119,71	114,01	123,77	138,99	109,42	118,55	123,52	123,52	158,00	178,42	141,95
15	L	50	31,16	40,05	47,33	12,50	13,50	15,50	158,17	202,91	245,48	0,05	0,05	0,05	1,80	2,32	2,84	115,39	148,32	175,26	142,52	153,92	176,72	116,56	149,54	180,91	82,07	90,36	90,36	99,28	127,74	156,64
16																																
17	L	50	38,29	27,31	25,44	11,00	8,00	7,50	181,27	134,86	121,36	0,05	0,06	0,06	2,54	2,03	2,00	141,78	101,13	94,20	125,42	91,21	85,51	133,59	99,39	89,44	84,56	103,63	105,28	139,97	111,58	110,10
18	L	20	14,56	11,69	10,55	6,00	4,50	4,50	88,96	68,37	64,70	0,05	0,05	0,06	0,80	0,59	0,59	53,92	43,28	39,05	68,41	51,31	51,31	65,56	50,39	47,68	86,22	88,70	94,51	44,26	32,49	32,46
19	L	10	23,70	21,87	28,05	5,50	5,00	6,50	108,44	102,09	131,50	0,11	0,10	0,11	2,81	2,24	3,18	87,75	80,99	103,88	62,71	57,01	74,11	79,92	75,23	96,91	177,41	169,12	174,09	154,49	123,59	175,25
20	L	50	51,85	52,07	55,98	12,00	14,50	15,00	235,71	242,73	259,52	0,04	0,04	0,04	2,56	2,52	2,87	192,00	192,82	207,28	136,82	165,32	171,02	173,71	178,88	191,26	67,98	67,98	68,81	140,85	139,01	158,29
21	L	40	25,42	30,31	23,96	8,00	9,00	5,00	131,29	155,38	117,67	0,06	0,06	0,06	1,68	2,02	1,60	94,14	112,23	88,73	91,21	102,61	57,01	96,76	114,51	86,72	91,19	93,68	97,82	92,60	111,17	87,90
22	R	40	33,22	27,03	25,51	9,50	8,00	9,00	163,12	136,29	128,21	0,06	0,06	0,07	2,40	1,79	1,82	123,02	100,09	94,46	108,31	91,21	102,61	120,21	100,44	94,49	103,63	104,46	108,60	131,89	98,76	100,45

23	**R**	**30**	12,72	2,95	6,43	7,00	2,00	4,50	85,34	17,78	45,78	0,05	0,04	0,04	0,64	0,12	0,29	47,09	10,93	23,80	79,81	22,80	51,31	62,89	13,10	33,74	82,90	72,95	71,30	35,10	6,80	16,02
24	**R**	**30**	36,56	37,72	34,71	9,50	8,50	7,00	172,77	162,66	144,06	0,06	0,07	0,07	2,65	2,78	2,68	135,37	139,68	128,52	108,31	96,91	79,81	127,33	119,87	106,17	102,80	117,72	117,72	145,64	152,97	147,40
25	**L**	**20**	14,65	16,36	13,72	4,00	4,00	4,00	72,95	84,81	67,59	0,08	0,08	0,08	1,20	1,38	1,13	54,24	60,57	50,79	45,61	45,61	45,61	53,76	62,50	49,81	124,35	133,47	130,16	65,96	76,20	62,43
26	**L**	**50**	32,35	34,26	41,51	10,00	8,00	11,00	154,63	152,86	197,18	0,04	0,05	0,05	1,47	1,76	2,44	119,78	126,88	153,72	114,01	91,21	125,42	113,96	112,66	145,32	68,81	80,41	87,88	81,03	96,65	134,61
MEAN			**27,01**	**27,99**	**26,51**	**8,77**	**8,71**	**8,06**	**135,69**	**138,37**	**130,61**	**0,06**	**0,06**	**0,06**	**1,82**	**1,84**	**1,80**	**100,00**	**103,65**	**98,16**	**100,00**	**99,29**	**91,92**	**100,00**	**101,97**	**96,25**	**100,00**	**99,76**	**104,11**	**100,00**	**101,57**	**99,03**

			D0										**D42**										**D84**									
			LEFT					**RIGHT**					**LEFT**					**RIGHT**					**LEFT**					**RIGHT**				
VOL	**SIDE**	**TH**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**	**AREA (mm2)**	**NUMBER (N)**	**PERIMETER (mm)**	**DEPTH (mm)**	**VOLUME (mm3)**
1	**L**	**30**	6,01	3,00	38,35	0,05	0,3212	12,44	6,00	62,90	0,05	0,61	2,76	2,00	16,86	0,05	0,14	8,51	3,00	48,93	0,05	0,38	7,23	4,00	49,13	0,05	0,391395	11,51	5,00	57,46	0,05	0,55
2	**L**	**10**	5,19	4,00	33,56	0,10	0,5396	1,51	1,00	12,55	0,08	0,12	0,00	0,00	0,00	0,00	0,00	1,14	1,00	8,02	0,09	0,09	2,26	1,00	11,56	0,09	0,206222	0,92	1,00	4,96	0,09	0,08
3	**L**	**30**	27,45	9,00	153,00	0,07	2,0039	24,49	7,00	134,88	0,07	1,78	29,76	8,00	153,99	0,07	2,17	32,05	9,00	168,23	0,07	2,25	26,01	6,00	135,42	0,07	2,023517	20,60	6,00	106,08	0,07	1,53
4	**L**	**10**	25,42	7,00	119,82	0,09	2,748	16,85	5,00	77,76	0,08	1,51	25,39	7,00	122,74	0,09	2,53	17,41	5,00	75,96	0,08	1,52	21,32	5,00	107,24	0,09	1,946596	19,19	6,00	92,51	0,07	1,54
5	**R**	**50**	27,07	13,00	155,04	0,04	1,0006	17,51	9,00	97,89	0,04	0,72	29,81	10,00	161,47	0,04	1,08	24,52	13,00	144,50	0,04	0,92	32,40	10,00	171,39	0,04	1,195622	16,02	10,00	99,31	0,04	0,61
6	**R**	**50**	33,39	11,00	177,96	0,05	1,8472	28,68	13,00	168,78	0,04	1,31	58,56	16,00	267,85	0,06	3,69	32,74	12,00	172,92	0,05	1,57	44,07	11,00	216,14	0,05	2,357197	31,87	12,00	170,71	0,05	1,54
7	**L**	**40**	18,44	14,00	121,72	0,05	0,8617	10,19	7,00	66,03	0,05	0,52	21,80	16,00	147,46	0,05	0,95	18,44	10,00	117,33	0,05	0,93	13,72	9,00	80,48	0,05	0,64796	13,21	10,00	89,59	0,05	0,67
8	**L**	**50**	33,39	12,00	179,45	0,04	1,3663	32,71	11,00	176,83	0,04	1,41	31,03	14,00	181,32	0,04	1,14	31,89	14,00	187,07	0,04	1,16	29,68	10,00	153,31	0,04	1,289518	27,13	12,00	162,83	0,04	1,18
9	**L**	**50**	52,59	13,00	212,77	0,06	3,9266	53,61	10,00	203,63	0,05	3,72	55,03	12,00	219,54	0,06	3,47	61,78	10,00	222,05	0,06	4,63	54,28	10,00	216,31	0,07	3,745752	65,73	8,00	235,08	0,06	4,74
10			20,98	8,00	117,06	0,04	0,9363	32,10	11,00	160,85	0,04	1,40																				
11	**R**	**30**	15,80	7,00	93,94	0,07	1,1813	6,24	4,00	43,28	0,06	0,40	11,50	6,00	62,29	0,08	0,88	14,16	8,00	83,67	0,07	0,89	10,03	6,00	57,39	0,07	0,7561	3,85	3,00	29,82	0,06	0,23
12	**L**	**40**	24,64	11,00	145,59	0,07	1,7811	19,02	9,00	102,82	0,06	1,34	23,39	9,00	131,04	0,07	1,62	29,74	13,00	155,99	0,06	1,99	21,88	9,00	123,28	0,07	1,557626	12,94	6,00	71,03	0,06	0,85
13	**R**	**50**	61,69	12,00	272,68	0,08	4,9141	47,01	11,00	220,83	0,08	4,43	57,05	15,00	264,79	0,07	4,87	45,69	14,00	228,96	0,08	4,07	58,46	16,00	279,48	0,07	4,878906	41,28	12,00	205,50	0,08	3,73
14	**R**	**30**	36,98	10,00	174,05	0,08	3,2709	29,02	12,00	161,84	0,07	2,47	42,00	9,00	190,60	0,09	4,07	34,16	12,00	186,59	0,06	2,41	33,45	6,00	141,68	0,09	3,362699	27,02	14,00	155,28	0,06	1,79
15	**L**	**50**	34,49	11,00	168,98	0,06	2,2151	27,83	14,00	147,36	0,04	1,39	36,00	13,00	179,79	0,06	2,38	44,11	14,00	226,03	0,05	2,26	43,16	11,00	207,74	0,06	2,762075	51,50	20,00	283,22	0,05	2,93
16			34,75	10,00	193,36	0,04	1,4695	25,15	11,00	151,64	0,05	1,30																				

17	**L**	**50**	47,78	13,00	216,85	0,06	3,3221	28,80	9,00	145,69	0,05	1,76	26,11	8,00	122,54	0,07	2,38	28,51	8,00	147,19	0,05	1,68	27,34	8,00	130,53	0,07	2,4427	23,54	7,00	112,20	0,05	1,56
18	**L**	**20**	16,41	8,00	100,91	0,06	1,0105	12,72	4,00	77,01	0,05	0,60	7,87	4,00	46,48	0,06	0,45	15,50	5,00	90,27	0,05	0,73	11,68	6,00	74,56	0,06	0,685499	9,41	3,00	54,84	0,05	0,49
19	**L**	**10**	22,17	5,00	95,37	0,09	2,2624	25,23	6,00	121,52	0,12	3,35	20,25	6,00	101,18	0,08	1,68	23,50	4,00	102,99	0,13	2,81	26,52	7,00	126,72	0,09	2,401526	29,58	6,00	136,27	0,12	3,96
20	**L**	**50**	51,83	14,00	250,68	0,04	2,3808	51,88	10,00	220,73	0,04	2,74	49,54	15,00	242,08	0,04	2,15	54,61	14,00	243,37	0,04	2,90	55,89	14,00	262,99	0,05	2,916208	56,06	16,00	256,05	0,04	2,83
21	**L**	**40**	31,56	10,00	164,25	0,05	2,0326	19,28	6,00	98,33	0,06	1,33	37,38	11,00	195,47	0,05	2,33	23,23	7,00	115,29	0,06	1,71	31,38	6,00	147,73	0,06	2,036709	16,55	4,00	87,62	0,06	1,16
22	**R**	**40**	33,05	11,00	168,06	0,06	2,4357	33,39	8,00	158,17	0,06	2,35	24,43	7,00	119,54	0,07	1,78	29,63	9,00	153,03	0,06	1,81	27,56	9,00	136,48	0,07	2,206653	23,46	9,00	119,95	0,06	1,44
23	**R**	**30**	9,02	5,00	57,87	0,05	0,4481	16,41	9,00	112,81	0,05	0,83	2,51	2,00	13,16	0,04	0,10	3,39	2,00	22,41	0,05	0,14	2,39	2,00	18,39	0,04	0,092829	10,47	7,00	73,17	0,05	0,49
24	**R**	**30**	39,22	10,00	184,25	0,06	2,6551	33,89	9,00	161,30	0,07	2,63	46,31	10,00	198,39	0,07	3,31	29,13	7,00	126,92	0,07	2,25	40,90	8,00	171,36	0,07	3,014469	28,52	6,00	116,76	0,08	2,34
25	**L**	**20**	13,15	3,00	63,89	0,08	1,1332	16,14	5,00	82,01	0,07	1,26	14,91	3,00	71,40	0,08	1,27	17,81	5,00	98,23	0,08	1,50	12,24	4,00	58,55	0,08	1,054875	15,19	4,00	76,64	0,08	1,21
26	**L**	**50**	30,93	9,00	147,29	0,05	1,5971	33,77	11,00	161,98	0,04	1,35	31,07	7,00	136,82	0,06	1,85	37,46	9,00	168,91	0,04	1,66	42,89	8,00	182,10	0,07	3,075773	40,14	14,00	212,26	0,04	1,81

