

An Assessment of Band Keratopathy Depth With Anterior Segment Optical Coherence Tomography

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Research article

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Abstract

Background: To describe the anterior segment optical coherence tomography (AS-OCT) findings in a series of patients with band keratopathy (BK) and discuss its possible clinical utility.

Methods: A retrospective review of 31 eyes from 31 consecutive patients with BK from November 2013 to October 2018. Lesion depth and central corneal thickness (CCT) were outputted from AS-OCT (RS-3000 Advance, NAVIS-EX 1.5.5 Nidek CO LTD, Japan).

Results: There were 20 cases of ocular trauma, 3 cases of retinal detachment, 2 cases of glaucoma, 2 cases of uveitis, 1 case of Coats' disease, 1 case of complicated cataract surgery, 1 case of non-clearing vitreous hemorrhage, and 1 case of unknown etiology. Mean duration of the opacity per patient history was 22.4 ± 11.3 (range 3-40) years. 26 eyes were no light perception (NLP), 3 eyes were light perception (LP) and 2 eyes were hand motion (HM). The calcium band as seen on AS-OCT corresponded to a hyperflective layer with posterior shadowing. The median depth of calcium was 100 μm (range 55-320) and the median CCT was 623 μm (range 534-785). The calcium depth was strongly correlated with the duration of the opacity per patient history ($r=0.68$, $p<0.001$).

Conclusions: AS-OCT may be utilized to assess BK depth. This depth has a wide distribution that is positively correlated with the duration of the opacity per patient history. Future studies will be required to measure BK depth across patients with less severe vision loss, test the consistency of AS-OCT measurements across different instruments, and confirm its clinical utility.

Background

Band keratopathy (BK) manifests clinically as the deposition of calcium within the interpalpebral exposure zone.¹ Histologic studies have shown the deposition of extracellular calcific materials to be predominantly in the basement membrane and Bowman's layer, but can also involve the epithelium and anterior stroma. Sometimes BK includes non-calcium components (mixed-type) thought to be from elastotic degeneration.¹⁻² Although BK may be idiopathic, it is often associated with co-morbidities such as chronic ocular diseases, chemical exposure, or systemic calcium or phosphate abnormalities.³

As BK progresses, accumulation of calcium can become symptomatic, affecting vision and/or disrupting the ocular surface causing photophobia, tearing, irritation and epithelial erosions. The mainstay of surgical treatment for BK is epithelial removal with ethylenediamine-tetraacetic acid (EDTA) chelation. Other options include manual debridement, phototherapeutic keratectomy (PTK) or superficial lamellar keratectomy. Amniotic membrane transplantation (AMT) is sometimes utilized as an adjuvant therapy.³⁻¹⁰

The surgical treatment for BK may in part depend on the depth of the lesion and the central corneal thickness (CCT). For example, Najjar et al reported EDTA chelation lasting 45 minutes for dense plaques, prompting Jhanji et al to propose that EDTA may not be ideal for thick or deep lesions.^{3,5} Additionally, the

appropriateness of PTK depends on predicting a sufficient residual stromal thickness. Spectral domain anterior segment optical coherence tomography (AS-OCT) is a non-contact imaging technology that uses tissue reflectance of near-infrared light to construct cross sectional images with a resolution similar to that of histopathology specimens.¹¹ The quantitative use of AS-OCT has been well described in the preoperative planning for a number of corneal pathologies.¹²⁻¹⁴ However, there have been limited reports on the application of AS-OCT to BK, with 2 more recent case reports and a small case series reported by Wirbelauer and Pham from 2004.¹⁵⁻¹⁷ The aim of the current work is to add to the literature on AS-OCT by reporting our findings from a series of 31 consecutive patients.

Methods

This is a retrospective review of the medical records of 31 eyes of 31 consecutive patients diagnosed with BK at Myongji hospital, Hanyang University College of Medicine between November 2013 and October 2018. The start time corresponded with the beginning of AS-OCT data collection on BK patients. The study adhered to the tenets of the Declaration of Helsinki and appropriate Institutional Review Board/Ethics Committee approvals were obtained.

