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Comparison of ultrasonic pachymetry and Fourier-domain optical coherence tomography for measurement of corneal thickness in dogs with and without corneal disease

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Abstract

Several ultrasonic and Fourier-domain optical coherence tomography (FD-OCT) pachymeters are used to measure corneal thickness in canine patients and research subjects. This study assessed the reliability of and consistency between two ultrasonic pachymetry (USP) devices, Pachette 3 and Accupach VI, as well as automated and manual measurements obtained using FD-OCT in dogs with and without corneal disease. Corneal thickness measurements were compiled from 108 dogs and analyzed using mixed effects linear regression, with Bonferonni adjustments for post-hoc comparisons, to determine the effects of age, weight and disease state. Data are presented as predicted mean ± standard error.

Canine corneal disease can result in marked increases in thickness that frequently exceed the upper limits of measurement of some pachymetry devices developed for human use. In this study, the corneas of dogs with endothelial disease or injury frequently exceeded the upper limits of quantitation of 999 and 800 μm for the Accupach VI and automated FD-OCT pachymeters, respectively. Using values <800 μm, the Pachette 3 generated significantly greater values for central corneal thickness (CCT) than the Accupach VI, manual FD-OCT and automated FD-OCT at 625 ± 7.0, 615 ± 7.2, 613 ± 7.2, and 606 ± 7.4 μm respectively ($P < 0.001$). Of the two devices where measurements >1000 μm were obtained, manual FD-OCT demonstrated less variability

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Conflict of interest statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

than the Pachette 3. Corneal thickness increased linearly with age and weight with an increase of 6.9 ± 1.8 μm/year and 1.6 ± 0.8 μm/kg body weight ($P < 0.005$ and $P = 0.038$, respectively).

Keywords

Canine; Corneal thickness; Ultrasonic pachymetry; Optical coherence tomography; Corneal endothelial dystrophy

Introduction

Multiple methods to measure corneal thickness are available to characterize corneal abnormalities and plan surgical procedures. Ultrasonic pachymetry (USP) utilizes contact of the instrument with the cornea and ultrasound technology to generate measurements while optical coherence tomography (OCT) measures corneal thickness through generation of a cross-sectional image (Alario and Pirie, 2013a; Amano et al., 2006; Kim et al., 2008; Realini and Lovelace, 2003; Sadoughi et al., 2015; Wolf et al., 2006). The handheld USP devices are commonly utilized due to their accessibility, portable nature, and ease of use. By contrast, OCT units offer a non-contact, non-invasive alternative for determining corneal thickness and provide detailed cross-sectional imaging of the cornea of human and veterinary patients (Alario and Pirie, 2013a; Ishibazawa et al., 2011). However, veterinary patients or animals used in research and ocular drug/device development typically require sedation or anesthesia in addition to physical restraint to obtain OCT images. The challenges of using OCT thus make USP devices more favorable if only corneal thickness measurements are required (Alario and Pirie, 2013a; Famose, 2013; Strom et al., 2015; Thomasy et al., 2016).

Corneal thickness is commonly evaluated in veterinary patients with ocular pathology including corneal disease, glaucoma and dry eye (Chaudhry, 2009; Famose, 2013; Strom et al., 2015; Thomasy et al., 2016). Numerous studies have evaluated the reliability and repeatability of USP and OCT devices in animals with no history of ocular disease and found high repeatability for individual techniques and positive correlation between techniques used to obtain corneal thickness measurements (Alario and Pirie, 2013a, 2014; Sadoughi et al., 2015; Strom et al., 2015; Wolf et al., 2006). However, few studies exist assessing the consistency of these techniques for patients with ocular abnormalities (Famose, 2013). The purpose of this study was to compare four techniques for measuring corneal thickness, two USP devices (Pachette 3 and Accupach VI) as well as automated and manual Fourier-domain OCT (FD-OCT) methods using retrospective data from dogs with normal and diseased corneas.

Materials and Methods

Animals

All aspects of the study were approved by the Institutional Animal Care and Use Committee of the University of California-Davis (#16547, 2 June 2011; #17324, 12 December 2012; #17680, 3 July 2013; #17798, 31 October 2013; #17847, 5 November 2013; and #18024, 3 March 2014) and were performed according to the Association for Research in Vision and

Ophthalmology resolution on the use of animals in research. Data was compiled retrospectively from six studies (Stewart et. al. unpublished results; Horikawa et al., 2016; Samuel et al., 2014; Shull et al., 2015; Stewart et al., 2014; Thomasy et al., 2016). Two hundred thirteen eyes of 108 dogs were evaluated; two right eyes and one left eye of three corneal endothelial dystrophy (CED)-affected Boston terriers were enucleated and thus these eyes were excluded from analysis. Forty-five Boston terriers (BT), 18 German shorthaired pointers (GSHP), 12 German wirehaired pointers (GWHP), 19 West highland white terriers (WHWT), eight dogs of miscellaneous breeds, and six Beagles were included in analysis; complete study demographics are in Table 1. Of the 108 dogs studied, 79 had corneal thickness measurements collected once, 22 had measurements collected 2–5 times, and seven had measurements collected >5 times.