***Table 8. Raw data for crow's feet wrinkles**. Raw and relative data from the 3D analysis of crow's feet wrinkles at the different time points, for each of the volunteers included in the study.*

Forehead wrinkles - AEVA-HE 3D - RAW DATA																		Forehead wrinkles - AEVA-HE 3D - RELATIVE DATA TO D0 (%)													
VOL	TH	AREA (mm2)			NUMBER (N)			PERIMETER (mm)			DEPTH (mm)			VOLUME (mm3)			AREA (%)			NUMBER (%)			PERIMETER (%)			DEPTH (%)			VOLUME (%)		
		D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84	D0	D42	D84
1	50	84,51	26,31	122,55	45,00	18,00	55,00	489,26	156,50	691,73	0,04	0,04	0,04	3,19	0,98	4,99	145,05	45,15	210,34	155,40	62,16	189,93	149,70	47,88	211,65	73,03	71,05	75,00	103,36	31,69	161,58
2	40	50,38	61,48	55,19	27,00	25,00	25,00	310,52	328,92	302,43	0,04	0,04	0,04	2,11	2,67	2,32	86,47	105,52	94,73	93,24	86,33	86,33	95,01	100,64	92,53	80,92	80,92	78,95	68,43	86,57	75,25
3	30	35,19	22,21	26,30	21,00	17,00	15,00	208,42	152,01	158,88	0,05	0,05	0,06	1,92	1,15	1,48	60,39	38,11	45,14	72,52	58,71	51,80	63,77	46,51	48,61	104,61	100,66	110,53	62,09	37,11	47,90
4	30	51,62	39,48	21,22	14,00	12,00	10,00	258,30	202,95	123,05	0,04	0,04	0,04	2,34	1,89	0,85	88,60	67,77	36,42	48,35	41,44	34,53	79,03	62,09	37,65	80,92	84,87	78,95	75,92	61,21	27,62
5	40	59,33	65,86	74,87	36,00	28,00	33,00	336,80	343,09	387,94	0,05	0,05	0,05	3,13	3,63	4,58	101,83	113,04	128,50	124,32	96,69	113,96	103,05	104,98	118,70	100,66	100,66	102,63	101,30	117,61	148,22
6	40	73,16	90,75	39,43	27,00	33,00	24,00	408,31	517,11	245,17	0,04	0,04	0,04	3,33	4,66	1,58	125,56	155,75	67,67	93,24	113,96	82,88	124,93	158,22	75,02	78,95	86,84	75,00	107,73	150,97	51,05
7	50	89,99	127,94	116,74	49,00	48,00	48,00	528,80	664,36	626,25	0,04	0,05	0,05	4,18	7,06	6,50	154,46	219,59	200,37	169,21	165,76	165,76	161,80	203,27	191,61	86,84	94,74	90,79	135,42	228,72	210,39
8	30	20,32	14,45	19,35	17,00	10,00	15,00	130,25	98,02	132,23	0,05	0,04	0,05	1,01	0,64	0,90	34,87	24,79	33,21	58,71	34,53	51,80	39,85	29,99	40,46	96,71	86,84	88,82	32,63	20,78	29,10
9	30	66,53	47,08	71,57	25,00	22,00	26,00	339,39	262,68	363,77	0,08	0,07	0,07	5,89	3,37	5,80	114,19	80,81	122,84	86,33	75,97	89,78	103,84	80,37	111,30	148,03	138,16	144,08	190,73	109,01	187,98
10	30	29,734*			13*			149,668*			0,053*			1,716*																	
11	20	17,79	37,45	10,29	12,00	21,00	8,00	110,47	237,90	60,11	0,04	0,04	0,04	0,68	1,74	0,41	30,53	64,28	17,65	41,44	72,52	27,63	33,80	72,79	18,39	75,00	84,87	78,95	22,07	56,52	13,38
12	40	66,84	66,33	48,11	37,00	37,00	32,00	388,89	383,93	302,23	0,05	0,05	0,04	3,15	3,22	2,11	114,73	113,85	82,57	127,77	127,77	110,50	118,99	117,47	92,47	90,79	90,79	84,87	102,10	104,17	68,30
13	50	92,54	37,57	3,76	54,00	27,00	3,00	530,91	209,92	23,19	0,04	0,04	0,04	3,84	1,48	0,14	158,84	64,49	6,45	186,47	93,24	10,36	162,44	64,23	7,09	80,92	76,97	71,05	124,24	47,88	4,42
14	40	41,24	47,02	66,31	30,00	32,00	47,00	259,56	300,76	434,21	0,04	0,05	0,04	1,71	2,16	2,87	70,79	80,69	113,80	103,60	110,50	162,30	79,42	92,02	132,86	78,95	90,79	84,87	55,32	69,92	93,07
15	20	24,69	25,41	36,39	12,00	14,00	20,00	136,20	142,15	217,02	0,09	0,09	0,08	2,22	2,29	3,14	42,37	43,61	62,46	41,44	48,35	69,06	41,67	43,49	66,40	171,71	173,68	161,84	71,99	74,31	101,58
16	30	54,252*			24*			331,262*			0,049*			3,1398*																	
17	40	34,63	29,32	13,64	18,00	15,00	6,00	204,10	172,38	72,15	0,07	0,06	0,08	2,48	1,95	1,09	59,43	50,33	23,41	62,16	51,80	20,72	62,45	52,74	22,07	136,18	124,34	157,89	80,36	63,16	35,45
18	50	40,45	44,78	52,51	26,00	27,00	31,00	249,80	268,12	309,81	0,03	0,03	0,03	1,35	1,45	1,72	69,42	76,86	90,12	89,78	93,24	107,05	76,43	82,04	94,79	63,16	61,18	61,18	43,74	46,99	55,58
19	30	51,65	46,64	51,04	19,00	15,00	24,00	278,70	245,92	279,68	0,07	0,07	0,07	3,94	3,41	3,71	88,65	80,05	87,61	65,61	51,80	82,88	85,27	75,24	85,57	136,18	134,21	132,24	127,54	110,40	120,17
20	20	36,93	28,17	48,79	19,00	16,00	23,00	214,61	153,44	285,74	0,08	0,08	0,08	3,05	2,49	4,13	63,39	48,34	83,74	65,61	55,25	79,42	65,66	46,95	87,43	159,87	153,95	161,84	98,91	80,76	133,93
21	20	75,68	75,63	71,82	10,00	21,00	26,00	287,78	329,83	346,09	0,07	0,06	0,05	5,66	4,60	3,70	129,90	129,80	123,27	34,53	72,52	89,78	88,05	100,92	105,89	134,21	114,47	100,66	183,37	149,09	119,89
22	40	102,33	73,26	118,01	52,00	32,00	57,00	548,01	371,62	646,34	0,04	0,04	0,04	4,64	3,33	5,25	175,64	125,74	202,54	179,57	110,50	196,83	167,67	113,70	197,76	80,92	82,89	82,89	150,19	107,85	170,20
23	40	29,29	14,67	7,00	24,00	11,00	6,00	194,68	96,87	46,85	0,03	0,04	0,04	0,96	0,52	0,24	50,26	25,18	12,01	82,88	37,99	20,72	59,57	29,64	14,34	63,16	69,08	69,08	30,95	16,69	7,91
24	50	112,39	107,10	94,07	39,00	34,00	29,00	592,25	541,82	490,48	0,05	0,05	0,05	6,91	6,69	5,81	192,91	183,82	161,46	134,68	117,41	100,14	181,21	165,78	150,07	106,58	102,63	106,58	223,76	216,67	188,20

25	**50**	73,16	88,56	84,78	41,00	44,00	50,00	427,14	505,61	504,42	0,05	0,05	0,05	3,63	4,54	4,25	125,57	152,01	145,52	141,58	151,94	172,66	130,69	154,70	154,34	94,74	92,76	92,76	117,42	147,20	137,59
26	**50**	67,68	102,94	112,46	41,00	39,00	49,00	410,82	549,34	641,31	0,04	0,04	0,04	2,79	5,08	5,50	116,16	176,68	193,02	141,58	134,68	169,21	125,70	168,08	196,22	76,97	84,87	84,87	90,42	164,50	178,01
MEAN		**58,26**	**55,02**	**56,92**	**28,96**	**24,92**	**27,58**	**326,83**	**301,47**	**320,46**	**0,05**	**0,05**	**0,05**	**3,09**	**2,96**	**3,04**	**100,00**	**94,43**	**97,70**	**100,00**	**86,04**	**95,25**	**100,00**	**92,24**	**98,05**	**100,00**	**99,26**	**99,01**	**100,00**	**95,82**	**98,61**

Table 9. Raw data for forehead wrinkles*. Raw and relative data from the 3D analysis of forehead wrinkles at the different time points, for each of the volunteers included in the study.*

