Ophthalmology Research: An International Journal

8(4): 1-7, 2018; Article no.OR.40561
ISSN: 2321-7227

Use of Ultrasound and Anterior Segment Optical Coherence Tomography to Compare Central Corneal Thickness Values in Patients with Open Angle Glaucoma

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Authors' contributions

This work was carried out in collaboration between all authors. Author PT designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author FR managed the analyses of the study. Author MS managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/OR/2018/40561
Editor(s):
(1) Tatsuya Mimura, Department of Ophthalmology, Tokyo Women's Medical University Medical Center East, Japan.
Reviewers:
(1) Nehal Samy El Gendy, Cairo University, Egypt.
(2) Tayo Julius Bogunjoko, Nigeria.
(3) Asaad Ahmed Ghanem, Mansoura University, Egypt.
Complete Peer review History: http://www.sciencedomain.org/review-history/23931

Original Research Article

Received 24th January 2018
Accepted 30th March 2018
Published 2nd April 2018

ABSTRACT

Purpose: To compare central corneal Thickness (CCT) using ultrasound (US) pachymetry and Anterior Segment Optical Coherence Tomography (AS-OCT), in patients with open-angle glaucoma (OAG).

Methods: Ninety patients above 50 years with healthy corneas were prospectively included for repeated measurements of central corneal Thickness (CCT), using ultrasound pachymetry (US) and Anterior Segment Optical Coherence Tomography (AS-OCT), during the same visit. The readings were averaged and compared by paired t-test. Both eyes of each participant were measured for our study.

Results: Ultrasound pachymetry showed significantly higher CCT values. The CCT measured by AS-OCT and ultrasound was 525 ± 32.1 µm and 533 ± 38 µm respectively for the right eye. For the left eye the values were 523 ± 31.2 µm and 532 ± 33.1 µm respectively for the AS-OCT and US. The difference in CCT measurement by AS-OCT and ultrasound was statistically significant

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(*P*<0.001) in both eyes with mean standard deviation of ultrasound CCT being 16.14 μm greater than the mean of AS-OCT CCT for the right and 15.12 μm for the left eye. A strong correlation was found (r >0.80) between the CCT measurement techniques. The Anova test didn't reveal serious differences neither with AS-OCT, nor with US pachymetry.

Conclusion: Central Cornea Thickness measurement by ultrasound pachymetry gives higher values compared to AS-OCT measurement in patients with OAG. This in clinical practice means, that they cannot be interchangeably used and both must be considered as methods of examination.

Keywords: Primary open-angle glaucoma; pachymetry; central corneal thickness; anterior segment optical coherence tomography.

1. INTRODUCTION

For the past years the clinical gold standard for glaucoma follow up is the measurement of the Intraocular Pressure (IOP). It has been shown that central corneal thickness (CCT) significantly affects IOP measurement and may be itself a risk factor for developing glaucoma [1-5].

CCT is also a predictive factor for glaucoma progression in patients with higher than normal Intraocular Pressure. Since IOP measurement by applanation tonometry is influenced by CCT, it is important to obtain a reliable corneal pachymetry value for each patient with glaucoma and adjust the IOP for the measured CCT [6,7]. There are many techniques available to measure CCT. Two of the most reliable are ultrasound, and anterior segment optical coherence tomography (AS-OCT).

During the last years ultrasound pachymetry has being incorporated into everyday practice as a screening tool, for it is easy and convenient to repeat several measurements. Ultrasound pachymetry is a contact procedure.

On the other hand, AS-OCT devices use a non-contact procedure, that detects minute differences in tissue depth and they provide high-resolution cross-sectional imaging of the cornea. Studies among non-glaucoma patients have confirmed that AS-OCT has an acceptable level of correlation with ultrasonic pachymetry although the two methods are not interchangeable [8,9].

The purpose of this study was to investigate if the same happens in open angle glaucoma patients.

2. MATERIALS AND METHODS

Hundred and eighty eyes were prospectively included in this study. Exclusion criteria included patients with any corneal pathology such as pterygium or ectasias, previous surgical intervention and any type of glaucoma other than OAG. All patients by the time of the study were under latanoprost therapy for a month, but did not take any antiglaucoma medication before our study and they were new patients.