The BT, GSHP, and GWHP studies consisted of 48 normal and 27 CED-affected dogs (Thomasy et al., 2016); one BT was surgically managed with a superficial keratectomy and conjunctival advancement hood flap (SCKAHF) (Horikawa et al., 2016). Eight dogs of miscellaneous breeds all had CED ($n = 6$) or corneal endothelial degeneration ($n = 2$); one dog with CED was treated with sodium chloride 5% ophthalmic ointment (5% NaCl, Bausch and Lomb, Tampa, FL, USA) while the remaining seven received a SKCAHF (Horikawa et al., 2016). The WHWT study consisted of 13 normal and six keratoconjunctivitis sicca (KCS)-affected dogs. The six Beagles used in this study were female intact research dogs with no ocular abnormalities at initial examination; five were treated with 5% NaCl in the right eye and artificial tear (AT) ophthalmic ointment (Rugby Laboratories) in the left eye 4–7 times a day for 10 days (Samuel et al., 2014). Following an interval of 268 days, the six Beagles underwent a transcorneal freezing procedure on the right eye. A 9-mm diameter steel probe immersed in liquid nitrogen to an approximate temperature of −196 °C was applied to the cornea of the right eye for 15–20 s to cause corneal endothelial injury (Okumura et al., 2013). Then, Beagles were treated with 1 drop of 10 mM Y27632 (LC Laboratories; $n = 3$), a rho kinase inhibitor, or phosphate buffered solution (PBS, GE Healthcare Life Sciences HyClone Laboratories; $n=3$) four times daily in the right eye for 56 days.

All dogs received a detailed ophthalmic examination, including handheld slit lamp biomicroscopy (SL-15, Kowa American Corporation) and indirect ophthalmoscopy with a 28D or 40D lens (Volk Optical) and a binocular indirect ophthalmoscope (Keeler Instruments) to determine disease status. Intraocular pressure (IOP) was measured with a Tono-Pen XL (Medtronic Solan) or Icare TonoVet (Icare TonoVet, Icare Finland) tonometer to exclude dogs with glaucoma, classified by IOP > 25 mm Hg. A Schirmer tear test (STT, Intervet) was performed on all dogs to confirm KCS in WHWT and exclude it in all other dogs.

USP

Ultrasonic pachymetry (USP; Accupach VI; Accutome Ultrasonic and Pachette 3; DGH Technology) was performed on both eyes of each dog in the central, superior, inferior, nasal and temporal perilimbal cornea as previously described (Thomasy et al., 2016). For clarity,

analyses of central corneal thickness will be abbreviated as CCT, whereas analyses including all locations of the cornea will be referred to as corneal thickness.

FD-OCT

Prior to performing FD-OCT, the dogs were sedated with acepromazine (0.01 mg/kg) and buprenorphine (0.01 mg/kg) administered intravenously (IV) for dogs ≥ 6 years of age and dexmedetomidine (1–3 μg/kg) IV for dogs <6 years of age. Then, FD-OCT imaging (RTVue 100, software version 6.1; Optovue; 26000 A scan/sec, 5 μm axial resolution, 840 nm superluminescent diode) of the central cornea was performed in both eyes of the dogs. For the automated FD-OCT measurement, the measuring device was centered over the pupil, and the RTVue pachymetry tool generated a 6-mm diameter corneal thickness map, from which the central corneal thickness (CCT) was recorded (Fig. 1A). For manual measurements, the RTVue measuring tool was used to generate a CCT value (Fig. 1B).

Statistical analysis

Mixed effects linear regression was used to evaluate the main effects of eye, method of measurement, body weight, age, breed, sex and, when appropriate, corneal location, and the interaction between method of measurement and corneal location. The individual dog was treated as a random effect; all other variables were considered fixed effects. Bonferonni multiple comparison adjustments were used for post-hoc analyses. Analyses were performed using Stata/IC 12.1 (StataCorp). Bland-Altman plots were constructed to compare the amount of agreement between techniques. Concordance correlation coefficients (CCCs) were interpreted in accordance with previous suggestions, with values > 0.75 indicating good reliability, values between 0.40 and 0.75 indicating moderate reliability, and values < 0.4 indicating poor reliability (Portney and Watkins, 2009; Sebbag et al., 2015). Data are presented as predicted mean ± standard error (SE) unless otherwise stated. For all analyses, values of $P \leq 0.05$ were considered significant. Upper limits of quantitation for the Accupach VI and automated FD-OCT scans were 999 and 800 μm, respectively. Both devices fail to generate a measurement for corneal thickness exceeding these values. Thus, statistical analyses were performed using all corneal thickness data as well as excluding values that exceeded those upper limits.

