Comparison of Ultrasound and Optical Coherence Tomography in Measurement of Pre-cut and Post-cut Descemet's Stripping Endothelial Keratoplasty Tissue

Abigail Gordon BA,[1] Abhinav Golla BS,[1] Li Wang MD, PhD,[1] Mitchell P. Weikert MD,[1,2] Sumitra S. Khandelwal MD[1,2]

ABSTRACT

Purpose: The purpose of this study is to evaluate corneal thickness using ultrasound pachymetry technology (US) in comparison to optical coherence tomography (OCT) in tissues pre resection for descemet stripping automated endothelial keratoplasty (DSAEK)

Methods: 30 donor corneas that were suitable for DSAEK were enrolled in this prospective study. All precut corneas were prepared for DSAEK using standard eye bank protocol. Prior to cutting and epithelial scraping, central and midperipheral (3 mm from center) thickness of donor corneas were measured via ultrasound pachymetry and OCT. Of these 30 corneas, 15 were also analyzed for post resection thickness. The anterior lamellar cap was removed and the measurements were taken again via ultrasound and parallel measurements were taken using OCT after 1.5 hours. Differences between measurements were studied using t-test and correlation coefficients.

Results: Both OCT and US provide similar central thickness of tissue pre resection (difference of -9 µm +/- 55 µm, P= 0.39) and post resection (difference of 5 µm +/- 59 µm, P= 0.75). However, while there was no difference in the post resection tissue midperipheral thickness between the two devices (difference of -15 +/- 52 µm, P= 0.28), there was a statistically significant in the pre resection midperipheral thickness (difference of -145 +/- 88 µm, P < 0.01).

Conclusion: OCT and US produce similar measurements for central thickness in both pre resection and post resection lenticules. However, while the post resection midperipheral thickness is similar between the two modalities, there is some variation in the pre resection thickness of the mid-periphery.

Keywords: Descemet Stripping Automated Endothelial Keratoplasty, Cornea Transplantation, OCT, optical coherence tomography, ultrasonic pachymetry

Descemet stripping automated endothelial keratoplasty (DSAEK) is a well-established surgical technique used to treat corneal diseases.[1] Increasingly, surgeons have preferred to obtain precut donor tissue from eye banks rather than prepare the tissue in the operating room.[2,3] Eye-bank prepared tissue has been shown to have similar outcomes, dislocation rates, and final endothelial cell loss as surgeon prepared tissue.[4,5]

Controversy currently exists as to whether the thickness of precut endothelial keratoplasty (EK) lenticules affects post-surgical outcomes. Recent studies have shown that there is insufficient evidence that graft thickness influences best corrected vision after DSAEK.[6,7] Other studies suggest thinner tissue may lead to better refractive outcomes.[8, 9] Additional studies have shown that, compared to DSAEK with central thickness of 200 microns, ultrathin DSAEK (central thickness less than 130 micrometers) results in better and faster recovery of best corrected visual acuity.[10,11] Given the correlation in hyperopic shift following DSAEK with central thickness of EK lenticules[12,13] as well as surgeon preference in lenticule thickness, accurate measurements of precut tissue thickness at eye banks are necessary.

While traditionally ultrasound pachymetry (USP) has been used to measure corneal thickness in eye banks due to its reliability and low cost, anterior segment optical coherence tomography (AS-OCT) has risen in favor due to the high-resolution images of the tissue.[14] OCT is a non-contact and repeatable method for evaluating corneal thickness that minimizes the stress placed upon the endothelium and risks of contamination; however, compared to ultrasound

Author Affiliation: [1]Cullen Eye Institute, Department of Ophthalmology, Baylor College of Medicine Houston, Texas, USA
[2]Lions Eye Bank of Texas, Houston Texas, USA

Author for Correspondence: Sumitra Khandelwal, MD, 1977 Butler Blvd., Houston, TX 77030

Meeting Presentation: The contents of this manuscript was presented as a poster at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) 2017.

