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Three-Dimensional Periocular Morphometry of Populations in the European Region

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DEDICATION

To my beloved parents

Yubin Ju and Hong Chen

who never stopped believing and supporting me to become a good doctor.

And to my future patients

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ABBREVIATIONS

3D	three-dimensional
2D	two-dimensional
VAM	VECTRA Analysis Module
En	Endocanthion, inner commissure of the palpebral fissure
Ex	Exocanthion, outer commissure of the lower and upper eyelash roots of the palpebral fissure
Pc	Pupillary center
Pm	Medial pupillary margin point horizontal to pupillary center
Pl	Lateral pupillary margin point horizontal to pupillary center
Lm	Medial corneoscleral limbus point horizontal to pupillary center
Ll	Lateral corneoscleral limbus point horizontal to pupillary center
Em	Inferior margin point of the medial eyebrow end (sometimes locates at the same place with EEn)
Em'	middle point of the medial eyebrow end
Em''	superior margin point of the medial eyebrow end
EEn	Inferior margin point of eyebrow vertical to En
EEn'	middle point of eyebrow vertical to En
EEn''	superior margin point of eyebrow vertical to En
Um	Middle point between En and Lm' at the upper palpebral margin on the lash roots
Um'	Middle point between En and Lm'' at the lower palpebral margin on the lash roots
EUm	Point vertical to Um at the inferior margin of eyebrows
EUm'	middle point vertical of eyebrows to Um
EUm''	superior margin point of eyebrows vertical to Um
Lm'	Point vertical to Lm at the upper palpebral margin on the lash roots
Lm''	Point vertical to Lm at the lower palpebral margin on the lash roots
ELm	Point vertical to Lm at the inferior margin of eyebrows
ELm'	middle point of eyebrows vertical to Lm
ELm''	superior margin point of eyebrows vertical to Lm
Ps	Palpebrale superioris, Point vertical to Pc at the upper palpebral margin on the lash roots
Pi	Palpebrale inferioris, Point vertical to Pc at the lower palpebral margin on the lash roots
EPs	Point vertical to Pc at the inferior margin of eyebrows

EPs'	middle point of eyebrows vertical to Pc
EPs''	uperior margin point of eyebrows vertical to Pc
Ll'	Point vertical to Ll at the upper palpebral margin on the lash roots
Ll''	Point vertical to Ll at the lower palpebral margin on the lash roots
ELl	Point vertical to Ll at the inferior margin of eyebrows
ELl'	middle point of eyebrows vertical to Ll
ELl''	superior margin point of eyebrows vertical to Ll
Ul	The middle between Ex and Ll' at the upper palpebral margin on the lash roots
Ul'	The middle between Ex and Ll'' at the lower palpebral margin on the lash roots
EUl	Point vertical to Ul at the inferior margin of eyebrows
EUl'	middle point of eyebrows vertical to Ul
EUl''	superior margin point of eyebrows vertical to Ul
EEx	Point vertical to Ex at the inferior margin of eyebrows
EEx',	middle point of eyebrows vertical to Ex
EEx''	superior margin point of eyebrows vertical to Ex
EExl	Point vertical to Ex at the inferior margin of eyebrows in lateral view
EExl'	middle point vertical to Ex of eyebrows in lateral view
EExl''	superior margin point vertical to Ex of eyebrows in lateral view
El	inferior margin of the lateral eyebrow end
El'	middle point of the lateral eyebrow end
El''	superior margin point of the lateral eyebrow end
PFW	Palpebral fissure width
PFH	Palpebral fissure height
EEnD_I	Eyebrow-endocanthion distance of the inferior point
EEnD_M	Eyebrow-endocanthion distance of the middle point
EEnD_S	Eyebrow-endocanthion distance of the superior point
EPDm_I	Eyebrow-palpebral margin distance (medial) of the inferior point
EPDm_M	Eyebrow-palpebral margin distance (medial) of the middle point
EPDm_S	Eyebrow-palpebral margin distance (medial) of the superior point
ELmD_I	Eyebrow-palpebral margin distance (medial limbus) of the inferior point
ELmD_M	Eyebrow-palpebral margin distance (medial limbus) of the middle point
ELmD_S	Eyebrow-palpebral margin distance (medial limbus) of the superior point
EPD_I	Eyebrow-palpebral margin (Ps) distance of the inferior point (similar to upper lid height)
EPD_M	Eyebrow-palpebral margin (Ps) distance of the middle point
EPD_S	Eyebrow-palpebral margin (Ps) distance of the superior point
ElD_I	Eyebrow-palpebral margin distance (lateral limbus) of the inferior point

ElID_M	Eyebrow-palpebral margin distance (lateral limbus) of the middle point
ElID_S	Eyebrow-palpebral margin distance (lateral limbus) of the superior point
EPDl_I	Eyebrow-palpebral margin distance (lateral) of the inferior point
EPDl_M	Eyebrow-palpebral margin distance (lateral) of the middle point
EPDl_S	Eyebrow-palpebral margin distance (lateral) of the superior point
EExD_I	Eyebrow-exocanthion distance of the inferior
EExD_M	Eyebrow-exocanthion distance of the middle point
EExD_S	Eyebrow-exocanthion distance of the superior point
ID	Iris diameter
PuD	Pupil diameter
PEn	Pupil center-endocanthion distance
LEn	Medial limbus-endocanthion distance
PEx	Pupil center-exocanthion distance
LEx	Lateral limbus-exocanthion distance
EnD	Inner intercanthal distance
ExD	Outer intercanthal distance
PD	Interpupillary distance
UPML	Upper palpebral margin length
LPML	Lower palpebral margin length
EL_I	Inferior eyebrow length
EL_M	Middle eyebrow length
EL_S	Superior eyebrow length
MCA	Medial canthal angle
LCA	Lateral canthal angle
CT	Canthal tilt
UA	Upper eyelid area
UV	Upper eyelid volume

1. DEUTSCHE ZUSAMMENFASSUNG

Für Patienten, die eine periokulare Operation benötigen, ist es entscheidend, die Abweichung der individuellen Gesichtsmorphologie vom normalen Zustand zu quantifizieren. Daher ermöglicht die Sammlung und Festlegung eines Datensatzes periokularer morphometrischer Messungen bei normalen Personen eine bessere Visualisierung und Quantifizierung der erwarteten Veränderungen im Rahmen des präoperativen Operationsplans und der postoperativen Veränderungen während der Nachuntersuchung. Die neueste Generation von dreidimensionaler (3D) digitaler stereoskopischer Fotogrammetrieausrüstung ermöglicht eine schnelle Erfassung der gesamten Gesichtsfläche in einem vollständig nicht-invasiven, hochauflösenden Modus, und die Genauigkeit und Präzision ihrer Bilder für anthropometrische Messungen ist mittlerweile gut etabliert.

Diese Studie zielt darauf ab, eine standardisierte Datenbank dreidimensionaler periokularer Messungen von Kaukasiern/Asiaten zu etablieren, die eine Standarddatenreferenz für verschiedene Arten therapeutischer und kosmetischer plastischer Operationen für alle Altersgruppen, Geschlechter und mehrere Ethnien bietet, die die Operationsplanung unterstützt und den Umfang der Operation abschätzt. Insgesamt wurden 369 Freiwillige an der Augenklinik der Universität zu Köln rekrutiert, im Alter zwischen 18,14 und 85,24 Jahren, darunter 304 Kaukasier und 65 Asiaten, 147 Männer und 222 Frauen. Von allen Teilnehmern wurden Bilder in neutraler Kopfposition aufgenommen. Insgesamt wurden 47 anthropometrische Landmarken der periokularen Region digital identifiziert und 42 Messungen an jedem Auge mit dem VECTRA-Analysemodul durchgeführt.

Für Augenbrauen gab es bilateral keine signifikanten Unterschiede, und sie ändern sich auch nicht signifikant mit dem Alter ($p>0.05$). Die Länge tendierte dazu, mit dem Alter kürzer zu werden, Männer hatten im Vergleich zu Frauen längere und breitere Augenbrauen ($p<0.001$); die Position nahm zwischen 18-40 Jahren ab, zwischen 60-70 Jahren zu, und war in anderen Altersgruppen relativ stabil, und Asiaten hatten insgesamt eine höhere Augenbrauenposition im Vergleich zu Kaukasiern.

Für augenbezogene Parameter hatten Kaukasier signifikant größere Spaltbreite der Augenlider, Höhe und Länge des unteren Augenlids, Irisdurchmesser, Pupillenzentrum/Nasenlimbus-mediale Kanthus-Distanz, lateraler Kanthuswinkel und Kanthalneigung ($p<0.001$,bzw.); Asiaten hatten längere obere Augenlider, Pupillendurchmesser und Interpupillar-/Intermediale Kanthus-/Interlaterale Kanthus-Distanzen und größere mediale Kanthuswinkel ($p<0.001$ bzw.). Zwischen den Geschlechtern hatten Männer eine größere Spaltbreite der Augenlider und Höhe, Irisdurchmesser, Pupillendurchmesser, Interpupillarabstände, Pupillenzentrum/Lidrand-mediale und laterale Kanthus-Distanzen, Interkanthus-Distanzen sowie obere und untere Lidränder; Frauen hatten größere mediale und laterale Kanthuswinkel und größere obere Lidbereiche ($p<0.001$, bzw.).

Mit dem Alter traten Parameteränderungen hauptsächlich vor dem 50. Lebensjahr und zwischen 60-70 Jahren auf. Die Länge der oberen und unteren Augenlider, die Spaltbreite und Höhe der Augenlider nahmen mit dem Alter ab, und das mediale Kanthus nahm mit dem Alter ab und war bei Frauen offensichtlicher ($p<0.001$,bzw.). Der Interpupillarabstand nahm mit dem Alter zu und war bei Männern offensichtlicher, während die Veränderungen zwischen den Kanthi bei Frauen signifikanter waren.

Diese Studie beschreibt die Verteilung und altersabhängigen Trends von Distanz-, Krümmungs-, Winkel-, Flächen- und Volumenparametern im Zusammenhang mit Augenbrauen und periokularer Region in einer multiethnischen, multialtersbezogenen Bevölkerung in der europäischen Region und vergleicht die Unterschiede zwischen Ethnien, Geschlechtern, Altersgruppen und Binokularen, wobei sie die Ergebnisse zuvor veröffentlichter Studien weiter ergänzt. Die anthropometrischen Daten unterstützen bei der Operationsplanung und ermöglichen eine quantitative Bewertung der chirurgischen Ergebnisse.

2. SUMMARY

For patients requiring periocular surgery, it is essential to quantify the deviation of the individual's facial morphology from the normal state. Therefore, collecting and establishing a dataset of periocular morphometric measurements in normal individuals will enable better visualization and quantification of the expected changes from the per-operative surgical plan and the post-operative changes occurring during follow-up. The latest generation of three-dimensional (3D) digital stereoscopic photogrammetry equipment allows rapid capture of the entire facial surface in a non-invasive, high-resolution mode, and the accuracy and precision of its images for anthropometric measurements have now been well established.

This study aims to establish a standardized database of Caucasian/Asian periocular three-dimensional measurements, which would provide a standard data reference for various types of therapeutic and cosmetic plastic surgeries for all ages, genders, and multiple ethnicities, guide operation design, and estimate the extent of surgery.

Three hundred sixty-nine volunteers were recruited at the Department of Ophthalmology, University of Cologne, aged between 18.14 and 85.24 years, including 304 Caucasians and 65 Asians, 147 men and 222 women. Images in a neutral head position were captured from all subjects. Forty-seven anthropometric landmarks of the periocular region were digitally identified, and 42 measures were performed on each eye using the VECTRA Analysis Module.

For eyebrows, there were no significant differences bilaterally, nor did they change significantly with age ($p>0.05$). Length tended to become shorter with age; males owned longer and wider eyebrows than females($p<0.001$); the position decreased between 18-40 years, increased between 60-70, and was relatively stable in other ages, and Asians had higher eyebrow positions overall compared with Caucasians.

For eye-related parameters, Caucasians had significantly greater palpebral fissure width, height and lower eyelid length, iris diameter, pupil center /nasal limbus-medial canthus distance, lateral canthus angle, and canthal tilt ($p<0.001$, respectively); Asians had longer upper eyelids, pupil diameters, and interpupillary/inter-medial canthus/inter-lateral canthus distances, and larger medial canthus angles ($p<0.001$, respectively). Between genders, males had greater palpebral fissure width and height, iris diameters, pupil diameters, interpupillary distances, pupil center/lid margin-medial and lateral canthus distances, inter-canthus distances, and upper and lower lid margins; females had larger medial and lateral canthus angles and larger upper lid areas ($p<0.001$, respectively). With age, parameter changes occurred mainly before 50 and between 60-70. Upper and lower eyelid length, palpebral fissure width, and height decreased, and the medial canthus decreased with age and was evident in females ($p<0.001$, respectively). Interpupillary distance increased with age and was evident in males, while changes between canthus in females were more significant.

This study describes the distribution and age-dependent trends of distance, curvature, angle, area, and volume parameters associated with the eyebrow and periocular region in a multiethnic, multiage population in the European region. It compares the differences between ethnicities, genders, age groups, and binoculars, further complementing the results of previously published studies. The anthropometric data assist in planning surgery and quantitatively evaluating surgical outcomes.

3. INTRODUCTION

3.1 Human craniofacial morphometry

Craniofacial anthropometry is the science of measuring the human face and head.[1] It provides a simple and non-invasive way to quantitatively assess the superficial changes in facial anatomy. Dr Leslie Gabriel Farkas is considered the pioneer of modern craniofacial anthropometry.[2] He innovatively explored the application of classical anthropometric techniques for the quantitative facial assessment and founded an extensive database of standardized North American white adults and children to serve as early standardized anthropometric reference data, adding several proportion indexes of the facial frame for assessing the face to make up for the shortcomings of using only linear measurements.[3,4] Several ratio indexes were added for facial frames evaluating to cover the deficiencies of using linear measurements only.[5]

A total of 47 craniofacial anthropometric landmarks (head, nose, eye, lip and mouth, chin, and ears) have been described in previous studies.[6] Most of them can be visually identified, while a few, as they are associated with skeletal structures, can only be located by palpation.[7] There are two methods of craniofacial anthropometry: direct manual and indirect measurements.

3.2 Direct manual measurements

For decades before the advent of modern indirect measurement methods, measurements for human morphology studies were derived mainly from direct measurements using tools such as calipers and soft rulers(Fig.1), [8] and proportions were calculated based on these results.

These manual measuring methods required physical contact with the subject and relied heavily on the subject's cooperation, and thus may not be suitable for young children or subjects unwilling to be directly touched for personal or cultural reasons.[9] Also, repetitive landmark positioning was required for each measurement, and the subject was required to remain still during measuring, which was laborious and could also increase working time and lead to errors. Moreover, the accuracy of measurements depends on the skill and experience of the measurer, and considerable errors can occur, especially when non-professionals take anthropometric measurements. It is also important to note that some errors may remain permanent since direct manual measurement leaves no image record of facial appearance other than a set of numbers.

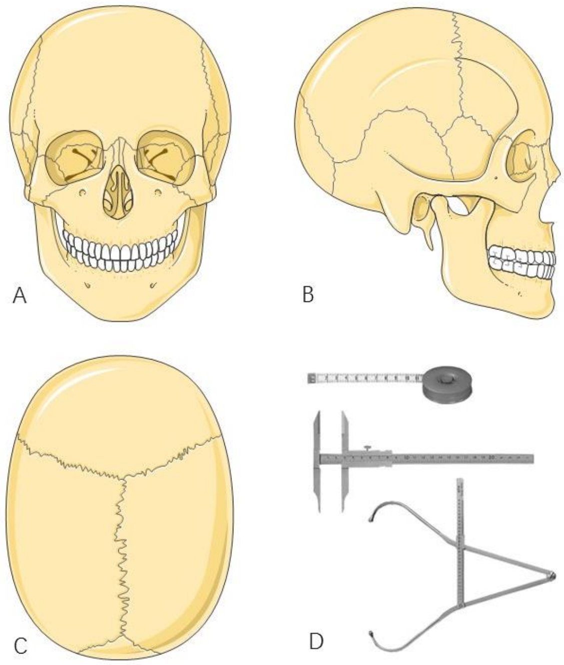


Figure 1. Skull anatomical morphology and manual anthropometry instruments.

A-C: Anatomical morphology of skull. Figure modified with text and annotation after adaptation of “Bone” from Servier Medical Art by Servier, licensed under a Creative Commons Attribution 3.0 Unported License. D: Instruments used for manual anthropometry. (Jayaratne YSN 2014)

In 1985, an anthropometric study of 18 patients with Treacher Collins syndrome was conducted by Kolar JC et al., and 27 to 65 anthropometric measurements of the head and face were performed.[10] In Another study of 61 Crouzon syndrome patients, 26 craniofacial surface measurements were taken directly,[11] partial data were inaccurate or unusable due to the weak co-operation of some patients. In a study of Down’s syndrome patients, 25 anthropometric measurements were conducted by one on each of 104 patients and 365 healthy volunteers, taking about 30 minutes for a single cooperating patient.[12] Fakhroddin M et al. performed craniofacial measurements on 101 patients diagnosed with chronic schizophrenia and an equal number of healthy controls. To achieve more accurate measures, two measurers were asked for measurement and spent as much time as possible on each subject.

3.3 Indirect measurements

Indirect anthropometric measurements, using camera imaging systems to capture two-dimensional (2D) or three-dimensional (3D) images of the human face and perform measurements on the images, have gradually replaced direct measurement methods as various imaging technologies have evolved. Less time is spent interacting with the patient, as shorter time is required for image acquisition, and measurements are taken after capture. The indirect method can reduce the risk of patient discomfort or injury in specific locations, such as periocular areas, which are difficult to obtain by direct measurement.[13] Additionally, indirect methods may be more appropriate for soft tissue feature assessment, where direct instrument contact may distort the soft surface and lead to data inaccuracies. Studies have demonstrated various 2D measurements to evaluate postoperative morphological changes in periocular biological features such as the eyelid and brow.[14,15]The 2D photographs lack the proper 3D depth and shape when measuring stereoscopic objects, which may cause magnification and distortion problems. Several variables, such as illumination changes and objective lens distance, can affect the standardization of the measurement.[16] A study by Tanner JM et al. proved that body and face photogrammetry inaccuracy can be attributed to posture.[17] The reliability of photogrammetry was assessed by Farkas LG et al. and showed that errors were found in some facial measurements obtained from 2D images compared to manual ones, with only 26 out of the 62 items being reliable and the majority of data from the lateral side being distorted.[18]

A variety of non-invasive 3D acquisition and quantification techniques have been widely used in clinical practice to date. The latest generation of 3D digital stereoscopic photogrammetry equipment allows rapid capture of the entire facial surface in a completely non-invasive, high-resolution mode compared to traditional ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and laser scanning. The accuracy and precision of its images for anthropometric measurements have now been well established.[19,20] Furthermore, parameters such as linear distance, curvature, angle, volume, and surface area can also be calculated.[21,22] These have been successfully applied to quantitatively assess facial features and outcomes of cosmetic or reconstructive surgery in healthy individuals and patients with craniofacial defects or deformities and facial changes with age.[23-26]
Morphological assessment of periocular soft tissues in 3D imaging systems has been involved in several studies, and initially, among the markers most widely used were the medial and lateral canthus, the superior and inferior palpebral point, and the upper lid crease point.[27,28] Guo Y and Heindl LM et al. set up a new 3D standardized coordinate system[29,30] based on a previous study demonstrating relevant measurements (linear distance, curvature and angle, area and volume[22,31-33]) in Caucasian populations at different ages,[34] genders, eye positions, facial expressions under various means of examination[35,36]and with different 3D image capture equipments.[25,37]Several studies have also proposed the use of smartphones/tablets as an alternative to stereoscopic photogrammetry systems, due to the limitations of the large size and high cost of the equipment and the necessity of frequent calibrations.[25,38,39] As multiple standard datasets have been established,[40-42] image acquisition has been standardized to make the data comparable across research projects.[43]

3.4 Purpose

For patients requiring periocular surgery, it is essential to quantify the deviation of the individual's facial morphology from the normal state. Therefore, collecting and establishing a dataset of periocular morphometric measurements in normal individuals will enable better visualization and quantification of the expected changes from the per-operative surgical plan and the post-operative changes occurring during follow-up.

