The efficiency of using mirror imaged topography in fellow eyes analyses of Pentacam HR data

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Abstract

Purpose: To investigate the effectiveness of flipping left corneas topography and analyse them quantitively along with fellow right corneas assuming they are mirror images of each other.

Methods: The study involved scanning both eyes of 177 healthy participants (aged 35.3 ± 15.8) and 75 keratoconic participants (aged 33.9 ± 17.8). Clinical tomography data has been collected from both eyes using the Pentacam HR and processed by a fully automated custom-built MATLAB code. For every case, the right eye was used as a datum fixed surface while the left corneal was flipped around the superior-inferior direction. At this position, the root-mean-squared difference (RMS) between flipped left cornea and the right cornea was initially determined for both anterior and posterior corneal surfaces. Next, the iterative closest point transformation algorithm was applied on the three-dimensional flipped cornea to allow the flipped left corneal anterior surface to translate and rotate in order to minimise the difference between it and the right cornea anterior surface, hence RMS differences were recalculated and compared.

Results: Comparing the dioptric power showed a significant difference between the RMS of both the flipped left eyes and right eyes, the healthy and the KC group ($p<0.001$). The RMS of the surfaces of the flipped left corneas and the right corneas was 0.6±0.4 D among the healthy group and 4.1±2.3 among the KC group. After transforming the flipped left corneas, RMS recorded 0.5±0.3 D and 2.4±2 D among healthy and KC groups respectively.

Conclusions: Although fellow eyes are highly related in their clinical parameters, they should be treated with care when one eye topography is flipped and processed with the other eye topography in an optic related research analysis where translation might be needed. In KC, an asymmetric disease, it has been observed that a portion of the asymmetry is due to corneal apex shift interfering with image acquisition therefore, transforming flipped left eyes by rotation and translation results in a fairer comparison between the fellow KC corneas.

1. Introduction

It is a common practice in anterior ocular topography-based studies that left eyes are superiorly-inferiorly flipped and quantitively analysed along with right eyes through the same analytical approach [1, 2]. This left eye mirror imaging technique of analysing corneal topography is well justified in the literature as bilateral fellow eyes were always found to be mirror-symmetric [3-6]. Conversely, and despite the several findings that the right and the mirrored image of the left anterior eye topographies are highly correlated, they are believed not to be equally aligned during the topography scan [7]. Only a little difference in their raw elevations, as measured, could make right and left eyes differ in their dioptric powers and astigmatic axes [8]. Additionally, two-thirds of the population are right-eye dominant [9-13], and the visual field of right eyes is different from that of left eyes [14]. Beyond the eye globe, the image merging processes carried out within the brain for the two eyes are different [15, 16]. These differences require different performances of the two eyes during the fixation process [17] where dominant eyes were believed to be dynamic during the fixation process.

The current study accepts the existence of the mirror symmetry among fellow eyes, but it investigates if only flipping left corneal topography data around a superior-inferior axis is an effective strategy for quantitively analysing right and flipped left corneas altogether, or if there should be an additional adjustment to compensate for the different eye alignments during the fixation process associated with the corneal topography and tomography scans. The study gives a clear pathway for the ocular anterior eye research community to enable analysing flipped left corneas with right corneas, if necessary, without affecting the results with misalignment artefacts.

2. Materials and Methodology

2.1. Participants

The study involved scanning fellow eyes of 177 healthy participants (aged 35.3 ± 15.8) and 75 keratoconic participants (aged 33.9 ± 17.8), selected from referrals to Instituto de Olhos Renato Ambrósio (Rio de Janeiro, Brazil). The current study utilises fully anonymised records retrospectively evaluated in solely secondary analyses. No clinical data was collected specially for this study; therefore, no ethical approval was required according to the policy of the University of Liverpool on research ethics. Nevertheless, the study was conducted in accordance with the standards set in the Declaration of Helsinki.