17.5 Attachment 5. Raw data – Skin biomechanical properties (Cutometer MPA Dual 580)

Elasticity (R2, %) - RAW DATA																MEAN VALUES			MEAN VALUES TO DAY 0 (%)		
VOL	D0					D42					D84					D0	D42	D84	D0	D42	D84
1	57,9	67,4	63,9	63,4	63,8	46,5	50,5	45,8	48,6	54,5	54,5	54,0	50,3	54,2	55,0	63,28	49,18	53,60	108,7%	84,5%	92,1%
2	56,8	55,7	70,0	61,5	59,3	71,5	65,1	64,2	64,3	74,1	54,3	62,0	56,5	51,8	56,9	60,66	67,84	56,30	104,2%	116,6%	96,8%
3	53,0	59,3	56,4	60,3	54,7	54,4	60,3	58,1	63,8	65,2	54,1	56,5	55,4	52,2	57,6	56,74	60,36	55,16	97,5%	103,7%	94,8%
4	52,7	49,6	56,2	48,7	45,4	53,8	58,1	59,9	51,3	54,5	55,9	48,9	52,4	48,1	51,1	50,52	55,52	51,28	86,8%	95,4%	88,1%
5	68,0	64,0	67,0	61,7	68,4	64,5	70,0	67,1	68,5	70,5	62,3	55,7	64,3	66,2	64,5	65,82	68,12	62,60	113,1%	117,1%	107,6%
6	68,1	69,5	63,9	68,6	67,2	70,1	65,9	65,6	65,5	70,5	65,3	72,4	69,7	68,1	67,4	67,46	67,52	68,58	115,9%	116,0%	117,9%
7	59,6	68,4	70,5	67,1	69,4	48,8	45,4	47,4	49,3	40,5	65,3	63,0	65,7	62,9	65,0	67,00	46,28	64,38	115,1%	79,5%	110,6%
8	61,7	72,2	55,4	62,1	68,0	54,2	48,8	50,6	62,6	55,5	45,9	53,9	47,2	45,6	44,8	63,88	54,34	47,48	109,8%	93,4%	81,6%
9	48,8	51,0	44,2	45,8	44,3	52,2	47,0	59,9	55,6	57,7	54,2	53,6	55,5	49,4	53,3	46,82	54,48	53,20	80,5%	93,6%	91,4%
11	47,6	57,5	56,6	57,2	61,8	50,9	60,2	54,5	53,7	53,6	40,8	46,0	46,6	46,7	54,6	56,14	54,58	46,94	96,5%	93,8%	80,7%
12	64,4	73,7	75,9	65,0	73,5	65,5	57,7	61,7	61,5	59,7	56,4	53,0	58,1	62,4	59,6	70,50	61,22	57,90	121,2%	105,2%	99,5%
13	58,5	61,7	60,5	64,4	57,8	59,0	55,0	60,3	57,0	63,2	51,5	42,8	50,6	46,3	44,0	60,58	58,90	47,04	104,1%	101,2%	80,8%
14	55,3	61,9	46,1	62,6	55,0	56,4	50,9	55,8	53,9	38,8	51,5	53,6	52,3	61,6	52,9	56,18	51,16	54,38	96,5%	87,9%	93,5%
15	51,7	54,0	57,9	56,8	48,4	68,1	68,3	59,5	67,4	52,6	52,9	56,0	61,5	56,1	56,7	53,76	63,18	56,64	92,4%	108,6%	97,3%
17	46,7	51,2	37,0	42,0	55,5	55,9	45,2	56,5	52,5	46,5	60,2	57,5	65,2	62,2	59,0	46,48	51,32	60,82	79,9%	88,2%	104,5%
18	62,4	62,7	60,0	61,6	66,7	64,9	64,8	65,1	64,5	62,3	65,6	62,6	67,6	71,9	53,1	62,68	64,32	64,16	107,7%	110,5%	110,3%
19	61,3	55,1	65,1	63,3	46,8	49,2	48,0	51,9	56,4	46,9	63,7	58,6	55,7	59,6	63,1	58,32	50,48	60,14	100,2%	86,7%	103,3%
20	53,0	56,2	50,9	55,1	52,6	49,7	57,5	53,2	57,8	53,3	60,2	55,0	60,8	49,0	52,8	53,56	54,30	55,56	92,0%	93,3%	95,5%
21	62,5	58,7	57,8	66,3	62,3	55,9	53,3	54,4	54,5	53,0	58,5	56,3	62,9	60,2	52,6	61,52	54,22	58,10	105,7%	93,2%	99,8%
22	51,3	47,8	52,4	52,8	52,9	41,8	42,5	46,8	48,0	51,5	49,0	45,1	51,3	55,9	46,2	51,44	46,12	49,50	88,4%	79,3%	85,1%
23	64,1	67,1	59,0	63,0	64,1	69,6	60,5	59,3	59,1	60,4	62,1	59,4	53,3	59,1	59,8	63,46	61,78	58,74	109,1%	106,2%	100,9%
24	54,5	53,0	52,4	56,9	52,7	57,3	47,3	41,5	50,7	42,7	48,7	46,5	47,4	44,2	40,1	53,90	47,90	45,38	92,6%	82,3%	78,0%
25	52,0	52,2	50,9	54,9	58,0	51,4	49,9	52,4	53,0	58,8	52,2	46,3	51,8	53,6	54,0	53,60	53,10	51,58	92,1%	91,3%	88,6%

26	57,6	60,1	44,1	43,7	55,9	41,7	41,7	46,3	50,6	46,8	50,4	44,9	41,5	41,0	48,1	52,28	45,42	45,18	89,8%	78,1%	77,6%
MEAN	**57,06**	**59,58**	**57,25**	**58,53**	**58,52**	**56,39**	**54,75**	**55,74**	**57,09**	**55,55**	**55,65**	**54,32**	**55,98**	**55,35**	**54,68**	**58,19**	**55,90**	**55,19**	**100,00%**	**96,07%**	**94,85%**

Elastic Recovery (R7, %) - RAW DATA																**MEAN VALUES**			**MEAN VALUES TO DAY 0 (%)**		
VOL	**D0**					**D42**					**D84**					**D0**	**D42**	**D84**	**D0**	**D42**	**D84**
1	36,2	37,1	37,8	35,3	36,1	24,6	28,1	24,6	26,9	31,6	31,5	29,7	26,8	31,8	30	36,50	27,16	29,96	115,4%	85,9%	94,7%
2	30,1	30,6	39,5	33,5	32,3	49,1	38,8	35,3	34,3	45,5	30,4	35,4	34,9	29,8	33,3	33,20	40,60	32,76	105,0%	128,4%	103,6%
3	33,8	35,3	32,2	30,7	30,7	30	33	32,6	36,8	41,4	28,5	30,3	33,3	27,7	30,7	32,54	34,76	30,10	102,9%	109,9%	95,2%
4	26,8	22	27,8	23,3	20	30,1	34	36	31,5	28	31,2	25,1	28,3	23,9	22,4	23,98	31,92	26,18	75,8%	100,9%	82,8%
5	40	35,2	39,3	34,7	40,2	38,9	42,5	42,8	44	43,2	35	32,2	40,3	37,7	39,9	37,88	42,28	37,02	119,8%	133,7%	117,1%
6	36	37,9	33,1	36,4	36,5	44,2	38,5	39,5	38,3	37,4	35,8	41,5	42,5	40,7	39,7	35,98	39,58	40,04	113,8%	125,2%	126,6%
7	39,9	41,8	46	39,6	41,8	28,1	27,6	26,3	26,4	24,8	42,1	37	39,6	38,4	36,8	41,82	26,64	38,78	132,2%	84,2%	122,6%
8	36,2	40	32,8	35,3	37,7	33,2	27,2	26,7	35,3	29,2	25	32,2	23	24	24,4	36,40	30,32	25,72	115,1%	95,9%	81,3%
9	26,5	26,6	21,9	24,2	20,2	28	22,8	32,9	32,7	32,5	28,6	29,6	29	25,7	30,5	23,88	29,78	28,68	75,5%	94,2%	90,7%
11	25,7	33,5	31,8	29,7	37	28,8	33,9	30,5	30	27,5	22,4	25	25,5	25,8	29,3	31,54	30,14	25,60	99,7%	95,3%	81,0%
12	38,2	50	50,3	41,6	46,8	39,20	32,20	39,90	33,80	36,30	32,1	29,2	30,8	37,3	29,5	45,38	36,28	31,78	143,5%	114,7%	100,5%
13	29,6	31	30,2	34,2	29,3	33,5	28,6	33,1	31,2	36,1	26,4	23,8	26,5	24,3	20,6	30,86	32,50	24,32	97,6%	102,8%	76,9%
14	32,2	34,1	24,3	35,2	31,1	31,5	24,7	30,3	30,2	19,8	29,5	29,4	28,6	32,5	28,5	31,38	27,30	29,70	99,2%	86,3%	93,9%
15	27,3	28	33,8	31,7	23,4	36,4	43,3	32,7	31,5	28,5	27,7	29	30,9	30,5	28,6	28,84	34,48	29,34	91,2%	109,0%	92,8%
17	22,9	27,2	18,6	21,2	30,6	30,4	26,6	33,4	31,7	24,1	32	31,5	36,2	31	33,6	24,10	29,24	32,86	76,2%	92,5%	103,9%
18	35,1	35,2	33,6	33,1	36,3	42,7	42,7	41,3	37,7	36	42,5	35,8	40	42,6	32,1	34,66	40,08	38,60	109,6%	126,7%	122,1%
19	33,2	26,9	31,6	30,7	26,3	23,3	23,3	31,1	32	23	30,6	30,4	27,8	31,9	34,5	29,74	26,54	31,04	94,0%	83,9%	98,2%
20	24,6	27,6	25,3	28,8	26,2	25,4	28,2	27,8	31,7	27	33,2	28	30,2	27,1	26,7	26,50	28,02	29,04	83,8%	88,6%	91,8%
21	34,6	31,5	29,8	34,1	33,2	29,3	27,2	27,8	28,8	29,3	34,2	31,4	32,3	31,3	28,2	32,64	28,48	31,48	103,2%	90,1%	99,5%
22	28,4	25,9	26,6	28	28,2	20,5	19,3	25,7	29	29,3	28,9	23,3	27,7	34,1	28,4	27,42	24,76	28,48	86,7%	78,3%	90,1%
23	37,4	40,7	31,8	35,2	35,3	35,6	35,2	32,8	31,5	33,6	38,3	35	26	31,1	32,3	36,08	33,74	32,54	114,1%	106,7%	102,9%

24	27,6	24	26,9	30,2	25,2	28,1	23,7	19,6	27,1	20	24,4	23,2	24,8	22,1	19,3	26,78	23,70	22,76	84,7%	74,9%	72,0%
25	25,1	22,4	26,2	29,6	30,4	29,50	26,40	30,20	27,40	33,80	25,9	22,4	28,2	28,2	29,9	26,74	29,46	26,92	84,6%	93,2%	85,1%
26	25,2	29,3	20,6	21,8	23,8	20,70	20,60	23,20	26,10	22,40	27,9	19,8	15,2	22,1	25,2	24,14	22,60	22,04	76,3%	71,5%	69,7%
MEAN	**31,4**	**32,2**	**31,3**	**31,6**	**31,6**	**31,7**	**30,4**	**31,5**	**31,9**	**30,8**	**31,0**	**29,6**	**30,4**	**30,5**	**29,8**	**31,6**	**31,3**	**30,2**	**100,0%**	**98,9%**	**95,6%**