This study aims to establish a standardized database of Caucasian/Asian periocular three-dimensional measurements, which would provide a standard data reference for various types of therapeutic and cosmetic plastic surgeries for all ages, genders, and multiple ethnicities, guide operation design, and estimate the extent of surgery.

4. MATERIAL AND METHOD

4.1 Material

4.1.1. Subjects

Volunteers were recruited at the Department of Ophthalmology, University of Cologne, Cologne, Germany. Subjects under 18 years old, with possible pathologies, facial deformities, signs of impairment, severe asymmetry, and medical histories of previous plastic surgery or aesthetic procedures involving the periocular area or operation affecting the facial morphology, were not considered. The university ethical committee approved the study and performed according to the Declaration of Helsinki. Written informed consent was obtained from all subjects.

4.1.2. Camera

The VECTRA M3 three-dimensional imaging system, developed by Canfield (Canfield Scientific, Fairfield, NJ), is designed to capture the surface shape, contours, and color of the human face with high precision.[44](Fig.2)

VECTRA captures the stereo anatomical shape of the subject by carefully photographing several two-dimensional views simultaneously. The capture system consists of six 1.2-millimeter geometric resolution lenses (polygon side length) mounted on a triangular steel stand in three sets (size: 122 cm wide×180 cm high×56 cm deep), equipped with on-board modular intelligent flash units, and the entire capture process is completed within a 3.5 millisecond capture time, enabling the system to capture qualified images without being affected by insufficient ambient light or the movement of the subject (e.g., an infant).

The information from the multiple views is then combined, and the photogrammetric algorithms in VECTRA image processing software are used to compute a highly accurate map of the observed surface's three-dimensional shape and color coordinates, ultimately generating a high-resolution three-dimensional computer model of the subject.[44] Unlike traditional 2D photography, data files of 3D images contain precise sub-millimeter measurement information. Using the VECTRA Analysis Module (VAM) makes it possible to analyze and compare multiple images of the subject over time with great accuracy, without concern for the precise positioning when captured.

Figure 2. The 3D imaging system

4.2 Method

General information, including their gender, date of birth, and ethnicity, was collected from volunteers after the informed consent was signed.

4.2.1. Image acquisition

4.2.1.1 Camera calibration

Calibration of the VECTRA 3D system is critical for creating geometrically accurate 3D models and is performed before volunteers' arrival or when the system is moved or altered.

There were two steps for calibration. For the first capture, stand about a meter from the VECTRA with the calibration target perpendicular to the floor and the L upright. Move closer /further /up/down from the VECTRA until the long/short leg of the L is between the vertical/ horizontal guides in the preview windows on the screen. Second capture: Stand with the calibration target about a meter from the VECTRA, the L upright, and the short leg of the L is between the horizontal guides in the top preview window. Tilt the calibration target forward about 30 degrees. Move the target until L's long/short leg is between the vertical/horizontal rails of the preview window. Volunteer image acquisition can be performed after the calibration is completed successfully. (Fig.3)

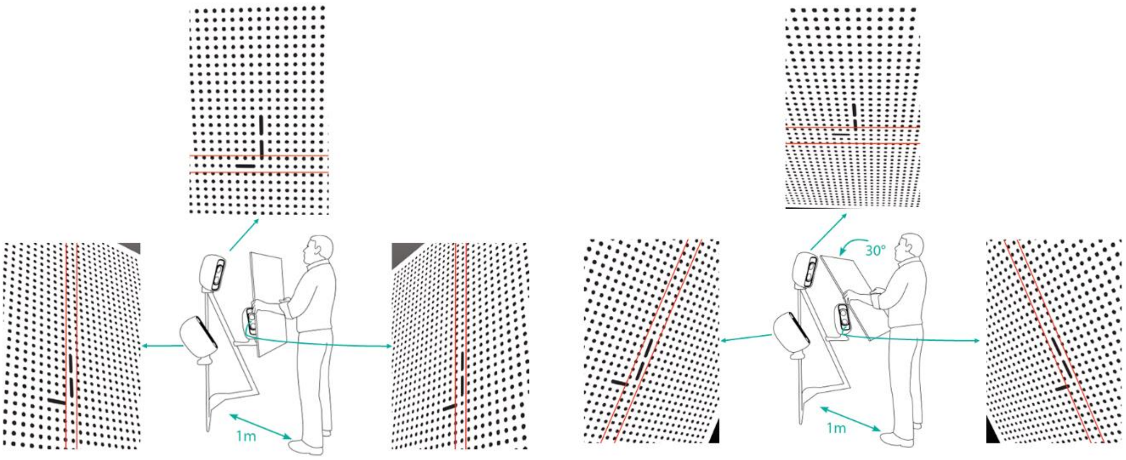


Figure 3. Calibration of the VECTRA 3D system

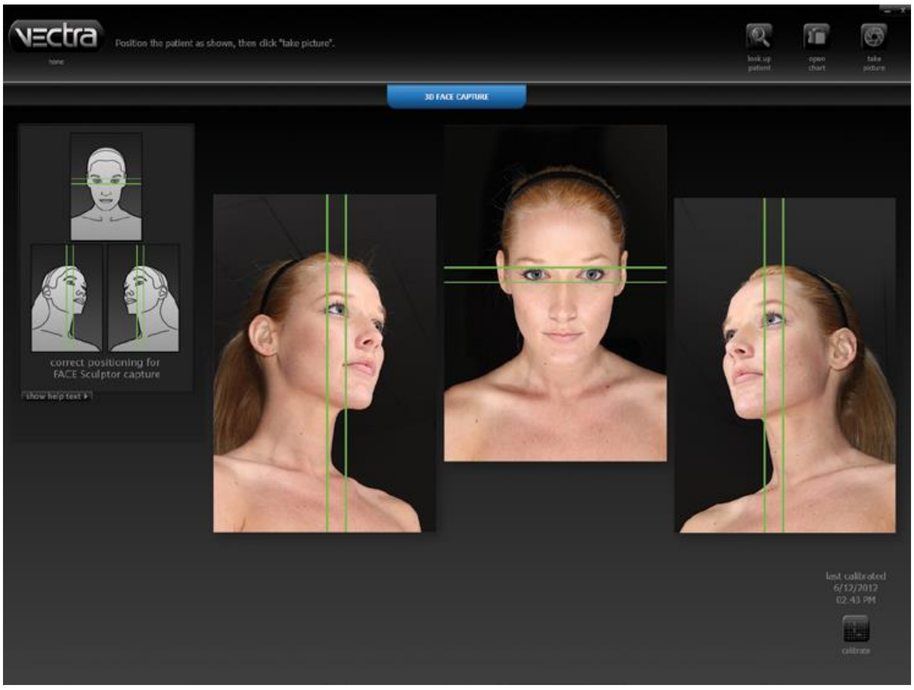


Figure 4. Position of the head and eyes presented on the screen.

4.2.1.2. Image capture

All images were captured in the same standard-illuminated clinical room with no external natural light, and an experienced operator performed the entire process according to the operating instructions. Before positioning the volunteers in front of the VECTRA, all make-up, jewelry, sweat, oils, or anything shiny from the skin were requested to be removed. Hair was secured away from the face, ears, and neck.

Volunteers sat on a stool, facing the camera and centered on both sides. Adjust the position and height until the eyes are centered between the preview images' horizontal and vertical guidelines. During image acquisition, all subjects were required to maintain a neutral head position with eyes naturally open, lips gently closed, and no other facial expression, such as a smile. (Fig. 4)

Capture images and the 3D facial images were automatically generated by the VAM software. Checked the quality of images; re-take or recalibrate was needed if the following situations occurred: the subject blinked, was in the wrong position, or images were blurred in the periocular region; 3D object exhibits geometric irregularities, including visible divisions in the object, dislocated image components, and/or image stitching flaws.

4.2.2. Landmarks and measurements

Forty-seven anthropometric landmarks of the periocular region on each eye were digitally identified using the VECTRA Analysis Module based on previous literature. (Fig. 5 and Tab. 1). The landmarks were selected and marked one after another as abbreviated labels according to the order listed in Table 1. Briefly, five easily identifiable landmarks(red) were first placed as prime points on the 3D model, including the pupillary center (Pc), medial and lateral corneoscleral limbus (Lm and Ll, horizontal to the pupillary center), endocanthion (En), and exocanthion (Ex). Then, most of the remaining landmarks were located by the horizontal or vertical coordinate axes passing through.

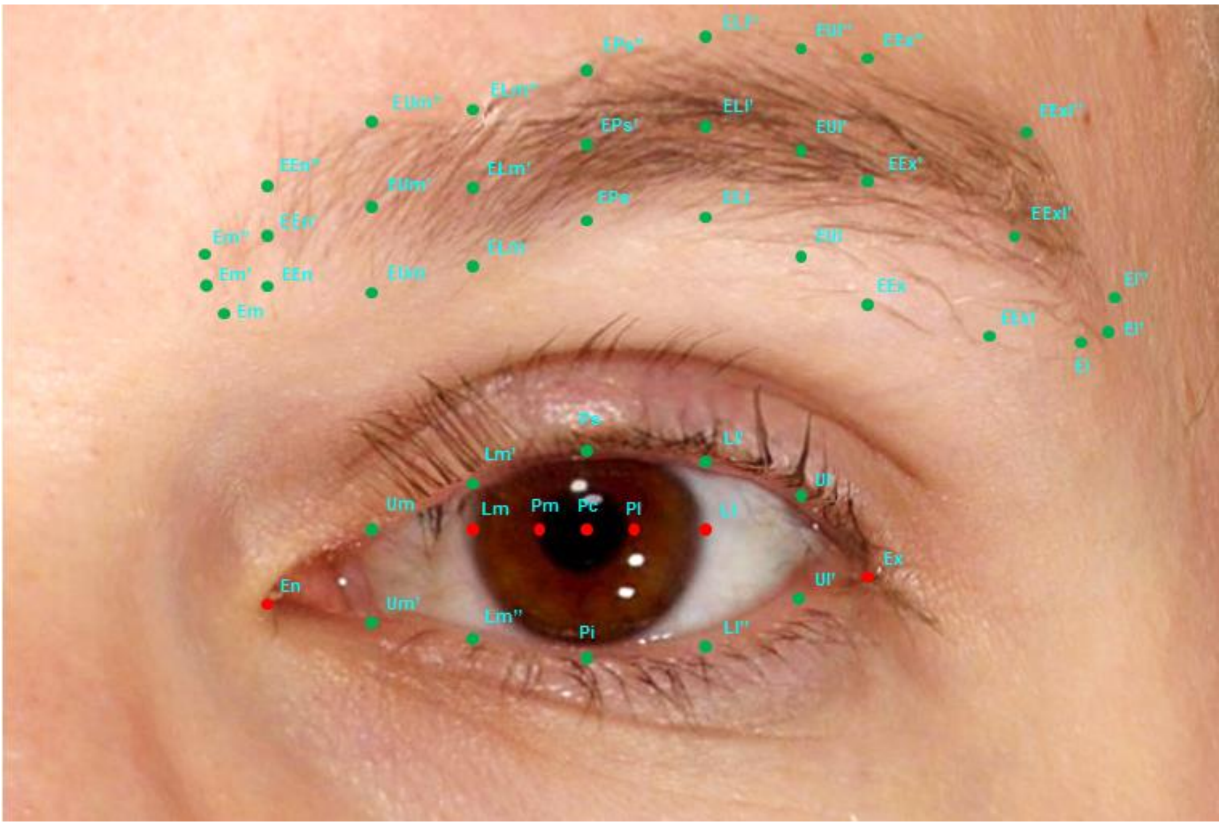


Figure 5. Forty-seven anthropometric landmarks in the periocular region.

Table 1. Definitions of 47 anthropometric periocular landmarks

Landmarks	Definitions
En	Endocanthion, inner commissure of the palpebral fissure
Ex	Exocanthion, outer commissure of the lower and upper eyelash roots of the palpebral fissure
Pc	Pupillary center
Pm	Medial pupillary margin point horizontal to pupillary center
Pl	Lateral pupillary margin point horizontal to pupillary center
Lm	Medial corneoscleral limbus point horizontal to pupillary center
Ll	Lateral corneoscleral limbus point horizontal to pupillary center
Em	Inferior margin point of the medial eyebrow end (sometimes locates at the same place with EEn); Em'', superior margin point; Em', middle point
EEn	Inferior margin point of eyebrow vertical to En; EEn'', superior margin point; EEn', middle point Um Middle point between En and Lm' at the upper

	palpebral margin on the lash roots
Um'	Middle point between En and Lm'' at the lower palpebral margin on the lash roots
EUm	Point vertical to Um at the inferior margin of eyebrows; EUm'', superior margin point; EUm', middle point
Lm'	Point vertical to Lm at the upper palpebral margin on the lash roots
Lm''	Point vertical to Lm at the lower palpebral margin on the lash roots
ELm	Point vertical to Lm at the inferior margin of eyebrows; ELm'', superior margin point; ELm', middle point
Ps	Palpebrale superioris, Point vertical to Pc at the upper palpebral margin on the lash roots
Pi	Palpebrale inferioris, Point vertical to Pc at the lower palpebral margin on the lash roots
EPs	Point vertical to Pc at the inferior margin of eyebrows; EPs'', superior margin point; EPs', middle point
Ll'	Point vertical to Ll at the upper palpebral margin on the lash roots
Ll''	Point vertical to Ll at the lower palpebral margin on the lash roots
ELl	Point vertical to Ll at the inferior margin of eyebrows; ELl'', superior margin point; ELl', middle point
Ul	The middle between Ex and Ll' at the upper palpebral margin on the lash roots
Ul'	The middle between Ex and Ll'' at the lower palpebral margin on the lash roots
EUl	Point vertical to Ul at the inferior margin of eyebrows; EUl'', superior margin point; EUl', middle point
EEx	Point vertical to Ex at the inferior margin of eyebrows; EEx'', superior margin point; EEx', middle point
EExl	Point vertical to Ex at the inferior margin of eyebrows in lateral view; EExl'', superior margin point; EExl', middle point
El	inferior margin of the lateral eyebrow end; El'', superior margin point; El', middle point

Modified from Guo Y. et al.[30]

Subsequently, measures were performed on each eye for four types of measurements: 32 linear distances, five curvatures, three angles, an area, and a volume. (Fig 6, Table 2)

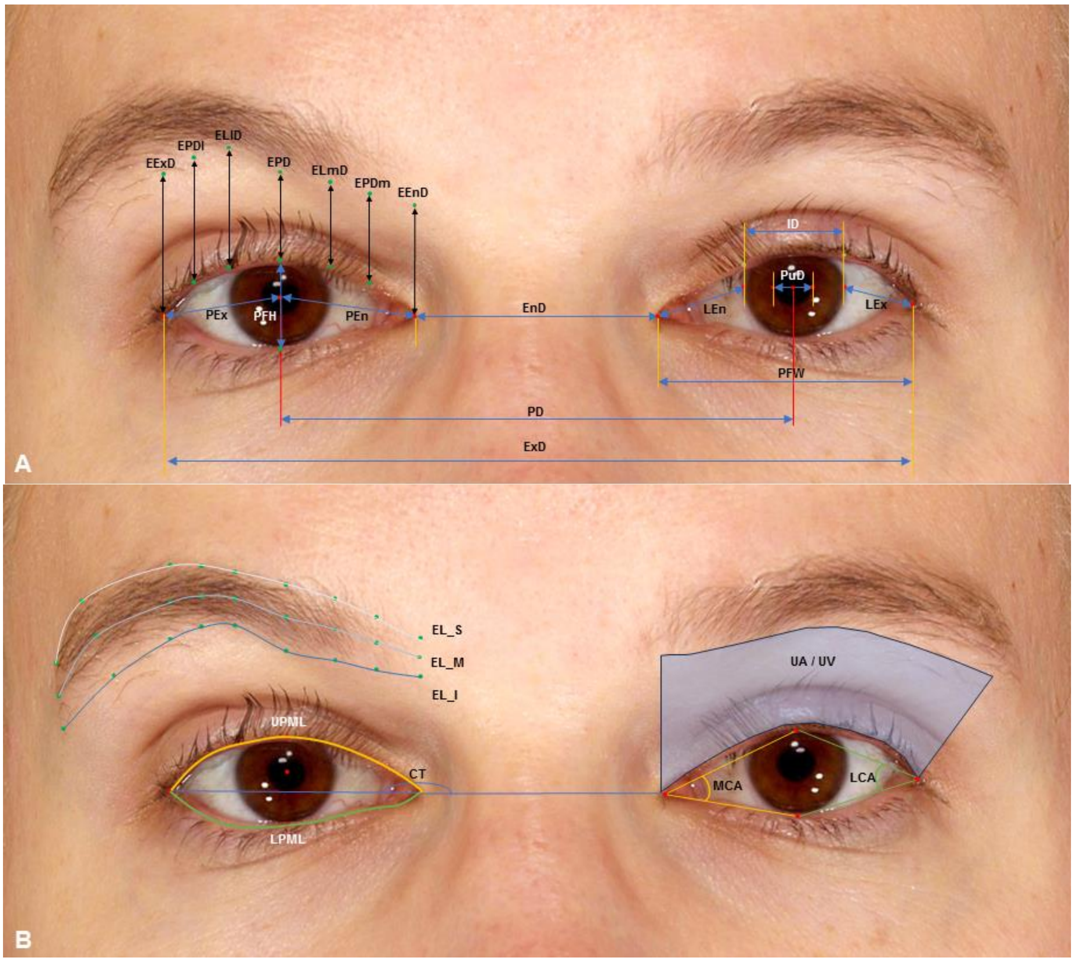


Figure 6. Thirty-two linear distance (A), five curvatures, three angles, an area and a volume (B) measured by 3D technology.

Table 2. List of 42 periocular measurements.

Abbreviations	Definitions	Landmarks
Linear distances		
PFW	Palpebral fissure width	En-Ex
PFH	Palpebral fissure height	Ps-Pi
EEnD_I, EEnD_M, or EEnD_S	Eyebrow-endocanthion distance of the inferior, middle, or superior point	EEn-En
EPDm_I, EPDm_M, or EPDm_S	Eyebrow-palpebral margin distance (medial) of the inferior, middle, or superior point	EUm-Um
ELmD_I, ELmD_M, or ELmD_S	Eyebrow-palpebral margin distance (medial limbus) of the inferior, middle, or superior point	ELm-Lm’
EPD_I, EPD_M, or EPD_S	Eyebrow-palpebral margin (Ps) distance of the inferior (similar to upper lid height), middle, or	Ps-EPs

	superior point	
ElID_I, ElID_M, or ElID_S	Eyebrow-palpebral margin distance (lateral limbus) of the inferior, middle, or superior point	ELl-Ll’
EPDl_I, EPDl_M, or EPDl_S	Eyebrow-palpebral margin distance (lateral) of the inferior, middle, or superior point	EUl-Ul
EExD_I, EExD_M, or EExD_S	Eyebrow-exocanthion distance of the inferior, middle, or superior point	EEx-Ex
ID	Iris diameter	Lm-Ll
PuD	Pupil diameter	Pm-Pl
PEn	Pupil center-endocanthion distance	Pc-En
LEn	Medial limbus-endocanthion distance	Lm-En
PEx	Pupil center-exocanthion distance	Pc-Ex
LEx	Lateral limbus-exocanthion distance	Ll-Ex
EnD	Inner intercanthal distance	En (left)-En (right)
ExD	Outer intercanthal distance	Ex (left)-Ex (right)
PD	Interpupillary distance	Pc (left)-Pc (right)
Curvatures		
UPML	Upper palpebral margin length	En-Um-Lm’-Ps-Ll’-Ul-Ex
PML	Lower palpebral margin length	En-Um’-Lm”-Pi-Ll”-Ul’-Ex
EL_I	Inferior eyebrow length	Em-EEn-EUm-ELm-EPs-ELl-EUl-EEx-EExl-El
EL_M	Middle eyebrow length	Em’-EEn’-EUm’-ELm’-EPs’-ELl’-EUl’-EEx’-EExl’-El’
EL_S	Superior eyebrow length	Em”-EEn”-EUm”-ELm”-EPs”-ELl”-EUl”-EEx”-EExl”-El”
Angles		
MCA	Medial canthal angle	Ps-En-Pi
LCA	Lateral canthal angle	Ps-Ex-Pi
CT	Canthal tilt	Ex (left)-En (left)-En (right), or Ex (right)-En (right)-En(left)
Area		

UA	Upper eyelid area	En-Um-Lm’-Ps-Ll’-Ul-Ex-EExl- EEx-EUl-ELl-EPs-ELm-EUm-EEn
Volume		
UV	Upper eyelid volume	En-Um-Lm’-Ps-Ll’-Ul-Ex-EExl- EEx-EUl-ELl-EPs-ELm-Eum-EEn

Modified from Guo Y. et al.[30]

4.3 Data collection and analysis

All data were entered into a database of Microsoft Excel 2016 for Windows (Microsoft Corp., Redmond, WA, USA) after finishing all landmark positioning and measurement. Further statistical analyses were performed using SPSS version 25 software (IBM Corp., Armonk, NY, USA).