Results

Of the 5,377 corneal thickness data points analyzed, 168 (3.1%) were >800 μm and 123 (2.3%) were >999 μm. Regardless of whether all data were included or values >999 and 800 μm were excluded, predicted mean CCT values from the Pachette 3 were significantly greater than those from Accupach VI and automated FD-OCT measurements ($P < 0.001$ and $P = 0.001$, respectively; Fig. 2). When all data were included, values from the manual FD-OCT measurements were also significantly greater than those from Accupach VI ($P = 0.032$; Fig. 2A). After excluding values >999 μm, manual FD-OCT measurements were significantly greater than automated measurements ($P = 0.005$; Fig. 2B). After excluding values >800 μm, CCT values from Pachette 3 were significantly greater than manual FD-OCT measurements as well as those from all other techniques; predicted mean CCT was 625

± 7.0, 615 ± 7.2, 613 ± 7.2 and 606 ± 7.4 μm for Pachette 3, Accupach VI, manual, and automated FD-OCT, respectively ($P < 0.001$; Fig. 2C).

To determine if similar trends were found at other corneal locations, data at the superior, inferior, nasal and temporal perilimbal cornea were compared between the USP devices. Following exclusion of values >999 μm, predicted corneal thickness values from the Pachette 3 were significantly greater than those from the Accupach VI at all five corneal locations ($P < 0.05$; Fig. 3). In addition, predicted CCT values in normal dogs were significantly lower than those from the nasal, temporal, superior, and inferior perilimbal cornea using data from both USP techniques ($P < 0.001$); values from the superior perilimbal cornea were significantly greater than all other locations ($P < 0.001$). The CCCs ranged from 0.52–0.87 for all techniques indicating moderate to good reliability between the six pairs of techniques (Table 2). The constructed Bland-Altman plots (Fig. 4) demonstrate variable 95% limits of agreements (LoAs) depending on which two techniques were compared (Table 2).

No significance difference ($P = 0.354$) in corneal thickness was identified between right and left eyes at 765 and 778 μm, respectively, using measurements from all dogs in the present study. Then, mixed effects linear regression was performed to determine if breed, age, weight, and sex had a significant effect on corneal thickness measurements in dogs free of corneal disease. A linear relationship existed between corneal thickness and age of 6.9 ± 1.8 μm for every year increase in age ($P < 0.005$). Similarly, corneal thickness significantly increased linearly with body weight by 1.6 ± 0.8 μm for every kilogram increase in body weight ($P = 0.038$). Males had significantly thicker corneas than females with predicted corneal thickness measurements of 677 ± 9.8 and 634 ± 9.8 um, respectively ($P = 0.002$). There was no significant difference in corneal thickness measurements amongst the five most common breeds included in this study – BT, WHWT, Beagle, GSHP and GWHP ($P > 0.05$).

Predicted corneal thickness and CCT for normal dogs was 744 ± 21 and 613 ± 9.4 um, respectively. Dogs affected with CED with or without treatment with SKCAHF had significantly greater corneal thickness compared to normal dogs at 865 ± 27, 804 ± 27, and 744 ± 27 μm, respectively ($P < 0.001$ and $P < 0.010$, respectively; Fig. 5). Similarly, Beagles treated with transcorneal freezing + phosphate buffer solution (TF + PBS) or transcorneal freezing + rho kinase inhibitor (TF + RKI) had significantly thicker corneas at 837 ± 23 and 847 ± 22 μm, respectively, compared to normal dogs ($P < 0.001$). Beagles treated with 5% NaCl and AT had significantly thinner and thicker corneas at 696 ± 2 and 775 ± 22 μm, respectively, than normal dogs ($P < 0.001$). Predicted corneal thickness in KCS-affected dogs was 702 ± 81 μm and did significantly differ from normal dogs ($P = 0.615$). In CED-affected, KCS-affected and corneal cryoinjured dogs, 225 of 314 (72%), 13 of 60 (22%), and 51 of 301 (17%) Pachette 3 CT measurements were >800 μm, respectively. Similarly, 193 of 314 (61%), 0 of 60 (0%,) and 30 of 301 (10%) Pachette 3 corneal thickness measurements were >999 μm in CED-affected, KCS-affected, and corneal cryoinjured dogs, respectively.

For the 108 dogs, median (range) IOP was 10 (4–17) mm Hg. Median (range) STT was 5.5 (0–10) mm/min in KCS-affected dogs and 21.5 (12–29) mm/min in normal dogs; the STT

values from one KCS-affected dog were excluded since it had received a parotid duct transposition for both eyes.

Discussion

The present study demonstrates that devices with the capability to measure corneal thickness greater than 1000 μm are required in spontaneous or induced models of corneal disease in dogs. The corneal thickness varied predictably with certain disease states and/or treatments such that CED and transcorneal freezing increased corneal thickness while 5% NaCl decreased corneal thickness. Thickness varied by location and was significantly thinner in the central versus peripheral cornea in normal dogs. In addition, the dorsal perilimbal cornea was significantly thicker than the nasal, temporal, and inferior perilimbal cornea. Finally, corneal thickness from normal dogs displayed a linear relationship with age and weight.