Fatigue (R9, mm) - RAW DATA																**MEAN VALUES**			**MEAN VALUES TO DAY 0 (%)**		
VOL	**D0**					**D42**					**D84**					**D0**	**D42**	**D84**	**D0**	**D42**	**D84**
1	0,056	0,062	0,052	0,051	0,05	0,047	0,044	0,046	0,055	0,047	0,04	0,051	0,056	0,051	0,056	0,05	0,05	0,05	107,3%	94,7%	100,6%
2	0,069	0,057	0,043	0,044	0,065	0,047	0,043	0,051	0,058	0,059	0,05	0,056	0,051	0,045	0,058	0,06	0,05	0,05	110,1%	102,2%	103,0%
3	0,048	0,06	0,047	0,046	0,063	0,038	0,046	0,052	0,046	0,057	0,04	0,041	0,042	0,05	0,045	0,05	0,05	0,04	104,6%	94,7%	86,3%
4	0,04	0,034	0,05	0,03	0,045	0,03	0,04	0,024	0,049	0,026	0,037	0,046	0,036	0,046	0,048	0,04	0,03	0,04	78,8%	66,9%	84,4%
5	0,068	0,062	0,064	0,057	0,053	0,086	0,068	0,067	0,071	0,072	0,059	0,056	0,06	0,059	0,056	0,06	0,07	0,06	120,4%	144,2%	114,9%
6	0,047	0,05	0,056	0,048	0,06	0,048	0,044	0,056	0,049	0,056	0,039	0,048	0,053	0,051	0,065	0,05	0,05	0,05	103,4%	100,2%	101,4%
7	0,058	0,061	0,051	0,075	0,057	0,034	0,035	0,033	0,03	0,037	0,066	0,077	0,075	0,079	0,068	0,06	0,03	0,07	119,6%	66,9%	144,6%
8	0,035	0,029	0,038	0,042	0,041	0,033	0,034	0,037	0,027	0,035	0,04	0,042	0,05	0,04	0,038	0,04	0,03	0,04	73,3%	65,7%	83,2%
9	0,051	0,065	0,063	0,057	0,063	0,038	0,043	0,042	0,046	0,043	0,039	0,039	0,048	0,055	0,052	0,06	0,04	0,05	118,4%	84,0%	92,3%
11	0,04	0,046	0,053	0,048	0,046	0,045	0,048	0,045	0,048	0,046	0,047	0,05	0,049	0,063	0,054	0,05	0,05	0,05	92,3%	91,9%	104,2%
12	0,042	0,052	0,053	0,05	0,046	0,03	0,04	0,05	0,06	0,04	0,053	0,069	0,067	0,07	0,072	0,05	0,04	0,07	96,2%	82,4%	131,1%
13	0,037	0,038	0,042	0,05	0,042	0,065	0,038	0,046	0,042	0,048	0,032	0,031	0,038	0,036	0,033	0,04	0,05	0,03	82,8%	94,7%	67,3%
14	0,037	0,042	0,044	0,049	0,045	0,037	0,038	0,042	0,039	0,046	0,042	0,046	0,04	0,049	0,051	0,04	0,04	0,05	85,9%	80,0%	90,3%
15	0,043	0,047	0,059	0,034	0,046	0,042	0,044	0,046	0,04	0,045	0,042	0,043	0,043	0,042	0,047	0,05	0,04	0,04	90,7%	85,9%	85,9%
17	0,051	0,044	0,046	0,051	0,04	0,053	0,062	0,059	0,065	0,056	0,042	0,044	0,036	0,053	0,069	0,05	0,06	0,05	91,9%	116,8%	96,6%
18	0,05	0,079	0,061	0,049	0,08	0,03	0,038	0,041	0,051	0,054	0,033	0,039	0,039	0,04	0,049	0,06	0,04	0,04	126,3%	84,8%	79,2%
19	0,045	0,049	0,035	0,029	0,044	0,032	0,034	0,052	0,051	0,047	0,032	0,04	0,053	0,045	0,044	0,04	0,04	0,04	80,0%	85,5%	84,8%
20	0,04	0,038	0,044	0,048	0,05	0,037	0,044	0,043	0,035	0,043	0,029	0,043	0,035	0,033	0,038	0,04	0,04	0,04	87,1%	80,0%	70,5%
21	0,045	0,067	0,066	0,046	0,048	0,041	0,066	0,054	0,051	0,051	0,049	0,051	0,054	0,062	0,066	0,05	0,05	0,06	107,7%	104,2%	111,7%

22	0,059	0,074	0,054	0,064	0,075	0,032	0,043	0,043	0,039	0,046	0,044	0,039	0,058	0,063	0,056	0,07	0,04	0,05	129,1%	80,4%	103,0%
23	0,044	0,05	0,048	0,036	0,042	0,04	0,038	0,035	0,035	0,038	0,033	0,04	0,049	0,069	0,059	0,04	0,04	0,05	87,1%	73,7%	99,0%
24	0,066	0,053	0,045	0,048	0,063	0,037	0,033	0,048	0,048	0,048	0,022	0,038	0,044	0,047	0,049	0,06	0,04	0,04	108,9%	84,8%	79,2%
25	0,046	0,048	0,056	0,056	0,074	0,05	0,05	0,05	0,05	0,06	0,046	0,053	0,063	0,059	0,063	0,06	0,05	0,06	110,9%	105,3%	112,5%
26	0,048	0,035	0,043	0,037	0,057	0,06	0,05	0,04	0,06	0,04	0,041	0,049	0,055	0,05	0,043	0,04	0,05	0,05	87,1%	98,2%	94,3%
MEAN	**0,05**	**0,05**	**0,05**	**0,05**	**0,05**	**0,04**	**0,04**	**0,05**	**0,05**	**0,05**	**0,04**	**0,05**	**0,05**	**0,05**	**0,05**	**0,05**	**0,05**	**0,05**	**100,0%**	**90,3%**	**96,7%**

Firmness (1/R0, mm) - RAW DATA																**MEAN VALUES**			**MEAN VALUES TO DAY 0 (%)**		
VOL	**D0**					**D42**					**D84**					**D0**	**D42**	**D84**	**D0**	**D42**	**D84**
1	0,378	0,366	0,415	0,442	0,38	0,361	0,317	0,378	0,331	0,336	0,35	0,34	0,36	0,34	0,32	2,52	2,90	2,92	103,9%	119,5%	120,1%
2	0,454	0,442	0,504	0,427	0,427	0,348	0,399	0,349	0,391	0,347	0,37	0,40	0,37	0,30	0,36	2,22	2,73	2,80	91,4%	112,3%	115,2%
3	0,364	0,391	0,354	0,361	0,4	0,327	0,355	0,393	0,366	0,336	0,32	0,31	0,33	0,34	0,29	2,67	2,81	3,14	110,1%	115,9%	129,3%
4	0,324	0,354	0,418	0,408	0,394	0,312	0,315	0,239	0,232	0,354	0,30	0,31	0,31	0,31	0,32	2,63	3,44	3,24	108,5%	141,8%	133,4%
5	0,435	0,43	0,419	0,508	0,415	0,411	0,492	0,449	0,462	0,444	0,43	0,40	0,40	0,41	0,47	2,27	2,21	2,37	93,3%	91,2%	97,8%
6	0,436	0,459	0,463	0,47	0,504	0,394	0,41	0,433	0,423	0,426	0,38	0,34	0,37	0,36	0,33	2,14	2,40	2,82	88,3%	98,7%	116,0%
7	0,482	0,488	0,47	0,48	0,538	0,213	0,275	0,217	0,258	0,23	0,41	0,45	0,46	0,45	0,43	2,03	4,19	2,27	83,8%	172,6%	93,6%
8	0,357	0,36	0,372	0,366	0,353	0,325	0,316	0,277	0,246	0,285	0,42	0,40	0,38	0,38	0,34	2,77	3,45	2,61	113,9%	142,1%	107,3%
9	0,373	0,402	0,392	0,404	0,391	0,346	0,36	0,356	0,327	0,317	0,37	0,33	0,37	0,36	0,36	2,55	2,93	2,79	105,0%	120,7%	114,8%
11	0,393	0,424	0,431	0,404	0,459	0,34	0,328	0,374	0,363	0,338	0,42	0,39	0,38	0,33	0,35	2,37	2,87	2,66	97,5%	118,1%	109,7%
12	0,432	0,43	0,433	0,436	0,449	0,37	0,36	0,39	0,46	0,30	0,48	0,50	0,47	0,47	0,47	2,29	2,66	2,11	94,5%	109,7%	86,8%
13	0,311	0,336	0,35	0,351	0,341	0,352	0,367	0,356	0,365	0,357	0,38	0,34	0,35	0,34	0,32	2,96	2,78	2,89	121,9%	114,6%	119,1%
14	0,385	0,436	0,453	0,415	0,418	0,406	0,344	0,396	0,351	0,358	0,33	0,30	0,32	0,39	0,34	2,37	2,70	2,98	97,7%	111,0%	122,6%
15	0,414	0,365	0,423	0,467	0,483	0,426	0,368	0,434	0,359	0,344	0,36	0,41	0,38	0,43	0,43	2,32	2,59	2,49	95,7%	106,6%	102,3%
17	0,42	0,408	0,408	0,48	0,51	0,451	0,425	0,389	0,457	0,468	0,39	0,45	0,40	0,46	0,45	2,25	2,28	2,32	92,5%	94,0%	95,7%
18	0,447	0,486	0,5	0,526	0,465	0,339	0,321	0,392	0,419	0,4	0,35	0,35	0,37	0,36	0,36	2,06	2,67	2,80	85,0%	110,1%	115,5%
19	0,352	0,319	0,358	0,313	0,37	0,424	0,421	0,376	0,403	0,452	0,44	0,47	0,52	0,40	0,43	2,92	2,41	2,21	120,3%	99,2%	91,2%

20	0,362	0,395	0,403	0,379	0,401	0,338	0,375	0,363	0,379	0,349	0,36	0,34	0,31	0,31	0,31	2,58	2,77	3,08	106,1%	114,1%	126,6%
21	0,391	0,435	0,426	0,457	0,474	0,426	0,372	0,331	0,424	0,379	0,35	0,38	0,43	0,42	0,42	2,29	2,59	2,50	94,3%	106,6%	102,8%
22	0,45	0,437	0,454	0,415	0,433	0,38	0,379	0,37	0,331	0,392	0,35	0,32	0,34	0,40	0,33	2,28	2,70	2,87	94,1%	111,2%	118,3%
23	0,367	0,42	0,4	0,324	0,289	0,303	0,301	0,305	0,327	0,34	0,37	0,37	0,40	0,39	0,40	2,78	3,17	2,60	114,4%	130,7%	106,9%
24	0,454	0,434	0,442	0,473	0,484	0,435	0,455	0,474	0,48	0,414	0,45	0,39	0,46	0,46	0,44	2,19	2,21	2,27	90,0%	91,2%	93,3%
25	0,402	0,437	0,42	0,403	0,477	0,36	0,41	0,40	0,41	0,37	0,44	0,39	0,39	0,42	0,43	2,34	2,58	2,41	96,3%	106,2%	99,1%
26	0,376	0,409	0,447	0,389	0,408	0,37	0,39	0,35	0,36	0,34	0,38	0,43	0,41	0,41	0,39	2,46	2,76	2,48	101,5%	113,5%	102,2%
MEAN	**0,40**	**0,41**	**0,42**	**0,42**	**0,43**	**0,36**	**0,37**	**0,37**	**0,37**	**0,36**	**0,38**	**0,38**	**0,39**	**0,39**	**0,38**	**2,43**	**2,78**	**2,65**	**100,0%**	**114,7%**	**109,2%**

