

# Repeatability of Scheimpflug Corneal Tomography in Patients with Keratoconus and Different Body Mass Indices

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## Abstract

**Objective:** To evaluate the repeatability of corneal tomographic parameters in keratoconus patients across different body mass index (BMI) categories.

**Methods:** This prospective study was conducted at the University of Auckland, New Zealand, from June 2021 to June 2022. A total of 243 eyes from keratoconus patients aged 18-45 years were categorized into normal (BMI  $\leq 24.9$ ; n=55), overweight (BMI 25.0-29.9; n=58), and obese (BMI  $\geq 30.0$ ; n=130) groups. Patients underwent three consecutive scans using the Pentacam AXL. The repeatability of flat simulated keratometry (K1A), steep simulated keratometry (K2A), maximum keratometry (Kmax), central corneal thickness (CCT), and thinnest corneal thickness (TCT) was assessed using within-subject standard deviation (Sw), repeatability limits, and intraclass correlation coefficients (ICC). A subgroup analysis was performed by matching patients for keratoconus severity to assess the influence of disease stage on repeatability.

**Results:** Repeatability decreased significantly with higher BMI across all parameters. K1A and K2A had the highest repeatability (ICC 0.992-0.998), while TCT had the lowest (ICC 0.983-0.988). Notably, the obese group showed greater variability in CCT and TCT compared to the normal and overweight groups. After adjusting for keratoconus severity, these differences were no longer statistically significant between BMI groups.

**Conclusions:** Tomographic parameter repeatability in keratoconus patients is excellent across BMI categories. Although repeatability decreases with increasing BMI, this effect is not significant after accounting for disease severity. These findings underscore the importance of using the most reliable tomographic parameters for monitoring keratoconus progression, particularly in patients with higher BMI and advanced stages of the disease.

**Keywords:** Keratoconus, Repeatability, BMI, Tomography, Intra-class correlation co-efficient, Corneal imaging, Corneal thickness

## Introduction

Keratoconus is a progressive, bilateral corneal ectasia characterized by corneal thinning, steepening and scarring [1,2]. Several studies have identified risk factors for keratoconus, including genetic predisposition, environmental factors, and ocular rubbing [3]. Additionally, recent epidemiological data suggest an increased prevalence of keratoconus in populations with higher rates of obesity [4]. In Aotearoa-New Zealand, keratoconus has also been demonstrated to disproportionately affect patients of Māori and Pacific Peoples

ethnicity [5], and the rates of obesity in these ethnicities are 1.9 and 2.5 times higher than in New Zealand Europeans, respectively [6].

The advent of corneal crosslinking (CXL) has revolutionized the treatment of this disease, arresting the underlying ectatic process and typically improving tomographic and visual parameters [7,8]. However, progression to late-stage disease may require a corneal transplant (keratoplasty) to provide visual rehabilitation [9]. Prompt intervention with CXL has been shown to significantly reduce the number of keratoplasties

required [10], highlighting the importance of accurate and timely diagnosis, as well as meticulous monitoring of disease progression.

While studies have been conducted on the repeatability of Scheimpflug-based tomography on keratoconus, it is unknown whether BMI itself may affect the repeatability of tomographic measurements [11,12]. To our knowledge, this is the first study to assess the effect of BMI on the repeatability of Scheimpflug-based tomography parameters in patients with keratoconus.

## Materials and Methods

Consecutive patients diagnosed with keratoconus and attending the University of Auckland Keratoconus and Crosslinking Service were enrolled between June 2021 and June 2022. The study included patients aged 18-45 years, categorized into normal ( $BMI \leq 24.9$ ), overweight ( $BMI 25.0-29.9$ ), and obese ( $BMI \geq 30.0$ ) groups. Inclusion criteria were a confirmed diagnosis of keratoconus and no prior corneal surgeries. Exclusion criteria included acute corneal hydrops, prior intraocular surgeries, or inability to obtain three consecutive tomographic scans of acceptable quality. Contact lens wearers were instructed to refrain from use for 48 hours before corneal tomography. The 48 hour period chosen aligned with current clinical practice and ensured feasibility for participants who rely on contact lenses [13].

As keratoconus is a bilateral, asymmetrical disease which does not consistently favor either eye [14,15], the patient's right eye was chosen for analysis, unless any of the exclusion criteria applied, in which case the left eye was analyzed (50 eyes, 20.6%).

The study was approved by the local Health and Disability Ethics Committee (approval number UAHPEC20294), a branch of the Ministry of Health in New Zealand, in accordance with the Declaration of Helsinki. The study was conducted with participants' understanding, and written informed consent was obtained from all participants prior to enrollment in the study.

## Instruments

The Penta Cam AXL® (Oculus, Wetzlar, Germany) is a partial coherence interferometry device that combines a rotating Scheimpflug system with optical biometry using a blue 475 nm light-emitting diode [16]. Over a maximum of 2 seconds per scan, the device acquires a total of 25 images to produce high-resolution corneal measurements. The system uses a second camera which detects and corrects eye movement. Three-dimensional images with up to 138,000 individual elevation points are created with a central fine-meshed dot matrix due to the rotation. The simulated keratometry measurements are taken from a 3 mm ring over the anterior surface of the cornea [16].