Numerous studies in dogs with healthy eyes demonstrate that USP and OCT devices generate relatively consistent corneal thickness measurements (Alario and Pirie, 2013a, 2014). In the present study, there was good agreement between the Accupach VI, automated and manual FD-OCT techniques when CCT was <800 μm with only the Pachette 3 generating significantly greater values than the 3 aforementioned devices; however, the greatest difference of 19 μm between Pachette 3 and automated FD-OCT was slight and likely to be clinically insignificant. Thus, all these devices may be appropriate for use in veterinary patients or research subjects in which corneal thickness is not anticipated to exceed 800 μm provided that the same device is used throughout the measurement period to prevent inter-device variability.

Few studies have assessed the reliability of the pachymetry devices to measure corneal thickness in canine patients with corneal disease (Famose, 2013). This study demonstrated that the Accupach VI and automated FD-OCT techniques have limited utility in canine patients with corneal disease as their corneal thickness frequently exceeds the 999 and 800 μm limits for these devices, respectively. Specifically, automated FD-OCT was unable to obtain 72%, 17 and 22% of measurements from CED-affected, corneal cryoinjured, and KCS-affected dogs respectively. The Accupach VI was unable to obtain 61% and 10% of measurements from CED-affected and cryoinjured dogs, respectively. While normal CCT in humans and dogs is relatively similar at 535 μm (Doughty and Zaman, 2000) and 613 μm respectively, the lack of a Bowman’s layer in dogs and differences in collagen fiber arrangement presumably allow canine corneas to swell more markedly with endothelial dysfunction in comparison to human corneas (Thomasy et al., 2016). Thus, OCT devices with manual measurement tools or USP devices such as the Pachette 3 which can measure up to 2000 μm are required in research studies where dog models of endothelial dysfunction are used (Horikawa et al., 2016) or for patients with exceptionally thick corneas.

It is noteworthy that the Pachette 3 consistently overestimated measurements in comparison to the Accupach VI and automated and manual FD-OCT techniques using CCT values <800 μm. This is consistent with other studies that demonstrate that USP devices generate greater corneal thickness measurements versus FD-OCT (Ishibazawa et al., 2011; Ponce et al., 2009; Strom et al., 2015), and more specifically, with one study that showed that a Pachette

device overestimated measurements in comparison to Scheimpflug and spectral-domain OCT devices in humans (Randleman et al., 2015). Pachymetry devices employ a default ultrasound velocity of 1640 m/s in their algorithms, the mean velocity through a human cornea, to calculate corneal thickness; this assumption may overestimate measurements in dogs (Alario and Pirie, 2013a) since the mean velocity through a canine cornea is estimated to be 1567–1585 m/s depending on the dog's age (Tang, 2012). Interestingly, corneal thickness measurements obtained at five corneal locations were significantly greater when obtained by the Pachette 3 vs. the Accupach VI after excluding values >999 μm. It has been previously speculated that these differences between the two USP devices could be due to slight variations in how each device generates readings (Samuel et al., 2014). The Pachette 3 generates 25 consecutive readings at a single position which can decrease user error. Alternatively, the Accupach VI acquires three separate readings that are averaged and requires new placement of the probe with sequential readings which could increase variability due to differences in probe position during applanation to the corneal surface.

After accounting for differences in thickness due to corneal location or measurement technique, the mixed effects regression model was used to determine the effects of age, weight, sex, and breed on corneal thickness. Central corneal thickness was significantly thinner than all other regions, which is consistent with previous studies (Bourges et al., 2009; Ortiz et al., 2014; Ponce et al., 2009; Samuel et al., 2014). A linear relationship between age and corneal thickness was identified with an increase of 6.9 ± 1.8 μm per year of age which is less than previous studies in dogs which reported increases of 17 μm/year (Gwin et al., 1982) and 14 μm/month (Gilger et al., 1991). A linear relationship between weight and corneal thickness was also identified in the present study with an increase of 1.6 ± 0.8 μm per kg of body weight and consistent with a previous study that found an increase of 1.83 ± 0.38 μm per kg of body weight (Gilger et al., 1991). Males had significantly thicker corneas than females, with predicted corneal thickness measuring 677 ± 19 compared to 633 ± 19 um for females, which is consistent with other studies (Gilger et al., 1991; Strom et al., 2015). No significant differences in corneal thickness were identified between the five breeds evaluated. The predicted mean corneal thickness of dogs without corneal disease was 744 ± 21 μm in the present study, which is thicker than means ranging from 535–598 μm presented in previous studies (Alario and Pirie, 2013a; Famose, 2013; Gilger et al., 1991). These differences in corneal thickness are likely attributable to age and weight differences between the study populations, variability in corneal location measured and/or differences in measurement devices used.