Before being anonymised, clinical topography data was collected from both eyes of normal and KC participants using the Pentacam HR (OCULUS Optikgeräte GmbH, Wetzlar, Germany). Participants with no history of ocular disease, trauma or ocular surgery, were selected for the healthy group and participants with a clear presence of keratoconus with no previous ocular procedures, such as collagen cross-linking were selected for the keratoconic group. Those with intraocular pressure (IOP) higher than 21 mmHg as measured by the Goldmann Applanation Tonometer, soft contact lens wear until less than two weeks before measurement, or rigid gas permeable (RGP) contact lens wear until less than four weeks before measurements were excluded.

At least three successive scans were taken for each eye with a total approximate period of 30 seconds between them. The measurements continued until three scans with an instrument-generated quality factor of at least 95% and 90% were obtained for the anterior and posterior surfaces, respectively. The scan with the highest quality was then selected for the analyses of the current study. Pentacam HR raw elevation data for the anterior surface was exported in comma-separated values (CSV) format and analysed using custom-built MATLAB (MathWorks, Natick, USA) codes.

2.2. Data collection and processing

Pentacam HR Data was extracted over a mesh grid covering -7 to 7 mm in 141 steps in both nasal-temporal and superior-inferior directions with missing raw elevation values around corners and edges set to NaN which stands for "Not a Number". A fully computerised custom-built MATLAB code was written especially for this study. The code was able to read the CSV files of both the right and left corneas of every participant before processing them. For every case, the right eye was used as a datum fixed surface while the left corneal was flipped around the superior-inferior direction. At this position, the root-mean-squared (RMS) difference between flipped left cornea and the right cornea is initially determined for both anterior and posterior corneal surfaces. The RMS difference was calculated as in Eq 1 as

$$RMS = \sqrt{\frac{\sum_{i=1}^{k}\left(Z_{OS\,flipped} - Z_{OD}\right)^2}{k}} \qquad \text{Eq 1}$$

where $Z_{os\,flipped}$ is the flipped left corneal raw elevation surface height and Z_{od} is the measured raw elevation right corneal surface height and k is the number of non-missing data points. In this context, the Latin notation OD stands for oculus dextrus which means the right eye, and OS stands for oculus sinister which means the left eye.

Later, the iterative closest point (ICP) transformation algorithm was applied on the three-dimensional (3D) flipped cornea to allow the flipped left corneal anterior surface to translate and rotate in order to minimise the difference between it and the right cornea anterior surface. The number of ICP iterations was set to 20 based on a preliminary study and the process outputs two matrices representing the 3D translation and the rotation. The flipped left cornea is then rotated (Eq 2) and translated (Eq 3) accordingly and as a result, the flipped left eye coordinates became unaligned with the right eye that was used as a datum. To allow a common coordinate among right and flipped left eyes, 3D triangulation-based cubic interpolation [18] was used to reconstruct the flipped left cornea that has been rotated and translated to be aligned with the right cornea.

The rotation matrix R that was resulted from the ICP algorithm can be expressed as in Eq 2 as

$$R = \begin{bmatrix} \cos\alpha\cos\beta & \cos\alpha\sin\beta\sin\gamma - \sin\alpha\cos\gamma & \cos\alpha\sin\beta\cos\gamma + \sin\alpha\sin\gamma \\ \sin\alpha\cos\beta & \sin\alpha\sin\beta\sin\gamma + \cos\alpha\cos\gamma & \sin\alpha\sin\beta\cos\gamma - \cos\alpha\sin\gamma \\ -\sin\beta & \cos\beta\sin\gamma & \cos\beta\cos\gamma \end{bmatrix} \quad \text{Eq 2}$$

where α is the rotation angle around the X-axis, β is the rotation angle around the Y-axis and γ is the rotation angle around the Z-axis. Likewise, the translation matrix T can be expressed as in Eq 3 as

$$T = \begin{bmatrix} X_t \\ Y_t \\ Z_t \end{bmatrix} \quad \text{Eq 3}$$

Where X_t, Y_t and Z_t are the translations in X, Y and Z directions respectively. Hence, the flipped left cornea coordinate can be expressed as shown in Eq 4 as