## Assessment

Participant-reported ethnicity was collected (European, Māori, Pacific Peoples, Indian, Asian, Other ethnicity), and their height and weight were measured using a calibrated stadiometer and digital scale, respectively. One investigator scanned each eye using automatic image acquisition where possible. Patients were instructed to blink immediately before each scan was acquired, and three consecutive scans of each eye were obtained within 15 minutes. Scans were assessed qualitatively by the investigator for eyelid, centration, or movement-related artefacts. All measurements were performed without pupil dilation under identical lighting conditions, between 1.00 pm and 5.00 pm to limit any influence of overnight, closed-eye, increase in pachymetry [17].

The BMI of each patient was calculated by taking the patient's weight, in kilograms, divided by their height, in meters squared. Patients were subsequently categorized, based on BMI, into three groups according to the World Health Organization (WHO) cut-off points [18]:

Normal weight: BMI less than or equal to  $24.9 \text{ kg/m}^2$

Overweight: BMI greater than or equal to  $25.0$  to  $29.9 \text{ kg/m}^2$

Obese: BMI greater than or equal to  $30.0 \text{ kg/m}^2$

The cutoffs provided by the WHO are used for White, Hispanic and Black individuals, with adjustments for patients of Asian ethnicity. Due to the small percentage of Asian, Indian and Other ethnicity patients in the study, no adjustments to the BMI calculations were made for these groups in this study. In addition, literature exploring whether ethnicity-specific adjustments are justified for people of Polynesian descent has suggested that the cutoffs are appropriate for this demographic [19].

Five main tomographic parameters were compared between groups: flat simulated keratometry of the anterior surface (K1A), steep simulated keratometry of the anterior surface (K2A), maximum keratometry ( $K_{\text{max}}$ ), central corneal thickness (CCT) and thinnest corneal thickness (TCT). These values were calculated as the mean of the three acquired scans.

## Statistical analysis

Initial statistical analysis was performed using SPSS (SPSS, IBM, Chicago, Illinois, USA). Further analysis and visualizations were performed with R version 4.3.2 (2024-04-01) using RStudio version 2024.04.2+764 (Posit Software, PBC), using *ggplot2*, *nnet*, *rstatix* and *dplyr* packages [20-24]. A complete list of packages and versions is available in the supplementary materials. The within-subject standard deviation ( $S_w$ ) was used to calculate precision ( $1.96 \times S_w$ ) and repeatability ( $2.77 \times S_w$ ) [25]. Repeatability was evaluated using the coefficient of variation (CV) and the intraclass correlation coefficient

(ICC). ICC estimates and their 95% confidence intervals were calculated based on a mean rating (k=3), absolute-agreement and a 2-way mixed-effects model. A one-way analysis of variance with Tukey's post-hoc was performed to assess the differences between the three groups for continuous variables. A Chi-squared test with Bonferroni correction was performed to assess for differences between categorical variables. The Bonferroni correction was used to reduce the chance of Type-1 error, while accepting the increased chance for Type-2 error [26].

A sub-group of patients in the normal and overweight groups were disease-matched to patients in the obese group based on their K<sub>max</sub>. A two-tailed t-test was used to assess differences between these groups.

Differences in BMI between ethnic groups were evaluated with Fisher's exact test (pairwise comparisons) and multinomial linear regression to calculate simple odds ratios.

A p-value of <0.05 was deemed significant for all statistical analyses, with adjustments to the α value made with the Bonferroni correction where required.

Results

The study included 243 eyes from 243 patients, divided into three BMI categories: normal (55 eyes), overweight (58 eyes), and obese (130 eyes). The mean age of patients was 20.73 ± 6.20 years in the normal BMI group, 25.97 ± 9.33 years in the overweight group, and 25.94 ± 6.71 years in the obese group. The age differences between the normal BMI group and both the overweight and obese groups were statistically significant (p<0.001) (Table 1). There were significantly more males in the overweight group (74.10%) compared to the normal (69.10%) and obese groups (53.10%) (p = 0.010) (Table 1).