Conflicts of interest: No conflicting relationships exist for any author.

Financial support: All studies supported in part by an unrestricted grant from Research to Prevent Blindness, New York, New York, U.S.A. (LW, SSK).

pachymetry, AS-OCT is a more expensive modality, which can limit its use.[15] AS-OCT can also provide a complete thickness profile of a tissue which may be valuable for surgeons, given that a non-uniform thickness profile as well as central thickness measurements influence the definite refractive outcome post-operatively.[16] A recent study has shown that AS-OCT might eventually be used as a pre-keratoplasty advanced screening technique in donor corneas.[17]

Previous studies have compared central thickness measurements with OCT and US. Some have found OCT measurements such as those with the Visante OCT are on average thicker than the traditional US measurements.[18,19] Still others have found that the AS-OCT Visante and RTVue measured thinner than US with a statistically significant difference in peripheral measurements.[20,21]

This study compared AS-OCT RTVue to ultrasound pachymetry in measuring corneal thickness of the pre resection cornea and post resection DSAEK lenticules both centrally and midperipheral. To our understanding, this is the first study to measure pre resection lenticules centrally and midperipherally with the RTVue using Life4˚C corneal preservation medium (NuMedis; Isanti, MN, USA).

MATERIALS AND METHODS

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Insitutional Review Board approval was obtained for research on these corneas.

We performed lamellar graft dissection on 30 corneas using standard eye bank protocol and measured corneal thickness via USP (PalmScan Pachymeter, MicroMedical Devices; Calabasas, CA, USA) and AS-OCT (RTVue, Optovue, Inc.; Fremont, CA, USA). Donor corneas were obtained from the Lion's Eye Bank of Texas, Cullen Eye Institute (Houston, TX). Tissues were stored in Life4˚C corneal preservation medium (Numedis; Isanti, MN, USA).

Prior to dissection, OCT images were taken of the tissues ("pre resection" tissues) at the Lion's Eye Bank using a mounted viewing chamber. Corneas were then marked at two locations to maintain orientation: centrally and at 0 degrees. Prior to epithelial scraping, ultrasound pachymetry was used to measure 5 points: center and 4 peripheral points located halfway between the center and limbus (3 mm from center) at 0, 90, 180 and 270 degrees. A microkeratome system (Moria, Inc; Doylestown, PA, USA) then dissected the anterior lamella following eye bank protocols. After microkeratome cut, 4 tissues with corneal perforation were excluded from the study. Another 11 tissues were excluded as the OCT technician was not available.

For 15 of the corneas, after dissection the anterior lamellar cap was removed and the residual graft was measured using USP again at the same 5 points. The corneas with cap were then transferred to a chamber containing Life4˚C media and a second OCT image was taken. All images using OCT were taken at least 1.5 hours after cutting. Using the ruler function of the RTvue, measurements of the central and mid-peripheral corneal thickness (3 mm from center) were taken.

STATISTICAL AND DATA ANALYSIS

All data were collected on an Excel sheet (Microsoft Office 2013), and the Data Analysis Tool Pack was used to calculate statistics. The midperipheral measurement was calculated by averaging the values taken a 0, 90, 180, and 270 degrees. A two sample T-test for equal or unequal variance was used to assess if the differences in central and mean midperipheral thickness measurements for US and OCT were statistically significant. A p-value < 0.05 was considered statistically significant. Bland-Altman plots were also used to evaluate agreement in the measurements.[22]

RESULTS

Pre resection central corneal thickness measurements by US and OCT in eye bank-prepared donor corneas were not statistically different. Average of 486 µm via US and 495 µm via OCT (difference of -9 µm +/- 55 µm, P= 0.39) (See Table 1). Central post resection thickness measurements were also not statistically different with an average of 112

Table 1

	Pre Resection US vs OCT center	Pre Resection US vs OCT Mid periphery	Post Resection US vs OCT center	Post Resection US vs OCT Mid Periphery
Mean Difference	-9	-145	5	-15
Standard Deviation	55	89	59	52
P value	0.40	<.01	0.75	0.29