As expected, increases in corneal thickness were observed in dogs with corneal endothelial dysfunction despite treatment with SKCAHF or 5% NaCl in comparison to normal dogs. However, SKCAHF significantly decreased corneal thickness and improved vision in dogs with endothelial dysfunction for up to 1 year following surgery (Horikawa et al., 2016). Transcorneal freezing in Beagles resulted in a temporary increase in corneal thickness that approached what was observed in dogs with CED suggesting that this may be an appropriate, albeit transient, model for endothelial injury if young dogs are used (Befanis et al., 1981). A mild decrease in corneal thickness in normal dogs receiving 5% NaCl was observed consistent with its hypertonicity and a previous study in normal rabbits (Green and Downs, 1973). In aggregate, these observations confirm that the mixed effects linear

regression model utilized in the present study was able to detect differences between clinical treatment groups and suggest that the model would be valid for assessing other variables such as technique, age, breed and sex.

Limitations of this study were typical of those commonly identified in retrospective studies. Specifically, the observer obtaining the measurements was not recorded so intra-observer and inter-observer variability could not be ascertained in the present study. However, low inter- and intra-observer variability has been previously reported for corneal thickness measurements obtained by both ultrasonic pachymetry (Kiddee and Horattanareung, 2009; Peyman et al., 2015) and FD-OCT (Alario and Pirie, 2013b) in dogs and humans, respectively. Thus, we do not expect these variables to dramatically influence the results of the present study.

Conclusions

Canine corneas exhibit marked increases in thickness with endothelial dysfunction that frequently exceed the upper limits of measurement of some pachymetry devices developed for human use such as the Accupach VI. The manual FD-OCT tool generated measurements most consistent with automated FD-OCT and Accupach VI measurements. While the Pachette 3 consistently overestimated CCT values in comparison to the Accupach VI, automated and manual OCT, these differences were relatively minor and unlikely to be of clinical consequence. Thus, the manual FD-OCT and Pachette 3 pachymeters would be most useful for measuring corneal thickness in dogs with spontaneous or induced endothelial disease.

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References

Alario A, Pirie C, 2013a Central corneal thickness measurements in normal dogs: a comparison between ultrasound pachymetry and optical coherence tomography. Veterinary Ophthalmology 17, 207–211. [PubMed: 23763504]

Alario A, Pirie C, 2014 Reliability of manual measurements of corneal thickness obtained from healthy canine eyes using spectral-domain optical coherence tomography (SD-OCT). The Canadian Journal of Veterinary Research 78, 221–225. [PubMed: 24982554]

Alario AF, Pirie CG, 2013b A spectral-domain optical coherence tomography device provides reliable corneal pachymetry measurements in canine eyes. The Veterinary Record 172, 605. [PubMed: 23716535]

Amano S, Honda N, Amano Y, Yamagami S, Miyai T, Samejima T, Ogata M, Miyata K, 2006 Comparison of central corneal thickness measurements by rotating Scheimpflug camera, ultrasonic pachymetry, and scanning-slit corneal topography. Ophthalmology 113, 937–941. [PubMed: 16751036]

Befanis P, JR RP, Brown D, 1981 Endothelial repair of the canine cornea. American Journal of Veterinary Research 42, 590–595. [PubMed: 7332117]

Bourges J, Alfonsi N, Laliberte J, Chagnon M, Renard G, Legeais J, Brunette I, 2009 Average 3-Dimensional models for the comparison of Orboscan II and Pentacam pachymetry maps in normal corneas. Ophthalmology 116, 2064–2071. [PubMed: 19744719]

Chaudhry I, 2009 Measurement of central corneal thickness in health and disease. Saudi Journal of Ophthalmology 23, 179–180. [PubMed: 23960857]

Doughty M, Zaman M, 2000 Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. Survey of Ophthalmology 44, 367–408. [PubMed: 10734239]

Famose F, 2013 Assessment of the use of spectral domain optical coherence tomography (SD-OCT) for evaluation of the healthy and pathological cornea in dogs and cats. Veterinary Ophthalmology 17, 12–22. [PubMed: 23356688]

Gilger B, Whitley R, McLaughlin S, Wright J, Drane J, 1991 Canine corneal thickness measured by ultrasonic pachymetry. American Journal of Veterinary Research 52, 1570–1572. [PubMed: 1767973]

Green K, Downs S, 1973 Reduction of corneal thickness with hypertonic solutions. American Journal of Ophthalmology 75, 507–510. [PubMed: 4697204]

Gwin R, Lerner I, Warren J, Gum G, 1982 Decrease in canine corneal endothelial density and increase in corneal thickness as functions of age. Investigative Ophthalmology and Visual Science 22, 267–271. [PubMed: 7056641]

Horikawa T, Thomasy S, Stanley A, Calderon A, Li J, Linton L, Murphy C, 2016 Superficial keratectomy and conjunctival advancement hood flap (SKCAHF) for the management of bullous keratopathy: validation in dogs with spontaneous disease. Cornea 35, 1295–1304. [PubMed: 27538190]

Ishibazawa A, Igarashi S, Hanada K, Nagaoka T, Ishiko S, Ito H, Yoshida A, 2011 Central corneal thickness measurements with Fourier-domain optical coherence tomographcy versus ultrasonic pachymetry and rotating Scheimpflug camera. Cornea 30 615–619. [PubMed: 21282999]

Kiddee W, Horattanareung O, 2009 Intraoperator repeatability and interoperator reproducibility in the ultrasonic pachymetry measurements of central corneal thickness. Journal of the Medical Association of Thailand 92, 672–676. [PubMed: 19459530]

Kim H, Budenz D, Lee P, Feuer W, Barton K, 2008 Comparison of central corneal thickness using anterior segment optical coherence tomography vs ultrasound pachymetry. American Journal of Ophthalmology 145, 228–232. [PubMed: 18054888]

Okumura N, Koizumi N, Kay E, Ueno M, Sakamoto Y, Nakamura S, Hamuro J, Kinoshita S, 2013 The ROCK inhibitor eye drop accelerates corneal endothelium wound healing. Investigative Ophthalmology and Visual Science 54.