All patients undergone ophthalmologic examination in the slit lamp, where fundus was examined and intraocular pressure (IOP) was measured. Refractive examination was also done. None had any significant spherical or cylindrical error and all measurements were made between 17.00 h and 20.00 h the same day by the same observer. Visante AS - OCT measurements were carried out first using the global pachymetry function. Patients' eye was aligned after head stabilization and cross-sectional images were obtained. Visante software processes the image and calculates automatically the map. The map is divided into eight zones: superior, temporal, superior temporal, inferior temporal, inferior, nasal, inferior nasal, superior nasal, and four rings of 2 mm, 5 mm, 7 mm and 10 mm diameter. Mean, maximum and minimum values of CCT were recorded.

Pachymetry was then performed using the NIDEK US – 1800 ultrasonic pachymeter after applying a topical anesthetic. Prior to the measurement, the US pachymeter was calibrated according to the manufacturer's instructions. A-scan velocity was set at 1640 m/s for all measurements. The above series of exams was strictly observed to keep the epithelium of the cornea intact. As per protocol two AS-OCT and ten US separate consecutive CCT measurements were obtained. The patient's age ranged from fifty to sixty-five years.

2.1 Statistical Analysis

All statistical analyses were performed using SPSS 15.0 software. SPSS is a comprehensive

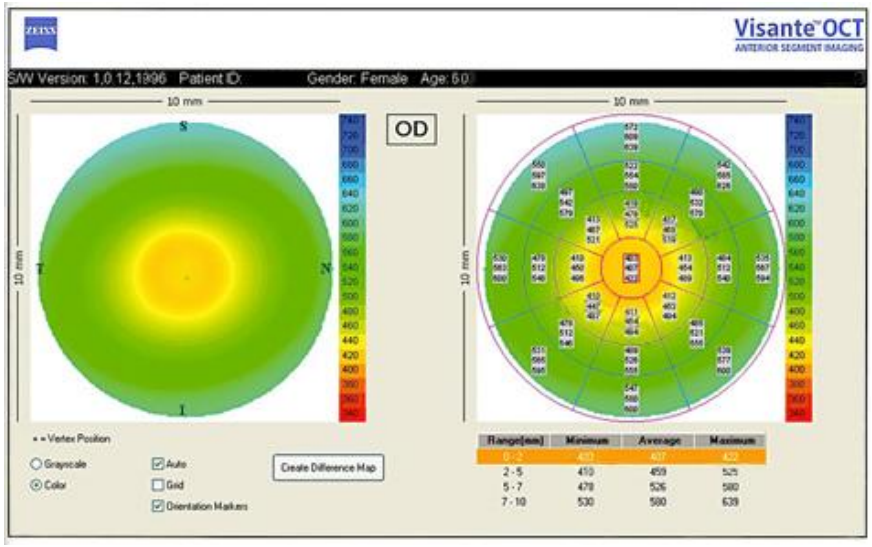

Fig. 1. Visante AS-OCT (anterior segment optical coherence tomography) global pachymetric map

system for analyzing data. It takes data and generates reports, charts, descriptive statistics and plots of distribution. A p-value less than 0.05 were considered statistically significant. In the statistical analysis the mean value of the measurements was used.

The agreement of CCT measured by AS-OCT and Ultrasound pachymetry was compared by paired t-test. Pearson test was also used to compare correlation between AS-OCT and Ultrasound.

We used the Bland-Altman method to calculate the mean and 95 per cent limits of agreement (LOA) [10,11] and to evaluate the agreement between the two methods.

3. RESULTS

Hundred and eighty eyes were enrolled in this study. There were 40 males and 50 females. Average age of the subjects was 51 ± 9 years and there were no significant differences in terms of age and gender. The age-sex distribution of the subjects is shown in Table 1.

Table 1. Demographic data

Number of patients	90
Age (mean)	55
Male	40
Female	50

All subjects were treated with latanoprost and they were new patients, participating in the study about a month after the beginning of their treatment. From the statistical analysis a positive correlation was observed between the measurements of AS-OCT and US (P<0.001).

Central cornea thickness was measured and the result was 525 ± 32.1μm with AS-OCT and 533 ± 38 μm for US pachymetry. For the left eye the values were 523 ± 31.2 μm and 532 ± 33.1 μm respectively for the AS-OCT and US. (Table 2)

From the statistic analysis with paired t-test we concluded that the differences between the two instruments were 9.90 ± 7.34 μm and 9.70 ± 7.12 for the right and left eyes (Table 3).