The Kolmogorov-Smirnov test was used to test the data normality of all measurements. The Wilcoxon signed-rank test for paired data was applied for nonnormally distributed measurements. An independent sample t-test was performed after the normal distribution was verified to analyze differences between groups. A paired Sample T-test was used to compare the differences between eyesides. Pearson's correlation coefficient (r) between the variables was calculated if the measurements were normally distributed; otherwise, spearman's rank correlation coefficient was used. Less than 0.4, 0.4 to 0.6, and over 0.6 were considered low, moderate, and high correlations between variables. $P < 0.05$ was considered statistically significant.

5. RESULTS

The demographic characteristics are presented in Table 3. A total of 369 volunteers, including 147 males and 222 females, were eligible for enrolment and received facial 3D image acquisition. Over 80% were Caucasian, and others were Asian. Seven hundred and thirty-eight sets of periocular data from both eyes were measured. No statistically significant age differences were identified between males (38.89±16.70 years) and females (41.89±19.91years, P=0.689 > 0.05).

Table 3. Demographic characteristics of volunteers

Categories	Count (%)	Age (years old), Mean ± SD (Range)
Gender		
Male	147(39.8)	38.89±16.70 (18.17-84.15)
Female	222(60.2)	41.89±19.91 (18.14-85.24)
Total	369	40.70±18.73 (18.14-85.24)
Race/Ethnicity		
Caucasian	304(82.4)	43.79±19.18 (18.14-85.24)
Asian	65(17.6)	26.22±3.90 (20.12-38.21)

5.1 Parameter differences between ethnic groups

Table 4 provides detailed data on ethnic and gender distributions.

Table 4. Demographic characteristics of volunteers between different races and genders.

		Male n=147	**Female** n=222
Caucasian n=304	n	120	184
	Age(years), Mean±SD (range)	41.52±17.29 (18.17-84.15)	45.27±20.20 (18.14-85.24)
Asian n=65	n	27	38
	Age(years), Mean±SD (range)	27.20±4.13 (20.63-38.21)	25.53±3.60 (20.12-30.91)

5.1.1. Overall

Overall, there were significant differences in the majority of measurements between the two ethnic groups, except for EPDm_I/M/S, EPDl_I, EExD_I, PFW, PFH, and UPML (p=0.979, 0.184, 0.131, 0.318, 0.885, 0.172, 0.142, 0.876, and 0.876, respectively). Of all measurements with significant differences, the Caucasian group (mean distance of 64.80±8.97, 11.94±0.60, 16.08±1.35, 10.56±1.25, 33.49±2.56, 38.29±3.84, 167.21±3.53 and 1.43±2.43mm, respectively) were larger than the Asian group(62.00±7.70, 11.57±0.49, 14.48±1.30, 9.48±1.19, 32.59±2.59, 34.64±3.75, 164.65±2.72 and 0.29±2.34mm, respectively) in EL_M, ID, PEn, LEn, LPML, LCA, CT, and UV. The remaining were significantly larger in Asian group.(Tab.5)

5.1.2. Parameter differences between ethnic groups(age-matched)

Different from the Caucasians enrolled in the group, the Asians enrolled were all under the age of 40 (range 20.63-38.21 years). Given the effect of age distribution on the overall results, the Caucasian population was age-matched with the Asian population.

Consistent with the overall data (Tab.5), most measurements differed significantly between the two racial groups, except for some parameters (EPDm_I/M/S, EPDl_I, p=0.211, 0.145, 0.085, 0.368, respectively). However, the EExD_M, PuD, and UA variables did not differ significantly after age matching (p=0.557, 0.093, 0.596, respectively), and some variables showed statistical differences (EExD_I, p=0.011; PFW and PFH, p<0.001; UPML, p=0.001). PD differed in both pre-and post-age matching, but its difference increased (p=0.003). Of all measurements with significant differences, the Caucasian group had larger measurements than the Asian group in EExD_I, EL, PFW, PFH, ID, PEn, LEn, UPML, LPML, MCA, LCA, CT, UA, and UV, and the remaining were significantly larger in the Asian group.

Table 5. Mean differences and significance tests between the races of all and age-matched volunteers.

	All							**Age-matched**						
	Overall n=369		**Caucasian** n=304		**Asian** n=65		**p-value**	**Overall** n=215		**Caucasians** n=150		**Asian** n=65		**p-value**
Parameters	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	Mean	SD	
EEnD_I	18.64	2.92	18.41	2.93	19.69	2.59	<0.001***	18.44	2.63	17.89	2.46	19.69	2.59	<0.001***
EEnD_M	23.17	2.61	22.89	2.54	24.48	2.57	<0.001***	23.44	2.52	22.99	2.37	24.48	2.57	<0.001***
EEnD_S	26.79	3.10	26.35	2.97	28.86	2.81	<0.001***	27.35	2.93	26.70	2.74	28.86	2.81	<0.001***
EPDm_I	15.46	2.75	15.46	2.85	15.46	2.23	0.979	15.25	2.33	15.16	2.36	15.46	2.23	0.211
EPDm_M	20.62	2.55	20.68	2.59	20.35	2.33	0.184	20.60	2.32	20.71	2.32	20.35	2.33	0.145
EPDm_S	24.38	2.84	24.31	2.87	24.73	2.67	0.131	24.39	2.64	24.25	2.62	24.73	2.67	0.085
ELmD_I	11.89	2.81	11.69	2.88	12.82	2.23	<0.001***	11.89	2.45	11.49	2.44	12.82	2.23	<0.001***
ELmD_M	17.09	2.57	16.97	2.60	17.69	2.37	0.004**	17.18	2.38	16.97	2.35	17.69	2.37	0.004**
ELmD_S	20.99	2.94	20.72	2.89	22.29	2.83	<0.001***	21.05	2.84	20.52	2.68	22.29	2.83	<0.001***
EPD_I	10.83	3.02	10.57	3.09	12.04	2.33	<0.001***	10.95	2.54	10.48	2.48	12.04	2.33	<0.001***
EPD_M	15.57	2.72	15.30	2.68	16.85	2.52	<0.001***	15.71	2.48	15.22	2.30	16.85	2.52	<0.001***
EPD_S	19.48	3.21	19.04	3.01	21.55	3.29	<0.001***	19.51	3.14	18.63	2.63	21.55	3.29	<0.001***
ELlD_I	11.85	3.36	11.70	3.49	12.56	2.54	0.001**	11.96	2.82	11.70	2.90	12.56	2.54	0.004**

ELID_M	16.47	2.88	16.21	2.87	17.68	2.60	<0.001***	16.63	2.56	16.19	2.41	17.68	2.60	<0.001***
ELID_S	20.63	3.34	20.17	3.12	22.76	3.53	<0.001***	20.66	3.27	19.74	2.69	22.76	3.53	<0.001***
EPDI_I	13.92	3.73	13.87	3.88	14.17	2.91	0.318	14.37	3.11	14.46	3.19	14.17	2.91	0.368
EPDI_M	18.67	2.94	18.45	2.96	19.67	2.62	<0.001***	19.13	2.49	18.90	2.40	19.67	2.62	0.003**
EPDI_S	22.94	3.36	22.49	3.15	25.09	3.46	<0.001***	23.18	3.19	22.36	2.69	25.09	3.46	<0.001***
EExD_I	18.11	3.89	18.11	4.04	18.07	3.10	0.885	18.69	3.35	18.96	3.42	18.07	3.10	0.011*
EExD_M	22.79	3.04	22.64	3.12	23.54	2.46	<0.001***	23.43	2.50	23.38	2.52	23.54	2.46	0.557
EExD_S	26.78	3.37	26.40	3.28	28.59	3.21	<0.001***	27.18	3.06	26.57	2.78	28.59	3.21	<0.001***
EL_I	52.78	9.01	52.27	9.50	55.20	5.61	<0.001***	57.33	6.67	58.25	6.89	55.20	5.61	<0.001***
EL_M	64.32	8.82	64.80	8.97	62.00	7.70	0.001**	64.43	8.31	65.46	8.36	62.00	7.70	<0.001***
EL_S	57.88	13.41	56.55	13.93	64.27	7.90	<0.001***	66.05	9.56	66.81	10.10	64.27	7.90	0.006**
UPML	39.72	3.18	39.71	3.23	39.75	2.98	0.876	40.45	2.96	40.75	2.91	39.75	2.98	0.001**
LPML	33.33	2.59	33.49	2.56	32.59	2.59	<0.001***	33.77	2.54	34.28	2.35	32.59	2.59	<0.001***
PFW	29.82	2.02	29.86	2.01	29.60	2.02	0.172	30.26	1.98	30.55	1.89	29.60	2.02	<0.001***
PFH	11.53	1.24	11.56	1.26	11.39	1.15	0.142	11.79	1.17	11.96	1.14	11.39	1.15	<0.001***
ID	11.87	0.60	11.94	0.60	11.57	0.49	<0.001***	11.91	0.66	12.05	0.67	11.57	0.49	<0.001***
PuD	4.13	0.81	4.05	0.80	4.54	0.77	<0.001***	4.45	0.70	4.41	0.66	4.54	0.77	0.093

PD	63.04	3.66	62.90	3.57	63.69	4.01	0.039*	62.86	3.67	62.49	3.45	63.69	4.01	0.003**
PEn	15.80	1.47	16.08	1.35	14.48	1.30	<0.001***	15.57	1.46	16.04	1.26	14.48	1.30	<0.001***
LEn	10.37	1.31	10.56	1.25	9.48	1.19	<0.001***	10.20	1.30	10.52	1.21	9.48	1.19	<0.001***
PEx	15.53	1.75	15.25	1.65	16.85	1.58	<0.001***	16.18	1.60	15.88	1.53	16.85	1.58	<0.001***
LEx	10.16	1.94	9.79	1.78	11.86	1.75	<0.001***	10.92	1.82	10.51	1.69	11.86	1.75	<0.001***
EnD	32.52	3.53	31.61	2.82	36.78	3.39	<0.001***	32.96	3.82	31.30	2.63	36.78	3.39	<0.001***
ExD	90.53	4.88	89.83	4.55	93.82	5.06	<0.001***	91.61	4.86	90.65	4.45	93.82	5.06	<0.001***
MCA	39.61	4.34	39.03	4.10	42.30	4.43	<0.001***	41.00	4.11	40.44	3.83	42.30	4.43	<0.001***
LCA	37.65	4.07	38.29	3.84	34.64	3.75	<0.001***	37.03	3.96	38.06	3.58	34.64	3.75	<0.001***
CT	166.76	3.54	167.21	3.53	164.65	2.72	<0.001***	165.86	3.02	166.38	2.99	164.65	2.72	<0.001***
UA	5.49	1.26	5.45	1.29	5.68	1.12	0.042*	5.72	1.18	5.74	1.21	5.68	1.12	0.596
UV	1.23	2.45	1.43	2.43	0.29	2.34	<0.001***	1.39	2.97	1.87	3.09	0.29	2.34	<0.001***

*p<0.05, **p<0.01, ***p<0.001.

5.2 Parameter differences between genders

5.2.1. Overall

Mean values, SD, and significance of differences of parameters between gender groups were shown in Table 7. In general, except for EPDm_I, EPD_M, EPDl_M, EExD_M, CT, and UV (p=0.057, 0.652, 0.052, 0.757, 0.089, and 0.084, respectively), the remaining variables differed significantly between gender groups. Of all the measures with significant differences, the inferior distance of EEnD, ELmD, EPD, ELlD, EPDl, EExD, and ELlD_M (18.85±2.94mm, 12.36±2.84mm, 11.42±3.09mm, 12.78±3.32mm, 14.96±3.76mm, and 19.09±4.03mm, respectively), and angles (MCA and LCA) were larger in the female group, and EEnD_M/S, EPDm_M/S, ELmD_M/S, EPD_S, ELlD_S, EPDl_S, EExD_S, EL_I/M/S and other eye-related parameters were larger in the male group.
In the Caucasian group, there were no significant differences (p=0.228, 0.726, 0.583, 0.061, and 0.281, respectively) between gender groups in EPDm_I, EPD_M, EExD_M, CT, and UV, which were similar to the total. However, EPDl_M was significantly different between genders (p=0.007) compared to overall (p=0.052), whereas it was not different in EEnD_I and ELlD_S (p=0.078 and 0.159, respectively) versus overall (p=0.013 and 0.002, respectively). In the Asian group, EPD_M, EPDl_M, and CT were similar to the overall, with no significant difference between genders (p=0.083, 0.341, and 0.729, respectively). EPDm_I, UV showed differences between genders (p=0.025 and 0.032, respectively), while EEnD_S, EPDm_M, ELmD_M, EPD_I, ELlD_M, PFH, ID, LEx showed no difference (p=0.051, 0.309, 0.231, 0.127, 0.099, 0.067,0.293, and 0.068, respectively) compared to the whole (p <0.05).

5.2.2. Parameter differences between genders (age-matched)

Mean values, SD, and significance of differences between genders after age-matching are shown in Table 7. In general, except for EPD_M, ELlD_M, EPDl_M, EExD_M, PFH, PuD, CT, and UV (p=0.440, 0.234, 0.114, 0.517, 0.469, 0.280, 0.918 and 0.068, respectively), other variables differed significantly between genders. In the Caucasian group, there were no significant differences between gender groups in EPDm_I, EPD_M, EExD_M, PFH, CT, and UV (p=0.238, 0.963, 0.301, 0.852, 0.635 and 0.351, respectively), which were similar to the total. However, ELlD_M and EPDl_M were greater in female group, with significant differences between genders (p=0.013 and 0.011) compared to overall (p=0.234 and 0.114), whereas it was not different in EEnD_I, EPDm_I, ELmD_M and ELlD_S, ID (p=0.056,0.238,0.053, 0.221, 0.079, respectively) versus overall (p=0.002, 0.025, 0.029, 0.003, 0.038, respectively). Other eye-related parameters with significant differences were greater in males, except for MCA, LCA, and UA, which were higher in females. In the Asian group, EPD_M, ELlD_M EPDl_M, EExD_M, PFH, and CT were similar to the overall with no significant difference between genders (p=0.083, 0.099, 0.341, 0.652, 0.067 and 0.729, respectively). PuD and UV showed differences between genders (p=0.032 and 0.032), while EEnD_M/S, EPDm_M, ELmD_M, EPD_I, ID, LEx showed no difference (p=0.611, 0.051, 0.309, 0.231, 0.127, 0.293, and 0.068, respectively) compared to the whole (p <0.05). Other eye-related parameters were similar to Caucasians.

Table 6. Mean differences and significance tests between gender and race of all volunteers.

	Overall					Caucasians					Asians				
	Male n=147		Female n=222		p-value	Male n=120		Female n=184		p-value	Male n=27		Female n=38		p-value
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
EEnD_I	18.31	2.85	18.85	2.94	0.013*	18.15	2.91	18.58	2.94	0.078	19.01	2.48	20.18	2.57	0.011*
EEnD_M	23.91	2.26	22.68	2.71	<0.001***	23.75	2.21	22.32	2.58	<0.001***	24.62	2.36	24.38	2.71	0.611
EEnD_S	27.99	2.65	25.99	3.12	<0.001***	27.67	2.58	25.48	2.90	<0.001***	29.43	2.50	28.45	2.96	0.051
EPDm_I	15.22	2.70	15.62	2.77	0.057	15.29	2.85	15.57	2.84	0.228	14.94	1.91	15.83	2.38	0.025*
EPDm_M	21.32	2.39	20.17	2.55	<0.001***	21.48	2.44	20.16	2.56	<0.001***	20.59	2.02	20.18	2.52	0.309
EPDm_S	25.34	2.63	23.75	2.80	<0.001***	25.33	2.69	23.65	2.79	<0.001***	25.39	2.34	24.26	2.81	0.018*
ELmD_I	11.18	2.61	12.36	2.84	<0.001***	10.93	2.65	12.18	2.92	<0.001***	12.27	2.11	13.21	2.24	0.017*
ELmD_M	17.37	2.48	16.91	2.61	0.018*	17.23	2.54	16.79	2.62	0.044*	17.99	2.13	17.48	2.51	0.231
ELmD_S	21.59	2.92	20.61	2.89	<0.001***	21.25	2.89	20.38	2.84	<0.001***	23.09	2.59	21.73	2.87	0.007**

EPD_I	9.94	2.67	11.42	3.09	<0.001***	9.55	2.61	11.24	3.19	<0.001***	11.67	2.20	12.31	2.40	0.127
EPD_M	15.63	2.59	15.54	2.80	0.652	15.26	2.49	15.33	2.80	0.726	17.31	2.37	16.52	2.59	0.083
EPD_S	20.00	3.24	19.14	3.14	<0.001***	19.40	2.93	18.81	3.05	0.021*	22.69	3.22	20.75	3.11	0.001**
ELID_I	10.44	2.90	12.78	3.32	<0.001***	10.12	2.94	12.73	3.44	<0.001***	11.86	2.25	13.05	2.64	0.008**
ELID_M	16.18	2.75	16.66	2.94	0.029*	15.75	2.63	16.51	2.97	0.001**	18.13	2.42	17.36	2.69	0.099
ELID_S	21.10	3.41	20.31	3.27	0.002**	20.39	3.01	20.03	3.19	0.159	24.28	3.31	21.70	3.30	<0.001***
EPDI_I	12.36	3.07	14.96	3.76	<0.001***	12.18	3.18	14.97	3.90	<0.001***	13.14	2.42	14.90	3.03	0.001**
EPDI_M	18.41	2.73	18.84	3.06	0.052	18.06	2.67	18.70	3.11	0.007**	19.93	2.48	19.48	2.71	0.341
EPDI_S	23.61	3.33	22.50	3.30	<0.001***	22.95	3.01	22.18	3.21	0.003**	26.57	3.13	24.04	3.32	<0.001***
EExD_I	16.63	3.16	19.09	4.03	<0.001***	16.61	3.34	19.09	4.16	<0.001***	16.70	2.19	19.05	3.29	<0.001***
EExD_M	22.75	2.78	22.82	3.19	0.757	22.55	2.90	22.69	3.27	0.583	23.66	2.01	23.46	2.74	0.652
EExD_S	27.66	3.32	26.20	3.28	<0.001***	27.18	3.23	25.88	3.22	<0.001***	29.82	2.83	27.71	3.19	<0.001***
EL_I	56.55	9.07	50.26	8.05	<0.001***	56.24	9.70	49.66	8.41	<0.001***	57.92	5.31	53.22	4.99	<0.001***

EL_M	70.04	8.32	60.50	6.87	<0.001***	70.51	8.65	61.05	6.98	<0.001***	67.91	6.28	57.71	5.49	<0.001***
EL_S	64.69	13.33	53.32	11.39	<0.001***	63.45	14.12	52.00	11.79	<0.001***	70.30	6.53	59.90	5.62	<0.001***
PFW	30.84	1.76	29.14	1.89	<0.001***	30.94	1.70	29.16	1.89	<0.001***	30.36	1.98	29.05	1.88	<0.001***
PFH	11.66	1.23	11.44	1.24	0.016*	11.78	1.20	11.42	1.27	0.001**	11.17	1.24	11.54	1.06	0.067
ID	11.99	0.59	11.80	0.60	<0.001***	12.07	0.58	11.86	0.60	<0.001***	11.62	0.44	11.53	0.52	0.293
PuD	4.26	0.89	4.05	0.75	0.001**	4.16	0.89	3.98	0.73	0.005**	4.71	0.79	4.42	0.74	0.032*
PEn	16.33	1.45	15.45	1.38	<0.001***	16.63	1.32	15.73	1.25	<0.001***	14.98	1.24	14.12	1.23	<0.001***
LEn	10.80	1.31	10.09	1.23	<0.001***	11.00	1.26	10.28	1.17	<0.001***	9.91	1.16	9.17	1.12	<0.001***
PEx	16.24	1.57	15.06	1.70	<0.001***	16.03	1.46	14.74	1.57	<0.001***	17.18	1.69	16.62	1.45	0.046*
LEx	10.87	1.82	9.68	1.87	<0.001***	10.58	1.67	9.28	1.67	<0.001***	12.19	1.93	11.62	1.59	0.068
EnD	33.38	3.65	31.95	3.33	<0.001***	32.40	2.96	31.09	2.60	<0.001***	37.70	3.29	36.13	3.33	0.009**
ExD	93.41	4.30	88.63	4.28	<0.001***	92.76	3.98	87.91	3.83	<0.001***	96.26	4.55	92.08	4.69	<0.001***

PD	65.00	3.50	61.74	3.16	<0.001***	64.82	3.42	61.65	3.08	<0.001***	65.81	3.75	62.19	3.50	<0.001***
UPML	41.18	2.84	38.75	3.03	<0.001***	41.34	2.67	38.64	3.12	<0.001***	40.45	3.45	39.26	2.50	0.024*
LPML	34.56	2.28	32.51	2.46	<0.001***	34.83	2.13	32.61	2.44	<0.001***	33.37	2.53	32.04	2.51	0.004**
MCA	38.86	4.28	40.10	4.31	<0.001***	38.56	4.29	39.34	3.95	0.021*	40.19	4.05	43.80	4.09	<0.001***
LCA	36.47	4.07	38.43	3.87	<0.001***	37.20	3.84	39.01	3.67	<0.001***	33.20	3.44	35.66	3.65	<0.001***
CT	166.49	3.56	166.94	3.51	0.089	166.88	3.67	167.43	3.42	0.061	164.75	2.32	164.58	2.99	0.729
UA	5.27	1.16	5.63	1.31	<0.001***	5.23	1.23	5.59	1.31	0.001**	5.43	0.81	5.86	1.27	0.024*
UV	1.43	2.30	1.10	2.54	0.084	1.56	2.27	1.35	2.53	0.281	0.81	2.39	-0.09	2.24	0.032*

*p<0.05, **p<0.01, ***p<0.001.