Within BMI groups, European patients were most prevalent in the normal BMI group (38.18%) and least prevalent in the obese group (10.00%) (p<0.001). Pacific Peoples were significantly overrepresented in the obese group, accounting for 62.31% of this category, compared to 12.73% in the normal BMI group and 25.86% in the overweight group (p<0.001). Indian ethnicity was more common in the normal BMI group, where 20.00% of the patients were Indian, compared to 15.52% in the overweight group and just 1.54% in the obese group (p = 0.001). Asian ethnicity followed a similar pattern,

| Table 1. Demographics and TKC of patients included in the study, p-values (p<0.05).                                                                                                                                        |                 |              |              |              |         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|--------------|--------------|--------------|---------|
| Demographic                                                                                                                                                                                                                |                 | Normal       | Overweight   | Obese        | p-value |
| Eyes (n)                                                                                                                                                                                                                   |                 | 55           | 58           | 130          |         |
| Males (n, %)                                                                                                                                                                                                               |                 | 38, 69.10%   | 43, 74.10%   | 69, 53.10%   | 0.010*  |
| Mean age (years, ± SD)                                                                                                                                                                                                     |                 | 20.73 ± 6.20 | 25.97 ± 9.33 | 25.94 ± 6.71 | <0.001* |
| Right eye (n, %)                                                                                                                                                                                                           |                 | 43, 78.20%   | 43, 74.10%   | 107, 82.30%  | 0.426   |
| Ethnicity (n, %)                                                                                                                                                                                                           | European        | 21, 38.18%   | 17, 29.31%   | 13, 10.00%   | <0.001* |
|                                                                                                                                                                                                                            | Māori           | 7, 12.73%    | 11, 18.97%   | 30, 23.08%   | 0.137   |
|                                                                                                                                                                                                                            | Pacific Peoples | 7, 12.73%    | 15, 25.86%   | 81, 62.31%   | <0.001* |
|                                                                                                                                                                                                                            | Indian          | 11, 20.00%   | 9, 15.52%    | 2, 1.54%     | 0.001*  |
|                                                                                                                                                                                                                            | Asian           | 6, 10.91%    | 5, 8.62%     | 3, 2.31%     | 0.013*  |
|                                                                                                                                                                                                                            | Other           | 3, 5.45%     | 1, 1.72%     | 1, 0.77%     | 0.044*  |
| Mean TKC ± SD                                                                                                                                                                                                              |                 | 2.09 ± 0.85  | 1.98 ± 0.91  | 2.52 ± 0.87  | 0.001*  |
| TKC 1 (n, %)                                                                                                                                                                                                               |                 | 15, 27.27%   | 21, 36.21%   | 19, 14.62%   | 0.001*  |
| TKC 1-2 (n, %)                                                                                                                                                                                                             |                 | 3, 5.45%     | 6, 10.34%    | 4, 3.08%     | 0.053   |
| TKC 2 (n, %)                                                                                                                                                                                                               |                 | 15, 27.27%   | 7, 12.07%    | 26, 20.00%   | 0.092   |
| TKC 2-3 (n, %)                                                                                                                                                                                                             |                 | 6, 10.91%    | 7, 12.07%    | 18, 13.85%   | 0.585   |
| TKC 3 (n, %)                                                                                                                                                                                                               |                 | 11, 20.00%   | 12, 20.69%   | 35, 26.92%   | 0.231   |
| TKC 3-4 (n, %)                                                                                                                                                                                                             |                 | 5, 9.09%     | 5, 8.62%     | 22, 16.92%   | 0.063   |
| TKC 4 (n, %)                                                                                                                                                                                                               |                 | -            | -            | 6, 4.62%     | 0.021*  |
| Normal BMI: <24.9 kg/m²; Overweight BMI: 25.0 to 29.9 kg/m²; Obese BMI: >30.0kg/m²; n: number; SD: Standard Deviation; TKC: Topographic Keratoconus Classification, * denotes statistical significance at the p<0.05 level |                 |              |              |              |         |

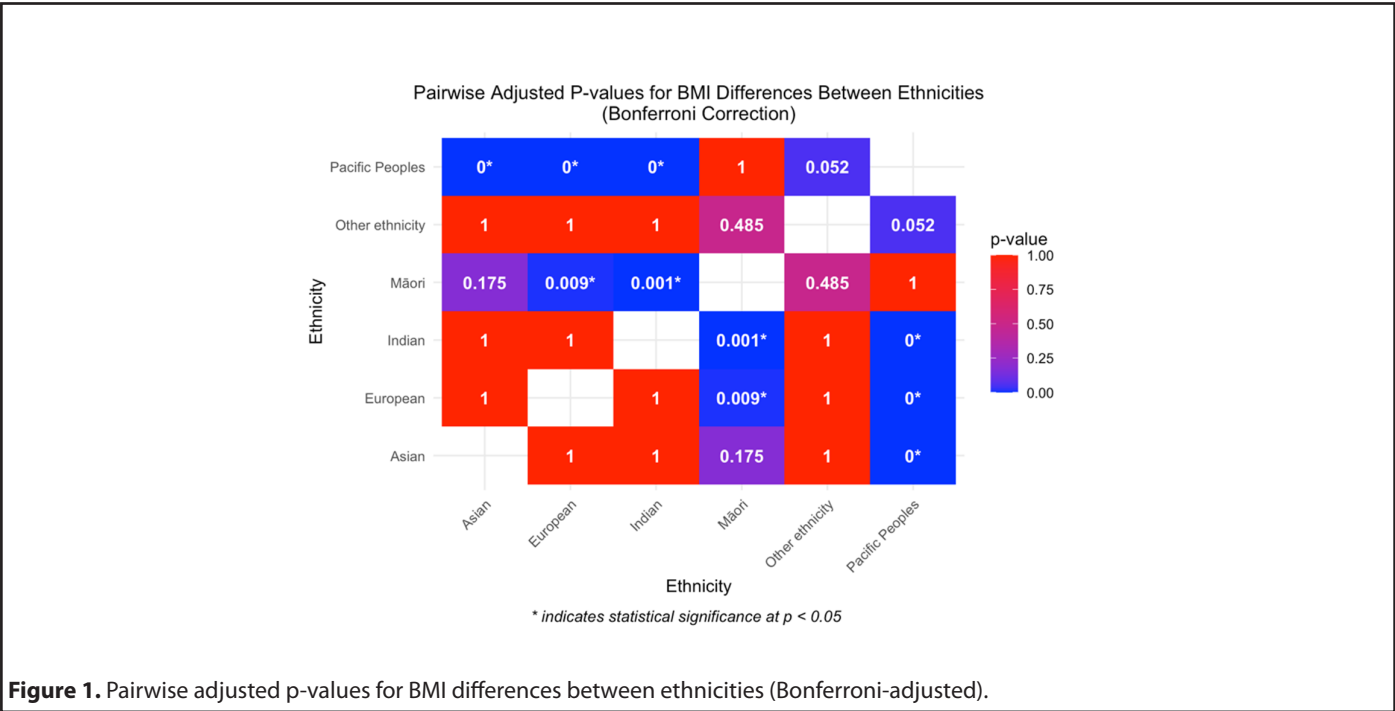
with 10.91% of the normal BMI group being Asian, 8.62% in the overweight group, and only 2.31% in the obese group (p=0.013) (**Table 1**).