Table 2. CCT as measured with AS-OCT and US

	Min value	Max value	Mean value
AS-OCT right eye	525 μm	557 μm	541 μm
US right eye	533 μm	571 μm	552 μm
AS-OCT left eye	523 μm	554 μm	538 μm
US left eye	532 μm	565 μm	548 μm

The Bland–Altman analyses of the data are displayed in Figs 2 and 3. From the graph we can see that agreement limits are from – 4.54 to 25.10 and from – 4.51 to 25.20 for the left and right eye respectively. The mean difference of measurements between the two methods was 9.90 µm and 9.70 for the right and left eyes, comparing AS-OCT and ultrasound pachymetry. We observe a greater discrepancy of the measurements between the two instruments above the value of about 520 µm in both eyes, whereas below this value there is a better agreement and a smaller difference.

The correlation of central corneal thickness with age was -0.078 (P> 0.05) for AS-OCT and -0.108 (P> 0.05) for US.

Table 3. Difference in CCT with paired t-test between the AS-OCT and US in both eyes

Paired t-test CCT	Mean value	*P*
US – AS-OCT right eye	9.90 (7.34)	<0.001
US – AS-OCT left eye	9,70 (7.12)	<0.001

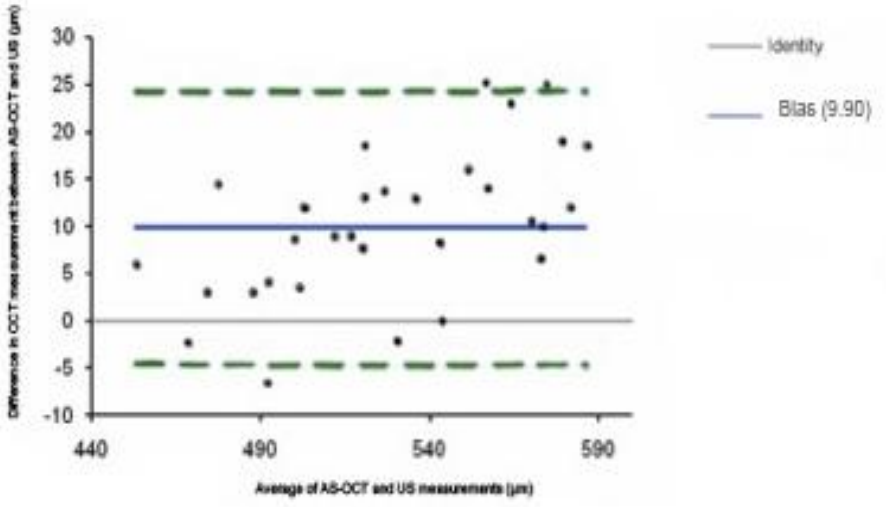

Fig. 2. Bland–Altman plot of AS-OCT and US, (right eye), showing a mean difference of 9.90 µm, LOA (Limits Of Agreement) - 4.54 to +25.1 µm

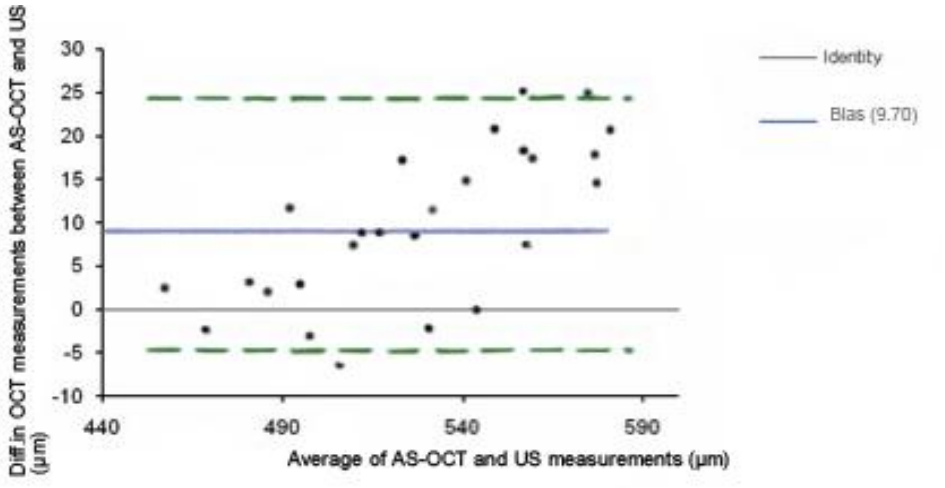

Fig. 3. Bland–Altman plot of AS-OCT and US, (left eye), showing a mean difference of 9.70 µm, LOA (limits of agreement) - 4.51 to +25.2 µm

4. DISCUSSION

According to the results of our study, measurements of CCT taken by AS-OCT differ significantly from the ultrasonic method. Bland–Altman Plots revealed that measurements using the AS-OCT were lower than with ultrasound, with mean difference of 9.88 mm.