$$\begin{bmatrix} x_{OS\,rt\,1} & x_{OS\,rt\,2} & x_{OS\,rt\,3} & \dots & x_{OS\,rt\,n} \\ y_{OS\,rt\,1} & y_{OS\,rt\,2} & y_{OS\,rt\,3} & \dots & y_{OS\,rt\,n} \\ z_{OS\,rt\,1} & z_{OS\,rt\,2} & z_{OS\,rt\,3} & \dots & z_{OS\,rt\,n} \end{bmatrix} = R * \begin{bmatrix} x_{OS\,1} & x_{OS\,2} & x_{OS\,3} & \dots & x_{OS\,n} \\ y_{OS\,1} & y_{OS\,2} & y_{OS\,3} & \dots & y_{OS\,n} \\ z_{OS\,1} & z_{OS\,2} & z_{OS\,3} & \dots & z_{OS\,n} \end{bmatrix} + T \quad \text{Eq 4}$$

before the RMS of the difference between the left cornea flipped, rotated and translated surface is recalculated as shown in Eq 5 as

$$RMS = \sqrt{\frac{\sum_{i=1}^{k}(Z_{OS\,rt} - Z_{OD})^2}{k}} \quad \text{Eq 5}$$

where $Z_{OS\,rt\,flipped}$ is the flipped left corneal raw elevation surface height that has been translated and rotated. Finally, the mean and standard deviation of the healthy and keratoconic participant groups were calculated and compared.

2.3. Axial radii of curvature and refractive power

Local axial curvatures were calculated for 359 meridians with a 1.0° angular step covering the assessed area of the cornea up to $x = 4$ mm radius. Centres of axial curvatures were assumed to lie on the corneal visual axis [19] as illustrated in Figure 1, the axial radius of curvature at any point was calculated as in Eq 6 as:

$$r = \frac{x}{\cos(90 - \alpha)} \qquad \text{Eq 6}$$

where α is the tangent angle at this point.

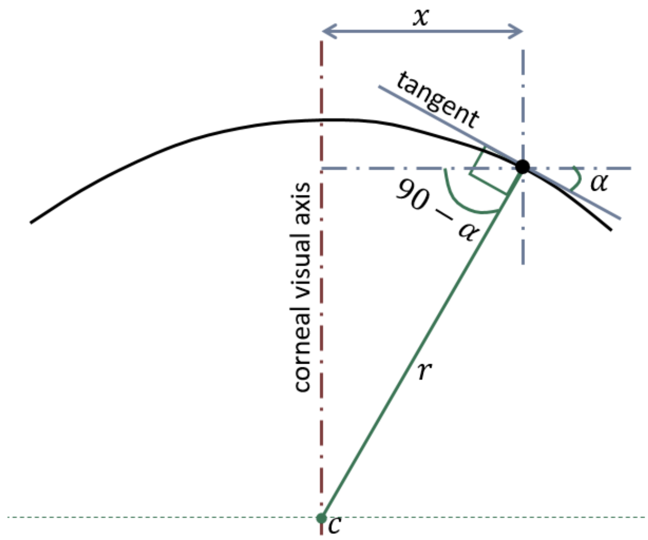

Figure 1: Determination of corneal surface axial radius of curvature (r) at a certain meridian plane. In this method, the centre of the curvature (c) was always restricted to the corneal visual axis.

This process was carried out for both corneal anterior and posterior surfaces and the corresponding radii of curvature, $R_{anterior}$ and $R_{posterior}$, were used to calculate the corneal optical power P using the Gaussian optics formula [20, 21]:

$$P = \frac{n_{cornea} - n_{air}}{R_{anterior}} + \frac{n_{aqueous} - n_{cornea}}{R_{posterior}} - \frac{t_c}{n_{cornea}}\left(\frac{n_{cornea} - n_{air}}{R_{anterior}}\right)\left(\frac{n_{aqueous} - n_{cornea}}{R_{posterior}}\right) \quad \text{Eq 7}$$

where the refractive indices of air, n_{air}, cornea, n_{cornea}, and aqueous, $n_{aqueous}$, were set at 1.0, 1.376 and 1.336, respectively, following Gullstrand relaxed eye model [22, 23]. The central corneal thickness, t_c, was determined by subtracting the corneal posterior raw elevation surface from anterior surface at the corneal apex.