Table 10. Raw data for skin biomechanical properties. *Raw and relative data from the skin biomechanical properties in the cheek at the different time points, for each of the volunteers included in the study.*

17.6 Attachment 6. Statistical analysis

One-way ANOVA of Crow's feet Wrinkles – Area (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	-3,650	-39,97 to 32,67	No	ns	0,9630	B	D42	
D0 vs. D84	1,837	-34,48 to 38,15	No	ns	0,9905	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	103,7	-3,650	16,08	24	24	0,2270	69
D0 vs. D84	100,0	98,16	1,837	16,08	24	24	0,1142	69
One-way ANOVA of Crow's feet Wrinkles – Number (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	0,7133	-26,48 to 27,91	No	ns	0,9974	B	D42	
D0 vs. D84	8,076	-19,12 to 35,27	No	ns	0,7271	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	99,29	0,7133	12,04	24	24	0,05924	69
D0 vs. D84	100,0	91,92	8,076	12,04	24	24	0,6707	69
One-way ANOVA of Crow's feet Wrinkles – Perimeter (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	-1,972	-33,08 to 29,13	No	ns	0,9851	B	D42	
D0 vs. D84	3,748	-27,36 to 34,85	No	ns	0,9474	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	102,0	-1,972	13,77	24	24	0,1432	69
D0 vs. D84	100,0	96,25	3,748	13,77	24	24	0,2721	69
One-way ANOVA of Crow's feet Wrinkles – Depth (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	0,2421	-18,02 to 18,50	No	ns	0,9993	B	D42	
D0 vs. D84	-4,111	-22,37 to 14,15	No	ns	0,8303	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	99,76	0,2421	8,085	24	24	0,02994	69
D0 vs. D84	100,0	104,1	-4,111	8,085	24	24	0,5085	69
One-way ANOVA of Crow's feet Wrinkles – Volume (%) – Comparison between timepoints to D0								

Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	A-?		
D0 vs. D42	-1,570	-42,15 to 39,01	No	ns	0,9944	B	D42	
D0 vs. D84	0,9712	-39,61 to 41,56	No	ns	0,9979	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	101,6	-1,570	17,97	24	24	0,08734	69
D0 vs. D84	100,0	99,03	0,9712	17,97	24	24	0,05405	69

Table S1. *Statistical analysis (ordinary one-way ANOVA with Dunnett's multiple comparisons) of results shown in Figure 15.*

One-way ANOVA of Forehead – Area (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	5,573	-30,08 to 41,23	No	ns	0,9134	B	D42	
D0 vs. D84	2,298	-33,36 to 37,95	No	ns	0,9846	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	94,43	5,573	15,79	24	24	0,3530	69
D0 vs. D84	100,0	97,70	2,298	15,79	24	24	0,1456	69
One-way ANOVA of Forehead – Number (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	13,96	-16,70 to 44,61	No	ns	0,4874	B	D42	
D0 vs. D84	4,750	-25,91 to 35,40	No	ns	0,9148	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	86,04	13,96	13,57	24	24	1,028	69
D0 vs. D84	100,0	95,25	4,750	13,57	24	24	0,3499	69
One-way ANOVA of Forehead – Perimeter (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	7,761	-25,90 to 41,42	No	ns	0,8231	B	D42	
D0 vs. D84	1,949	-31,71 to 35,61	No	ns	0,9875	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	92,24	7,761	14,91	24	24	0,5206	69
D0 vs. D84	100,0	98,05	1,949	14,91	24	24	0,1308	69
One-way ANOVA of Forehead – Depth (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	0,7413	-18,63 to 20,11	No	ns	0,9945	B	D42	
D0 vs. D84	0,9871	-18,38 to 20,35	No	ns	0,9903	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	99,26	0,7413	8,576	24	24	0,08643	69
D0 vs. D84	100,0	99,01	0,9871	8,576	24	24	0,1151	69
One-way ANOVA of Forehead – Volume (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	4,175	-33,73 to 42,08	No	ns	0,9558	B	D42	

D0 vs. D84	1,384	-36,52 to 39,29	No	ns	0,9950	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	95,82	4,175	16,78	24	24	0,2488	69
D0 vs. D84	100,0	98,62	1,384	16,78	24	24	0,08247	69

Table S2. *Statistical analysis (ordinary one-way ANOVA with Dunnett's multiple comparisons) of results shown in Figure 16.*

One-way ANOVA of Firmness - 1/R0 (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	-14,65	-24,06 to -5,238	Yes	**	0,0025	B	D42	
D0 vs. D84	-9,150	-15,99 to -2,311	Yes	**	0,0084	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	114,7	-14,65	3,995	24	24	3,667	23
D0 vs. D84	100,0	109,2	-9,150	2,903	24	24	3,152	23
One-way ANOVA of Elasticity – R2 (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	3,925	-2,063 to 9,913	No	ns	0,2319	B	D42	
D0 vs. D84	5,146	-0,4278 to 10,72	No	ns	0,0725	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	99,99	96,07	3,925	2,542	24	24	1,544	23
D0 vs. D84	99,99	94,85	5,146	2,366	24	24	2,175	23
One-way ANOVA of Elastic Recovery – R7 (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	1,129	-7,808 to 10,07	No	ns	0,9376	B	D42	
D0 vs. D84	4,371	-3,223 to 11,96	No	ns	0,3130	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	98,87	1,129	3,794	24	24	0,2977	23
D0 vs. D84	100,0	95,63	4,371	3,224	24	24	1,356	23
One-way ANOVA of Fatigue – R9 (%) – Comparison between timepoints to D0								
Dunnett's multiple comparisons test	**Mean Diff,**	**95,00% CI of diff,**	**Below threshold?**	**Summary**	**Adjusted P Value**	**A-?**		
D0 vs. D42	9,658	0,1834 to 19,13	Yes	*	0,0454	B	D42	
D0 vs. D84	3,317	-5,421 to 12,05	No	ns	0,5806	C	D84	
Test details	**Mean 1**	**Mean 2**	**Mean Diff,**	**SE of diff,**	**n1**	**n2**	**q**	**DF**
D0 vs. D42	100,0	90,34	9,658	4,022	24	24	2,401	23
D0 vs. D84	100,0	96,68	3,317	3,709	24	24	0,8943	23

Table S3. *Statistical analysis (ordinary one-way ANOVA with Dunnett's multiple comparisons) of results shown in Figure 17.*

17.7 Attachment 7. Raw data – Panelist self-assessment

QUESTIONNAIRE AFTER 6 WEEKS (D42)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	17	18	19	20	21	22	23	24	25	26
SENSORY EXPERIENCE																									
1. How much the application of the Bracelet is simple	4	4	4	4	3	1	4	4	4	4	4	4	4	4	4	4	4	3	2	4	4	4	4	4	4
2. How much the appearance of the Bracelet is pleasant	4	4	1	3	3	1	4	4	4	4	4	3	3	4	3	3	4	3	3	4	4	4	3	4	3
3. How much the feeling (texture) of the Bracelet is pleasant	4	4	1	4	3	1	4	4	4	4	3	4	4	4	3	3	4	3	3	4	3	4	4	4	3
4. How much the odor of the Bracelet is pleasant	4	4	1	2	4	3	2	4	3	2	3	3	2	3	1	4	3	3	3	4	2	4	3	4	2
5. How much the design of the Bracelet is attractive	3	4	1	3	3	1	4	4	4	4	3	2	3	4	2	3	4	2	2	3	4	4	3	4	3
TREATMENT EFFECTIVENESS																									
6. My fine lines are smoothed	3	4	1	3	2	2	2	4	3	3	2	2	4	3	2	3	3	2	2	1	3	3	2	2	2
7. My crow's feet / forehead wrinkles appear less visible	3	4	1	3	3	2	2	4	3	3	2	1	4	2	2	3	3	2	2	1	2	3	2	2	2
8. My skin looks younger	3	4	1	4	3	2	1	4	3	3	2	1	4	3	2	3	3	3	3	2	2	2	2	2	2
9. My skin is more hydrated	3	4	1	4	3	1	2	4	3	4	2	2	4	3	2	3	2	3	3	2	2	3	3	3	2
10. My skin seems firmer	4	4	1	3	3	1	2	4	3	4	2	2	4	2	2	2	3	3	3	2	2	2	2	2	2
11. My skin seems more elastic (flexible)	4	4	1	3	3	1	2	4	3	3	2	1	4	2	2	2	3	3	3	2	2	3	2	2	2
12. How much the Bracelet improves your muscle tension	3	4	1	3	2	1	2	4	3	4	2	1	2	2	1	3	2	2	2	2	2	3	1	2	2
13. How much the Bracelet improve your joints flexibility	3	4	1	3	2	2	2	4	4	5	2	1	2	2	1	2	2	3	3	2	1	3	1	2	2
14. How much the Bracelet relieves the pain in the joints	3	4	1	3	1	2	1	3	3	1	2	1	2	2	1	2	2	2	3	2	1	3	1	2	1
15. How much the Bracelet helps you to do your daily tasks	3	4	1	3	1	2	1	3	3	2	2	1	2	2	1	4	2	1	1	1	1	4	1	3	1
16. The treatment improve hair appearance	3	4	1	4	2	2	1	4	3	2	2	1	1	1	1	2	2	2	2	2	2	2	1	2	2
17. The treatment improve nail appearance	3	4	1	3	1	2	1	4	4	2	3	1	2	1	1	2	1	1	2	1	1	2	1	2	2
CONSUMER BEHAVIOUR																									
18. I am satisfied with the tested treatment	3	4	1	4	3	1	2	4	4	4	2	1	4	3	3	3	3	2	2	2	2	3	2	3	2
19. I would use the treatment again	4	4	1	4	3	1	1	4	4	3	2	1	4	2	3	3	3	2	2	2	2	3	2	4	2
20. I would recommend the treatment	4	4	1	4	2	1	1	4	4	3	2	1	4	3	2	3	3	2	2	2	2	3	1	3	2
21. I think the price of the tested treatment should be (€)	30	30	1	25	-	20	1	5	40	20	20	0	30	40	15	20	28	10	10	30	20	15	20	23	12