Table 7. Mean differences and significance tests between gender and race of age-matched volunteers.

	Overall					Caucasians					Asians				
	Male n=93		Female n=122		p-value	Male n=66		Female n=84		p-value	Male n=27		Female n=38		p-value
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
EEnD_I	18.00	2.41	18.77	2.74	0.002**	17.59	2.27	18.13	2.57	0.056	19.01	2.48	20.18	2.57	0.011*
EEnD_M	23.95	2.21	23.06	2.67	<0.001***	23.67	2.10	22.45	2.43	<0.001***	24.62	2.36	24.38	2.71	0.611
EEnD_S	28.23	2.62	26.68	2.99	<0.001***	27.75	2.51	25.87	2.63	<0.001***	29.43	2.50	28.45	2.96	0.051
EPDm_I	14.97	2.15	15.47	2.44	0.025*	14.98	2.25	15.30	2.45	0.238	14.94	1.91	15.83	2.38	0.025*
EPDm_M	21.19	2.10	20.15	2.39	<0.001***	21.44	2.09	20.14	2.33	<0.001***	20.59	2.02	20.18	2.52	0.309
EPDm_S	25.25	2.37	23.74	2.65	<0.001***	25.19	2.39	23.51	2.55	<0.001***	25.39	2.34	24.26	2.81	0.018*
ELmD_I	11.28	2.36	12.36	2.42	<0.001***	10.87	2.34	11.98	2.41	<0.001***	12.27	2.11	13.21	2.24	0.017*
ELmD_M	17.47	2.30	16.96	2.42	0.029*	17.26	2.35	16.73	2.34	0.053	17.99	2.13	17.48	2.51	0.231
ELmD_S	21.65	2.79	20.59	2.79	<0.001***	21.07	2.66	20.08	2.61	0.001**	23.09	2.59	21.73	2.87	0.007**
EPD_I	10.23	2.43	11.49	2.48	<0.001***	9.65	2.28	11.13	2.44	<0.001***	11.67	2.20	12.31	2.40	0.127
EPD_M	15.81	2.52	15.62	2.45	0.440	15.21	2.32	15.22	2.28	0.963	17.31	2.37	16.52	2.59	0.083
EPD_S	20.05	3.32	19.10	2.95	0.002**	18.97	2.70	18.36	2.55	0.048*	22.69	3.22	20.75	3.11	0.001**
ELID_I	10.76	2.64	12.87	2.60	<0.001***	10.31	2.67	12.79	2.59	<0.001***	11.86	2.25	13.05	2.64	0.008**
ELID_M	16.47	2.69	16.76	2.46	0.234	15.80	2.50	16.49	2.31	0.013*	18.13	2.42	17.36	2.69	0.099
ELID_S	21.20	3.56	20.24	2.98	0.003**	19.96	2.83	19.58	2.57	0.221	24.28	3.31	21.70	3.30	<0.001***
EPDI_I	12.96	2.75	15.45	2.93	<0.001***	12.88	2.88	15.71	2.85	<0.001***	13.14	2.42	14.90	3.03	0.001**

EPDI_M	18.91	2.54	19.29	2.45	0.114	18.50	2.45	19.21	2.32	0.011*	19.93	2.48	19.48	2.71	0.341
EPDI_S	23.82	3.36	22.69	2.97	<0.001***	22.72	2.78	22.08	2.59	0.042*	26.57	3.13	24.04	3.32	<0.001***
EExD_I	17.24	2.98	19.81	3.18	<0.001***	17.45	3.23	20.15	3.08	<0.001***	16.70	2.19	19.05	3.29	<0.001***
EExD_M	23.34	2.43	23.50	2.56	0.517	23.21	2.58	23.52	2.48	0.301	23.66	2.01	23.46	2.74	0.652
EExD_S	27.95	3.01	26.58	2.97	<0.001***	27.20	2.75	26.08	2.72	<0.001***	29.82	2.83	27.71	3.19	<0.001***
EL_I	60.54	6.68	54.85	5.52	<0.001***	61.60	6.91	55.58	5.60	<0.001***	57.92	5.31	53.22	4.99	<0.001***
EL_M	70.07	6.87	60.04	6.50	<0.001***	70.93	6.92	61.08	6.65	<0.001***	67.91	6.28	57.71	5.49	<0.001***
EL_S	72.19	8.38	61.27	7.47	<0.001***	72.95	8.93	61.88	8.10	<0.001***	70.30	6.53	59.90	5.62	<0.001***
PFW	31.06	1.87	29.65	1.84	<0.001***	31.34	1.75	29.92	1.75	<0.001***	30.36	1.98	29.05	1.88	<0.001***
PFH	11.74	1.22	11.82	1.13	0.469	11.97	1.13	11.95	1.14	0.852	11.17	1.24	11.54	1.06	0.067
ID	11.98	0.63	11.85	0.67	0.038*	12.13	0.64	11.99	0.68	0.079	11.62	0.44	11.53	0.52	0.293
PuD	4.49	0.68	4.42	0.71	0.280	4.40	0.60	4.42	0.71	<0.001***	4.71	0.79	4.42	0.74	0.032*
PEn	16.03	1.42	15.22	1.39	<0.001***	16.46	1.26	15.72	1.15	<0.001***	14.98	1.24	14.12	1.23	<0.001***
LEn	10.58	1.26	9.91	1.25	<0.001***	10.86	1.20	10.25	1.16	<0.001***	9.91	1.16	9.17	1.12	<0.001***
PEx	16.59	1.64	15.87	1.51	<0.001***	16.34	1.55	15.53	1.42	<0.001***	17.18	1.69	16.62	1.45	0.046*
LEx	11.30	1.93	10.62	1.68	<0.001***	10.94	1.81	10.17	1.51	<0.001***	12.19	1.93	11.62	1.59	0.068
EnD	33.78	3.84	32.33	3.69	<0.001***	32.17	2.75	30.61	2.31	<0.001***	37.70	3.29	36.13	3.33	0.009**
ExD	94.02	4.52	89.77	4.27	<0.001***	93.10	4.19	88.73	3.63	<0.001***	96.26	4.55	92.08	4.69	<0.001***
PD	64.71	3.57	61.44	3.07	<0.001***	64.26	3.41	61.11	2.80	<0.001***	65.81	3.75	62.19	3.50	<0.001***
UPML	41.36	3.02	39.75	2.72	<0.001***	41.73	2.76	39.98	2.80	<0.001***	40.45	3.45	39.26	2.50	0.024*

LPML	34.63	2.47	33.11	2.39	<0.001***	35.15	2.26	33.59	2.18	<0.001***	33.37	2.53	32.04	2.51	0.004**
MCA	39.81	3.97	41.92	3.98	<0.001***	39.65	3.95	41.06	3.63	0.001**	40.19	4.05	43.80	4.09	<0.001***
LCA	35.93	3.93	37.87	3.78	<0.001***	37.04	3.56	38.87	3.40	<0.001***	33.20	3.44	35.66	3.65	<0.001***
CT	165.84	3.04	165.87	3.01	0.918	166.29	3.19	166.46	2.83	0.635	164.75	2.32	164.58	2.99	0.729
UA	5.45	1.12	5.93	1.19	<0.001***	5.46	1.22	5.96	1.16	<0.001***	5.43	0.81	5.86	1.27	0.024*
UV	1.69	2.67	1.17	3.16	0.068	2.06	2.71	1.73	3.35	0.351	0.81	2.39	-0.09	2.24	0.032*

*p<0.05, **p<0.01, ***p<0.001

5.3 Correlation between parameters and age of Caucasians

The composition of each age group is shown in Figure 7.

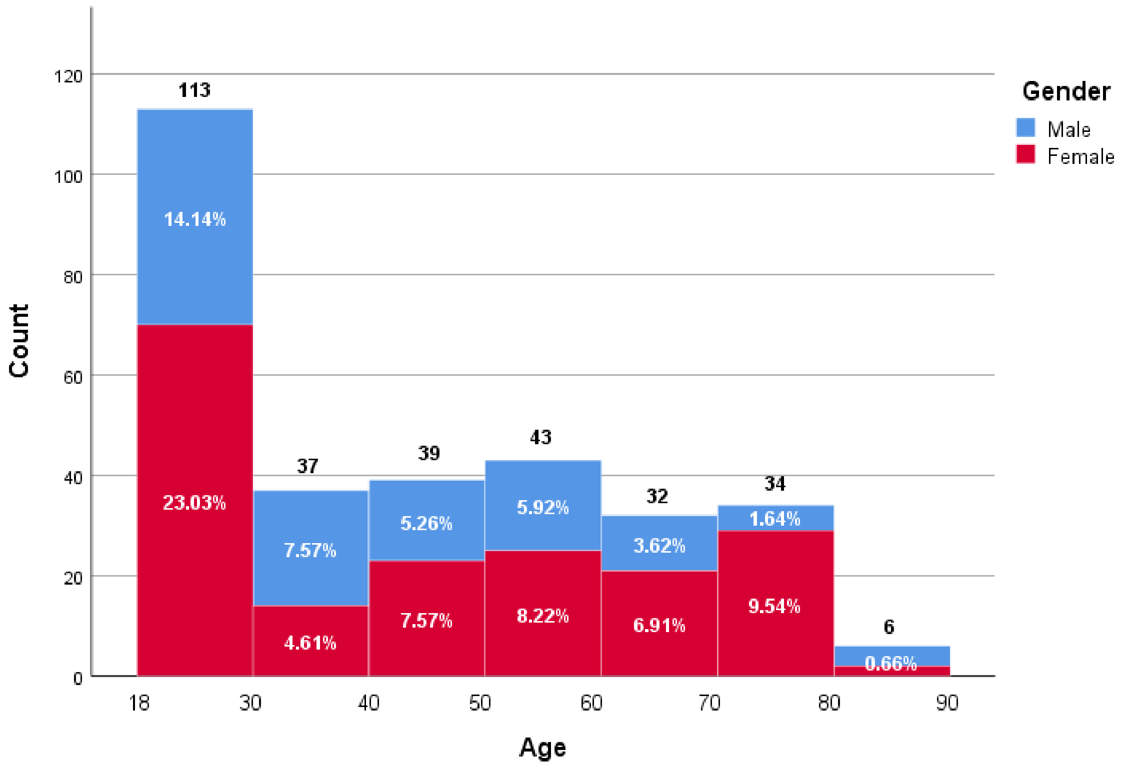


Figure 7. Gender and age distribution of the Caucasian population

5.3.1. Correlation between parameters and age

All the data generally fits a normal distribution, and a linear relationship between the two variables was demonstrated through a scatterplot before the Pearson correlation analysis was carried out (Fig.8-10). The Pearson's correlation coefficient (r) of all measurements in different gender groups are shown in Table 8. EL_S (r=-0.675, p<0.001) was strongly negatively correlated with age (Fig.8A), whereas EL_I, PuD, PEx, and LEx (r=-0.568, -0.475, -0.429 and -0.415, P<0.001, respectively) were moderately negatively correlated with age (Fig.8B-E). PFW, LPML, UPML, PFH, MCA, ID, ExD (r= -0.388, -0.367, -0.362, -0.352, -0.344, -0.254 and -0.246, P<0.001, respectively) and age were weak negatively related (Fig.9), while EEnD_I, CT and ELID_S (r= 0.249, 0.236 and 0.208, P<0.001, respectively) were weak positively related (Fig.10).

In male group, EL_S (r= -0.636, p<0.001) was strongly negatively correlated with age (Fig.11A), whereas EL_I (r= -0.517, p<0.001) was moderately negatively correlated (Fig.11B). EEnD_I, EPDm_I and PD showed a positive weak correlation with age (r= 0.357, 0.260 and 0.238, p<0.001, respectively), while PuD, PFW, PEx, MCA, EExD_I, EPDl_I, LEx and ID (0.2<|r|<0.3, p≤0.001) showed a negative weak correlation.

In the female group, EL_S, EL_I and PuD (r= -0.755, -0.618 and -0.608, p<0.001) correlated with age strongly and negatively (Fig.12A-C), whereas PEx, LEx, UPML, LPML, PFH, PFW and MCA (r=-0.519, -0.516, -0.457, -0.447, -0.445, -0.443 and -0.424, p<0.001, respectively) correlated moderately (Fig.13A-G). ExD and ID (r=-0.294 and -0.256, p<0.001) showed a negative weak correlation with age (Fig.14B), while CT, EnD, ELID_S and EPD_S (r=0.274, 0.245, 0.243 and 0.228, p<0.001, respectively) were positively correlated with age (Fig.14A, C-E).

Table 8. Pearson's correlation analysis and significance between parameters and age in different gender groups of Caucasians.

	Overall (n=304)				Male (n=120)				Female (n=222)			
Parameters	Mean	SD	r	p-value	Mean	SD	r	p-value	Mean	SD	r	p-value
EEnD_I	18.41	2.93	0.249	<0.001***	18.15	2.91	0.357**	<0.001***	18.58	2.94	0.182**	<0.001***
EEnD_M	22.89	2.54	0.003	0.940	23.75	2.21	0.133*	0.040*	22.32	2.58	-0.016	0.763
EEnD_S	26.35	2.97	-0.112	0.006**	27.67	2.58	-0.004	0.953	25.48	2.90	-0.120*	0.022*
EPDm_I	15.46	2.85	0.199	<0.001***	15.29	2.85	0.260**	<0.001***	15.57	2.84	0.160**	0.002**
EPDm_M	20.68	2.59	0.058	0.159	21.48	2.44	0.125	0.055	20.16	2.56	0.064	0.223
EPDm_S	24.31	2.87	0.069	0.090	25.33	2.69	0.114	0.079	23.65	2.79	0.095	0.068
ELmD_I	11.69	2.88	0.161	<0.001***	10.93	2.65	0.144*	0.025*	12.18	2.92	0.145**	0.005**
ELmD_M	16.97	2.60	0.076	0.062	17.23	2.54	0.071	0.279	16.79	2.62	0.093	0.077
ELmD_S	20.72	2.89	0.122	0.003**	21.25	2.89	0.105	0.107	20.38	2.84	0.159**	0.002**
EPD_I	10.57	3.09	0.123	0.002**	9.55	2.61	0.012	0.854	11.24	3.19	0.142**	0.006**
EPD_M	15.30	2.68	0.114	0.005**	15.26	2.49	0.070	0.282	15.33	2.80	0.134*	0.011*
EPD_S	19.04	3.01	0.199	<0.001***	19.40	2.93	0.177**	0.006**	18.81	3.05	0.228**	<0.001***
ElD_I	11.70	3.49	0.085	0.036*	10.12	2.94	-0.055	0.398	12.73	3.44	0.106*	0.042*
ElD_M	16.21	2.87	0.103	0.012*	15.75	2.63	0.017	0.790	16.51	2.97	0.127*	0.015*
ElD_S	20.17	3.12	0.208	<0.001***	20.39	3.01	0.164*	0.011*	20.03	3.19	0.243**	<0.001***
EPDl_I	13.87	3.88	-0.070	0.086	12.18	3.18	-0.229**	<0.001***	14.97	3.90	-0.057	0.273
EPDl_M	18.45	2.96	-0.042	0.300	18.06	2.67	-0.127	0.051	18.70	3.11	-0.018	0.728
EPDl_S	22.49	3.15	0.130	0.001**	22.95	3.01	0.109	0.091	22.18	3.21	0.162**	0.002**
EExD_I	18.11	4.04	-0.122	0.003**	16.61	3.34	-0.232**	<0.001***	19.09	4.16	-0.126*	0.016*

EExD_M	22.64	3.12	-0.129	0.002**	22.55	2.90	-0.147*	0.024*	22.69	3.27	-0.125*	0.017*
EExD_S	26.40	3.28	0.042	0.307	27.18	3.23	0.070	0.283	25.88	3.22	0.057	0.273
EL_I	52.27	9.50	-0.568	<0.001***	56.24	9.70	-0.517**	<0.001***	49.66	8.41	-0.618**	<0.001***
EL_M	64.80	8.97	-0.080	0.049*	70.51	8.65	-0.001	0.984	61.05	6.98	-0.059	0.259
EL_S	56.55	13.93	-0.675	<0.001***	63.45	14.12	-0.636**	<0.001***	52.00	11.79	-0.755**	<0.001***
UPML	39.71	3.23	-0.362	<0.001***	41.34	2.67	-0.145*	0.025*	38.64	3.12	-0.457**	<0.001***
LPML	33.49	2.56	-0.367	<0.001***	34.83	2.13	-0.187**	0.004**	32.61	2.44	-0.447**	<0.001***
PFW	29.86	2.01	-0.388	<0.001***	30.94	1.70	-0.272**	<0.001***	29.16	1.89	-0.443**	<0.001***
PFH	11.56	1.26	-0.352	<0.001***	11.78	1.20	-0.150*	0.020*	11.42	1.27	-0.445**	<0.001***
ID	11.94	0.60	-0.254	<0.001***	12.07	0.58	-0.217**	0.001**	11.86	0.60	-0.256**	<0.001***
PuD	4.05	0.80	-0.475	<0.001***	4.16	0.89	-0.283**	<0.001***	3.98	0.73	-0.608**	<0.001***
PD	62.90	3.57	0.140	0.001**	64.82	3.42	0.238**	<0.001***	61.65	3.08	0.184**	<0.001***
PEn	16.08	1.35	-0.017	0.670	16.63	1.32	0.131*	0.044*	15.73	1.25	-0.053	0.312
LEn	10.56	1.25	0.010	0.803	11.00	1.26	0.130*	0.044*	10.28	1.17	-0.016	0.760
PEx	15.25	1.65	-0.429	<0.001***	16.03	1.46	-0.251**	<0.001***	14.74	1.57	-0.519**	<0.001***
LEx	9.79	1.78	-0.415	<0.001***	10.58	1.67	-0.223**	0.001**	9.28	1.67	-0.516**	<0.001***
EnD	31.61	2.82	0.183	<0.001***	32.40	2.96	0.164*	0.011*	31.09	2.60	0.245**	<0.001***
ExD	90.53	4.88	-0.246	<0.001***	93.41	4.30	-0.142*	0.015*	88.63	4.28	-0.294	<0.001***
MCA	39.03	4.10	-0.344	<0.001***	38.56	4.29	-0.249**	<0.001***	39.34	3.95	-0.424**	<0.001***
LCA	38.29	3.84	0.052	0.204	37.20	3.84	0.082	0.205	39.01	3.67	0.000	0.995
CT	167.21	3.53	0.236	<0.001***	166.88	3.67	0.163*	0.012*	167.43	3.42	0.274**	<0.001***
UA	5.45	1.29	-0.146	<0.001***	5.23	1.23	-0.109	0.095	5.59	1.31	-0.187**	<0.001***

UV	1.43	2.43	-0.120	0.003**	1.56	2.27	-0.140*	0.032*	1.35	2.53	-0.104*	0.046*

*p<0.05, **p<0.01, ***p<0.001.