Further analyses revealed significant differences between ethnic groups and BMI category.

After pairwise Fisher’s exact tests with Bonferroni correction (**Table 2**), significant differences were observed between: Pacific Peoples and Asian, European, and Indian groups. Māori also had significantly different BMI distributions compared to Europeans and Indians. These were visualized in a heat map (**Figure 1**).

| Table 2. Bonferroni-corrected pairwise comparisons between ethnicity categories (Fisher's exact test), p value<0.05. |                 |                  |
|----------------------------------------------------------------------------------------------------------------------|-----------------|------------------|
| Ethnicity 1                                                                                                          | Ethnicity 2     | Adjusted p-value |
| Asian                                                                                                                | European        | 1                |
| Asian                                                                                                                | Indian          | 1                |
| Asian                                                                                                                | Māori           | 0.176            |
| Asian                                                                                                                | Other ethnicity | 1                |
| Asian                                                                                                                | Pacific Peoples | 0.00028*         |
| European                                                                                                             | Indian          | 1                |
| European                                                                                                             | Māori           | 0.0086*          |
| European                                                                                                             | Other ethnicity | 1                |
| European                                                                                                             | Pacific Peoples | 2.15e-9*         |
| Indian                                                                                                               | Māori           | 0.00051*         |
| Indian                                                                                                               | Other ethnicity | 1                |
| Indian                                                                                                               | Pacific Peoples | 7.25e-9*         |
| Māori                                                                                                                | Other ethnicity | 0.485            |
| Māori                                                                                                                | Pacific Peoples | 1                |
| Other ethnicity                                                                                                      | Pacific Peoples | 0.052            |

\* denotes statistical significance at the  $p<0.05$  level



**Figure 1.** Pairwise adjusted p-values for BMI differences between ethnicities (Bonferroni-adjusted).

A multinomial logistic regression model (**Table 3**) was used to examine the association between ethnicity and BMI category, with European ethnicity and Normal weight as the reference groups. A forest plot (**Figure 2**) illustrates the simple odds ratios (ORs) and 95% confidence intervals for each ethnicity and BMI category.

Key findings from the model were that Māori individuals had significantly higher odds of being obese compared to Europeans (OR=6.92, 95% CI: 2.36–20.28,  $p<0.001$ ). Pacific Peoples had the highest odds of obesity compared to Europeans (OR=18.69, 95% CI: 6.63–52.70,  $p<0.0001$ ). No significant differences were observed for overweight status across ethnicities. Asian, Indian, and Other Ethnicity groups did not have statistically significant differences in obesity

prevalence compared to Europeans. These results align with national obesity data [27].

A stacked bar chart was used to illustrate the relative proportions of participants in each BMI category; stratified by ethnicity (**Figure 3**).