Ortiz S, Mena L, Cristobal A, Martin R, 2014 Relationships between central and peripheral corneal thickness in different degrees of myopia. Journal of Optometry 7, 44–50. [PubMed: 24646900]

Peyman M, Tai LY, Khaw KW, Ng CM, Win MM, Subrayan V, 2015 Accutome PachPen handheld ultrasonic pachymeter: Intraobserver repeatability and interobserver reproducibility by personnel of different training grades. International Ophthalmology 35, 651–655. [PubMed: 25189684]

Ponce CP, Rocha K, Smith S, Krueger R, 2009 Central and peripheral corneal thickness measured with optical coherence tomography, Scheimpflug imaging, and ultrasound pachymetry in normal, keratoconus-suspect, and post-laser in situ keratomileusis eyes. Journal of Cataract and Refractive Surgery 35, 1055–1062. [PubMed: 19465292]

Portney L, Watkins M, 2009 Foundations of clinical research: Applications to practice, 3rd edition Upper Saddle River, NJ: Prentice Hall.

Randleman J, Lynn M, Perez-Straziota C, Weissman H, Kim S, 2015 Comparison of central and peripheral corneal thickness measurements with scanning-slit Scheimpflug and Fourier-domain ocular coherence tomography. British Journal of Ophthalmology 99, 1176–1181. [PubMed: 25824260]

Realini T, Lovelace K, 2003 Measuring central corneal thickness with ultrasound pachymetry. Optometry and Vision Science 80, 437–439. [PubMed: 12808403]

Sadoughi M, Einollahi B, Einollahi N, Rezaei J, Roshandel D, Feizi S, 2015 Measurement of central corneal thickness using ultrasound pachymetry and Orbscan II in normal eyes. Journal of Ophthalmic and Vision Research 10, 4–9. [PubMed: 26005545]

Samuel M, Thomasy S, Calderon A, Collins B, Murphy C, 2014 Effects of hypertonic saline on central corneal thickness in normal dogs. Veterinary Ophthalmology 17, E31–E49.

Sebbag L, Kass P, Maggs D, 2015 Reference values, interest correlations, and test-retest repeatability of selected tear film tests in healthy cats. Journal of the American Veterinary Medical Association 246, 426–435. [PubMed: 25632817]

Shull O, Thomasy S, Davis L, Murphy C, 2015 Phenotypic characterization of corneal endothelial dystrophy in German Shorthaired and Wirehaired Pointers using *in vivi* advanced corneal imaging. Veterinary Ophthalmology 18, E17–E34.

Stewart K, Thomasy S, Stanley A, Davis L, Murphy C, 2014 Quantitative and qualitative evaluation of the tear film in West Highland White Terriers with and without keratoconjunctivitis sicca Proceedings, Comparative Ocular Surface Disease Workshop, Forth Worth, TX.

Strom A, Cortes D, Rasmussen C, Thomasy S, McIntyre K, Lee S, Kass P, Mannis M, Murphy C, 2015 *In vivo* evaluation of the cornea and conjunctiva of the normal laboratory beagle using time- and Fourier-domain optical coherence tomography and ultrasound pachymetry. Veterinary Ophthalmology, 1–7.

Tang J, 2012 Ultrasonic characterization of corneal and scleral biomechanics, Doctoral Dissertation, The Ohio State University.

Thomasy S, Cortes D, Hoehn A, Calderon A, Li J, Murphy C, 2016 In vivo imaging of corneal endothelial dystrophy in Boston Terriers: a spontaneous, canine model for Fuch's endothelial corneal dystrophy. Investigative Ophthalmology and Visual Science 57, 495–503. [PubMed: 26868753]

Wolf B, Stojanac D, Sacu S, Drexler W, Findl O, 2006 Comparison of three methods of measuring corneal thickness and anterior chamber depth. . American Journal of Ophthalmology 142, 7–12.

Highlights

- Corneal thicknesses measured by ultrasonic pachymetry (Pachette 3 & Accupach VI) and two FD-OCT methods were compared.
- Corneal thickness varied predictably depending on age, weight, and corneal disease status.
- The Pachette 3 produced higher corneal thickness measurements than the other three methods.
- Canine corneas markedly thickened with endothelial disease and sometimes exceeded the upper measurement limits of pachymetry devices.