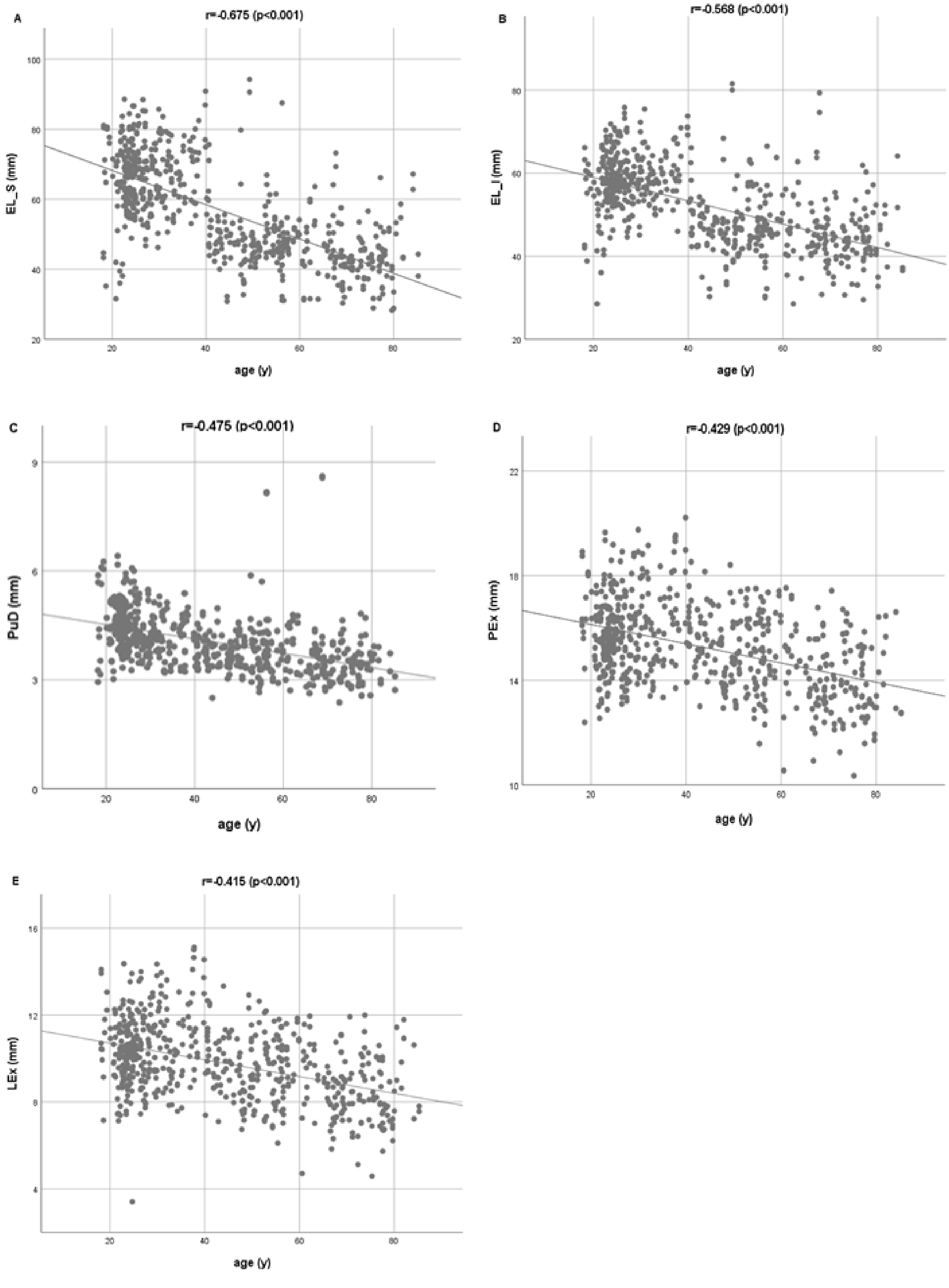


Figure 8. Parameters strong/moderate negatively correlated with age.

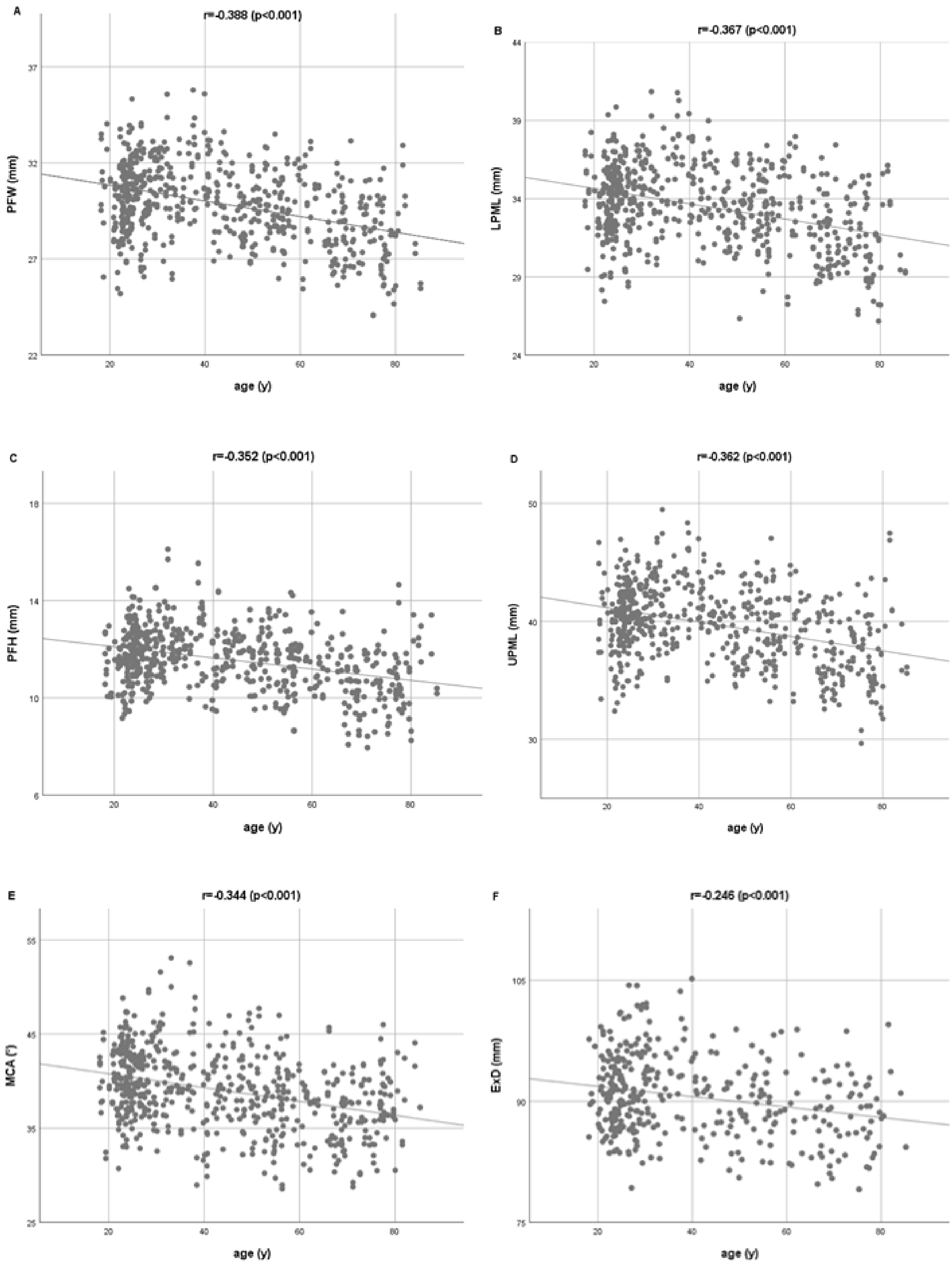


Figure 9. Parameters weak negatively related to age.

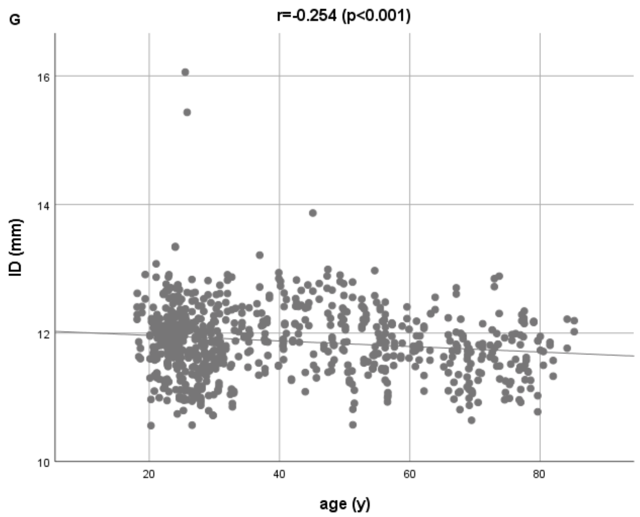


Figure 9. Parameters weak negatively related to age. (continued)

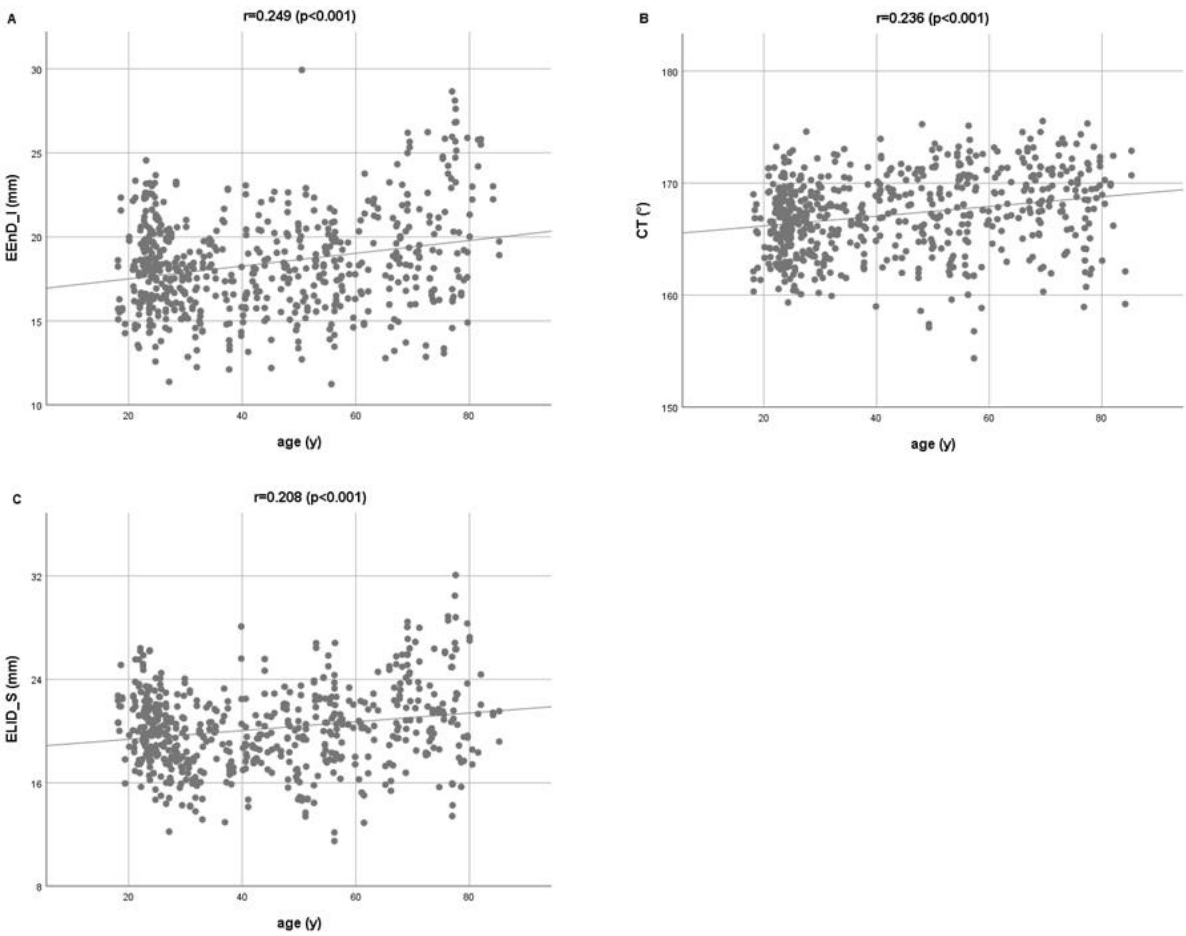


Figure 10. Parameters weak positively related to age.

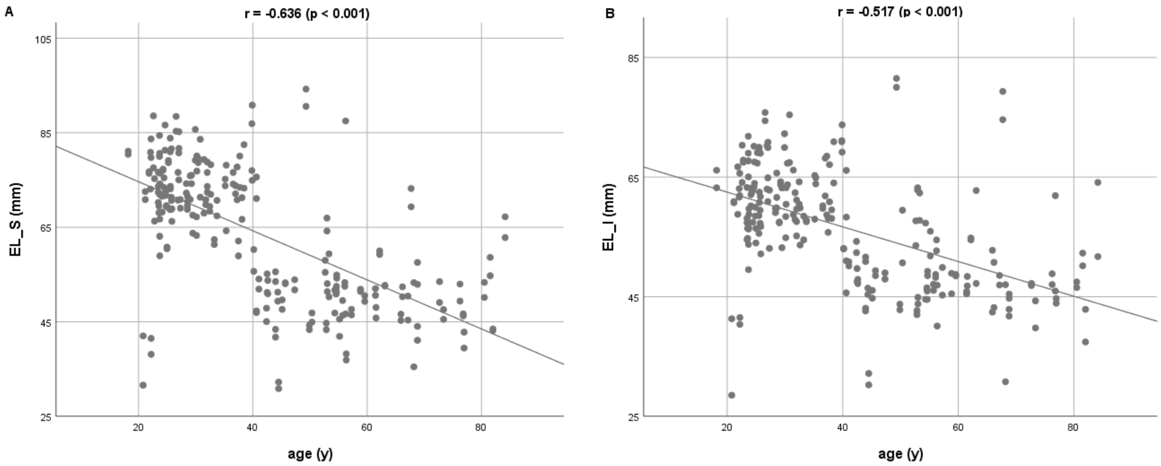


Figure 11. Parameters negatively correlated with age in the male group

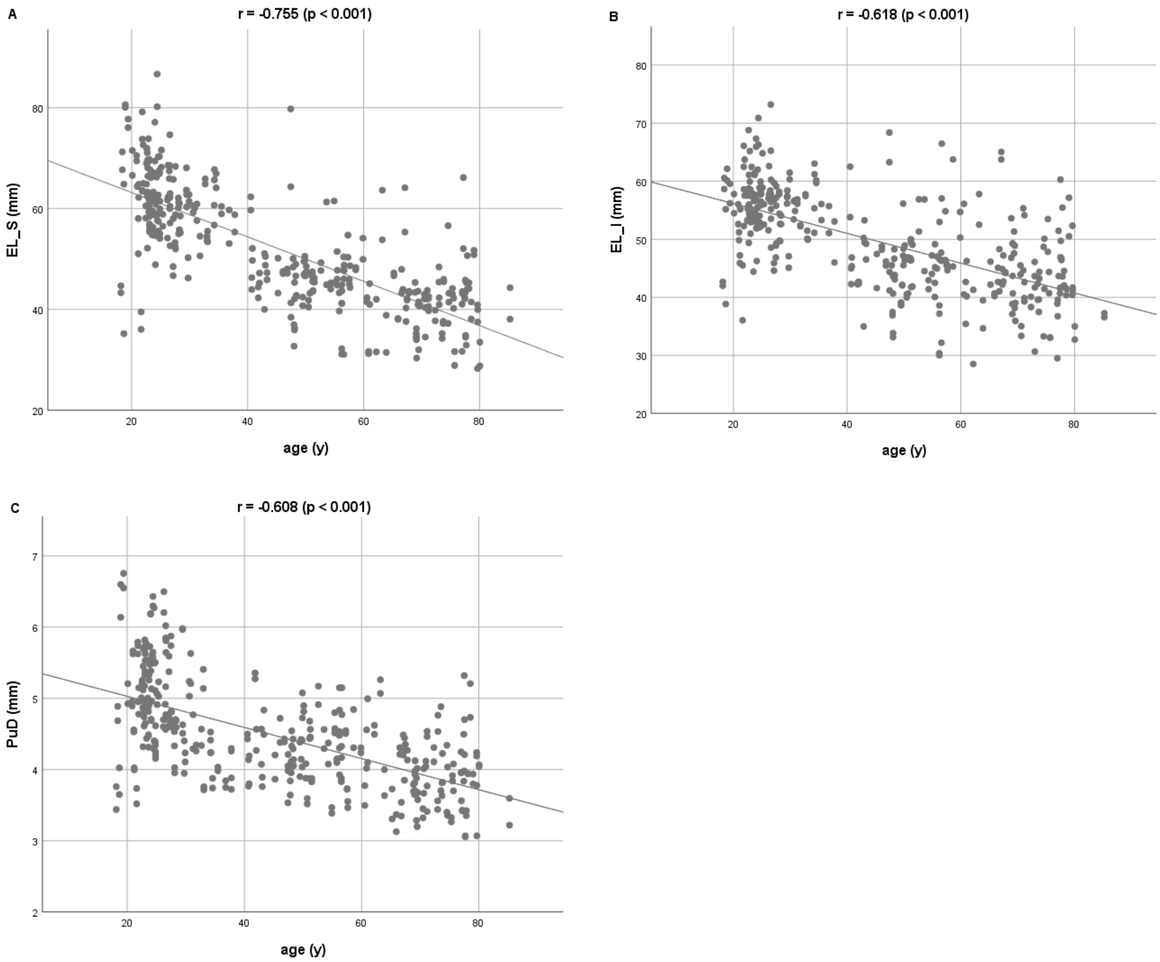
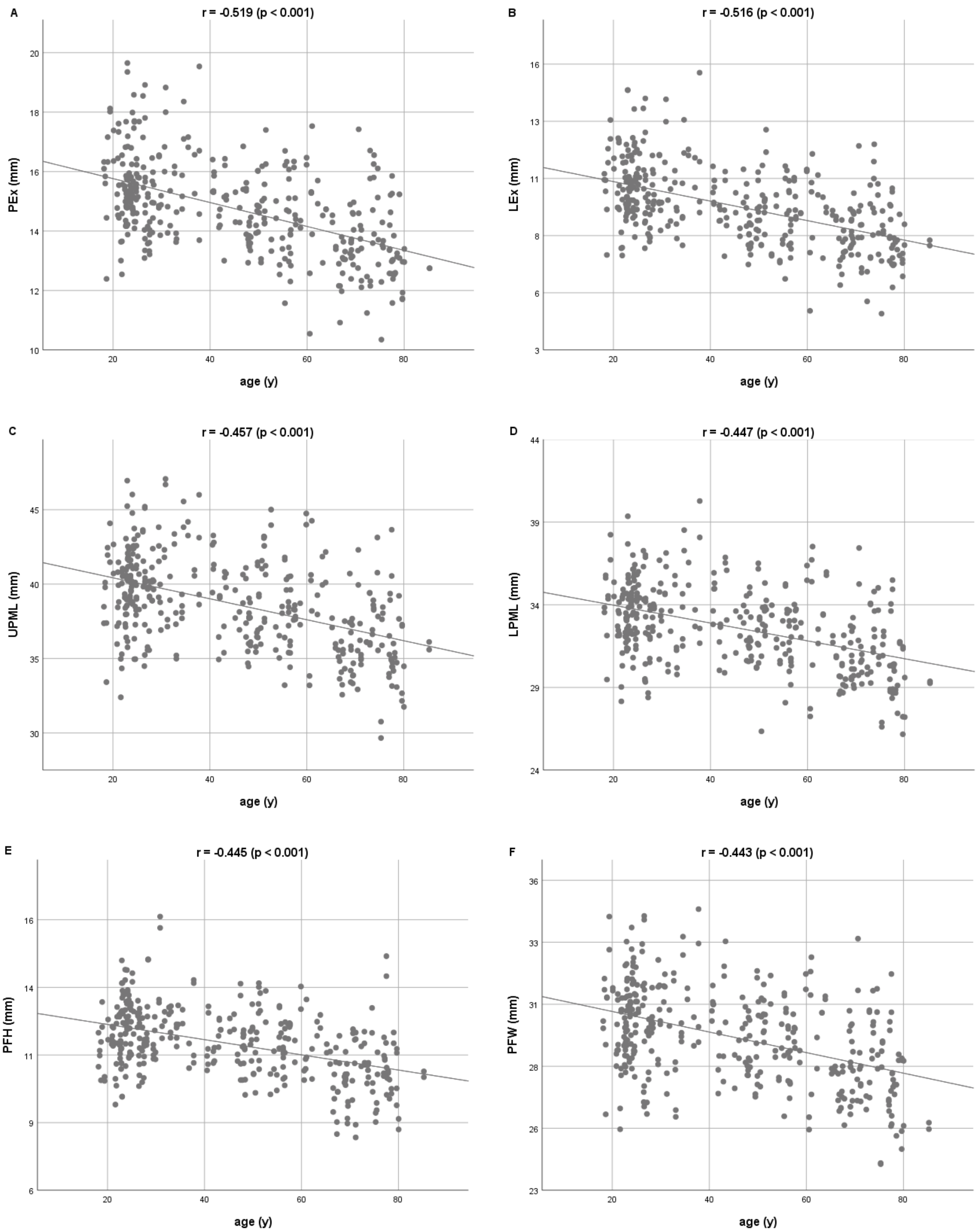


Figure 12. Parameters strong negatively correlated with age in the female group.