22. Comments	
1	I notice improvement in my skin
2	It's good
3	I don't like the smell, I find it unpleasant. It opens, it is impossible to keep it attached to the skin.
4	Being able to fix it with something so that you don't have to adjust the wristband every moment. It's soft, it's nice sometimes you forgot you took it.
5	Honestly, if I have had any changes I don't know, the bracelet is not super comfortable, but it can be worn
6	Simple treatment with positive results
7	I haven't noticed anything
8	I liked it a lot
9	I liked the bracelet aesthetically. It has hydrated my face, but I have not noticed any improvement compared to creams used previously. It has kept my face hydrated. For the rest I have not observed any changes. My nails have improved
10	My skin is firm
11	I don't notice any improvement in my skin.
12	I haven't noticed anything
13	I think it works very well for me, the bracelet peels off over time and at first the smell is not pleasant, otherwise I am very happy.
14	I think that over time, it could be more effective.
15	change the smell
16	Excellent
17	The only thing I have noticed are the wrinkles on my face that are a little less visible.
18	At first it smelled quite a bit and was not unpleasant, but after a week the smell was negligible.
19	Poor closure loosens the tension and is uncomfortable.
20	The closure is very uncomfortable, it comes loose easily
21	.
22	I haven't noticed most of the things that are asked. Not noticing it doesn't mean it doesn't work, it just means that I don't notice it.
23	I consider that I have had it for a short time to be able to give a reliable assessment. It would be easier to have before and after photos. Even so, I thought my skin would notice drier and tighter and that hasn't been the case. The general evaluation is positive. tn
24	It's very comfortable
25	I am comfortable wearing the bracelet, although it tends to come loose easily

26	I haven't really noticed any visible changes.

QUESTIONNAIRE AFTER 12 WEEKS (D84)	1	2	3	4	5	6	7	8	9		11	12	13	14	15		17	18	19	20	21	22	23	24	25	26
SENSORY EXPERIENCE																										
1. How much the application of the Bracelet is simple	4	4	4	4	4	4	4	4	3		4	4	4	4	4		4	4	4	4	4	4	4	4	4	3
2. How much the appearance of the Bracelet is pleasant	4	4	4	4	3	4	4	4	4		3	2	3	4	3		3	4	4	3	4	4	4	4	4	2
3. How much the feeling (texture) of the Bracelet is pleasant	4	4	4	4	3	4	4	4	4		3	3	3	4	4		3	3	4	3	4	4	4	4	4	3
4. How much the odor of the Bracelet is pleasant	4	4	1	3	4	3	2	4	3		2	2	2	4	3		3	2	2	3	3	2	4	3	4	2
5. How much the design of the Bracelet is attractive	4	4	1	3	3	4	2	4	4		3	2	3	4	3		3	4	3	3	4	4	4	4	4	2
TREATMENT EFFECTIVENESS																										
6. My fine lines are smoothed	3	4	1	3	2	4	2	3	3		2	3	4	2	2		2	2	3	3	1	2	3	2	2	1
7. My crow's feet / forehead wrinkles appear less visible	3	4	1	3	2	4	2	3	3		2	2	4	2	1		2	2	3	3	1	2	3	2	2	1
8. My skin looks younger	3	4	1	3	2	4	2	3	3		2	3	4	1	1		1	2	3	3	1	2	3	2	2	1
9. My skin is more hydrated	2	4	1	3	3	4	2	3	3		1	3	4	2	1		2	2	3	3	2	2	2	3	3	1
10. My skin seems firmer	3	4	1	4	2	4	2	3	3		1	2	4	1	1		1	2	2	3	2	2	2	2	2	1
11. My skin seems more elastic (flexible)	3	4	1	4	2	4	2	3	3		1	3	3	2	1		2	2	2	3	1	2	3	3	3	1
12. How much the Bracelet improves your muscle tension	3	4	1	4	2	4	1	3	3		2	3	2	1	1		1	3	2	3	1	2	2	2	2	1
13. How much the Bracelet improve your joints flexibility	4	5	1	4	2	4	1	3	4		2	1	2	1	1		1	3	2	2	1	2	3	3	2	1
14. How much the Bracelet relieves the pain in the joints	3	4	1	4	2	4	1	2	3		2	1	2	1	1		1	3	3	2	1	1	2	2	2	1
15. How much the Bracelet helps you to do your daily tasks	3	4	1	4	4	4	1	3	3		1	1	3	1	1		4	3	2	2	1	1	4	2	2	1
16. The treatment improve hair appearance	4	4	1	3	2	4	1	3	3		2	1	2	1	1		2	3	2	3	1	1	2	2	2	1
17. The treatment improve nail appearance	4	4	1	3	2	4	1	3	4		2	1	2	1	1		2	2	3	2	1	1	2	2	2	1
CONSUMER BEHAVIOUR																										
18. I am satisfied with the tested treatment	4	4	1	4	2	4	2	3	4		1	3	4	2	1		2	2	3	3	2	3	2	3	2	1
19. I would use the treatment again	3	4	1	4	2	4	1	3	4		1	2	4	2	1		2	2	3	3	2	3	3	3	3	1
20. I would recommend the treatment	3	4	1	4	2	4	1	3	4		1	1	4	3	1		1	2	3	3	2	3	3	3	2	1
21. I think the price of the tested treatment should be (€)	40	30	1	25	-	30	5	5	40		-	10	40	50	10		10	22	10	15	60	35	15	25	25	8

22. Comments	
1	Comfortable but you have to tighten it as it gets wider
2	None
3	I don't notice anything in fact my skin on my face has just been showered or washed and I look like a lizard. The only relief I have felt was when I put on sunscreen. That improved my tightness and left me looking good. I still have the same or more wrinkles.
4	For dry skin apply the sunscreen two or three times. The bracelet loses its smell in the first few days. The bracelet loses its hardness a little and is comfortable you get used to it. My joints are renewed every morning. Thank you.
5	It is not very comfortable but if the results are good it is better than applying creams
6	Very easy to use bracelet improves the skin
7	The smell the first few days is not pleasant. I have not noticed anything with the treatment
8	Rs nonite
9	When traveling to very cold places a little more hydration on my face would have been nice. In both bracelets after two weeks the washer that holds the excess ulcer broke and it was somewhat uncomfortable since it became loose more easily.
10	
11	My skin is very dry because I was not able to apply any moisturizer during the study.
12	I haven't noticed practically anything.
13	I really liked the bracelet over time it falls apart a little and at first it smells bad but the results on the skin are wonderful
14	No comment
15	I don't see any improvement
16	
17	I haven't noticed any changes
18	At the beginning of the treatment the skin seemed to improve but over time I have not seen any changes.
19	It is comfortable and easy to use
20	It is comfortable to wear it hydrates my skin and I find it more luminous.
21	.
22	It is very comfortable to use but I am not aware of the results.
23	I thought my skin would be drier by not using any moisturizer.
24	On some occasions I have been stung in the area by the heat
25	It tends to loosen easily
26	I have had days with visibly dry and tight skin

17.8 Attachment 8. Raw data and clinical pictures

Original raw data obtained directly from for each of the experimental measurements, are enclosed in a digital file, delivered together with this report, in order to assure full transparency and the traceability of the results.

Original clinical pictures are enclosed in a digital file, delivered together with this report, according to the following folder structure:

HD Macroscopic Pictures

Macroscopic pictures using Nikon D8400 and HeadScan Bench Light Face, as explained in 10.5.3:

- **V1 (Volunteer 1):**
  - 288_01_F000_CP_00. Volunteer 1, cross polarized, front side at D0.
  - 288_01_F000_CP_01. Volunteer 1, cross polarized, front side at D42.
  - 288_01_F000_CP_02. Volunteer 1, cross polarized, front side at D84.
  - 288_01_F000_PP_00. Volunteer 1, parallel polarized, front side at D0.
  - 288_01_F000_PP_01. Volunteer 1, parallel polarized, front side at D42.
  - 288_01_F000_PP_02. Volunteer 1, parallel polarized, front side at D84.
  - 288_01_F000_HP_00. Volunteer 1, half polarized, front side at D0.
  - 288_01_F000_HP_01. Volunteer 1, half polarized, front side at D42.
  - 288_01_F000_HP_02. Volunteer 1, half polarized, front side at D84.
  - 288_01_R045_CP_00. Volunteer 1, cross polarized, right side at D0.
  - 288_01_R045_CP_01. Volunteer 1, cross polarized, right side at D42.
  - 288_01_R045_CP_02. Volunteer 1, cross polarized, right side at D84.
  - 288_01_R045_PP_00. Volunteer 1, parallel polarized, right side at D0.
  - 288_01_R045_PP_01. Volunteer 1, parallel polarized, right side at D42.
  - 288_01_R045_PP_02. Volunteer 1, parallel polarized, right side at D84.
  - 288_01_ R045_HP_00. Volunteer 1, half polarized, front side at D0.
  - 288_01_ R045_HP_01. Volunteer 1, half polarized, front side at D42.
  - 288_01_ R045_HP_02. Volunteer 1, half polarized, front side at D84.
  - 288_01_L045_CP_00. Volunteer 1, cross polarized, left side at D0.
  - 288_01_L045_CP_01. Volunteer 1, cross polarized, left side at D42.
  - 288_01_L045_CP_02. Volunteer 1, cross polarized, left side at D84.

- 288_01_L045_PP_00. Volunteer 1, parallel polarized, left side at D0.
- 288_01_L045_PP_01. Volunteer 1, parallel polarized, left side at D42.
- 288_01_L045_PP_02. Volunteer 1, parallel polarized, left side at D84.
- 288_01_ L045_HP_00. Volunteer 1, half polarized, front side at D0.
- 288_01_ L045_HP_01. Volunteer 1, half polarized, front side at D42.
- 288_01_ L045_HP_02. Volunteer 1, half polarized, front side at D84.

AEVA-HE 3D

1. **Repos**: Black and white images obtained with AEVA-HE system, before processing.
   - V01-L-T0. Volunteer 1, left side, D0.
   - V01-L-T1. Volunteer 1, left side, D42.
   - V01-L-T2. Volunteer 1, left side, D84.
   - V01-R-T0. Volunteer 1, right side, D0.
   - V01-R-T1. Volunteer 1, right side, D42.
   - V01-R-T2. Volunteer 1, right side, D84.

2. **Multiple comparison 3D:** Combination of the 3D reconstructions obtained after processing with AEVA-HE system, for each different side (left or right) and each different time point (D0, D42 and D84).
   - V01-L-T0. Volunteer 1, left side, D0.
   - V01-L-T1. Volunteer 1, left side, D42.
   - V01-L-T2. Volunteer 1, left side, D84.
   - V01-R-T0. Volunteer 1, right side, D0.
   - V01-R-T1. Volunteer 1, right side, D42.
   - V01-R-T2. Volunteer 1, right side, D84.

3. **Extractzone:** Individual 3D reconstruction obtained after processing with AEVA-HE system, indicating in red the Region of Interest (ROI) analyzed.
   - V01-L-T0. Volunteer 1, left side, D0.
   - V01-L-T1. Volunteer 1, left side, D42.
   - V01-L-T2. Volunteer 1, left side, D84.
   - V01-R-T0. Volunteer 1, right side, D0.