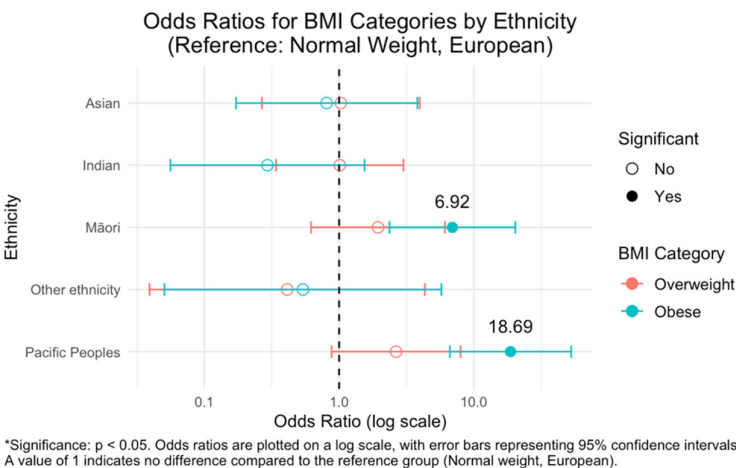
Topographic Keratoconus Classification (TKC, which classifies keratoconus into five grades: 0 (normal) to 4 (severe)) varied significantly across the BMI groups [28].

In the normal BMI group, 27.27% of the eyes were classified as TKC 1, while this classification was more common in the overweight group (36.21%) and less common in the obese group (14.62%) ( $p=0.001$ ). TKC 3, representing a more advanced keratoconus, was present in 20.00% of the normal

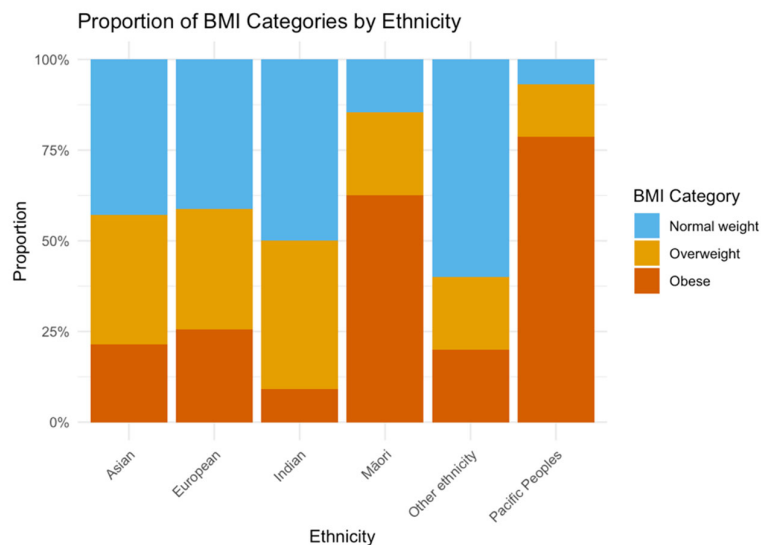
**Table 3.** Multinomial logistic regression of ethnicity and Body Mass Index; simple odds ratios, 95% Confidence Intervals (CI) and p-values ( $p<0.05$ ).

| Ethnicity       | BMI Category | Odds Ratio | CI (Lower–Upper) | p-value  |
|-----------------|--------------|------------|------------------|----------|
| Asian           | Overweight   | 1.03       | 0.27–3.96        | 0.97     |
| Asian           | Obese        | 0.81       | 0.17–3.80        | 0.79     |
| Indian          | Overweight   | 1.01       | 0.34–3.00        | 0.98     |
| Indian          | Obese        | 0.29       | 0.06–1.54        | 0.15     |
| Māori           | Overweight   | 1.94       | 0.62–6.09        | 0.26     |
| Māori           | Obese        | 6.92       | 2.36–20.28       | 0.0004*  |
| Other           | Overweight   | 0.41       | 0.04–4.32        | 0.46     |
| Other           | Obese        | 0.54       | 0.05–5.74        | 0.61     |
| Pacific Peoples | Overweight   | 2.65       | 0.88–7.96        | 0.08     |
| Pacific Peoples | Obese        | 18.69      | 6.63–52.70       | 3.09e-8* |

\* denotes statistical significance at the  $p<0.05$  level



**Figure 2.** Simple odds ratios for BMI categories by ethnicity (Reference: normal BMI; European).



**Figure 3.** Stacked bar chart of proportions of participants in each BMI category, by ethnicity.

BMI group, 20.69% of the overweight group, and 26.92% of the obese group ( $p=0.231$ ). The most severe classification, TKC 4, was found exclusively in the obese group (4.62%) ( $p=0.021$ ) (**Table 1**).

For tomographic parameters, the mean flat simulated keratometry of the anterior surface (K1A) was  $45.19 \pm 3.50$  D in the normal group,  $44.84 \pm 3.50$  D in the overweight group, and  $47.76 \pm 7.03$  D in the obese group. The repeatability limits for

K1A were 0.72 D in the normal group, 0.82 D in the overweight group, and 2.29 D in the obese group. The intraclass correlation coefficient (ICC) for K1A was 0.998 in both the normal and overweight groups and 0.995 in the obese group (**Table 4**).