µm via US and 107 µm via OCT (difference of 5 µm +/- 59 µm, P= 0.75). Central measurements were correlated (Pre resection: r= 0.66, P < 0.01; Post resection: r= 0.62, P= 0.01). Pre resection midperipheral thickness measurements were statistically different with an average of 563 µm via US and 709 µm via OCT (difference of -145 +/- 88 µm, P < 0.01). However, post resection midperipheral thickness measurements were not statistically different with an average of 164 µm via US and 178 µm via OCT (difference of -15 +/- 52 µm, P= 0.28). Midperipheral measurements were correlated (post resection: r= 0.72, P < 0.01; pre resection r= 0.53, P < 0.01). (See Figures 1-4). Bland-Altman Plots were generated for all measurements (Figure 5). The 95% confidence interval for the pre resection midperipheral thickness measurements was between 28 µm and -319 µm.

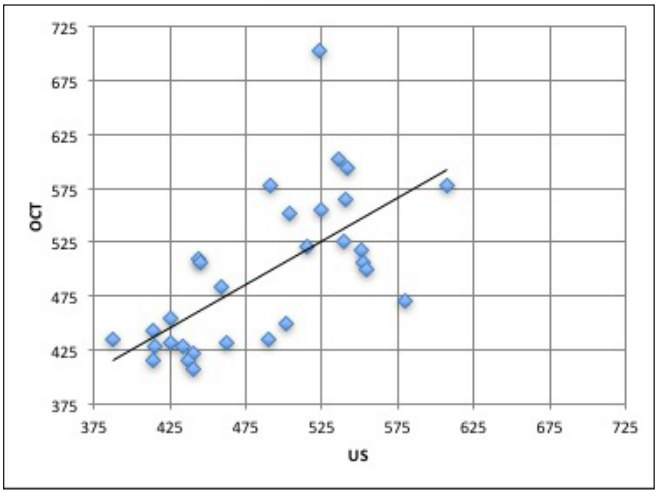

Figure 1: *Pre resection ultrasound vs optical coherence tomography central thickness correlation*

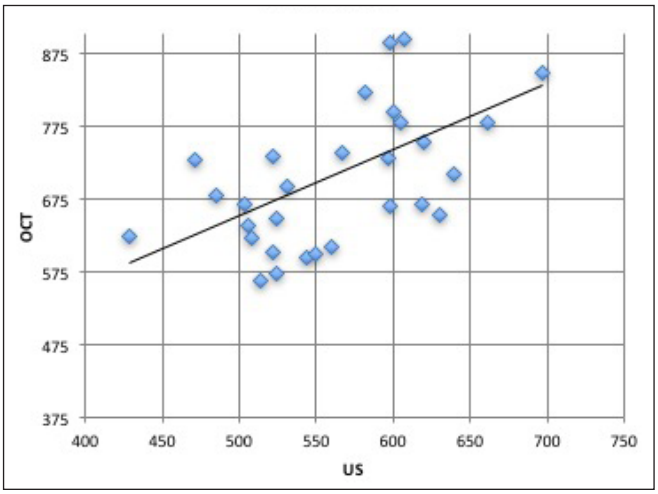

Figure 2: *Pre resection ultrasound vs optical coherence tomography midperipheral thickness correlation*

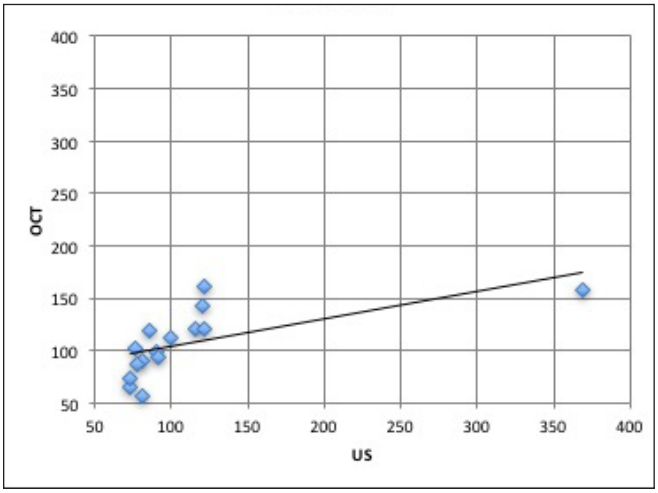

Figure 3: *Post resection ultrasound vs optical coherence tomography central thickness correlation*