2.4 Statistical Analysis

The results were subjected to statistical analysis through the use of the MATLAB Statistics and Machine Learning Toolbox. A significance level of 5% was set and the probability of the null hypothesis (p-value) was computed using a two-sample t-test [24]. This calculation was carried out on pairs of data sets to ensure that the observed effects were not occurring as a result of sampling error. Due to the choice of significance level, the observed effects were deemed significant if they achieved a p-value lower than 0.05.

3. Results

When left corneas were only flipped around the superior-inferior axis, heathy corneas recorded RMS difference in raw elevation between flipped left corneas and right corneas of 26.3±11.5 and 39.6±14.5 µm for anterior and posterior surfaces respectively. Values of RMS were up to 109.11±66 (anterior) and 104.5±53.6 (posterior) among KC corneas, Figure 2. Once the ICP algorithm was applied, RMS values went down to 12.3±6, 25.4±10.8 µm among healthy corneas and 26.8±15.8, 41.9±19.6 µm among KC for anterior and posterior corneas respectively Figure 3.

The rotations associated with the ICP algorithm were hardly observable as can be seen in Figure 3. Associated translation with the ICP transformation algorithm recorded -0.27±2, 2.5±19 and 1.5±5 μm among health corneas and -1.1±7, -1±10 and -4.9±36.8 μm among KC corneas, Figure 4. When the RMS values were compared without and with the use of the ICP transformation algorithm, it was found that using the ICP transformation algorithm reduced the RMS significantly among both healthy ($p<0.001$) and KC groups ($p<0.001$) for both anterior and posterior surfaces.

Comparing the dioptric power showed a significant difference between the RMS of the flipped left corneas and right corneas for both the healthy and the KC group ($p<0.001$). The RMS of the surfaces of the flipped left corneas and the right corneas was 0.6±0.4 D among the healthy group and 4.1±2.3 D among the KC group. After transforming the flipped left corneas, RMS recorded 0.5±0.3 D and 2.4±2 D among healthy and KC groups respectively, Figure 5.

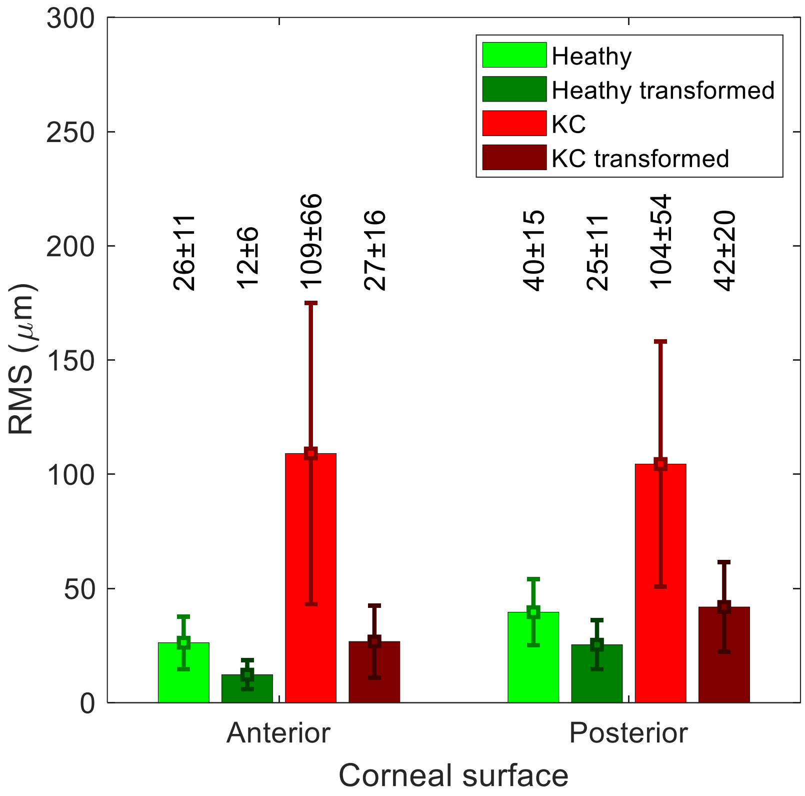

Figure 2: RMS difference between the flipped left corneas and right corneas for both anterior and posterior surfaces. It shows the difference before and after flipped left corneas being transformed (rotated and translated).