The mean steep simulated keratometry of the anterior surface (K2A) was  $48.77 \pm 4.73$  D in the normal group,  $48.52 \pm 4.94$  D in the overweight group, and  $52.41 \pm 8.13$  D in the obese group. The repeatability limits for K2A were 1.02 D in

| Table 4. Repeatability of keratometry and pachymetry measurements in eyes with different body mass indices.                                                                                                                                                                                                                                                                                                                                                                                              |                   |                 |                |                 |         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-----------------|----------------|-----------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Group             | Mean Difference | Standard Error | 95% CI          | p-value |
| TCT (μm)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Normal-Overweight | -6.75           | 9.23           | -28.51 to 15.02 | 0.75    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Normal-Obese      | 18.53           | 7.89           | -0.07 to 37.14  | 0.05    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Overweight-Obese  | 25.28           | 7.74           | 7.02 to 43.54   | <0.001* |
| S <sub>w</sub> TCT (μm)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Normal-Overweight | -1.59           | 1.09           | -4.17 to 0.98   | 0.31    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Normal-Obese      | -1.63           | 0.93           | -3.83 to 0.57   | 0.19    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Overweight-Obese  | -0.04           | 0.91           | -2.19 to 2.12   | 1.00    |
| K <sub>max</sub> (D)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Normal-Overweight | 0.89            | 1.75           | -3.24 to 5.02   | 0.87    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Normal-Obese      | -4.80           | 1.50           | -8.33 to -1.27  | <0.001* |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Overweight-Obese  | -5.69           | 1.47           | -9.16 to -2.22  | <0.001* |
| S <sub>w</sub> K <sub>max</sub> (D)                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Normal-Overweight | -0.05           | 0.13           | -0.35 to 0.25   | 0.92    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Normal-Obese      | -.27            | 0.11           | -0.53 to -0.01  | 0.04*   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Overweight-Obese  | -0.22           | 0.11           | -0.47 to 0.04   | 0.11    |
| N: number; Normal BMI: ≤ 24.9 kg/m <sup>2</sup> ; Overweight BMI: 25.0 to 29.9 kg/m <sup>2</sup> ; Obese BMI >30 kg/m <sup>2</sup> ; CI: Confidence Interval; SD: Standard Deviation; Sw: Within-subject standard deviation; D: Dioptres; K1A: Flat Simulated Keratometry of Anterior Surface; K2A: Steep Simulated Keratometry of Anterior Surface; Kmax: Maximum Keratometry; CCT: Central Corneal Thickness; TCT: Thinnest Corneal Thickness; * denotes statistical significance at the p<0.05 level. |                   |                 |                |                 |         |

the normal group, 1.27 D in the overweight group, and 3.45 D in the obese group. The ICC for K2A ranged from 0.998 in the normal group to 0.992 in the obese group (**Table 4**).

The maximum keratometry (Kmax) mean values were  $54.07 \pm 7.83$  D in the normal group,  $53.18 \pm 7.24$  D in the overweight group, and  $58.87 \pm 10.60$  D in the obese group. The repeatability limits for Kmax were 1.32 D in the normal group, 2.05 D in the overweight group, and 2.80 D in the obese group. The ICC for Kmax was 0.999 in the normal group, 0.997 in the overweight group, and 0.997 in the obese group (**Table 2**).

Regarding pachymetry, the mean central corneal thickness (CCT) was  $478.23 \pm 39.44$   $\mu$ m in the normal group,  $486.16 \pm 44.39$   $\mu$ m in the overweight group, and  $461.65 \pm 53.40$   $\mu$ m in the obese group. The repeatability limits for CCT were 10.28  $\mu$ m in the normal group, 12.64  $\mu$ m in the overweight group, and 16.63  $\mu$ m in the obese group. The ICC for CCT ranged from 0.997 in the normal group to 0.996 in the obese group (**Table 4**).

The mean thinnest corneal thickness (TCT) was  $471.66 \pm 38.78$   $\mu$ m in the normal group,  $478.41 \pm 43.87$   $\mu$ m in the overweight group, and  $453.13 \pm 54.72$   $\mu$ m in the obese group.

The repeatability limits for TCT were 20.20  $\mu$ m in the normal group, 27.55  $\mu$ m in the overweight group, and 28.36  $\mu$ m in the obese group. The ICC for TCT was 0.988 in the normal group, 0.983 in the overweight group, and 0.988 in the obese group (**Table 4**).

Significant differences in tomographic parameters were observed between the normal and obese groups for K1A, K2A, and Kmax, with mean differences of -2.58 D ( $p=0.01$ ), -3.64 D ( $p<0.001$ ), and -4.80 D ( $p<0.001$ ), respectively. The differences between the overweight and obese groups were also statistically significant for these parameters, with mean differences of -2.92 D for K1A ( $p=0.00$ ), -3.89 D for K2A ( $p<0.001$ ), and -5.69 D for Kmax ( $p<0.001$ ) (**Table 5**).

In pachymetric measurements, significant differences were found particularly between the overweight and obese groups, with mean differences of -24.50  $\mu$ m for CCT ( $p<0.001$ ) and -25.28  $\mu$ m for TCT ( $p<0.001$ ) (**Table 5**).

Regarding the ICC overall, the lower bound of the 95% confidence interval for all parameters was greater than 0.90, indicating excellent repeatability [29].