- V01-R-T1. Volunteer 1, right side, D42.
- V01-R-T2. Volunteer 1, right side, D84.

4. **Texture:** Black and white images of the Region of Interest (ROI), obtained with AEVA-HE system, before processing.
   - V01-L-T0. Volunteer 1, left side, D0.
   - V01-L-T1. Volunteer 1, left side, D42.
   - V01-L-T2. Volunteer 1, left side, D84.
   - V01-R-T0. Volunteer 1, right side, D0.
   - V01-R-T1. Volunteer 1, right side, D42.
   - V01-R-T2. Volunteer 1, right side, D84.

5. **Topographies extracted area:**

I. Crow's feet wrinkles

a. **Wrinkles analysis**: Images showing the wrinkles analysis detected by the AEVA-HE system after the threshold plane object detection module processing. The multiple timepoints (D0, D42 and D84) comparison is also included.
   - ValleyTHRESH_V01-Crowsfeet-L/R-. Volunteer 1, left/right side.

b. **3D ROI**: Images showing the surface structure detected by the AEVA-HE system after processing. The multiple timepoints (D0, D42 and D84) comparison is also included.
   - Topo_V01-Crowsfeet-L/R-. Volunteer 1, left/right side.

II. Forehead wrinkles

a. **Wrinkles analysis**: Images showing the wrinkles analysis detected by the AEVA-HE system after the threshold plane object detection module processing. The multiple timepoints (D0, D42 and D84) comparison is also included.
   - ValleyTHRESH_V01-Forehead-L/R-. Volunteer 1, left/right side.

b. **3D ROI**: Images showing the surface structure detected by the AEVA-HE system after processing. The multiple timepoints (D0, D42 and D84) comparison is also included.
   - Topo_V01-Forehead-L/R-. Volunteer 1, left/right side.

17.9 Attachment 9. Informed consent

CONSENTIMIENTO INFORMADO DE PARTICIPACIÓN EN EL ESTUDIO DE INVESTIGACIÓN COSMÉTICA DC.288.36.077

${nombreyapellidos}** con DNI **${dni_contacto} he sido invitado a participar en el estudio DC.288.36.077 de investigación cosmética, el cual será llevado a cabo por Dermaclaim Lab S.L., CIF: B16909699, con sede fiscal en Parc Cientific de la Universitat de Valencia, Calle Catedràtico Agustín Escardino Benlloch, 9, 46980 Paterna (Valencia).

El objetivo de este consentimiento informado es que usted reciba la información correcta y suficiente para que pueda evaluar y juzgar si quiere o no participar en el estudio. Para ello, lea esta hoja informativa de atención y nosotros le aclararemos las dudas que le puedan surgir al respecto.

Debe saber que su participación en este estudio es voluntaria y que puede decidir no participar y retirar el consentimiento en cualquier momento, sin que por ello se altere la relación con Dermaclaim Lab S.L.

OBJETIVO DEL ESTUDIO

El objetivo principal del estudio es evaluar los efectos beneficiosos para la piel de una pulsera con liberación controlada de Colágeno. Para ello, se tomarán las medidas necesarias para cuantificar las arrugas y la firmeza y elasticidad de la piel.

Además, como objetivo secundario, se obtendrá información subjetiva de la percepción de los voluntarios sobre la eficacia del producto, mediante un cuestionario de evaluación.

FUNCIONAMIENTO

Esta nueva tecnología funciona mediante el contacto directo con la piel. Los principios activos se liberan de forma controlada, de forma que una pulsera pueda ofrecer tratamiento durante semanas. Contiene péptidos de colágeno hidrolizado y aceite de semilla de granada, que mejoran la calidad de la piel y el aspecto de las arrugas, entre otros beneficios.

Para poder valorar su efecto de forma apropiada, es **imprescindible dejar de usar cualquier otro cosmético** o producto de la piel, a **excepción de protector solar.** Es la única manera de relacionar unos efectos positivos con un solo producto de estudio, ya que de otra manera podrían deberse a otro producto o rutina.

MODO DE USO

Deberá llevar puesta una pulsera 24 horas durante la duración del estudio. Es resistente al agua, al sudor, al calor... por lo que no deberá preocuparse por quitársela. Una vez puesta correctamente, puede olvidarse de ella.

Es más, **solo funciona cuando está en contacto directo con la piel**, por lo que no debe quedar mucho espacio entre su muñeca y la pulsera.

Por las mañanas, debe aplicar **PROTECTOR SOLAR obligatoriamente** a primera hora, aunque la exposición al sol vaya a ser mínima.

Puede mantener sus hábitos de maquillaje (a excepción de los días de visita), siendo el último paso TRAS EL PROTECTOR SOLAR y recordando desmaquillarse correctamente al finalizar el día. Una higiene diaria y específica del rostro es muy importante para el cuidado de la piel.

Importante: Debe evitar una exposición directa e intensa el sol durante el estudio en la medida de lo posible. Además del SPF puede utilizar gorro, gorra o gafas de sol siempre que se exponga al sol, aunque sea de forma leve.

CONTRAINDICACIONES

No utilizar en niños, embarazadas o mujeres lactantes.

Duración de Tratamiento y Medidas

Duración del tratamiento: 84 días

Medidas: 3 visitas

1) Inicial (Día 0): 6 SEPTIEMBRE
2) Intermedia: 18 OCTUBRE
3) Final (Día 84): 29 NOVIEMBRE

OBLIGACIONES

- **No aplicar ningún producto cosmético** sobre el rostro durante la duración del estudio.
- No aplicarse ningún otro dispositivo ni tomar fármacos destinados a la mejora de la salud de la piel, ni complejos vitamínicos que puedan tener ese efecto.
- No llevar cabo ningún tratamiento/proceso estético que pueda interferir en el aspecto del rostro (**microblading en labios o cejas, extensiones de pestañas, peeling clínico, etc**).
- Ponerse en contacto con Dermaclaim en caso de duda, molestia o cambio que perjudique al correcto funcionamiento del estudio.
- Completar los cuestionarios en la fecha indicada.
- Acudir a las visitas con el ROSTRO LIMPIO (con agua y jabón facial) desde 2 horas antes.

Compensación económica

- En el caso de completar el estudio siguiendo las indicaciones correspondientes, recibirá una compensación económica de 60€.

  *La compensación económica se recibirá vía transferencia bancaria al finalizar el tratamiento si se han cumplido todas las condiciones de estudio, lo cual puede detectarse con el control de consumo y los resultados analizados en clínica.

3

Persona de contacto durante el estudio

Lucía Fernández Gómez, Clinical Project Manager

clinica@dermaclaim.com +34 644 03 50 20

CONSENTIMIENTO INFORMADO DE PARTICIPACIÓN

Yo, **${nombreyapellidos}** a fecha **${fecha_hoy}**:

- He recibido suficiente información sobre el estudio y he comprendido la información que se me ha facilitado.
- He podido hacer preguntas sobre el estudio a las personas responsables del mismo.
- Comprendo que mi participación es voluntaria.
- Confirmo que los datos personales aportados son ciertos, soy mayor de 18 años y capaz de firmar un contrato jurídicamente vinculante.
- Autorizo a Dermaclaim Lab S.L. a comunicarse conmigo por los medios que consideren oportunos.

17.10 Attachment 10. Informed consent for clinical pictures

1

AUTORIZACIÓN DE CESIÓN DE DERECHOS DE IMAGEN PARA EL ESTUDIO DE INVESTIGACIÓN COSMÉTICA DC.288.36.077

${nombreyapellidos}** con DNI **${dni_contacto} ha sido invitado a participar en el estudio DC.288.36.077 de investigación cosmética, el cual será llevado a cabo por Dermaclaim Lab S.L., CIF: B16909699, con sede fiscal en Parc Cientific de la Universitat de Valencia, Calle Catedràtico Agustín Escardino Benlloch, 9, 46980 Paterna (Valencia).

Debe saber que la cesión de los derechos de imagen en este estudio es voluntaria y que puede decidir no autorizarlo, sin que por ello se prohíba su participación en el estudio.

Autorización de cesión de derechos de imagen

Al amparo de lo dispuesto en la Ley Orgánica 1/1982, de 5 de Mayo, de protección civil del derecho al honor, a la intimidad personal y familiar y a la propia imagen, como parte del estudio citado y en la hipótesis de una futura explotación publicitaria del tratamiento analizado:

Yo, **${nombreyapellidos}** a fecha **${fecha_hoy}** autorizo la reproducción y difusión de las mencionadas imágenes, o partes de las mismas con las siguientes condiciones:

- La cesión se efectúa a título gratuito, de manera que el cedente no recibe contraprestación alguna a cambio de la cesión de sus derechos de imagen.
- El promotor únicamente podrá identificarme por mi código de voluntario y no tendrá acceso a mis datos personales.
- Para marketing y publicidad, con la única salvedad y limitación de aquellas utilizaciones o aplicaciones que puedan atentar al derecho al honor en los términos previsto en la Ley Orgánica 1/1982.

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FT-03-05 | Rev.00

17.11 Attachment 11. AEVA-HE technical datasheet

DATASHEET

EOTECH
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AEVA-HE 190662
5.0 Megapixel

System

Object	3D metrology system	EOTECH reference	2021-050-2525 and 2021-050-2526
Manufacturer	AICON 3D Systems GmbH	Customer reference	-
Type	Aeva^{3D}-HE	Identification number	Eotech-P127
Serial number	AE190662	Ordering customer	Dermaclaim

Configuration

Sensor	Existing measuring ranges		AEHE190662-S	AEHE190662-L
	Field of view (diagonal)	[mm]	110	250
Camera	Camera type		Manta G-507B	
	Camera	#	50-0503448429 | 50-0503448430	
	Digitization (X, Y)	[pixel]	2464 x 2056	
	Camera connection		GigE	
	Pixel size (X, Y)	[mm]	0.030	0.075
	X, Y resolution (interpolated)	[µm]	30	75
	Camera shutter	[ms]	0.06 ... 15, default 10, grey panel	0.06 ... 15.04, default 0.66
	Camera angle	[degree]	+18° | -11°	
	Camera aperture**	[f | number]	4+ | 4+	4+ | 4+
	Camera focal distance	[mm]	50 | 50	25 | 25
	Intermediate ring	[mm]	5 | 5	- | -
Projector	Projector	#	ASN190662	
	Projector light source		LED White, cyan filer	
	Projector pattern		-	
	Projector angle	[degree]	0°	
	Projector aperture**	[f | number]	5.6	4+
	Projector focal distance	[mm]	25	25
	Intermediate ring	[mm]	-	-
	Filter		Schneider BG 39	
Characteristics	Weight	[kg]	4.1 (LED)	
	Maximum field of view	[mm²]	90 x 70	200 x 150
	Depth of measuring volume	[mm]	50	120

Abbreviations on the lenses (system seen from the rear side): CR = Camera Right | CL = Camera Left | P = Projector
** The scaling of lens apertures are photographic standard f-stops

System components

Software	Application	AEVA V4	
	Dongle ID	980115R31	
	License	HASP dongle based	
Calibration tools for model based calibration	Calibration plates	-	
Equipment	opto*LINK* II	#	ASN210092
	Camera color	#	17475048
	Bench VTOP 500 LED option	#	1903-06
	4M-CAL-EOT	#	
	Step Gauge holder	YES	
	System cable	[m]	4.5
	USB cable	[m]	1.8
Computer configuration	HP Z2 G4	CZC116BGW8	
	Graphic card	NVIDIA Quadro P2200	
	Hard Drive	PCIe SSD 1 To Zturbo drive	
	Processor	I7 10700K 3.8 GHz	
	RAM	32 Go	
	Cameras board	Intel Ethernet I350-T2 Dual Port	
	Operating system	**Microsoft Windows 10 x64** Pro EN	

EOTECH
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EOTECH SA
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17.12 Attachment 12. AEVA-HE calibration report

MAINTENANCE REPORT AEVA-HE²

EOTECH
more for science

Date : 31 January 2023.
Eotech reference : 23-950-2659.
Customer reference : Upon signed agreement as of 13/01/2023.