Patient medical history included age, sex, and ocular co-morbidities. During the initial visit, patients and/or family members were asked when they first noticed the presence of a white opacity on the affected eye. This time (in years) was recorded as the duration of the opacity. Examination included best-corrected visual acuity (BCVA), slit-lamp biomicroscopy (Haag-Streit model BQ-900; Haag-Streit AG, Koeniz, Switzerland), and AS-OCT (RS-3000 Advance, NAVIS-EX 1.5.5 Nidek CO LTD, Japan). The diagnosis of BK was made based by the presence on slit lamp examination of a superficial calcific appearing band in the interpalpebral zone.

AS-OCT images were acquired three times at five minute intervals for each patient. Images were reviewed for adequacy; if they were decentered or contained artifact, they were repeated until an optimal image was obtained. Figure 1 presents the AS-OCT of a healthy control. Differences in tissue reflectivity allow for sufficient resolution to identify tear film, epithelial, stromal, and endothelial layers. The CCT was automatically calculated based on data from 12 radial scans centered on the pupil. Resolution reported by the manufacturer was 4 μm . To determine calcium depth, the 12 radial scans for each patient were reviewed, the highest image quality scan was chosen, and the deepest rim of the lesion on that scan was manually identified on a computer screen using a cursor. The CCT was measured as the thickness of stromal bed including the epithelial layer, and the depth of the calcium was measured from the epithelial layer to the inferior margin of the calcium invasion layer. The software then generated the depth. Two ophthalmologists (JWK and HJS) performed this step and were blinded to each other's results. Calcium depth was measured and compared by two ophthalmologists. The within-subject standard deviation (SD), coefficient of variation (CV), and intraclass correlation coefficient (ICC) were calculated to assess repeatability. The correlations were also evaluated via the Pearson's correlation coefficient. The reported calcium depth was the average between the 2 observers. Statistical analyses were conducted using SPSS statistical software (version 26.0, SPSS Inc., Chicago, IL). Means are reported with \pm the standard

deviation. Histograms were used to determine distributions. Correlations were determined with the Pearson's Correlation.

Results

There were 5 females (16.1%) and 26 males (83.9%) in the study. The age at presentation was normally distributed with a mean of 44.3 ± 13.9 (range 13-70) years old. There was a history of ocular trauma in 20 cases (64.5%), retinal detachment in 3 cases (9.7%), glaucoma in 2 cases (6.5%), and uveitis in 2 cases (6.5%). There was one case each of Coats' disease, complicated cataract surgery, and non-clearing vitreous hemorrhage. There was one case of unknown etiology. The mean duration of the opacity was 22.4 ± 11.3 (range 3-40) years. The majority of cases were no light perception (NLP) (26 eyes, 83.9%). The remaining were 3 cases of light perception (LP) and 2 cases of hand motion (HM). The average follow-up period was 13.9 ± 15.9 months (range, 1-69).

AS-OCT of BK revealed a high intensity reflective layer in the anterior cornea with variable degrees of posterior shadowing (Figure 1). The median depth of calcium was 100 μm (range 55-320) and the median CCT was 623 μm (range 534-785). The distribution of both parameters was positively skewed (Figure 2). The calcium depth was strongly correlated with the duration of the opacity by patient history ($r=0.68$, $p<0.001$) with a best-fit slope of 5 $\mu\text{m}/\text{year}$ duration (Figure 3).

The SD of examiner 1 and examiner 2 for calcium depth were 11.07 μm and 10.85 μm respectively, and were not significantly different between the two examiners. The respective CV and ICC values were 8.3%, 0.99 for examiner 1, and 8.0%, 0.99 for examiner 2. The Pearson's correlation coefficients of calcium depth between the two ophthalmologists were statistically significant ($r=0.975$, $p<0.001$).

Discussion

In recent years, Fourier-Domain OCT imaging has become a valuable tool in the clinical and experimental assessment of the ocular surface, allowing for the examination of anatomical structure and measuring the thickness of various corneal layers.¹⁸ We confirm the findings of previous AS-OCT reports that corneal calcium deposits appear hyperreflective and exhibit posterior shadowing.¹⁵⁻¹⁷ Similar to Wirbelauer and Pham, we found that the depth of calcium as determined by AS-OCT has a wide range, close to 300 μm .¹⁷ Our distribution was skewed to more superficial lesions.