A
r = -0.519 (p < 0.001)
PEx (mm)
age (y)
B
r = -0.516 (p < 0.001)
LEx (mm)
age (y)
C
r = -0.457 (p < 0.001)
UPML (mm)
age (y)
D
r = -0.447 (p < 0.001)
LPML (mm)
age (y)
E
r = -0.445 (p < 0.001)
PFH (mm)
age (y)
F
r = -0.443 (p < 0.001)
PFW (mm)
age (y)

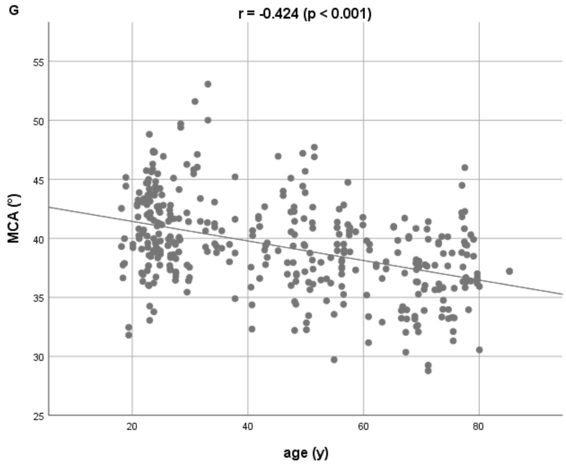


Figure 13. Parameters moderate negatively correlated with age in the female group.

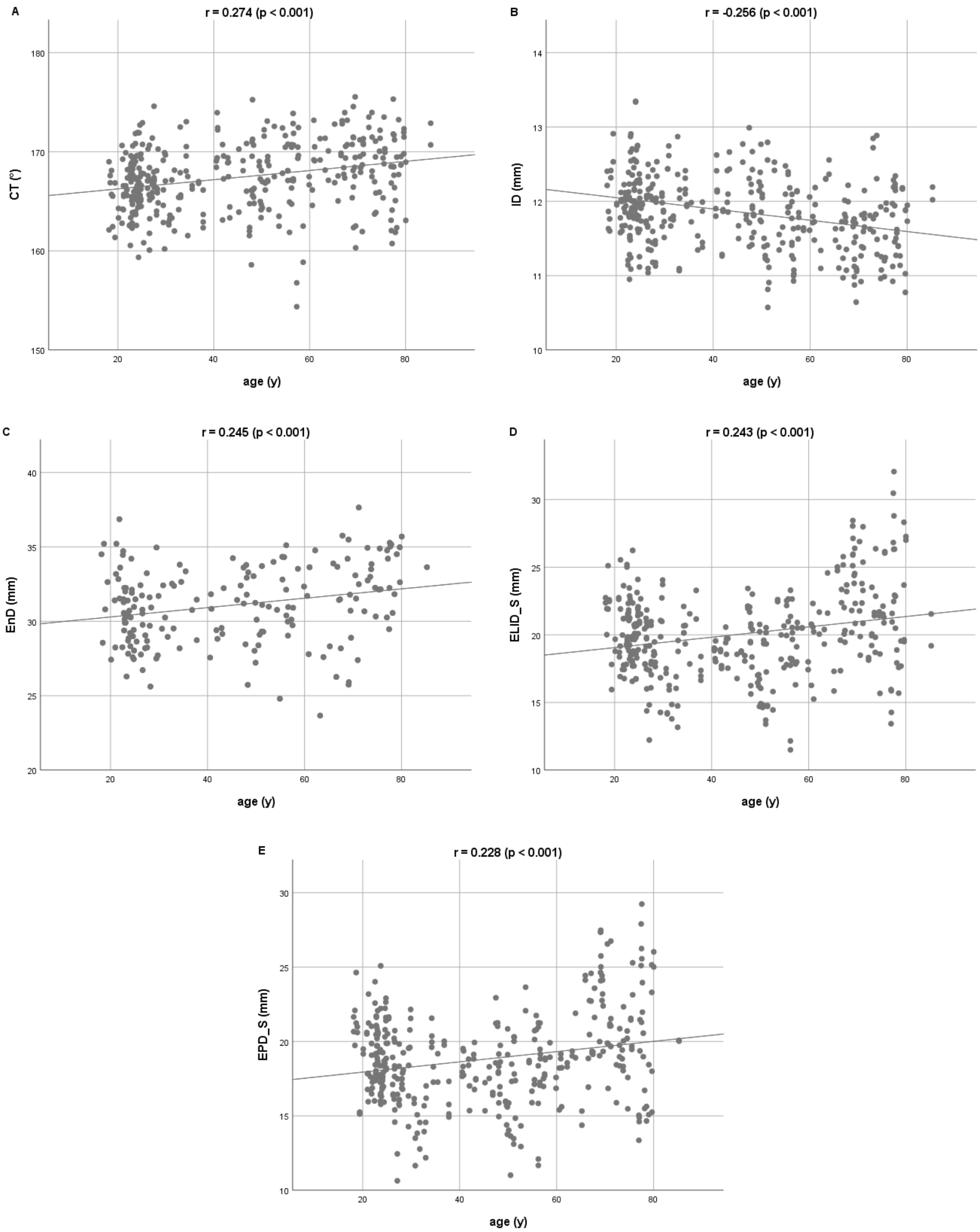


Figure 14. Parameters weak correlated with age in the female group.

Distributions of measurements among all ages are shown in Table 9.

Table 9. Mean and standard deviation of parameters between age groups of Caucasians.

	G1		G2		G3		G4		G5		G6		G7	
Parameters (mm/°)	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
EEnD_I	18.14	2.41	17.14	2.44	17.93	2.52	18.12	2.63	19.36	3.16	19.98	4.07	22.64	2.38
EEnD_M	23.12	2.33	22.60	2.46	22.56	2.04	22.40	2.64	22.73	2.47	23.14	3.40	25.55	1.95
EEnD_S	26.77	2.66	26.50	2.99	26.19	2.52	26.02	3.47	25.55	3.17	25.79	3.37	28.26	2.32
EPDm_I	15.45	2.31	14.28	2.33	14.75	2.74	14.80	2.33	16.49	2.80	16.91	4.26	18.55	2.50
EPDm_M	20.89	2.23	20.15	2.49	20.02	2.44	20.20	2.77	20.91	2.26	21.37	3.57	22.81	2.38
EPDm_S	24.40	2.48	23.78	2.96	23.72	2.80	24.13	3.41	24.56	2.68	24.92	3.36	26.21	2.43
ELmD_I	11.86	2.36	10.38	2.38	10.83	2.49	10.92	2.48	12.91	3.26	13.09	4.09	13.30	2.69
ELmD_M	17.25	2.29	16.10	2.35	16.23	2.36	16.34	2.52	17.54	2.79	17.83	3.39	18.45	1.96
ELmD_S	20.78	2.56	19.69	2.88	20.17	2.61	20.45	3.11	21.40	3.13	21.70	3.33	22.16	2.50
EPD_I	10.84	2.39	9.35	2.42	9.58	2.40	9.61	2.92	11.92	3.96	12.02	4.22	11.08	4.00
EPD_M	15.55	2.20	14.19	2.30	14.41	2.09	14.64	2.63	16.31	3.21	16.37	3.64	16.82	2.64
EPD_S	18.96	2.46	17.60	2.86	18.27	2.38	18.89	3.15	20.35	3.56	20.37	3.68	20.92	2.66
ELlD_I	12.11	2.86	10.46	2.64	10.55	2.56	10.65	3.55	12.67	4.05	13.42	4.72	11.53	5.52
ELlD_M	16.54	2.33	15.11	2.36	15.15	2.02	15.40	2.75	17.01	3.47	17.65	3.97	17.27	3.91
ELlD_S	20.06	2.55	18.76	2.88	19.30	2.27	19.94	3.35	21.38	3.51	21.91	3.99	21.64	3.20
EPDl_I	14.88	3.16	13.20	2.93	12.47	3.02	12.05	3.92	14.63	4.54	14.66	5.22	12.53	5.33
EPDl_M	19.23	2.33	17.87	2.35	17.13	2.25	16.92	2.80	18.90	3.56	19.39	4.09	19.08	3.85
EPDl_S	22.65	2.55	21.49	2.92	21.44	2.42	21.84	3.39	23.17	3.57	24.07	4.20	24.34	2.91
EExD_I	19.24	3.42	18.13	3.28	16.63	3.22	16.48	4.10	17.93	4.52	18.54	5.50	16.78	4.74

EExD_M	23.57	2.47	22.81	2.63	21.16	2.75	21.23	2.82	22.38	3.65	22.84	4.42	23.62	3.25
EExD_S	26.73	2.68	26.10	3.05	25.12	3.14	25.74	3.24	26.69	3.73	27.20	4.44	28.57	3.01
EL_I	57.84	7.09	59.53	6.10	47.50	8.75	47.91	6.89	46.46	8.91	43.86	6.56	44.51	9.24
EL_M	65.21	8.05	66.22	9.26	65.77	8.40	64.26	9.25	62.75	8.87	62.92	10.26	67.89	14.62
EL_S	66.32	10.36	68.36	9.13	49.65	10.84	48.26	7.53	45.05	9.28	42.58	6.44	48.19	11.73
UPML	40.35	2.71	41.96	3.17	39.80	2.78	39.73	2.93	37.79	2.96	36.85	2.85	39.41	4.90
LPML	33.98	2.20	35.17	2.57	33.84	2.26	33.32	2.05	32.21	2.59	31.26	2.40	31.98	3.09
PFW	30.35	1.81	31.13	2.02	29.96	1.76	29.72	1.52	28.79	1.91	28.17	1.86	28.56	2.41
PFH	11.81	1.05	12.40	1.28	11.74	0.97	11.44	1.24	10.66	1.11	10.62	1.20	11.46	1.74
ID	12.06	0.71	12.04	0.49	12.15	0.51	11.81	0.49	11.64	0.46	11.67	0.47	11.80	0.27
PuD	4.48	0.68	4.21	0.57	3.81	0.44	3.83	0.88	3.72	1.04	3.42	0.53	3.40	0.40
PD	62.09	3.19	63.71	3.94	62.67	3.69	63.93	3.28	62.48	3.97	63.50	3.37	66.08	3.88
PEn	15.93	1.20	16.39	1.36	16.25	1.40	16.45	1.13	16.00	1.72	15.68	1.30	16.08	2.08
LEn	10.41	1.16	10.83	1.31	10.62	1.36	10.87	1.07	10.54	1.42	10.32	1.15	10.67	2.00
PEx	15.76	1.44	16.27	1.72	15.33	1.28	15.05	1.42	14.22	1.46	13.76	1.46	14.43	1.54
LEx	10.37	1.60	10.91	1.89	9.61	1.49	9.53	1.50	8.75	1.45	8.29	1.53	9.24	1.63
EnD	31.13	2.63	31.80	2.57	31.12	2.87	31.90	2.62	31.16	3.31	33.00	2.71	34.76	1.99
ExD	90.12	4.07	92.29	5.13	89.67	4.54	90.11	3.95	87.31	4.67	88.21	4.38	90.77	5.07
MCA	40.34	3.47	40.76	4.79	39.19	3.93	37.68	4.00	36.40	3.41	37.02	3.55	37.98	4.25
LCA	37.99	3.48	38.29	3.90	38.95	3.47	38.42	4.11	37.82	4.40	38.64	4.14	39.36	5.04
CT	166.33	2.97	166.53	3.08	167.53	3.63	167.47	4.26	168.79	3.39	168.58	3.64	167.81	4.29
UA	5.85	1.17	5.42	1.29	5.03	1.08	4.80	1.12	5.45	1.43	5.44	1.52	5.47	1.13
UV	1.85	3.14	1.94	2.93	0.75	1.81	0.83	1.33	1.19	1.22	1.29	1.32	1.43	1.01

G1, age<=30; G2, 30-40; G3, 40-50; G4, 50-60; G5, 60-70; G6, 70-80; G7, age >80.

5.3.2. Eyebrow-related parameters

Eyebrow-related parameters included inferior, middle, or superior distance of EEnD, EPDm, ELmD, EPD, ELlD, EPDl, EExD, and EL. (Fig.15)

In all age groups, except for EL, there was an overall increasing trend in measurements with age. From G1 to G2, there were no significant changes in EEnD_M/S, EPDm_S, and EExD_S (p=0.098, 0.470, 0.104, and 0.092, respectively), while the remaining measurements decreased significantly; from G2 to G3, most measurements did not change significantly, while EPDl_M (p=0.049) and EExD_I/M (p<0.01) decreased; from G4 to G5, most measurements increased except for EEnD_M/S, EPDm_M/S, ELmD_S, and EExD_S, which did not change significantly(p>0.05), and a decrease in EEnD_I(p=0.012). In G3-G4, G5-G6, and G6-G7, there were no significant changes in all measurements, except for an increase of EEnD from G6 to G7(p=0.004,0.003 and 0.017, respectively). In EL, there was a significant decrease in EL_I/S at G2-3 and EL_S at G4-5 (p<0.001), with no significant difference in the EL_M group. (Fig.15, Tab.10).

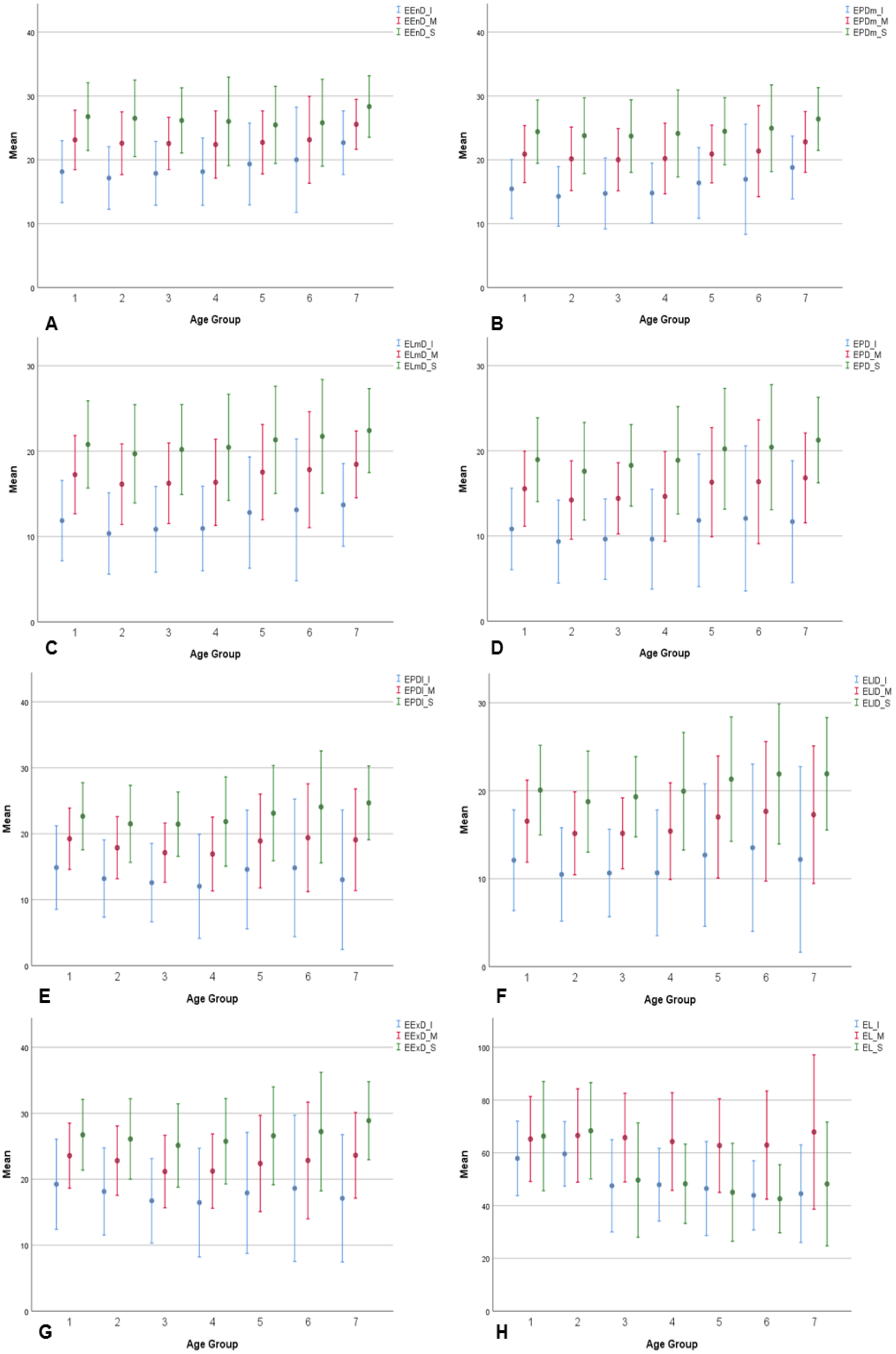


Figure 15. Distribution of eyebrow-related parameters across age groups

Table 10. Differences of eyebrow-related parameters in Caucasian populations across age groups (p value).