**Table 5.** Differences between mean keratometry and pachymetry measurements in eyes between different body mass groups (normal n=55, overweight n=58, and obese n=130).

|                               | Group             | Mean Difference | Standard Error | 95% CI         | p-value |
|-------------------------------|-------------------|-----------------|----------------|----------------|---------|
| K1A (D)                       | Normal-Overweight | 0.35            | 1.07           | -2.17 to 2.87  | 0.94    |
|                               | Normal-Obese      | -2.58           | 0.91           | -4.73 to -0.42 | 0.01*   |
|                               | Overweight-Obese  | -2.92           | 0.90           | -5.04 to -0.81 | 0.00*   |
| S <sub>w</sub> K1A (D)        | Normal-Overweight | 0.00            | 0.10           | -0.24 to 0.25  | 1.00    |
|                               | Normal-Obese      | -0.20           | 0.09           | -0.41 to 0.02  | 0.08    |
|                               | Overweight-Obese  | -0.20           | 0.09           | -0.41 to 0.01  | 0.06    |
| K2A (D)                       | Normal-Overweight | 0.25            | 1.28           | -2.77 to 3.28  | 0.98    |
|                               | Normal-Obese      | -3.64           | 1.10           | -6.22 to -1.06 | <0.001* |
|                               | Overweight-Obese  | -3.89           | 1.08           | -6.43 to -1.36 | <0.001* |
| S <sub>w</sub> K2A (D)        | Normal-Overweight | 0.00            | 0.17           | -0.4 to 0.39   | 1.00    |
|                               | Normal-Obese      | -0.17           | 0.14           | -0.51 to 0.17  | 0.46    |
|                               | Overweight-Obese  | -0.17           | 0.14           | -0.5 to 0.17   | 0.46    |
| CCT ( $\mu$ m)                | Normal-Overweight | -7.92           | 9.13           | -29.45 to 13.6 | 0.66    |
|                               | Normal-Obese      | 16.58           | 7.80           | -1.81 to 34.97 | 0.09    |
|                               | Overweight-Obese  | 24.50           | 7.66           | 6.45 to 42.56  | <0.001* |
| S <sub>w</sub> CCT ( $\mu$ m) | Normal-Overweight | -0.56           | 0.78           | -2.4 to 1.27   | 0.75    |
|                               | Normal-Obese      | -1.02           | 0.67           | -2.59 to 0.55  | 0.27    |
|                               | Overweight-Obese  | -0.46           | 0.65           | -2 to 1.08     | 0.76    |

\* denotes statistical significance at the  $p<0.05$  level

Following disease-matching for severity of keratoconus, no significant differences were found between the topographical parameters or their within-subject standard deviations for normal and obese and overweight and obese groups.

## Discussion

This study evaluated the repeatability of tomographic parameters in keratoconus in patients with a range of BMI from normal to obese. It has been suggested that BMI can be treated as an independent risk factor for keratoconus [4], and disease severity has been linked with BMI in previous studies [3]. A large body of literature has reported on the repeatable nature of Pentacam derived tomographic and pachymetric parameters in keratoconus of varying severity [12,30]. Whilst previous studies have reported absolute values of anterior segment parameters in patients with obesity, there is a lack of studies investigating whether BMI *per se* could affect the repeatability of tomographic and pachymetric measurements [31].

The ability to obtain repeatable tomographic measurements is essential in tracking the progression of keratoconus, and serial Scheimpflug corneal tomography has become the standard of care in developed countries [32]. Indeed, tomographic progression of keratoconus is said to have occurred if key keratometry values have increased beyond the repeatability limits [33]. Although CXL for keratoconus is effective it is not without risk, and post-procedural persistent stromal haze, corneal melt, and microbial keratitis with perforation have all been reported in the literature [34,35]. Therefore, it is critical that the procedure is not offered to patients indiscriminately and that clinical decisions are based on repeatable data that confirm disease and progression.

The results of this study showed that the repeatability of tomographic parameters decreased as BMI increased. However, sub-group analysis showed this difference was not statistically significant after accounting for disease severity. This study found excellent repeatability as assessed by the ICC of all tomographic parameters regardless of BMI. A significant ethnic disparity between BMI groups was found, with Pacific Peoples with keratoconus being over-represented in the obese group. Although elucidating reasons behind this observation is beyond the scope of this paper, this has important implications for healthcare planning within a New Zealand context and warrants further investigation. The over-representation of the obese group and Pacific Peoples in our study sample could introduce bias in interpreting the effect of BMI on tomographic repeatability, which should be considered when generalizing our findings.

The absolute repeatability limits of K2A,  $K_{max}$  and CCT measurements in this study were higher than those reported by other investigators, which ranged between 0.48–1.56 D, 0.86–1.66 D and 8.1–12.6  $\mu\text{m}$  respectively [30–37]. However,

the repeatability limits for K1A and TCT were similar to those reported in the literature, ranging from 0.51–2.08 D and 8.26–28.15  $\mu\text{m}$  respectively [36]. Reduced repeatability in this study could be explained by increased disease severity, with the majority of patients having a  $\geq 2$ -3 TKC Grade.