An important consideration is how well the AS-OCT calculations correspond to actual lesion depth and CCT. The AS-OCT calculations are based on refractive indices, absorptions and autocorrelations from presumed normal corneas.¹¹ There are a number of studies looking at the consistency of AS-OCT calculations in non-calcific lesions.¹⁹⁻²¹ The true gold standard for accurate assessment of depth is comparison with corresponding histopathology specimens. Wirbelauer et al. showed no statistically significant difference between non-calcific lesion depth on AS-OCT (4Optics AG, Lübeck, Germany) and light microscopy from paired histologic specimens.²⁰ Khurana et al. found no statistically significant

difference between CCT calculated on AS-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) and paired ultrasound pachymetry (Corneo-Gage Plus; Sonogage, Cleveland, OH) in eyes with non-calcific corneal opacities.²¹ A unique source of error in calcific lesions comes from the relatively dense posterior shadows, sometimes blocking all signals from deeper structures. The software algorithm extrapolated a CCT even in cases with dense shadowing and in calculating calcium depth we assumed it was not present within the shadow.

Nioi et al. reported cornea morphological modifications after death using portable SD-OCT on an animal model.^{22,23} Based on their report, we can speculate that local cornea thickness measurements or reflectivity on OCT could be altered by partial metabolic changes due to hypoxia after cornea damage. To prove this, prospective and experimental studies are needed. If these findings are revealed, the causative mechanism of changes in corneal thickness and reflectivity found in our BK study may be clarified.

We found an expected significant correlation between the depth of the calcific lesion and the duration in years of a white opacity, as determined by patient history. The regression slope was 5 μm of increased depth annually. A limitation of the study was the subject report of opacity duration. Ideally this variable would be defined by examination. An additional bias may exist due to the wide range of follow-up periods. Although there may be a certain degree of error in the reported years of duration, the correlation is still significant when the precision is rounded to decades of duration. Furthermore the correlation is supported by histologic evidence that BK begins with deposits in the epithelial basement membrane and Bowman's layer that over time become fractured, followed by calcification of the epithelium and the anterior stroma.²

Najjar et al. found that patients with worse baseline vision had less visual improvement after mechanical debridement with EDTA.⁵ Similarly O'Brart et al. reported that patients with worse baseline vision had less visual improvement after PTK.⁶ The visual acuity in our series was primarily NLP. The predominance of severe blindness in our BK patient population may be due to local referral practice patterns. Future studies will be needed to determine whether visual acuity might correlate with outputted calcium depth, and if so, then calcium depth may be a useful prognosticator for visual improvement.

Our current treatment algorithm utilizes AS-OCT. EDTA chelation is our first line treatment, but in our experience it is less effective and efficient at removing thick plaques that extend deep into the anterior stroma. In the past we were unable to consistently identify these deep BK patients preoperatively with slit lamp biomicroscopy alone, and frequently we needed to perform a manual superficial lamellar keratectomy in addition to EDTA chelation. This operative challenge prolonged surgical time and led to unnecessary EDTA use, a chemical that is difficult to obtain in South Korea. With AS-OCT we now preoperatively stratify BK depth and only use EDTA on superficial lesions. Another potential use of AS-OCT in BK is in the prediction of post-PTK refractive outcomes. Cleary et al and Rush et al have already demonstrated the utility of preoperative AS-OCT measurements in non-calcific lesions.^{24,25} The current study is a first step in evaluating the potential benefit of AS-OCT, as this series is limited to patients with

primarily NLP vision. As the next step, a study will be required to address the question of whether patients with better baseline vision have similar AS-OCT profiles.

Conclusions

In conclusion, AS-OCT can be used to output a BK depth. This depth has a wide distribution that is positively correlated with the duration of the opacity per patient history. Future studies will be required to examine the AS-OCT profiles in patients with less severe vision loss, test the consistency of AS-OCT measurements across different instruments, and test the clinical utility of AS-OCT in the treatment of BK.