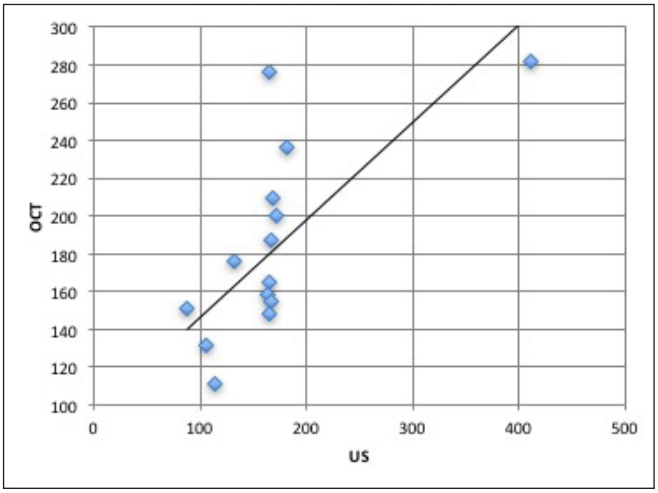

Figure 4: *Post resection ultrasound vs optical coherence tomography midperipheral thickness correlation*

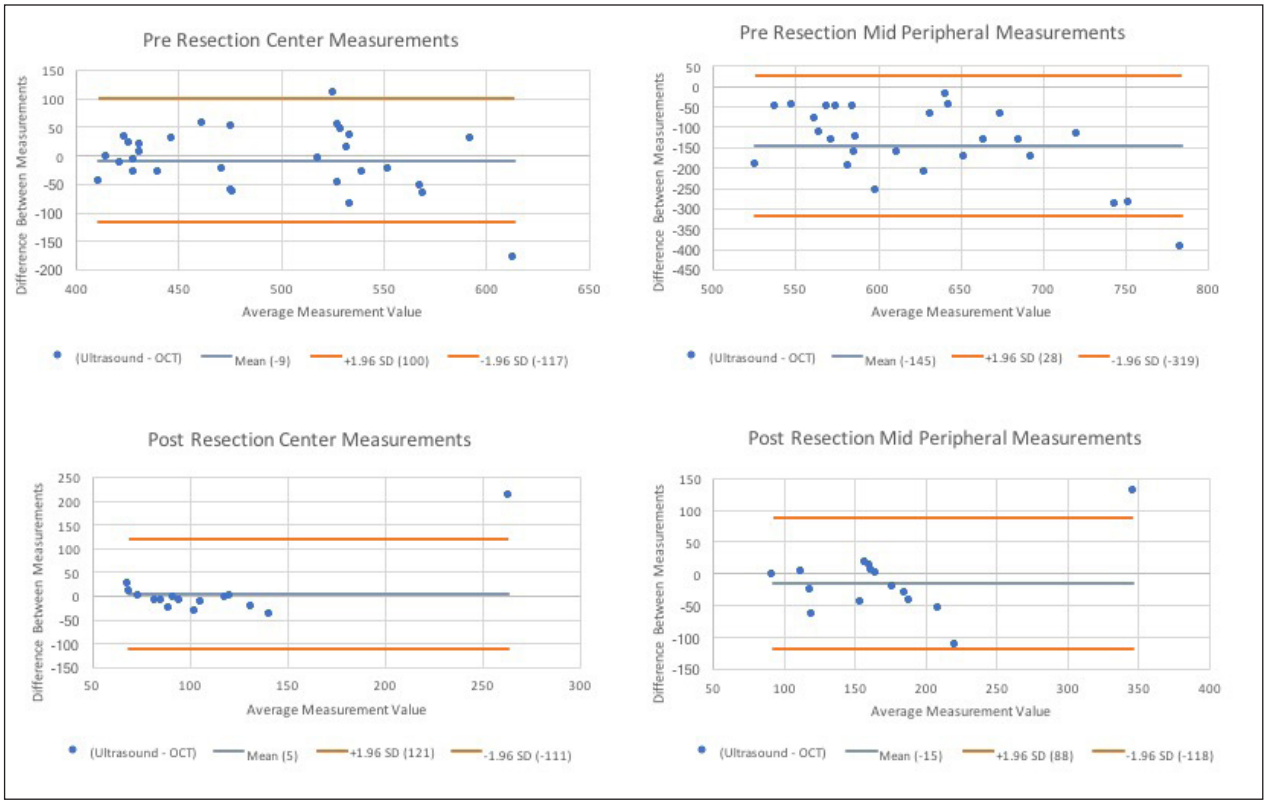

Figure 5: *Bland-Altman plots of ultrasound vs optical coherence tomography measurements.*

DISCUSSION

Both OCT and US provide similar central thickness of tissue pre resection and post resection. However, while the post resection midperipheral tissue thickness was similar between the two devices, the pre resection was not.

These results suggest that both OCT and US provide similar central thickness measurements in the same tissue. This finding agrees with previous studies.[18,20] While a previous study has shown that the post resection midperiphery thicknesses may be statistically different[20] our study suggested that they are not. However, in the midperiphery with pre resection tissue, the two modalities may provide different values. The most likely reason for this would be the measurement error involved in measuring the tissue via US by hand rather than an automated system. While a central measurement would be more likely to be repeatable, midperiphery measurements require a technician to estimate of the midperipheral distance, as it was not directly marked.