	G1-2	G2-3	G3-4	G4-5	G5-6	G6-7
EEnD_I	0.002	[illegible]	0.642	0.012	0.330	0.004
EEnD_M	0.098	0.930	0.657	0.443	0.431	0.003
EEnD_S	0.470	0.493	0.719	0.400	0.675	0.017
EPDm_I	0.000	0.258	0.899	0.000	0.506	0.077
EPDm_M	0.016	0.742	0.651	0.101	0.389	0.104
EPDm_S	0.104	0.900	0.401	0.412	0.496	0.206
ELmD_I	0.000	0.252	0.823	0.000	0.780	0.863
ELmD_M	0.000	0.734	0.782	0.007	0.598	0.401
ELmD_S	0.002	0.286	0.537	0.066	0.605	0.650
EPD_I	0.000	0.573	0.929	0.000	0.893	0.475
EPD_M	0.000	0.535	0.543	0.001	0.923	0.697
EPD_S	0.000	0.117	0.159	0.009	0.976	0.622
ELlD_I	0.000	0.832	0.825	0.001	0.331	0.215
ELlD_M	0.000	0.906	0.504	0.002	0.335	0.772
ELlD_S	0.000	0.206	0.152	0.012	0.423	0.829
EPDl_I	0.000	0.135	0.440	0.000	0.972	0.198
EPDl_M	0.000	0.049	0.597	0.000	0.469	0.813
EPDl_S	0.001	0.901	0.386	0.022	0.188	0.782
EExD_I	0.015	0.005	0.795	0.043	0.488	0.300
EExD_M	0.026	0.000	0.886	0.032	0.525	0.575
EExD_S	0.092	[illegible]	0.219	0.098	0.476	0.194
EL_I	0.070	0.000	0.739	0.262	0.058	0.767
EL_M	0.373	0.754	0.277	0.316	0.918	0.152
EL_S	0.139	0.000	0.336	0.025	0.080	0.132

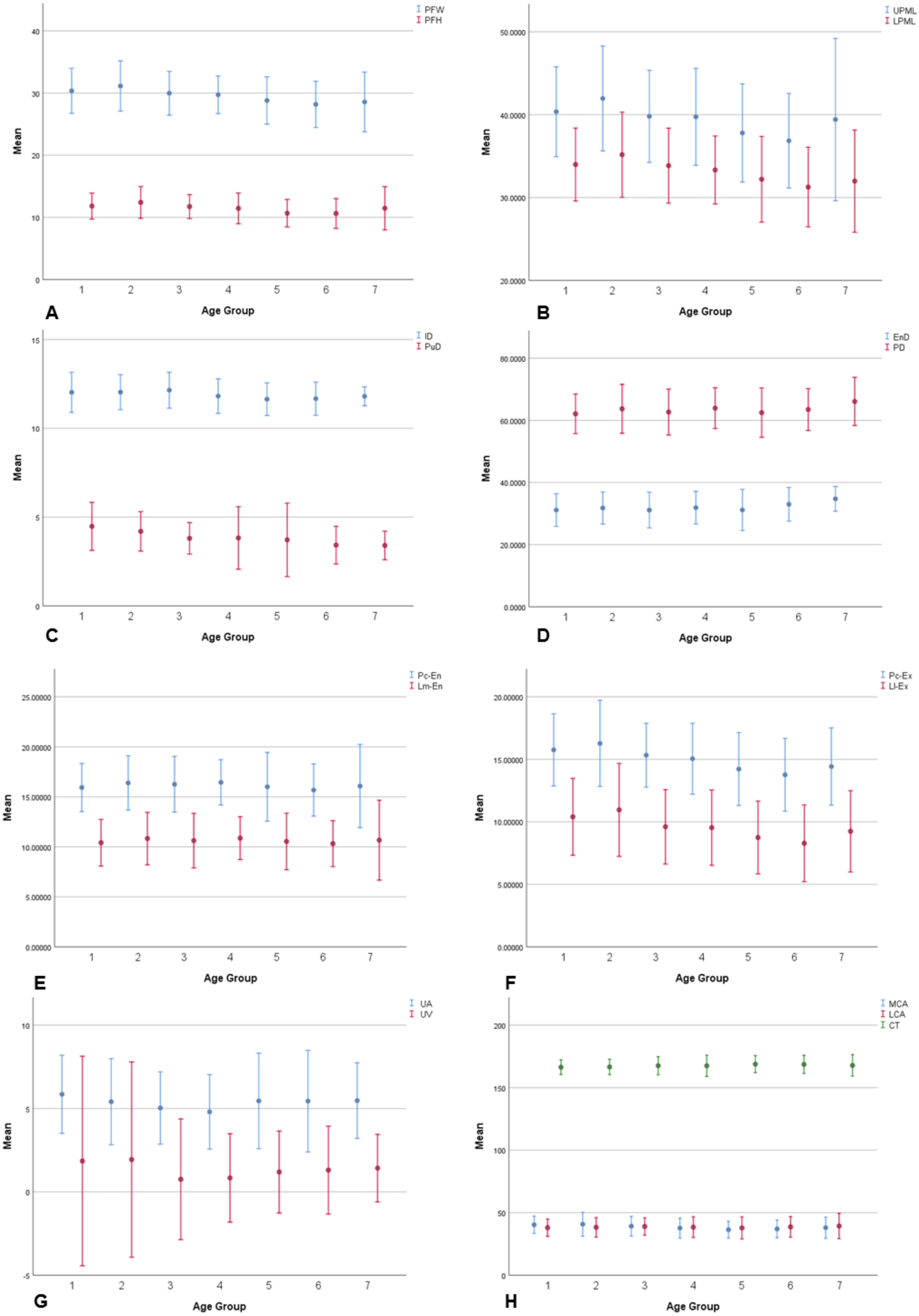
0.000 0.050 1.000

G1, age<=30; G2, 30-40; G3, 40-50; G4, 50-60; G5, 60-70; G6, 70-80; G7, age >80.

5.3.3. Ocular-related parameters

Ocular-related parameters included PFW, PFH, UPML, LPML, ID, PuD, EnD, ExD, PD, PEn, LEn, PEx, LEx, MCA, LCA, CT, UA and UV. (Fig.16)

Among all linear measurements (PFW, PFH, UPML, LPML, ID, PuD, EnD, ExD, PD, PEn, LEn, PEx, LEx), from G1 to G2, ID, and EnD changed insignificantly, while PuD decreased and the remaining measurements increased significantly ($p<0.05$); from G2 to G3, significant decreases were observed in PFW, PFH, UPML, LPML, PuD, ExD, PD, PEx and LEx ($p \leq 0.001$), with non-significant changes in other measurements; from G3 to G4, there were no notable changes in most of the measurements, except for a significant decrease in ID and an increase in PD; from G4 to G5, all measurements decreased except PuD, EnD, PEn and LEn, with no significant changes; from G5 to G6, LPML and PuD were significantly decreased, while EnD was increased, leaving no significant changes in the remaining measurements ($p>0.05$); from G6 to G7, most of the measurements did not show significant changes except for the increase in PFH, EnD, and PD. For other measurements, MCA decreased significantly ($p<0.05$) in G2-G3, G3-G4, and G4-G5; CT increased from G4 to G5; LCA did not show any significant change between all groups; UA decreased significantly from G1 to G2 and G2 to G3, increased from G4 to G5; UV decreased from G2 to G3. (Fig.16, Tab.11)


A
PFW
PFH
Mean
Age Group
B
UPML
LPML
Mean
Age Group
C
ID
PuD
Mean
Age Group
D
EnD
PD
Mean
Age Group
E
Pc-En
Lm-En
Mean
Age Group
F
Pc-Ex
Ll-Ex
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MCA
LCA
CT
Mean
Age Group

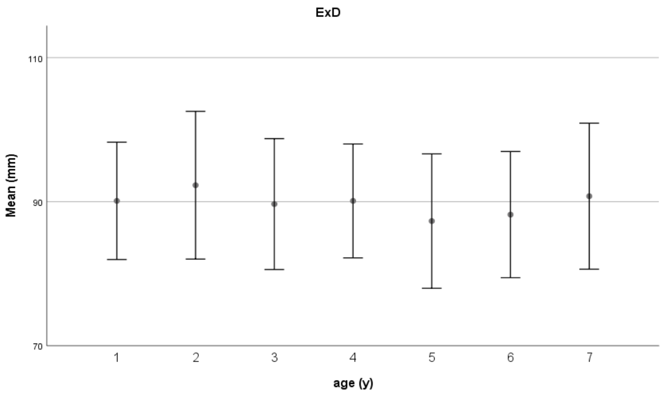

Figure 16. Distribution of palpebral fissure-related parameters in Caucasians across age groups

Table 11. Differences of ocular-related parameters in Caucasian populations across age groups (p value).

	G1-2	G2-3	G3-4	G4-5	G5-6	G6-7
UPML	0.000	0.000	0.883	0.000	0.066	0.103
LPML	0.000	0.001	0.125	0.005	0.031	0.362
PFW	0.002	0.000	0.345	0.002	0.060	0.522
PFH	0.000	0.000	0.091	0.000	0.822	0.040
ID	0.808	0.175	0.000	0.030	0.724	0.173
PuD	0.003	0.000	0.834	0.489	0.039	0.901
PD	0.000	0.094	0.022	0.016	0.116	0.019
PEn	0.006	0.541	0.333	0.074	0.228	0.536
LEn	0.011	0.345	0.201	0.123	0.324	0.566
PEx	0.022	0.000	0.186	0.001	0.073	0.153
LEx	0.029	0.000	0.753	0.002	0.078	
EnD	0.057	0.127	0.071	0.129	0.001	0.036
ExD	0.000	0.001	0.509	0.000	0.258	0.720
MCA	0.491	0.029	0.016	0.040	0.311	0.400
LCA	0.530	0.274	0.375	0.390	0.271	0.593
CT	0.633	0.069	0.921	0.042	0.734	0.511
UA	0.008	0.047	0.179	0.003	0.960	0.945
UV	0.832	0.004	0.745	0.093	0.675	0.728

0.000 0.050 1.000

G1, age<=30; G2, 30-40; G3, 40-50; G4, 50-60; G5, 60-70; G6, 70-80; G7, age >80.

5.4 Parameter differences between eyes

The data were tested as normally distributed, and the paired-sample t-test was used to compare the differences for each parameter between eyes.

In Table 12, the differences between the right and left eyes of each measure (Δ), the correlation with age (r) and significance (p) were shown. EPDl_M, ELlD_M, EPDm_I, ELlD_I, ELmD_I, LEn, PEn showed a low positive correlation with aging (r=0.111, 0.117, 0.120, 0.131, 0.133, 0.133, 0.174, $p<0.05$, respectively), while MCA, UV showed low negative correlation (r=-0.117, -0.157, p=0.024 and 0.003, respectively).

Table 12. Differences between left and right eye measurements and their correlation with age

Difference (Δ)	Mean	SD	r	p
ΔEEnD_I	-0.13	1.91	0.096	0.064
ΔEEnD_M	-0.38	1.51	0.099	0.062
ΔEEnD_S	-0.53	1.79	0.095	0.069
ΔEPDm_I	0.16	1.72	0.120*	0.021
ΔEPDm_M	-0.13	1.49	0.053	0.319
ΔEPDm_S	-0.27	1.53	0.023	0.660
ΔELmD_I	0.16	1.72	0.133*	0.010
ΔELmD_M	-0.01	1.53	0.081	0.127
ΔELmD_S	-0.16	1.63	0.044	0.406
ΔEPD_I	-0.22	1.84	0.013	0.799
ΔEPD_M	-0.19	1.55	-0.021	0.691
ΔEPD_S	-0.15	1.61	-0.046	0.379
ΔELlD_I	-0.06	2.10	0.131*	0.012
ΔELlD_M	-0.02	1.67	0.117*	0.026
ΔELlD_S	-0.06	1.73	0.034	0.516
ΔEPDl_I	-0.01	2.48	0.102	0.050
ΔEPDl_M	0.11	1.89	0.111*	0.036
ΔEPDl_S	0.09	1.83	0.088	0.093
ΔEExD_I	-0.32	2.66	-0.018	0.738
ΔEExD_M	-0.17	1.94	-0.047	0.378
ΔEExD_S	-0.10	1.85	-0.067	0.199
ΔEL_I	0.19	5.19	0.066	0.207
ΔEL_M	-0.31	5.45	-0.059	0.261
ΔEL_S	0.07	5.79	-0.019	0.718
ΔUPML	0.20	1.88	0.003	0.955
ΔLPML	0.26	1.21	0.101	0.054
ΔPFW	0.19	0.93	0.082	0.115
ΔPFH	0.01	0.74	0.013	0.804
ΔID	0.06	0.50	0.000	0.998
ΔPuD	0.00	0.42	-0.048	0.354

∆PEn	0.29	1.05	0.174^{**}	0.001
∆LEn	0.27	1.00	0.133^{*}	0.011
∆PEx	-0.08	1.16	-0.077	0.141
∆LEx	-0.11	1.35	-0.087	0.096
∆MCA	-0.43	2.93	-0.117^{*}	0.024
∆LCA	0.08	2.84	0.077	0.139
∆CT	-0.73	3.38	-0.045	0.389
∆UA	0.01	0.67	0.067	0.208
∆UV	0.66	2.78	-0.157^{**}	0.003

*p<0.05, **p<0.01, ***p<0.001.

5.4.1. Eyebrow-related parameters

Among the eyebrow-related parameters, there were highly significant differences between the right and left eye in EEnD_M/S, EPD_I distance (p<0.001). Differences also existed in EPDm_S, EPD_M, and EExD_I (p=0.001, 0.022, 0.021, respectively), with the mean of the left eye greater than that of the right. No significant differences were found in other measurements between the two sides. (Tab.13)

Table 13. Mean values and significance of differences in eyebrow-related parameters between eyes

	Overall		**Right**		**Left**		**p-value**
Parameters	Mean	SD	Mean	SD	Mean	SD	
EEnD_I	18.64	2.92	18.57	2.93	18.70	2.91	0.187
EEnD_M	23.17	2.61	22.98	2.57	23.35	2.64	<0.001***
EEnD_S	26.79	3.10	26.53	3.03	27.04	3.14	<0.001***
EPDm_I	15.46	2.75	15.54	2.75	15.38	2.75	0.081
EPDm_M	20.62	2.55	20.56	2.57	20.68	2.54	0.093
EPDm_S	24.38	2.84	24.24	2.84	24.52	2.84	0.001**
ELmD_I	11.89	2.81	11.97	2.84	11.81	2.78	0.071
ELmD_M	17.09	2.57	17.10	2.58	17.09	2.57	0.863
ELmD_S	20.99	2.94	20.91	2.92	21.08	2.96	0.060
EPD_I	10.83	3.02	10.72	3.05	10.95	2.98	<0.001***
EPD_M	15.57	2.72	15.50	2.71	15.65	2.73	0.022*
EPD_S	19.48	3.21	19.39	3.17	19.58	3.25	0.083
ELlD_I	11.85	3.36	11.82	3.44	11.88	3.28	0.568
ELlD_M	16.47	2.88	16.48	2.90	16.46	2.86	0.831
ELlD_S	20.63	3.34	20.58	3.33	20.68	3.36	0.520

EPDl_I	13.92	3.73	13.92	3.70	13.92	3.76	0.956
EPDl_M	18.67	2.94	18.74	2.88	18.59	2.99	0.289
EPDl_S	22.94	3.36	22.98	3.27	22.90	3.44	0.346
EExD_I	18.11	3.89	17.94	3.96	18.27	3.82	0.021*
EExD_M	22.79	3.04	22.73	3.11	22.86	2.96	0.108
EExD_S	26.78	3.37	26.73	3.39	26.83	3.36	0.302
EL_I	52.78	9.01	52.88	8.86	52.68	9.17	0.474
EL_M	64.32	8.82	64.14	8.83	64.50	8.83	0.276
EL_S	57.88	13.41	57.89	13.29	57.88	13.54	0.823

*p<0.05, **p<0.01, ***p<0.001.

The differences in age groups are shown in Table 14. Most of the eyebrow-related measurements were not significantly different between the eyes, with the differences mainly found in volunteers aged lower than 30 years (G1) and between 50-60 years (G4). In G1, the differences were primarily found in EnD_I/M/S, EPDm_S and EPD_I/M (P<0.05), with a larger left than right eye; in G4, the differences were mainly in EEnD_M/S, EPDm_S, ELmD_S, EPD_M, EExD_I/M, EL_M (p=0.017, 0.020, 0.007, 0.038, 0.027, 0.030, 0.018 and 0.018, respectively) and the left eyes were larger. EPDl_S in G5 and ELmD_I in G6 also differed significantly; the data were larger in the right eye.

Table 14. Significant differences in eyebrow-related parameters between eyes across age groups (p value).

	Overall	G1	G2	G3	G4	G5	G6	G7
EEnD_I	0.187	0.002	0.075	0.428	0.699	0.564	0.484	0.764
EEnD_M	0.000	0.000	[illegible]	0.979	0.017	0.385	0.963	0.749
EEnD_S	0.000	0.000	0.071	0.901	0.020	0.369	0.719	0.171
EPDm_I	0.081	0.670	0.400	0.403	0.270	0.969	0.047	0.355
EPDm_M	0.093	0.133	0.201	0.825	0.071	0.276	0.427	0.458
EPDm_S	0.001	0.004	0.475	0.318	0.007	0.271	0.877	0.536
ELmD_I	0.071	0.561	0.089	0.307	0.463	0.285	0.018	0.772
ELmD_M	0.863	0.644	0.510	0.812	0.280	0.793	0.084	0.236
ELmD_S	[illegible]	0.073	0.769	0.672	0.038	0.769	0.668	0.198
EPD_I	0.000	0.037	0.026	0.824	0.252	0.955	0.874	0.175
EPD_M	0.022	0.013	0.952	0.226	0.027	0.647	0.471	0.223
EPD_S	0.083	0.083	0.372	0.722	0.150	0.982	0.276	0.348
ElD_I	0.568	0.216	[illegible]	0.086	0.292	0.509	[illegible]	0.894
ElD_M	0.831	0.226	0.413	0.565	0.611	0.451	0.177	0.838
ElD_S	0.520	0.377	0.355	0.561	0.870	0.799	0.708	0.790
EPDl_I	0.956	0.232	0.047	0.299	0.691	0.713	0.236	0.903
EPDl_M	0.289	0.541	0.282	0.156	0.521	0.181	0.278	0.715
EPDl_S	0.346	0.742	0.276	0.256	0.711	0.033	0.550	0.390

EExD_I	0.021	0.177	0.146	0.471	0.030	0.705	0.916	0.486
EExD_M	0.108	0.872	0.614	0.275	0.018	0.588	0.775	0.474
EExD_S	0.302	0.522	0.764	0.114	0.167	0.978	0.127	0.380
EL_I	0.474	0.776	0.110	0.425	0.304	0.595	0.961	0.177
EL_M	0.276	0.421	0.478	0.329	0.018	0.947	0.572	0.226
EL_S	0.823	0.288	0.659	0.471	0.460	0.781	0.979	0.114

0.000 0.050 1.000

G1, age<=30; G2, 30-40; G3, 40-50; G4, 50-60; G5, 60-70; G6, 70-80; G7, age >80.

5.4.2. Eye-related parameters

Among eye-related parameters (Tab.15), a highly significant difference was found between the right and left eyes in LPML, PFW, PEn, LEn, CT, and UV (p<0.001). UPML, ID, and MCA values also differed (p=0.047, 0.032 and 0.005).

Table 15. Mean values and significance of differences in eye-related parameters between eyes

	Overall		Right		Left		p-value
	Mean	SD	Mean	SD	Mean	SD	
UPML	39.72	3.18	39.81	3.14	39.62	3.23	0.047*
LPML	33.33	2.59	33.46	2.58	33.20	2.59	<0.001***
PFW	29.82	2.02	29.91	2.00	29.72	2.03	<0.001***
PFH	11.53	1.24	11.53	1.23	11.53	1.25	0.846
ID	11.87	0.60	11.90	0.59	11.85	0.61	0.032*
PuD	4.13	0.81	4.14	0.82	4.13	0.81	0.968
PEn	15.80	1.47	15.94	1.49	15.66	1.45	<0.001***
LEn	10.37	1.31	10.50	1.35	10.24	1.26	<0.001***
PEx	15.53	1.75	15.49	1.77	15.57	1.73	0.205
LEx	10.16	1.94	10.10	1.94	10.21	1.95	0.121
MCA	39.61	4.34	39.38	4.46	39.84	4.22	0.005**
LCA	37.65	4.07	37.68	4.00	37.61	4.13	0.571
CT	166.76	3.54	166.39	3.50	167.13	3.55	<0.001***
UA	5.49	1.26	5.49	1.26	5.48	1.27	0.737
UV	1.23	2.45	1.55	2.38	0.91	2.48	<0.001***

*p<0.05, **p<0.01, ***p<0.001.

Among the linear measurements (UPML, LPML, PFW, PFH, ID, PuD, PD, EnD, ExD, PEn, LEn, PEx, LEx), differences were mainly in PFW, PEn, LEn, and LPML in G3, G4, and G6, and also appeared in PFW in the G1 group and ID in G2, with the right being greater than the left in all of the above measurements. In other parameters, such as MCA in G4 and CT in G1 and G5, left eyes were larger; in contrast to UV in G1 and G2, the right side was larger than the left. (Table 16)

Table 16. Significant differences in eye-related parameters between eyes across age groups

	Overall	G1	G2	G3	G4	G5	G6	G7
UPML	0.047	0.167	0.932	0.157	0.419	0.488	0.074	0.722
LPML	0.000	0.069	0.830	0.004	0.085	0.423	0.000	0.770
PFW	0.000	0.032	0.987	0.027	0.012	0.631	0.002	0.781
PFH	0.846	0.797	0.418	0.446	0.721	0.536	0.559	0.585
ID	0.032	0.454	0.000		0.428	0.974	0.092	0.155
PuD	0.968	0.255	0.520	0.347	0.253	0.798	0.505	0.307
PEn	0.000	0.309	0.320	0.001	0.000	0.032	0.008	0.655
LEn	0.000	0.114	0.621	0.002	0.000	0.075	0.024	0.613
PEx	0.205	0.523	0.579	0.136	0.109	0.143	0.679	0.998
LEx	0.121	0.526	0.231		0.117	0.157	0.392	0.935
MCA	0.005	0.654	0.951	0.080	0.007		0.077	0.824
LCA	0.571	0.189	0.374	0.145	0.506	0.423	0.902	0.485
CT	0.000	0.006	0.262	0.567	0.167	0.015	0.212	0.821
UA	0.737	0.630	0.702	0.169	0.399	0.853	0.114	0.820
UV	0.000	0.000	0.016	0.083	0.398	0.776	0.956	0.634

0.000 0.050 1.000

We analyzed the distribution of interocular differences across race and gender. (Tab.17) Except for ΔELmD_I, ΔELmD_M, ΔPuD (P<0.01, respectively), which were predominantly between genders in Caucasian populations, and ΔEPDI_M (P<0.01), EL_M, LEn and MCA (P<0.05, respectively), which were predominantly between races, there were no gender or racial variations in the inter-binocular differences.