Obese individuals have decreased total respiratory system compliance and exhibit a shallow, rapid breathing pattern [38,39]. In addition, these patients may have a narrowed interpalpebral fissure, thickened tear film, and an increased orbital fat content [40,41]. It is postulated that these factors might interfere with the ability of the Penta Cam's second camera to detect and control eye movement while obtaining the scan.

These physiological characteristics could theoretically impair image quality by affecting the stability of the eye during scanning or by altering the tear film dynamics. However, after matching for disease severity, no statistically significant differences in tomographic parameters were observed across BMI categories. This finding suggests that while these factors were initially considered as potential confounders, they did not significantly impact the repeatability of tomographic parameters in our dataset.

Despite this, it is important to recognize that these physiological factors might still affect the quality of imaging in certain contexts, particularly in populations where more extreme variations in respiratory function or eyelid anatomy are present. Therefore, while our study did not find these factors to be significant confounders in the relationship between BMI and tomographic repeatability, they may still be relevant in other clinical or research settings where such physiological variations are more pronounced.

Furthermore, it is known that glycation and natural corneal collagen crosslinking are caused by aging and type 2 diabetes [42]. As patients were significantly older in the overweight and obese groups, and increasing BMI is associated with a greatly increased risk of developing type 2 diabetes, it is possible that these factors impacted the reliability of the results between cohorts [43]. However, after adjusting for disease severity, there were no significant differences seen between groups in relation to the tomographic parameters measured or the within-subject standard deviation of the measurements obtained. This suggests that the differences between these parameters during our baseline comparison are likely due to differences in disease severity between groups. Despite adjustments for disease severity, differences in repeatability may still be partly attributable to the inherent variability associated with advanced stages of keratoconus.

This study had several limitations, including the use of only a single tomography device and the inclusion of scans without quality scores of 'OK' in severe keratoconus patients (166 of 729 total scans, 22.77%). In clinical practice, obtaining tomographic scans, which are all graded as 'OK', can be

challenging, as patients with severe disease can suffer fixation loss and photophobia [44]. However, scans can be of adequate quality if enough data points are sampled to generate a topography map. Therefore, this study did not exclude scans without a quality score of 'OK' for analysis. Furthermore, using the mean measurements from several scans in advanced keratoconus may be more useful than single measurements from a scan with an 'OK' quality score [36]. The algorithms used by the Penta Cam software to acquire images and generate parameters are also more likely to perform poorly in advanced disease, necessitating manual alignment and capture. In addition, the corneas of patients with advanced disease may have scarring, hindering the ability of the device to interpret tissue boundaries and affecting the output of the algorithms. Furthermore, the obese weight group were overrepresented in population, potentially impacting the results.

Although participants were asked to remove their contact lenses 48 hours prior to scans being performed, we did not collect information on the proportion of contact lens wear. Corneal warpage from contact lens wear can take between one to eight weeks to stabilize and it is not always practical to request patients with advanced disease who are often reliant on contact lens wear to abstain from use for such a prolonged period [45]. In addition, all three scans for each patient were conducted within a 15-minute timeframe, so the effect of any corneal warpage is likely to be consistent between scans. Therefore, while absolute measurements of keratometry and pachymetry may have been affected, it is unlikely to have influenced the repeatability of these measures. However, the possibility of residual corneal warpage affecting measurements cannot be excluded, particularly in severe cases. In addition, conducting all scans within a 15-minute timeframe may not account for diurnal variations or longer-term changes, limiting the assessment of repeatability over extended periods. Future studies may further explore contact lens wear history and cessation in more detail.

Finally, measurements were conducted using one device based on partial coherence interferometry and a rotating Scheimpflug system. Future studies should be completed using tomography devices with different imaging modalities to further explore the effect of BMI on repeatability.

In conclusion, our study demonstrates that BMI does not significantly affect the repeatability of tomographic parameters obtained using the Penta Cam AXL. We found statistically significant differences in BMI between ethnic groups, with Māori and Pacific Peoples being 6.92 and 18.69 times more likely, respectively, to be obese than Europeans. This finding aligns with national obesity trends [27]. Parameters such as TCT are critical in determining CXL treatment modality, and while this was the least repeatable measure in our study, it did not vary with BMI. Given K1A and K2A were the most repeatable metrics in all BMI groups, we suggest that a classification system such as ABCD is used incorporating these parameters [46].

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## Conflicts of Interest

There are no conflicts of interest to declare.

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There is no specific funding for this study to declare.

## Author Contribution Statement

JL was responsible for data collection, literature search, draft of the manuscript, statistical analysis and manuscript editing. LA was responsible for data collection and manuscript drafting and editing. AG was responsible for data collection, statistical analysis and manuscript editing. CM was responsible for study design and manuscript editing. MZ was responsible for study design and manuscript editing.

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