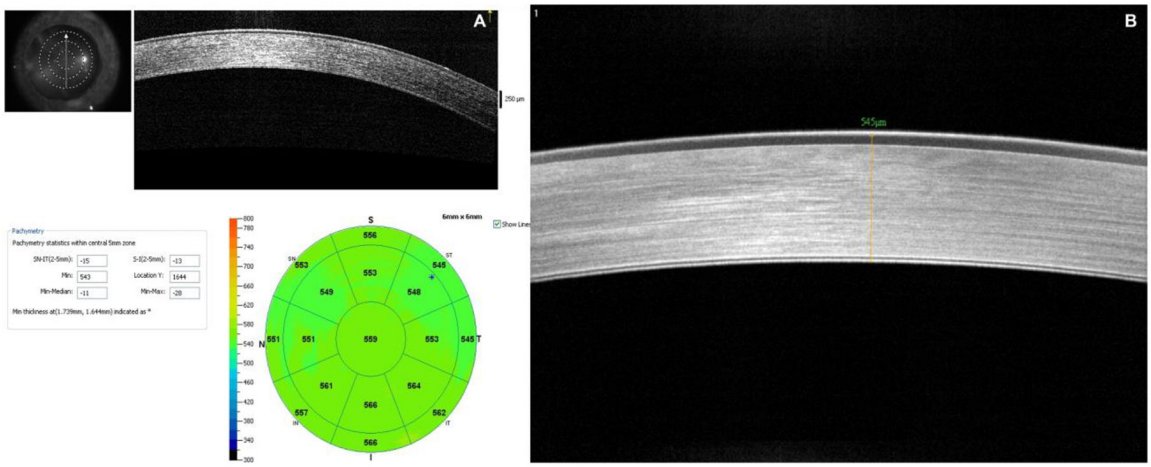
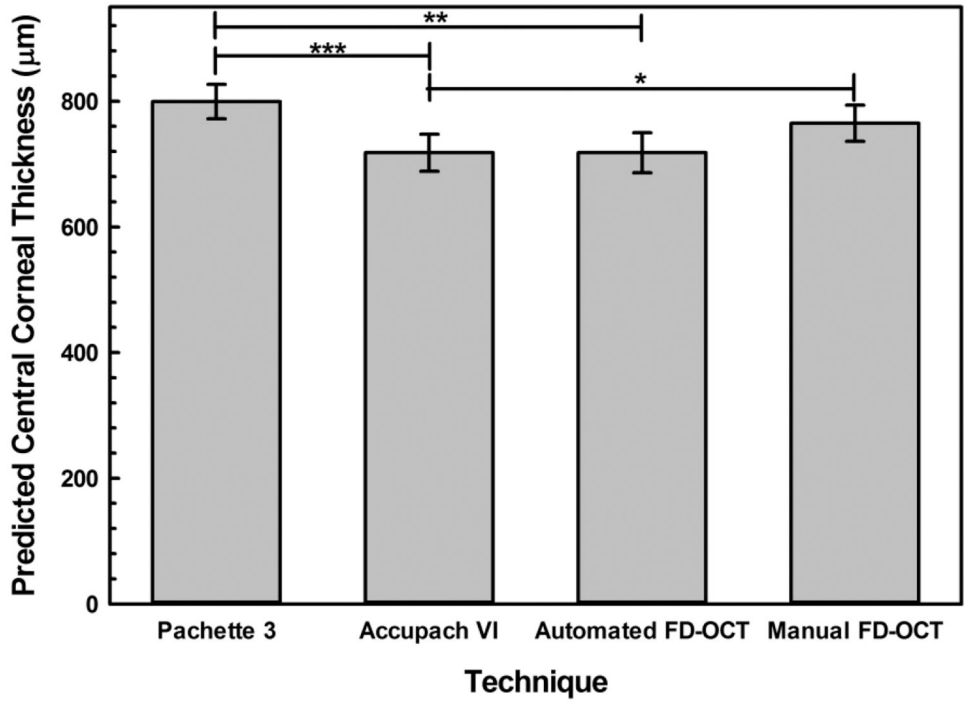
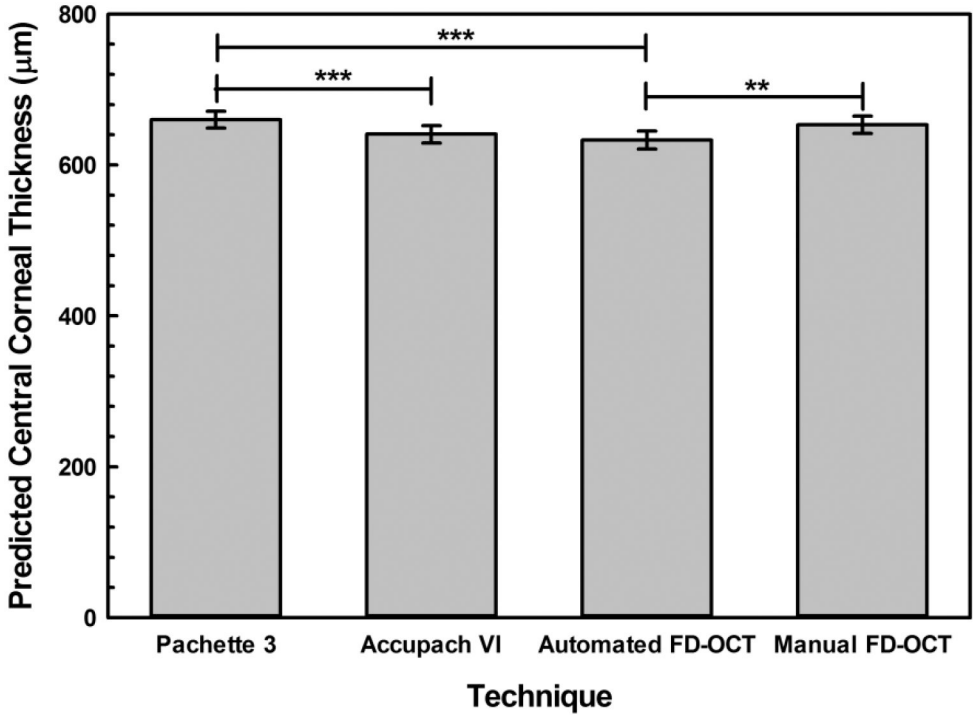