Abbreviations

AMT = Amniotic Membrane Transplantation

AS-OCT = Anterior Segment Optical Coherence Tomography

BCVA = Best Corrected Visual Acuity

BK = Band Keratopathy

CCT = Central Corneal Thickness

CV= Coefficient of Variation

EDTA= Ethylenediamine-Tetraacetic Acid

HM= Hand Motion

ICC=Intraclass Correlation Coefficient

LP = Light Perception

NLP = No Light Perception

PTK = Phototherapeutic Keratectomy

SD= Standard deviation

Declarations

Ethics approval and consent to participate

The study received approval from Seonam University College of Medicine Institutional Review Board (MJH 2019-05-001).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HJS collected and analyzed the data and was a major contributor to the writing of the manuscript. GMR analyzed the data and was a major contributor to the writing of the manuscript. RSC was a major contributor to the writing of the manuscript. JWK collected the data and was major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures

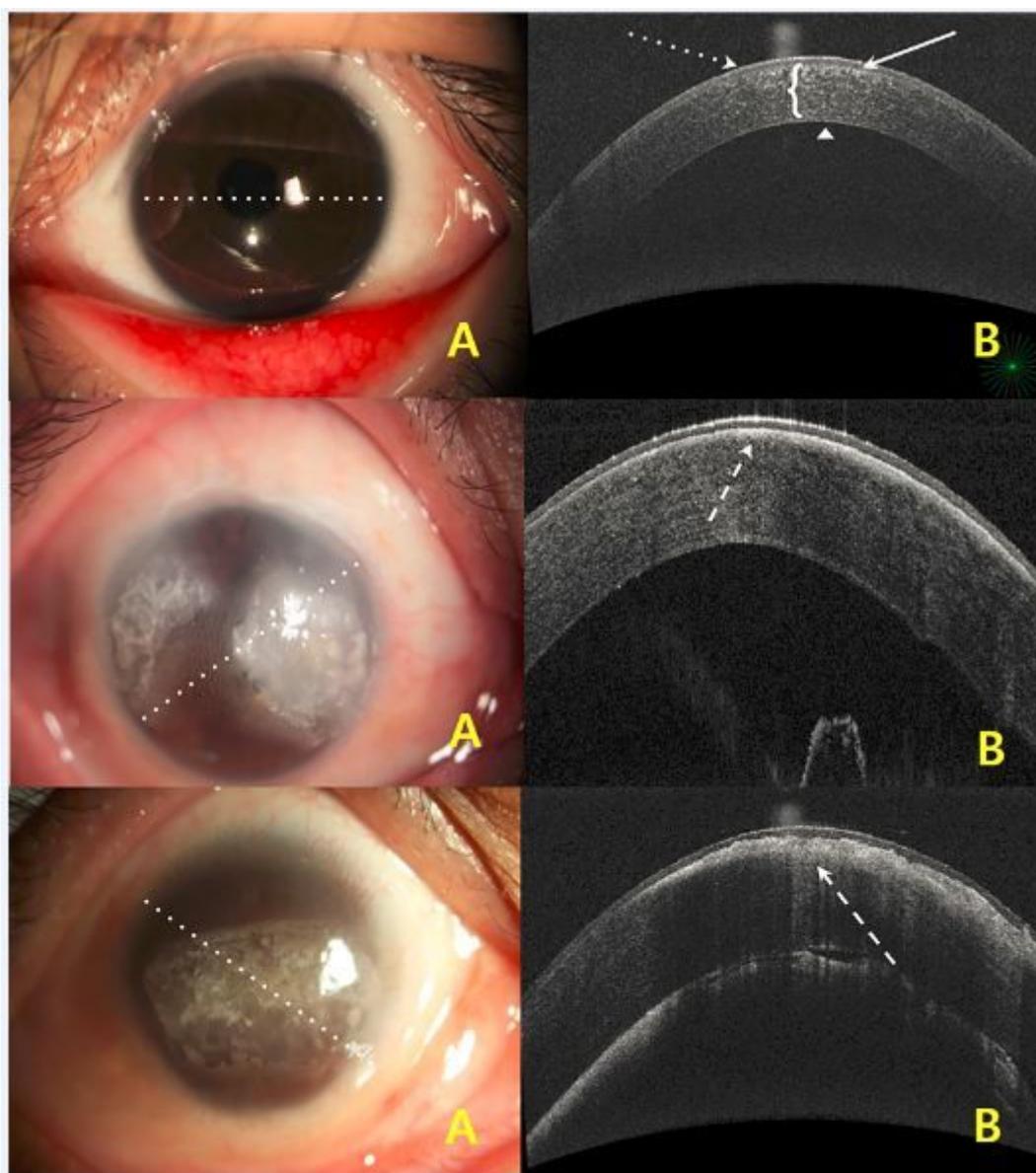


Figure 1

Slit lamp photographs (A) and corresponding anterior segment optical coherence tomographs (AS-OCT) (B). Top row: 38 year-old male with a normal cornea. The tear film is the most anterior hyperreflective anterior layer (dashed arrow), followed by the hyporeflective epithelium (solid arrow), the variably reflective stroma (bracket) and the hyperreflective endothelium (arrowhead). Middle row: 43 year-old male with band keratopathy (BK). There is a smooth, thin hyperreflective band deep to the epithelium (dashed arrow) and moderate posterior shadowing nasally. Bottom row: 51 year-old male with BK. There is a thick, hyperreflective band with rough edges (white arrow) and severe posterior shadowing.

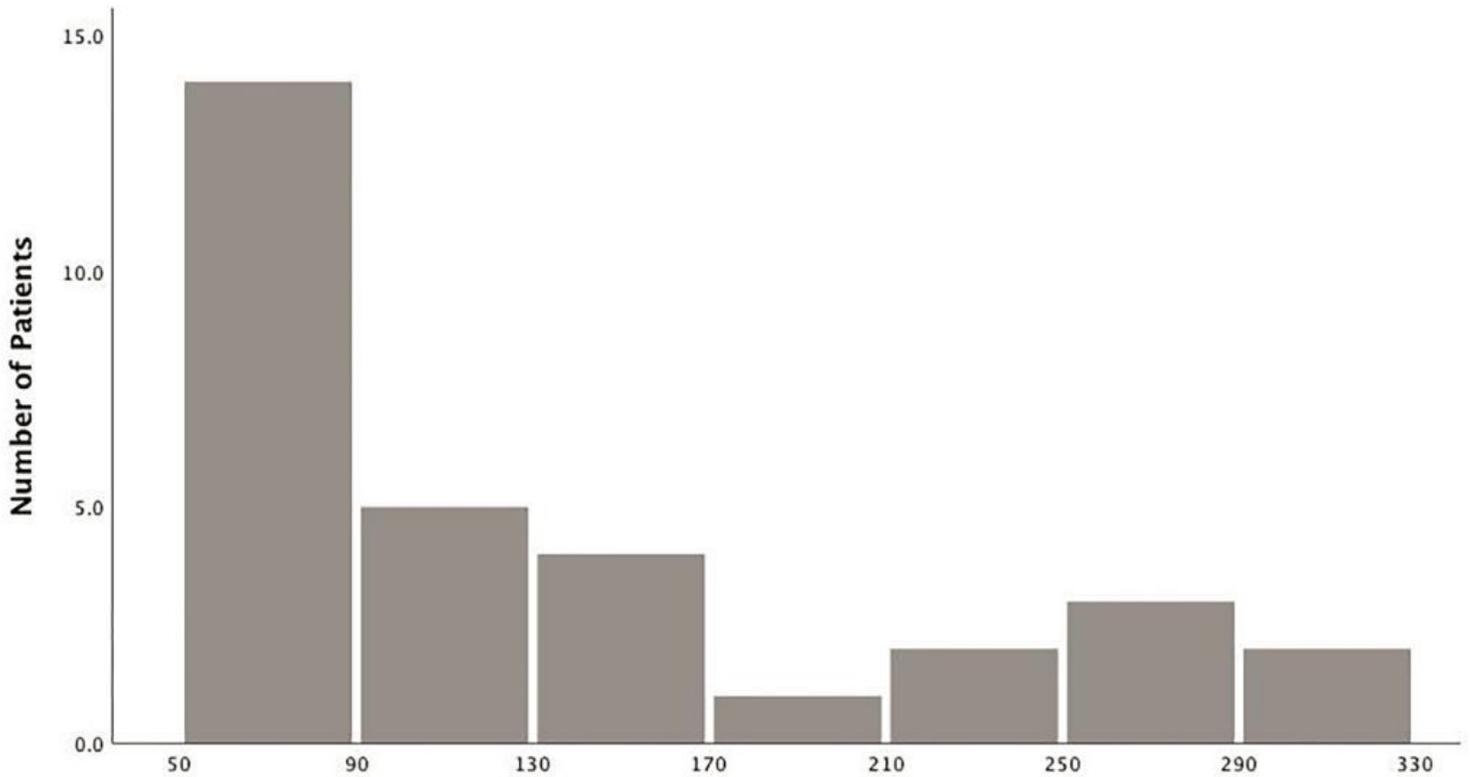


Figure 2

Calcium depth distribution across 31 consecutive patients with band keratopathy. The height of the bar represents the number of cases having a depth contained within the width of the bar.