Repeatability of the measurements using AS-OCT was as good as with US.

The repeatability of the two machines has been confirmed by other studies [12-15].

Central corneal thickness after statistic analysis was found to be 525 ± 32.1 μm with AS-OCT and 530 ± 38 μm with ultrasound pachymetry.

The measurement of central corneal thickness with ultrasonic pachymetry is the method of choice among doctors because of its established reliability, low cost and ease of use. However, measurement by ultrasonic pachymetry requires a contact examination on the corneal epithelium and a correct technic. It is necessary to put the probe as much vertically as possible so the measurement correlates with the 2 -3 mm centrally. To have a correct measurement is also necessary to handle it with care and not force it on the cornea.

Ultrasonic pachymetry is also dependent on the reflection of the sound from the anterior and posterior corneal surfaces without calculating the thickness of the tear layer that is displaced by the probe socket [16].

On the other hand, AS-OCT offers a non-contact mapping of the anterior surface of the cornea and a calculation of the CCT as well as high resolution imaging of the anterior chamber. Anterior segment OCT imaging was first described in 1994 by Izatt et al. [17] using the same wavelength of light as retinal OCT, namely 830 nm.

This wavelength is suboptimal for imaging the angle due to limited penetration through scattering tissue such as the sclera. OCT imaging of the anterior segment with a longer wavelength of 1310 nm was developed later on and had the advantages of better penetration through sclera as well as real-time imaging at 8 frames per second. In clinical practice AS-OCT offers also an excellent qualitative and quantitative assessment of the anterior chamber and the angle and is useful as an adjunct to gonioscopy.

The mean value of the measurements of CCT with AS-OCT was lower than the measurements with US in the POAG patients.

The reason for the difference between the two equipment is not completely known. It could be partly explained by the different methodology, the algorithmic differences of the two machines as mentioned above and the uncertainty about the true index of refraction of the laser light source used by AS-OCT. We must also not forget that AS-OCT offers a corneal mapping and CCT measurement in the central 2 mm. Ultrasound on the other hand offers focal on site measurement. Most of the results in previous studies comparing measurements of CCT in normal eyes, report also differences between AS-OCT and US values. One possible reason could be the number of patients participated or even the different US equipment used. In clinical practice systemic equipment errors should be considered when measuring central corneal thickness.

Corneal swelling due to local anesthetic even by 8.9 μm [18,19], is another reason that we may encounter as to why AS-OCT readings may be lower than ultrasound's.

We should also keep in mind that according to the Bland-Altman plots, there is a greater discrepancy of the measurements between the two instruments above the value of about 520 μm in both eyes, whereas below this value there is a better agreement and a smaller difference.

A meta-analysis by Doughty and Zaman showed that a 10% difference in the central corneal thickness could lead to a difference in intraocular pressure of up to 3.4 mmHg.

They calculated that for every 10 μm difference in the central corneal thickness, a change of 0.2 mmHg occurs in IOP measurements [20].

Although the difference in CCT measurements between the two equipment was less than 20 μm in this study, the importance of CCT difference in tonometry should not be clinically ignored.

5. CONCLUSION

The aim of our study was to compare Central Corneal Thickness (CCT) using ultrasound (US) pachymetry and Anterior Segment Optical

Coherence Tomography (AS-OCT), in patients with open-angle glaucoma (OAG).

The CCT measurement by ultrasound pachymetry gives higher values compared to AS-OCT measurement in patients with OAG. This in clinical practice means, that they cannot be interchangeably used and both must be considered as methods.

Nevertheless, further research would be useful with larger numbers of patients and longer follow-ups are required to confirm these findings and improve patient care.

CONSENT AND ETHICAL APPROVAL

This study was performed with an institutional review board approval and all authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. After a detailed explanation of the procedure benefits and risks, consent was obtained from all patients. None of the patients refused to enroll and none were lost to follow-up during the course of the study.

All authors declare that written informed consent was obtained from the patients for publication of this study and accompanying images.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
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