1) IDENTIFICATION :

- System : **AEVA-HE²**
- Serial number : **AEHE190662**
- Customer : **DERMACLAIM**
- User : **Mr. David GONZALEZ FERNANDEZ**

- Visit date : **31st January 2023.**
- Operator : **Gabriel KOËLLER**

2) USED HARDWARE :

- Calibration plate for Aeva-HE system FOV S, n° #1906_100.
  Calibration certificate n° CER210112 dated 24/02/2021.
- Calibration plate for Aeva-HE system FOV L, n° #1906_200.
  Calibration certificate n° CER210113 dated 24/02/2021.
- Calibration plate for Aeva-HE system FOV XL, n° #2026_L_400.
  Calibration certificate n° CER210115 dated 25/02/2021.
- Depth sample (step gauge) 4M-CAL-ETC, n°24010-10.
  Grooves 50µm, 100µm, 500µm and 900µm.
  Calibration report n°20220028 dated 07/09/2022.

3) CALIBRATION :

- Calibration of the 3 configurations of the Aeva-HE system :
  - AEHE190662-S
  - AEHE190662-L
  - AEHE190662-XL

- Hardware : Calibration plates.

- "MBC" method : calibration by detection of the gravity centers of the calibration plate targets at different positions and comparison to the photogrammetric measurement of the calibration plate.

- The results of the statistical analysis of the calibration are recorded into the files AE180469-S.TST, AE180469-HE-160.TST, AE180469-L.TST, AE180469-XL.TST.

EOTECH SAS, 1 ZI du fond des prés – 91460 Marcoussis – France – Tel. +33 (0) 164 497 130 – www.eotech.fr
Au capital de 100 000 € – code NACE 4669B – RCS 39038204200021 – TVA FR51390382042

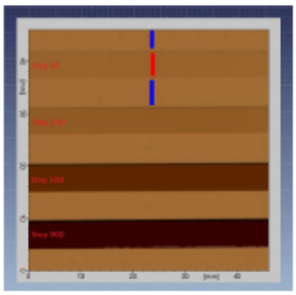
- **Results :**

Sensor	Specifications (µm)	Result (µm)
AEHE190662-S	dxMax=15 dyMax=15 dzMax=15 dsMax=15	**dx = 4.18** **dy = 4.14** **dz = 6.05** **ds = 8.44**
AEHE190662-L	dxMax=25 dyMax=25 dzMax=25 dsMax=25	**dx = 7.04** **dy = 7.93** **dz = 7.16** **ds = 12.79**
AEHE190662-XL	dxMax=45 dyMax=45 dzMax=45 dsMax=45	**dx = 18.86** **dy = 15.85** **dz = 31.05** **ds = 39.64**

4) SPECIFICATIONS AND PERFORMANCES:

4-1 Vertical measurement exactness check :

- Hardware : Depth sample 4M-CAL-ETC.
- Method :
  - Put the sample at the working distance with the corner reference being oriented on top right (horizontal grooves).
  - Adjust the operating distance (focus).
  - Center the sample: horizontally with help of the center holes matching the vertical central line on the video image; vertically in order to be able to measure the depth grooves.
  - Process the surface topography with plane compensation calculated using automatic selection of top surface of the topography.
  - Automatic selection of the areas close to the center of the sample and corresponding to the top of the step to evaluate, and then of the area at the bottom of the step.



  - Calculation of the step height by difference of the mean heights top / bottom of the groove.

- Repeat these steps for each groove of the step gauge and each configuration of the instrument.

- **Results :**

Sensor	Specifications (µm)	Measured (µm)
AEHE190662-S	61.4 ±10 120.9 ±10 515.5 ±10 910.0 ±10	**62.9** **122.9** **518.1** **911.2**
AEHE190662-L	61.4 ± 15 120.9 ± 15 515.5 ± 15 910.0 ± 15	**63.3** **123.0** **517.1** **910.0**
AEHE190662-XL	515.5 ±20 910.0 ±20	**513.5** **909.0**

4-2 Horizontal measurement exactness check :

- Hardware : Calibration plate.

- Method :
  - Put the plate at the plane 0 (center of measurement volume).
  - Set the sensor distance and center the calibration plate.
  - Launch the function "Check XY" from the Calibration taskbar.
  - Note the distances values.
  - Repeat these steps for each configuration of the instrument.

- **Result :**

Sensor	Reference points	Specifications (mm) +/- 1 pixel (mm)	Measured (mm)
AEHE190662-S	**10 - 11** **10 - 13**	31.0060 ± 0.030 30.9939 ± 0.030	**30.9937** **30.9854**
AEHE190662-L	**20 - 21** **20 - 23**	61.9744 ± 0.069 61.9929 ± 0.069	**61.9579** **61.9736**
AEHE190662-XL	**40 - 41** **40 - 43**	124.0950 ± 0.138 123.9951 ± 0.138	**124.1222** **124.0028**

MAINTENANCE REPORT
Author: GabrielKOËLLER
Date : 31 janvier 2023

5) MISCELLANEOUS

- Minor Aeva V4 software update to version 4.1.02, not activated because of currently running studies.
- AEVA-HE² : Installation of an additional FOV XL.
- VisioTOP 500 : Tightening of the head rest device.
- Arrangement of cables and advice.
- Check of step gauge #40012-4 : Conform.
  Results :

Filename	Step Nominal	Step Measured
4MCALETC_400124-Step50-	56.8µm ± 10 µm	55.9µm
4MCALETC_400124-Step100-	101.6µm ± 10 µm	101.4µm
4MCALETC_400124-Step500-	503.9µm ± 10 µm	503.7µm
4MCALETC_400124-Step900-	900.2µm ± 10 µm	900.1µm

For Eotech :

Gabriel KOËLLER

17.13 Attachment 13. CameraScan software calibration report

1

INTERNAL CALIBRATION

Manufacturer's name: Orion TechnoLab Concept

Manufacturer's address: 56 rue de Suède 37100 Tours, France

Software: FrameScan V4

Equipment: Professional photography studio setup

- *Camera Nikon D5600 24 Mpx + objective 40mm macro-2.8.*
- *HeadScan Bench Light Face (Orion Concept)*
- *Vinsetto Table with automatic adjustable height*
- *Flash Leds 2x2 white led spots 4000°K, IRC95*
- *Flashes Xenon 2 Elinchrom 400, drived by the camera*
- *Automatic polarization gelatin filter wheel of camera flashes.*

CALIBRATION PROCEDURE

The software for image analysis and the components of the professional photography studio are calibrated using an official colochart, provided by the manufacturer (Orion TechnoLab), mounted in the HeadScan Bench Light Face. This colorchart offers 24 different color-targets which cover different color tones. The Camera setting are adjusted to get specific RGB values for white and grey targets and these values are settled as **Calibration Standards:**

	Red	Green	Blue
CP White	237	228	223
CP Gray	203	191	186
PP White	243	232	227
PP Gray	216	201	194
HP White	243	233	226
HP Gray	209	194	189

CROSS-POLARIZED **PARALLEL POLARIZED**

The calibration is made by RGB color image detection in the color target. RGB value are selected using a color dropper. The difference between the RGB values and the Calibration Standard should be less than 3% in order to consider the equipment as "Calibrated".

Target	Red Channel	Green Channel	Blue Channel	Difference (%)		
White CP	239	228	226	-0,8	0,0	-1,3
White PP	241	230	224	0,8	0,9	1,3
Grey CP	206	197	190	-1,5	-1,6	-2,2
Grey PP	212	197	190	1,9	2,0	2,1

CLINICAL PROJECT MANAGER

Lucía Fernández Gómez, MSc 05/05/2023

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FT-RH-01 | Rev.00

17.14 Attachment 14. Courage-Khazaka calibration report

CHECK CALIBRATION CERTIFICATE

Manufacturer's name: **Courage + Khazaka electronic GmbH**

Manufacturer's address: **Mathias-Brüggen-Straße 91**
50829 Köln, Germany
++ 49 221 - 956499 - 0
++ 49 221 - 956499 - 51

Probe: Name: **Cutometer**

S/N: **21366253**

Cutometer *calibration* *

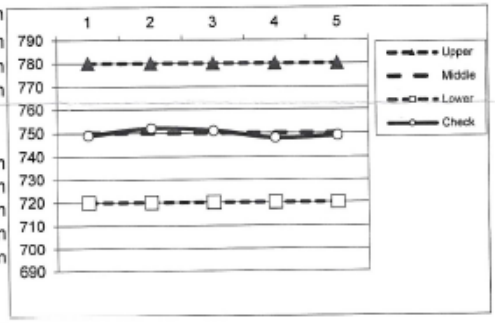
The device calibration is done according to the device calibration procedure AACTCHK750 and with the *working measurement standard** supplied by the Courage-Khazaka electronic GmbH (Germany) Quality Assessement Laboratory.

The penetration depth is measured within an *indication interval** from 0 µm to 2500 µm.
The *working measurement standard* is 750 µm ±30 µm long under the standard environmental conditions to run the device calibration:
- Temperature 20 ±5°C
- Relative humidity: 50 ±10%

Cutometer calibration check

*nominal value**		750,0	µm
*uncertainty**	±	30,0	µm
Upper limit:		780,0	µm
Lower limit:		720,0	µm

n	Check	
1	749	µm
2	752	µm
3	751	µm
4	748	µm
5	749	µm



measurement result*

average :		749,8	µm
standard deviation (<= 3) :		1,6	µm
uncertainty (3sigma)	±	4,9	µm
pass/ fail:		pass	
valid until:		15.9.2022	

average	± uncertainty	± 3 sigma = 99% interval for *true value**
749,8 µm	+30,2 µm	+4,9 µm = 784,9 µm
	-29,8 µm	-4,9 µm = 715,1 µm

*) International vocabulary of metrology – Basic and general concepts and associated terms (VIM) JCGM 200:2012

Cologne, 15.09.2021 In charge of product check calibration: DEC