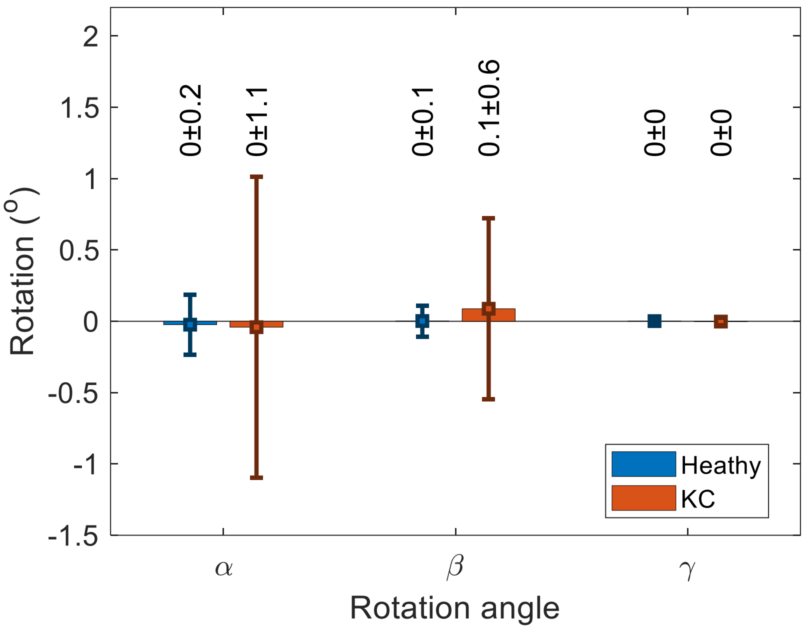

Figure 3: Flipped left cornea rotation angles around X, Y and Z axes respectively.

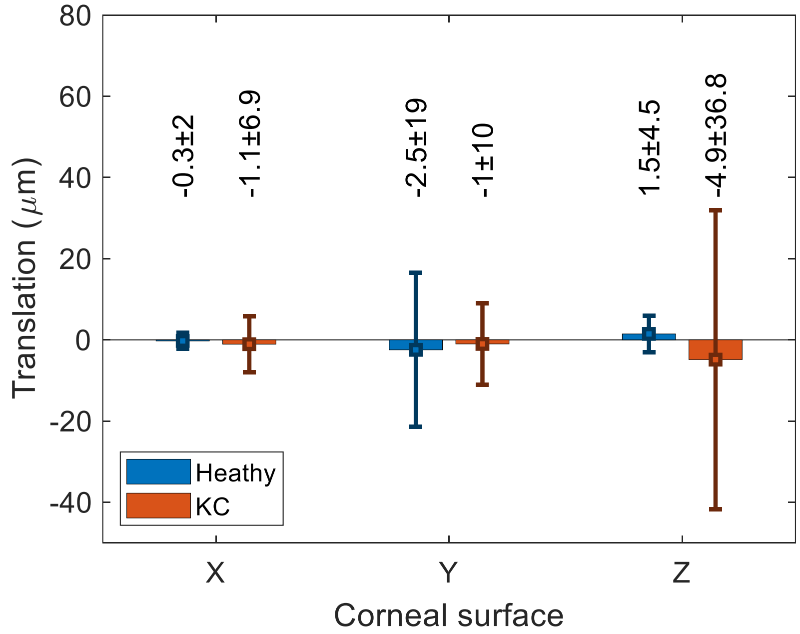

Figure 4: Flipped left cornea translation in X, Y and Z directions respectively.