Our study was limited by the small sample size and that post resection OCT and US measurements were only acquired on half of our tissues. The study was also limited by our inability to directly mark the center and midperiphery of the post resection corneas, resulting in a loss of orientation. We were thus unable to do a direct comparison of each of the midperipheral measurements and instead used the average of four different locations. Additionally, because of the curvature of the cornea, it can be challenging to set the US perpendicular to the tissue repeatably. While OCT allows for the user to measure a line perpendicular to the endothelium, this process is more challenging for peripheral measurements than central. However, this study was unique in that it compared both the pre resection and post resection measurements of the same tissues at the center and periphery with different imaging modalities.

Further research is needed to determine the repeatability of both the ultrasound and OCT measurements, especially at the mid-periphery of the tissue. Regardless, as DSAEK currently aims to be as thin as possible in regard to lenticule size, various modalities of measurement will become more important to surgeons and the eye bank. Surgeons often utilize OCT imaging in clinics may wish to utilize imaging of their eye bank prepared tissue in the future.

REFERENCES

1. Gorovoy MS. (2006). Descemet-stripping automated endothelial keratoplasty. *Cornea*. 2006; 25:886-889.
2. Kitzmann AS, Goins KM, Reed C, et al. Eye Bank Survey of Surgeons Using Precut Donor Tissue for Descemet Stripping Endothelial Keratoplasty. *Cornea*. 2008;27:634-639.