Table 17. Differences in binocular measurements by gender and race

p-value	Between Gender All	Between Gender Caucasian	Between Gender Asian	**Between Race**
ΔEEnD_I	0.290	0.162	0.300	0.842
ΔEEnD_M	0.583	0.285	0.225	0.218
ΔEEnD_S	0.921	0.669	0.169	0.444
ΔEPDm_I	0.241	0.186	0.834	0.777
ΔEPDm_M	0.299	0.388	0.496	0.437
ΔEPDm_S	0.833	0.762	0.867	0.159
ΔELmD_I	0.006**	0.001**	0.298	0.409

∆ELmD_M	0.040*	0.010*	0.385	0.314
∆ELmD_S	0.295	0.124	0.305	0.740
∆EPD_I	0.232	0.122	0.427	0.571
∆EPD_M	0.980	0.492	0.088	0.536
∆EPD_S	0.997	0.387	0.044*	0.572
∆ElD_I	0.163	0.037*	0.104	0.979
∆ElD_M	0.236	0.069	0.080	0.775
∆ElD_S	0.489	0.231	0.270	0.817
∆EPDl_I	0.763	0.860	0.694	0.121
∆EPDl_M	0.785	0.830	0.732	0.008**
∆EPDl_S	0.960	0.751	0.280	0.075
∆EExD_I	0.256	0.346	0.374	0.390
∆EExD_M	0.499	0.723	0.257	0.289
∆EExD_S	0.782	0.860	0.728	0.327
∆EL_I	0.258	0.219	0.962	0.855
∆EL_M	0.326	0.219	0.661	0.017*
∆EL_S	0.369	0.271	0.736	0.209
∆UPML	0.480	0.652	0.581	0.325
∆LPML	0.461	0.496	0.812	0.257
∆PFW	0.242	0.361	0.447	0.273
∆PFH	0.158	0.279	0.331	0.215
∆ID	0.085	0.070	0.927	0.395
∆PuD	0.040*	0.005**	0.242	0.653
∆PEn	0.404	0.474	0.727	0.053
∆LEn	0.711	0.814	0.768	0.025*
∆PEx	0.855	0.971	0.735	0.767
∆LEx	0.919	0.903	0.584	0.615
∆MCA	0.056	0.127	0.259	0.012*
∆LCA	0.108	0.160	0.451	0.664
∆CT	0.898	0.811	0.240	0.682
∆UA	0.238	0.255	0.690	0.287
∆UV	0.239	0.163	0.651	0.373

*p<0.05, **p<0.01, ***p<0.001.

6. DISCUSSION

In previous studies, direct and 2D anthropometry were the standard eye and brow-related parameter measurement methods. With the increasing diversity of measurement needs and demands for accuracy, 3D digital stereophotogrammetry, a non-invasive and fast modern measurement method, seems to be an optimal and accurate tool in soft tissue assessment, especially for measuring the depth of facial structures. Stereoscopic measurement technology is capable of accurate linear distance and angle measurements, and the accuracy, reliability, and repeatability of linear distance (curve), area, and volume measurements on facial surfaces have been proven in several studies. They are gradually replacing traditional measurement methods in practical applications. Most current research on periocular measurements uses landmarks labeled on 3D facial models, and measurements covering almost the entire surface of the periocular area are later obtained from these landmarks for quantitative analysis of periocular morphological features.

In the present study, based on the results of landmark studies of established periocular tissues, over 300 Caucasians and 60 Asians underwent facial 3D digital stereoscopic image acquisition, and periocular data were measured and analyzed to evaluate the effects of gender, age, and ethnicity on these parameters, and to assess binocular symmetry.

6.1 Eyebrow-related parameters

Regarding eyebrows, the following findings can be obtained from our research. Overall, there were no significant differences between the right and left eyes and no obvious changes with age, with a few differences occurring below 30 and between 50 and 60. Regarding the shape of the eyebrows, compared to women, the brows in men were longer and wider, the upper edge further away from the upper lid while the lower edge of the eyebrows was closer to the upper lid; the length of the eyebrows, in general, tends to become shorter with age, increasing slightly before the age of 40 and becoming shorter after that age. For eyebrow position, in general, it decreases between the ages of 18-40 years, is relatively stable between the ages of 40-60 years, increases between the ages of 60-70 years, and is relatively stable after the age of 70 years; in males, the eyebrow is positioned higher on the nasal side, whereas on the temporal side, it appears to be higher in females. All of the above is more evident in Caucasians. In Asians, like Caucasians, men have longer and wider eyebrows, with no significant differences between the genders; however, the overall position of the eyebrows is higher in Asians than in Caucasians.

In previous studies, several different methods have been used to assess and measure the shape and position of the eyebrows. According to earlier findings, the underlying facial skeleton differs between the genders, with males having a greater forehead height and width compared to females,[45] with more prominent supraorbital ridges[46] and therefore, males tend to have thicker, heavier, flatter eyebrows and smaller vertical distance between the eyebrows and the eyes[47,48].

The aging process leads to brow position and shape changes. Asaad's study showed that the shape changes, as evidenced by an increase in the medial height of the brow while the lateral height remains stable or decreases[49]; meanwhile, another study on the female brow with age showed that the stability or elevation of the medial part, coupled with a decrease in the height of the peak of the brow, results in a decrease in brow slant [50], which is similar to our findings. The changes mentioned above in brow position and morphology can be explained by a variety of mechanisms, such as the influence of the balance of the surrounding muscles and tensions[51,52], aging of the periocular skin[53], skeletal changes[54], ligamentous attenuation[55,56], and redistribution of fat[57,58]. In recent years, with the maturity and popularity of procedures such as blepharoplasty, related studies have found that patients' brow position decreases after surgery.[51,59,60] This indirectly supports a new hypothesis that visual field obstruction caused by lateral brow pseudoptosis and weakness of the levator system stimulates frontalis muscle contraction, which lifts the brow. Moreover, in several brow movement-related muscle groups (frontalis, orbicularis oculi, and frowning muscles), the proportionality index of movement was greater in older subjects than younger ones[61]. Gender-related differences in eyebrow aging may also exist, with one study finding a significant increase of eyebrow height in medial canthus and middle brow height with age in females but not in males[49]. In a study of white males[62], the eyebrows were wide and flat, with no obvious arch shape, and were positioned much lower in males than in females, which was consistent with the findings described by Gunter et al.[63] In a study by Price KM et al.,[64] a significant difference in eyebrow height (decline with age) was shown for different age groups in African American males, but not in females or white males, possibly reflecting ethnically relevant differences in eyebrow aging; while there are still studies that report no significant changes. [65,66,67] Based on an interracial brow and eyelid anthropometric analysis, Kunjur J et al. compared data from Whites and and found that the central height of the brow was significantly greater in Chinese ($p<0.001$) [68].

The brow is a 3-dimensional structure; age-related brow changes can be more complex and may not follow a 2D description, and 3D analyses can provide a more accurate assessment of the brow. However, there are few studies and limited parameters available for comparison. Lu TY et al. measured the eyebrow-related parameters of Malays and Chinese, and the Malays appeared to have shorter eyebrow heights (11.10 mm) compared to the Chinese (11.79 mm). There was a prevalence of asymmetry on both sides, possibly due to the detection of minor discrepancies between the right and left eyes through the use of 3D photogrammetry as compared to direct measurements. [69] Guo et al. developed a landmark system for eyebrow and periocular soft tissue parameter measurements. [70,71] In eyebrow-related measurements, height (the distance between the lower edge of the eyebrow and the upper eyelid margin, was significantly higher in females than males ($p < 0.001$, respectively). In contrast, males had significantly longer eyebrows than females (EL male 69.73±5.57mm, female 58.59±4.65mm, $p < 0.001$, respectively).

6.2 Eye-related measurements

The results of the eye-related measurements are shown in the following table. (Tab.18)

Table 18. Distribution of eye-related parameters among ethnicity, gender, binocular differences, and changing with age

	Race		**Gender**		**Trends with age**	**Binocular difference**		**Age of differences**
	Caucasian	Asian	M	F		R	L	
UPML		↑	↑		↓(F)	↑		
LPML	↑		↑		↓(F)	↑		40-50, 70-80
PFW	↑		↑		↓(F)	↑		<30,40-60,70-80
PFH	↑		↑(Asian ND)		↓(F)			
ID	↑		↑(Asian ND)		↓	↑		30-40
PuD		↑-	↑		↓(F)			
PD		↑	↑		↑(M)			
EnD		↑	↑		↑(F)			
ExD		↑	↑		↓(F)			
PEn/ LEn	↑		↑		↑(M) ↓(F)	↑		>40
PEx/ LEx		↑	↑		↓(F)			
MCA		↑		↑	↓(F)		↑	50-60
LCA	↑			↑				
CT	↑				↑(F)		↑	<30,60-70
UA			↑		↓			
UV	↑				↓	↑		<40

↑, parameter increase/ larger; ↓, parameter decrease/ smaller; ND, no difference; M, male; F, female; R, right; L, left.

Between races, Caucasians have significantly larger lid height, width, and lower eyelid length than Asians, while the upper eyelid is longer in Asians. The iris diameter and pupil center/nasal limbus-medial canthus distance were significantly larger in Caucasians than in Asians, who had large pupil diameters and interpupillary/medial /lateral canthus distances. The medial canthus angles are larger in Asians, and the lateral canthus angles and canthal tilt are larger in Caucasians. Among the different genders in Caucasians, males had high eyelids, wide lid fissures, large iris diameters, pupil diameters, interpupillary distances, pupil center/limbus-medial and lateral canthus distances, inter-canthus distances, and long upper and lower lid margins; females had large medial and lateral canthus angles and large upper lid areas. There was no difference in canthal tilt or upper lid volume. Asians were similar to Caucasians in all parameters except for no significant difference in middle lid height and iris diameter. With age, parameter changes mainly occur before 50 and between 60 and 70. Upper and lower eyelid length, lid height, and width decreased and became more evident in females, and pupil diameter was similar. Among the interocular parameters, the interpupillary distance increased with age and was more pronounced in males, while the intercanthal distance changes were more pronounced in females (increase in the medial intercanthal distance, decrease in the lateral intercanthal distance). The lateral canthus angle did not change significantly with age, but the medial canthus angle decreased simultaneously, which was more obvious in females. The results of our analyses regarding lid fissure regional morphometry were similar to some other studies.[62] We found that for Caucasians, PFW, PFH, and EnD were 29.86 ± 2.01, 11.56 ± 1.26, and 31.61 ± 2.82 mm, respectively, which is in line with Farkas's reported results for young white North Americans (PFW 32 ± 1.3 mm, EnD 32.9 ± 3.6 mm[72]) as well as several other studies (PFW 26.7 ± 1.7 mm, 29.17 ± 1.92 mm; PFH 9.4 ± 1.3 mm, 9.26 ± 1.35 mm[62,64]; EnD of 31.49 ± 2.68 mm[62]). Furthermore, according to several studies[73-76], PFW, PFH, EnD, and ExD values in Chinese women aged 18-35 years ranged from 25.37-27.65 mm, 9.36-11.64 mm, 33.17-38.27 and 85.63-93.02 mm, which were similar to our results (29.05±1.88mm, 11.54±1.06mm, 36.13±3.33mm and 92.08±4.69mm, respectively). Furthermore, in a study of eye morphology that included 3600 women of different races and ages, [77] EnD and ExD were higher in Asians, while the change in EnD with age was more significant (12%) than ExD (7%), PFW was lower in Asians than in Caucasians, and there was a negative correlation between age and PFW, PFH, and a stronger correlation among women over 60 years of age. These findings strongly support our results.

In recent 3D measurement analysis studies, lid width, upper and lower lid margin length, inner and outer inter-canthus distance, and interpupillary distance, which are all in the transverse direction, were significantly greater in males compared to females in lid width and eyelid measurements according to Guo et al. ($p \le 0.001$, respectively) [70] These results agree with our results and with the results using 2D photogrammetry by Li et al. [73]and Wu et al. [76] as well as using 3D photogrammetry by Jayaratne et al.[74] In a quantitative analysis of eyelid aging in Chinese women by 3D anthropometry, PFW and ExD were significantly correlated with age[78], with the decline accelerating with age, and speeding up after 40 years of age. PFH decreased, and EnD did not change significantly with age.

Findings from our study showed that with increasing age, lid width became smaller (r=-0.388, p<0.001) and the distance between the medial canthus was greater (r=0.183, p<0.001); whereas, according to Liu JH et al. [34] the medial canthus position did not significantly correlate with gender but tended to move temporally and inferiorly with age, while the lateral canthus position tended to move nasally and inferiorly (young/old; PFW, 30.856 ± 2.052/28.761 ± 2.228mm; En-En, 31.346 ± 2.769/33.306 ± 3.267mm; Pu-Ex, 16.258 ± 1.585/14.149 ± 1.388mm, p< 0.001, respectively). These changes become more significant after age 70 for females and 80 for males, and the results are consistent for both studies. In a 3D visual modeling study of facial aging involving 594 subjects, [79] the lateral canthus moved medially, and the upper and lower eyelids moved closer to each other with age. According to our results, PEx decreased with age (r = -0.429, p < 0.001), and Liu's results also showed that there was a significant difference in PEx between the younger and older groups (PEx, 16.258 ± 1.585mm vs. 14.149 ± 1.388mm, p < 0.001, respectively). [34] Also, our data show that upper and lower eyelid length decreases with age, more significantly in females.

We selected MCA (Ps-En-Pi) and LCA (Ps-Ex-Pi) for 3D measurements of the medial and lateral canthus angles, which, according to Guo's studies, [32] are significantly more accurate when compared to the midpoint-formed angles MCAm (Um-En- Um') and LCAm (Um-En- Um'). are considerably more accurate. Results indicated that females (40.10 ± 4.31° and 38.43 ± 3.87°) tended to have larger values than males (38.86 ± 4.28° and 36.47 ± 4.07°), with a statistically significant difference (p < 0.001), which is in line with the results of a three-dimensional study in Caucasians (MCA 40.28±3.42° in female, 38.33±4.31°in male, *p* = 0.030; LCA 38.01±3.16° in female, 34.35±4.87° in male, *p* < 0.001)[70] and 2D study by Li in Asians (MCA 59.98 ± 9.62° in female, 56.64 ± 11.28° in male, p = 0.058; LCA 84.68 ± 15.31° in female, 74.69 ± 12.64° in male, p < 0.001) [73]. However, comparisons of values between studies could not be performed due to different definitions of angles. An age-related downward trend was also observed for MCA (r=-0.344, p<0.001).

Direct and 2D techniques cannot accurately measure the periocular area and volume, and using 3D measurements provides a new possible approach. Liu et al.[33], Fan et al. [31]. and Guo et al.[22] evaluated the accuracy of stereophotogrammetric area measurements in the periocular region with different 3d imaging systems, race, and gender, respectively, showing good intra-rater, inter-rater, and intra-method reliability. For volume measurement, most of the studies are about the lower eyelids. Miller evaluated the volume changes of patients' tear troughs and deep fat compartments of the upper cheeks pre- and post-lower blepharoplasty using the fat repositioning technique,[80], and the results were reproducible. Cristel and Caughlin[81] reported the reliability of 3D volumetric measurements that could accurately quantify volumetric changes in the lacrimal sulcus and inferior periorbital area after lower blepharoplasty with fat pad displacement and autologous fat grafting. Only a few studies have been performed on the

upper eyelid region area and volume measurements. A 3D stereophotogrammetry was used by Figueiredo et al. to perform measurements of volume changes in the lateral brow-eyelid complex after internal brow fixation,[82] and Hyer et al.'s study demonstrated the accuracy of 3D image reconstruction for periorbital region volume changes assessment with excellent inter-observer reproducibility and suitability for clinical use. However, according to Fan et al.[31] and Guo et al.,[22] upper lid region volume measurements using different systems and single images directly all showed poor reliability. This study may be the first to evaluate the correlation of eyelid area and volume with age changes using a 3d measurement system, and no similar studies have been done. Based on our findings, the upper lid area generally decreases with age, while it is larger in males compared to females; for volume measurements, similar to the area, it also decreases with age, with the most significant changes before the age of 40 years, and the upper lid volume is larger in Caucasians than in Asians. There was no difference in area between the left and right eyes but a difference in volume ($p<0.001$), which tended to decrease with age ($r=-0.157$, $p=0.003$). However, according to the results of previous studies, the accuracy of 3D volume measurements is still controversial.
The above changes may be related to the following reasons. First, it may result from the weakening of the orbicularis oculi muscle; the lower eyelid is subjected to laxity of the lower eyelid skin and lateral tarsal ligament and gravity, leading to tendon attenuation and lower eyelid laxity[83]. Also, it may be related to the mechanism that facial bones have an uneven absorptive recession with growing age[84,85], especially the greater recession of the supra-medial (old age) and infra-lateral (middle age) orbital rims, corresponding to the facial regions showing the most evident signs of aging[86]. Third, the degree of proptosis may be another reason for parameter change. Previous studies reported a general trend of increased ocular prominence due to significant growth of the ocular axis or orbital soft-tissue volume increasing before age 30, with greater ocular prominence values in males than in females. Then, a net decrease in facial fat volume was observed over time, [87] stable or decreasing between the ages of 30-50 and decreases significantly from 50-70 years. [88-92] Age-related convergence insufficiency exotropia caused by accommodative amplitude decreases leading to changes in axis position can also affect measurements. Uneven resorption of the orbital skeleton may also be associated with these changes.

The ethnicity and age distribution of the population enrolled limit our results. Most subjects were Caucasians, with fewer Asians and predominantly young and middle-aged adults. Results may not be generalizable among different races. Moreover, fewer older Caucasians were included, which may have affected the measurements and thus led to deviations in the results. Further, according to Lambros[93], some subjects unconsciously raise their eyebrows in front of a camera or mirror to appear younger, and this may cause inaccuracies and inconsistencies in the brow and periocular height measurements. Additionally, the different positions (sitting/lying) during photography and surgery can cause skin elasticity, muscle tension, and fat distribution changes, leading to data variations. Therefore, this point should be considered when 3D systems are used for surgical design. Notably, the accuracy of volumetric measurements remains unsatisfactory, and the overlayed images may make the results more reliable. Therefore, further studies are needed to assess the accuracy and reliability of the standardized landmark system combined with this.

This study described the distribution and age-dependent trends of distance, curvature, angle, area, and volume parameters associated with the eyebrow and periocular region in a multiethnic, multiage population in the European region. We compared the differences between ethnicities, genders, age groups, and binoculars, further complementing the results of previously published studies. The anthropometric data collection can improve our understanding of the aging process, provide information on inter-gender and inter-ethnic differences, be used for comparative studies with other brow and eyelid area selection methods of using the orbital rim as a boundary, and be used as a standard dataset to assist in the planning of rejuvenation and therapeutic plastic surgery. For future work, as 3D photogrammetry has shown excellent accuracy and reliability in most of the parameters and has a wide range of potential clinical applications, it is recommended to include this technique as a routine pre- and post-operative examination to identify any asymmetry and manage it accordingly like in clinical patients with deformities of the brow and eyelids and post-traumatic reconstructive or plastic surgery or tumors, as well as quantitatively evaluating surgical outcomes. For volumetric measurements, overlayed images or other possibilities need to be tested and evaluated for effectiveness. Precise measurements combined with 3D printing techniques would achieve better postoperative morphological and functional results. Furthermore, artificial intelligence has been gradually applied to oculoplastic research. Surgical prediction system development for multi-disease, multi-operator, and multi-surgical scenarios based on pre- and post-surgical images and data of patients in standard groups and various diseases could be carried out in future work.

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8. APPENDIX

8.1 Figures

8.2 Tables