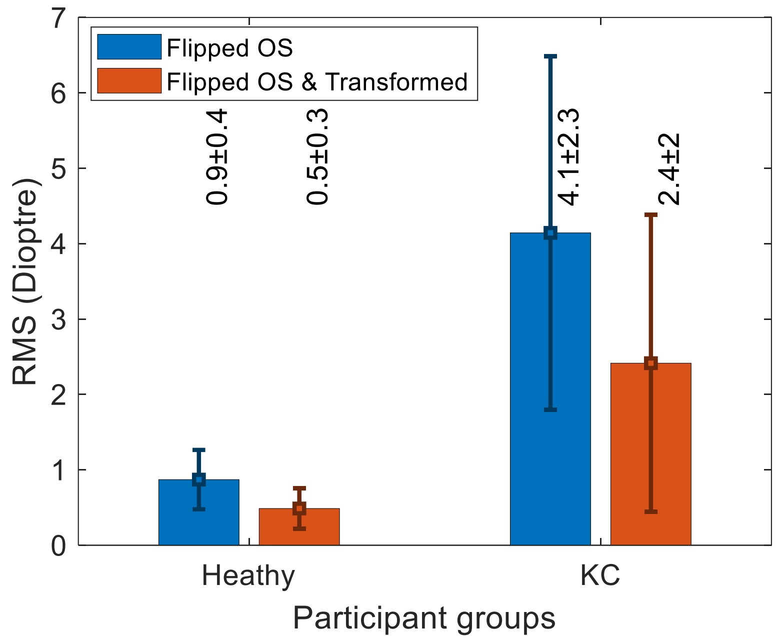

Figure 5: Axial power RMS difference between right corneas and flipped left corneas without and with ICP transformation.

4. Discussion

The results of the current study confirm the fellow anterior eyes match in terms of the topographical shape (see Appendix A) but suggests fellow corneas should not be considered mirror images of each other in collective analysis without constraints. Flipping the left corneas in order to analyse right and left corneas together may not be a good strategy if the aim of a study is related to evaluating the corneal optical performance. It was clear from the results that flipped left eyes needed to be translated a few microns to fit the right eyes, and these little translations caused a change of 0.5 D to 2 D in the corneal optical power. As these power mismatches are high enough to require refractive correction [25], flipped left corneas should not be used as an equivalent to right corneas without further processing. The results suggest that the main mismatch between flipped left corneas and right corneas was caused by the surface translation. This indicates that the measured apex position of the flipped left corneas was not a mirror image of the measured right corneas.

When comparing corneal power, flipped left corneas of KC participants showed an important asymmetry in the average dioptric power RMS difference of more than 4 D. However, there was a significant reduction of more than 2D ($p<0.001$) when the flipped left corneal surface was transformed using the ICP algorithm. These big differences in KC cases power could be a result of the fact that some KC patients have difficulty in focusing on the topographer target during the scan process. This makes the alignment of the KC right and left corneas vary a lot, artificially increasing their asymmetries. The study has some limitations as the ICP algorithm was applied on the central 8 mm diameter corneal zone only, so the peripheral corneal surface effect was not considered. It also used a Scheimpflug imaging tomography instrument, which has its limitations like imaging discrete 2D meridians and using them to reconstruct the corneal surfaces instead of measuring the surface as a 3D surface. Finally, grading of keratoconus was not taken into account of the o utcome of this study and all keratoconic corneas were analysed together as a single group. The current study findings are in agreement with Bao [3] who reported mirror symmetry between fellow corneas among healthy subjects and with Bussières who reported both symmetrical and asymmetrical patterns among fellow corneas in patients with keratoconus based on corneal tomography [26]. Dienes [6] also concluded that severe keratoconus patients are more asymmetric in their disease status. In addition, the current study raises the concern that reasonable mirror symmetry in topography does not mean mirror symmetry in refractive power and a few microns misalignment in topography could cause a significant difference in refractive power calculations.

In conclusion, fellow corneas are highly related in their clinical parameters, but they should be treated with care when one corneal topography is flipped and processed with the other corneal topography in an optic related research analysis and translation might be needed. A portion of the asymmetry in KC is due to corneal apex shift interfering with image acquisition therefore, transforming flipped left corneal surfaces by rotation and translation leads to a sensible comparison between the fellow KC corneas since it reduces the power difference between fellow eyes from 4 to 2D. This can be of relevance to the KC diagnosis since it has historically been described as an asymmetric disease [27-29].

5. Financial Disclosure

None of the authors have financial disclosures.

6. Declaration of interest

The authors report no conflicts of interest.