   Rose L, Briceño CA, Stark WJ et al. Assessment of eye bank-prepared posterior lamellar corneal tissue for endothelial keratoplasty. *Ophthalmology*. 2008;115: 279-286.
3. Price MO, Baig KM, Brubaker JW, et al. Randomized prospective comparison of precut vs surgeon-dissected grafts for Descemet stripping automated endothelial keratoplasty. *Am J Ophthalmology*. 2008; 146: 36-41.
4. Terry MA, Shamie N, Chen ES, et al. Precut Tissue for Descemet's stripping automated endothelial keratoplasty: vision, astigmatism and endothelial survival. *Ophthalmology*. 2009;116: 248-256.
5. Wacker K, Bourne WM, Patel SV. Effect of Graft Thickness on Visual Acuity After Descemet Stripping Endothelial Keratoplasty: A Systematic Review and Meta-Analysis. *American Journal of Ophthalmology*. 2016; 163:18-28.
6. Terry MA, Straiko MD, Goshe JM et al. Descemet's Stripping Automated Endothelial Keratoplasty: The Tenuous Relationship between Donor Thickness and Postoperative Vision. *Ophthalmology*. 2012; 119: 1988-1996.
7. Busin M and Albé E. Does thickness matter: ultrathin Descemet stripping automated endothelial keratoplasty. *Current Opinion in Ophthalmology*. 2014; 25: 312-318.
8.
9. Busin M, Madi S, Santorum P, et al. "Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty with the Microkeratome Double-Pass Technique: Two-Year Outcomes." *Ophthalmology*. 2013;120:1186-1194.
10. Neff KD, Biber JM, and Holland EJ. "Comparison of Central Corneal Graft Thickness to visual Acuity Outcomes in Endothelial Keratoplasty." Cornea. 2011;30:388-391.
11. Dickman MM, Kruit PJ, Remeijer L, et al. A Randomized Multicenter Clinical Trial of Ultrathin Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) versus DSAEK. *Ophthalmology*., 2016; 123: 2276-2284.
12. Nieuwendaal CP, van Velthoven MEJ, Biallosterski C et al. Thickness measurements of donor posterior disks after descemet stripping endothelial keratoplasty with anterior segment optical coherence tomography. *Cornea*. 2009; 28: 298-303.
13. Esquenazi S and Rand W. Effect of the shape of the endothelial graft on the refractive results after Descemet's stripping with automated endothelial keratoplasty. *Canadian Journal of Ophthalmology*. 2009; 44:557-561.
14. Li Y, Shekhar R, and Huang D. Corneal Pachymetry Mapping with High-Speed Optical Coherence Tomography. *Ophthalmology*. 2006; 113: 797-799.
15. Amato D, Lombardo M, Oddone F, et al. Evaulation of a new method for the measurement of corneal thickness in eye bank posterior corneal lenticules using anterior segment optical coherence tomography. *Br J Ophthalmology*. 2011; 95: 580-584
16. Holz HA, Meyer JJ, Espandar L, et al. Corneal profile analysis after Descemet stripping endothelial keratoplasty and its relationship to postoperative hyperopic shift. *Journal of cataract and refractive surgery*. 2008; 34: 211-214.
17. Janunts E, Lagenbucher A, Seitz B. In Vitro Corneal Tomography of Donor Cornea Using Anterior Segment OCT. *Cornea*. 2016; 35: 647-653.
18. Tang M, Ward D, Ramos JLB et al. Measurements of Microkeratome cuts in Donor Corneas with Ultrasound and Optical Coherence Tomography. *Cornea*. 2012; 31:145-149.
19. Kanavi MR, Fahim P, Rahmanian M, et al. Measurements of Donor Endothelial Keratoplasty Lenticules Prepared from Fresh Donated Whole Eyes Using Ultrasound and Optical Coherence Tomography. *Cell and Tissue Banking*. 2017;12: 99-104.
20. Fante RJ, Shtein RM, Titus MS, et al. Anterior Segment Optical Coherence Tomography Versus Ultrasound Pachymetry to Measure Corneal Thickness in Endothelial Keratoplasty Donor Corneas. *Cornea*. 2013;32:79-82.
21. Şimşek A, Bilak S, Güler M et al. Comparison of Central Corneal Thickness Measurements Obtained by RTVue OCT, Lenstar, Sirius Topography, and Ultrasound Pachymetry in Healthy Subjects. *Seminars in Ophthalmology*. 2016;31:467-472.
22. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res*. 1999;8:135–160.