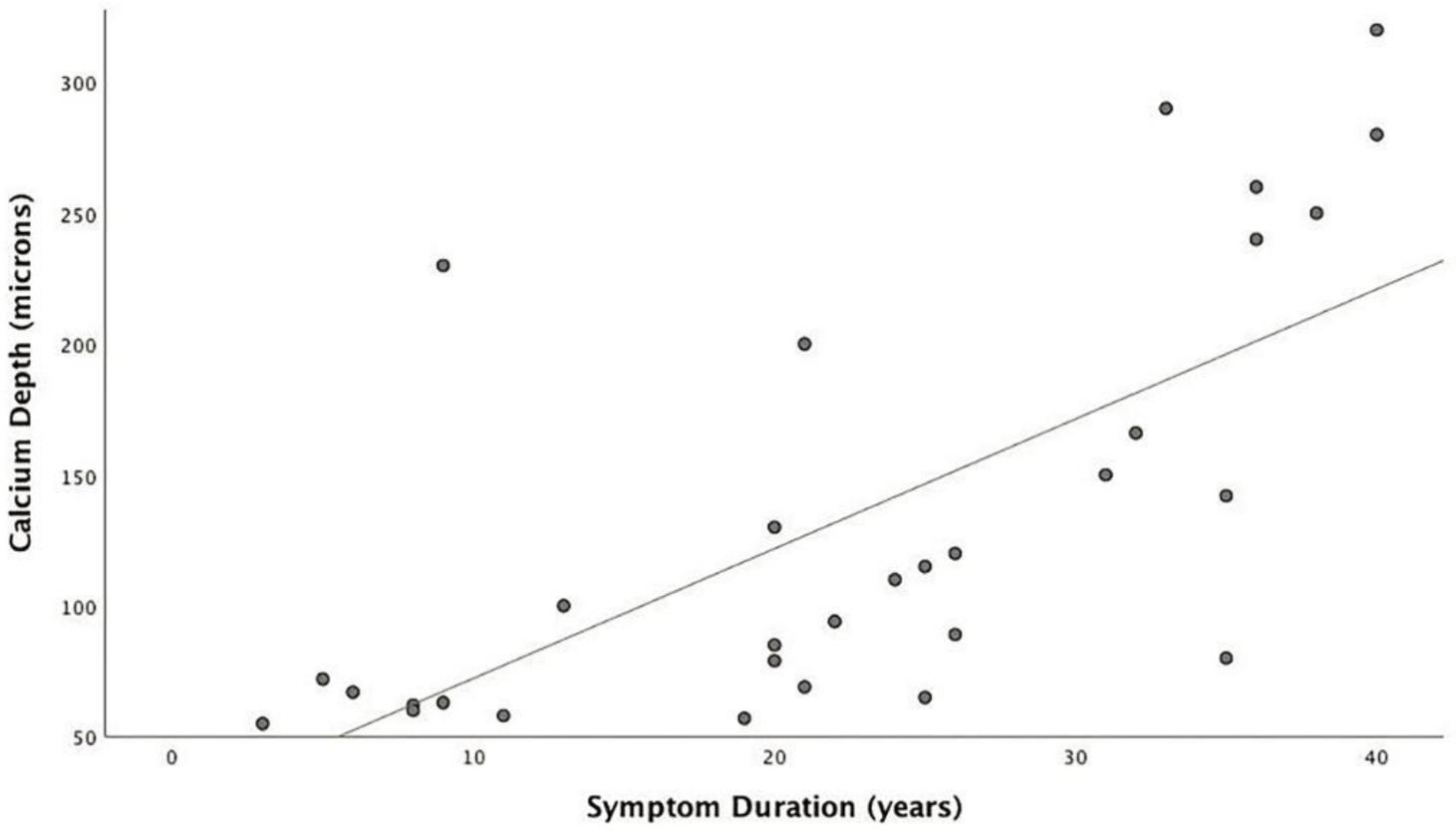


Figure 3

Correlation of calcium depth and duration of eye opacity. Pearson's Correlation, $r=0.68$ ($p<0.001$).