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Appendix A

This appendix reports the measured clinical correlation between right (OD) and left (OS) corneas as measured by the Pentacam HR. High correlations were noticed among most of the clinical parameters among healthy subjects except the location of the minimum pachymetry (R=0.5) and the astigmatism axes (R=0.5) where moderate correlations were recorded, Figure 6. When the KC clinical parameters were investigated, only the chamber height recorded a high correlation among right and left corneas. It was clear that the weakest correlations were recorded when the horizontal location of the minimum pachymetry was investigated (R=0.2), Figure 7.

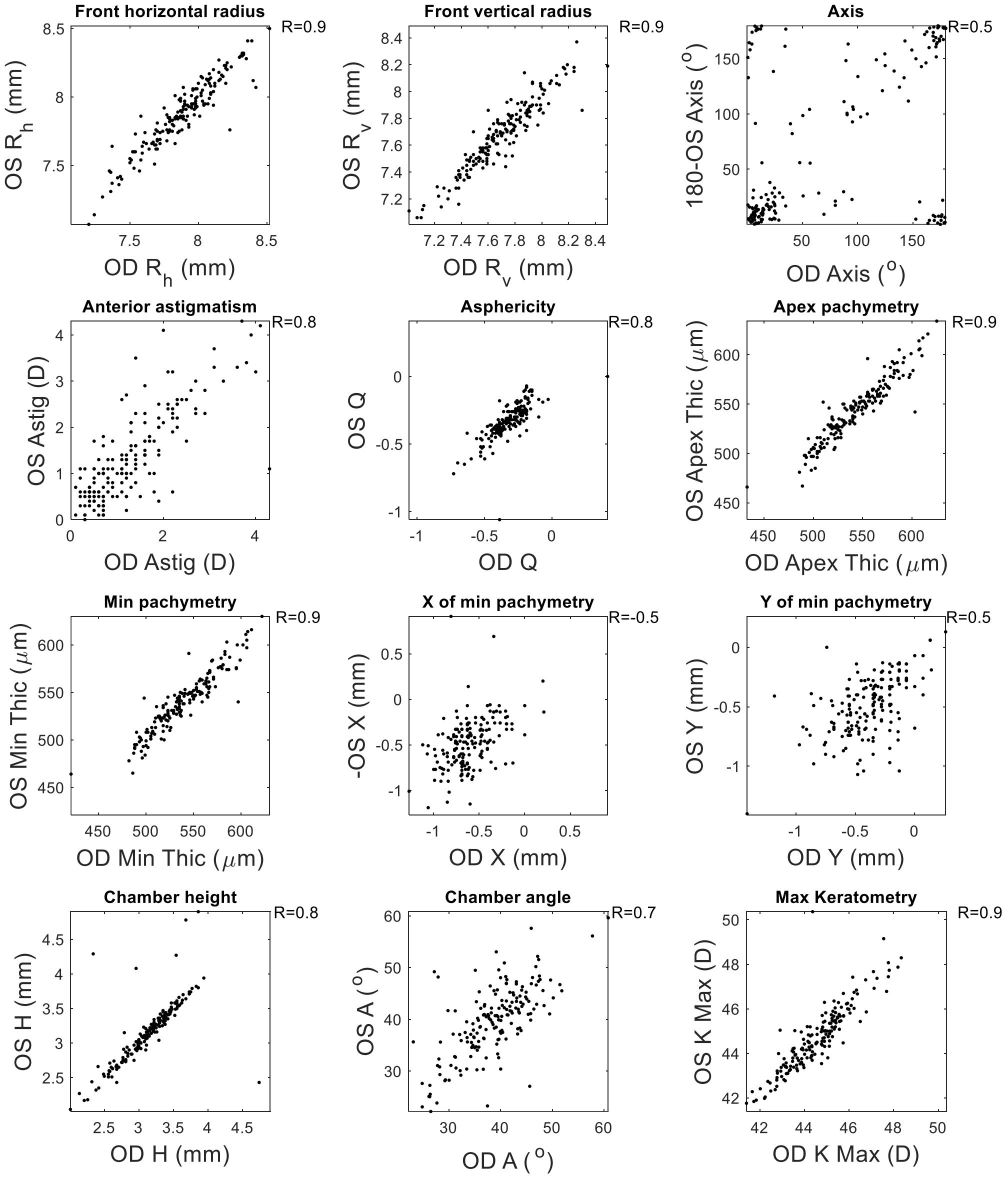

Figure 6: Correlation between right and left corneas clinical parameters among healthy subjects.

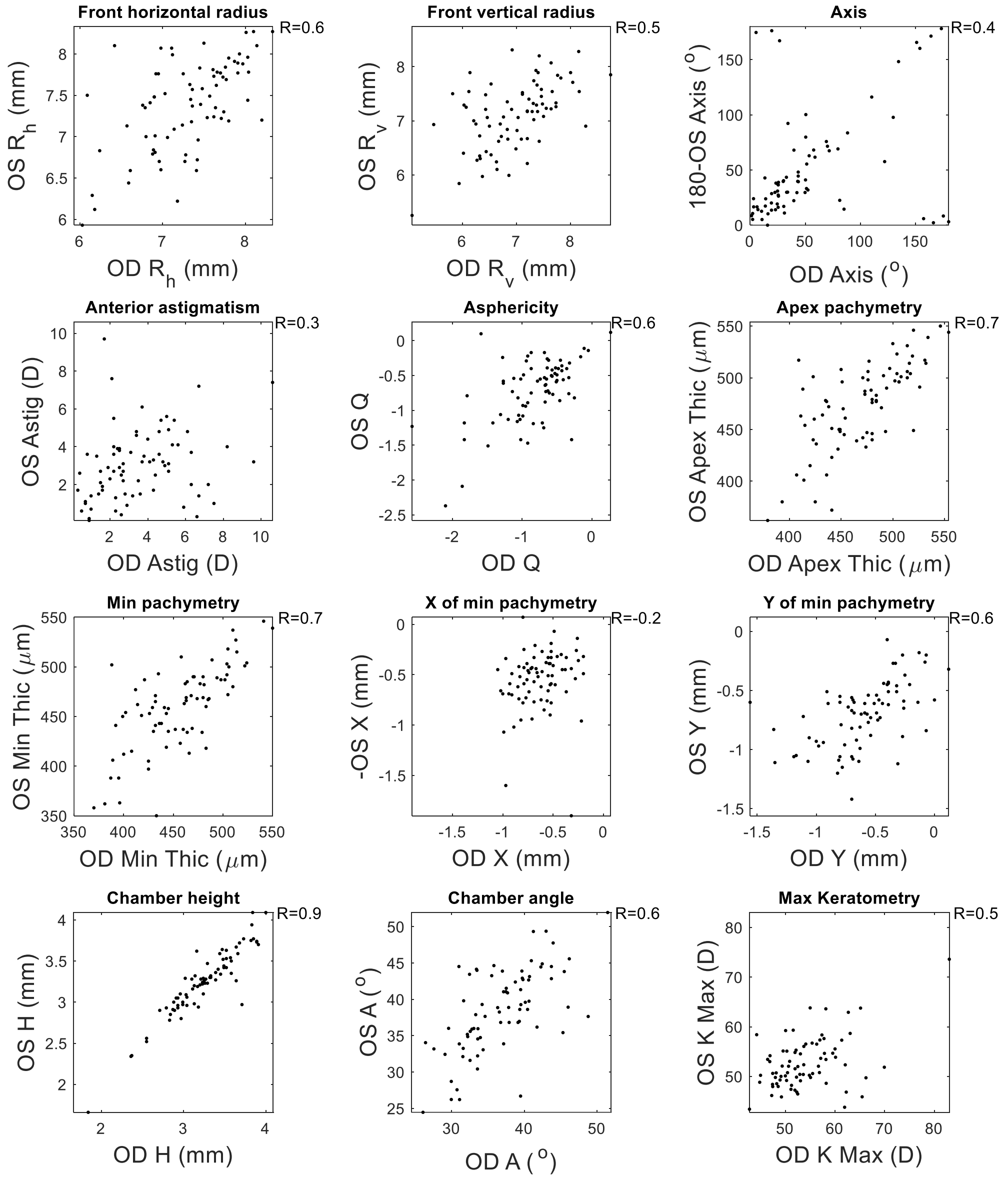

Figure 7: Correlation between right and left corneas clinical parameters among KC subjects.