Fig. 1.

Central corneal thickness is automatically generated (A) and measured manually (B) using Fourier-domain optical coherence tomography (FD-OCT) images. Images were obtained from an 11-year-old castrated male Boston terrier with a clear cornea and no ophthalmic abnormalities. The automated measurement generated by the pachymetry software was 559 µm and the value obtained manually using the RTVue measurement tool was 545 µm.





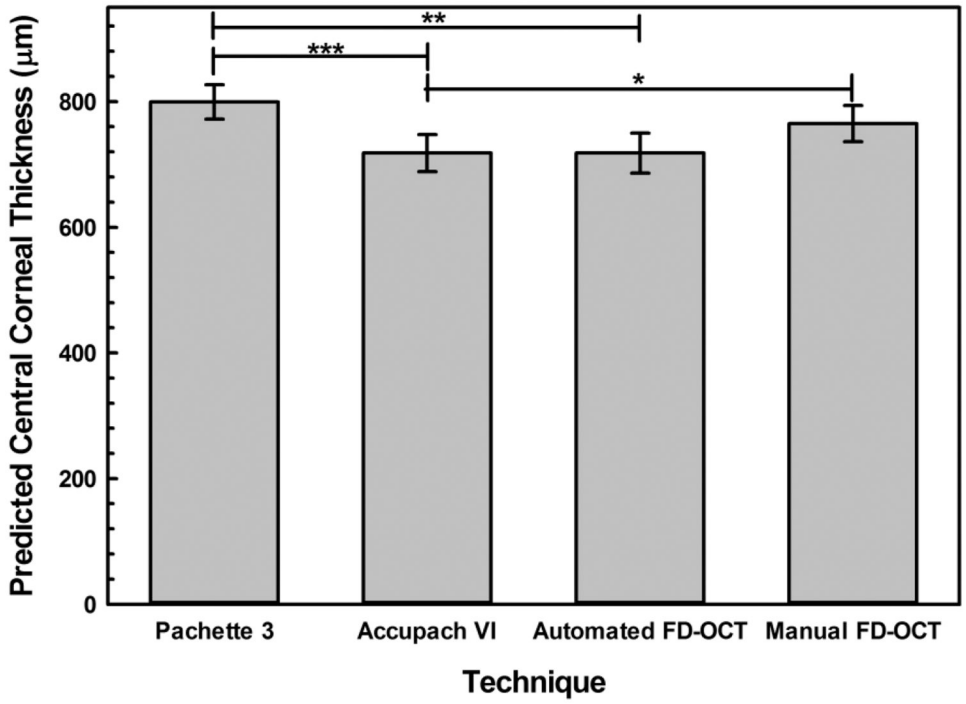


Fig. 2.

Predicted mean ± standard error (SE) central corneal thickness (CTT) for four measurement techniques including all data from 108 dogs with or without corneal disease (A). The CTT values from Pachette 3 were significantly greater than those from Accupach VI ($P < 0.001$) and automated Fourier-domain optical coherence tomography (FD-OCT) measurements ($P = 0.001$). Values from the manual FD-OCT measurements were significantly greater than those from Accupach VI ($P = 0.032$). All other techniques were not significantly different from one another. Predicted mean CCT ± SE for four measurement techniques excluding data >999 µm from 98 dogs with or without corneal disease (B). The CCT values from Pachette 3 were significantly greater than Accupach VI ($P < 0.001$) and automated FD-OCT measurements ($P < 0.001$). The manual FD-OCT measurements were significantly higher than automated measurements ($P = 0.005$). All other techniques were not significantly different from one another. Predicted mean CCT ± SE for four measurement techniques excluding data >800 µm from 91 dogs with or without corneal disease (C). The CCT values from Pachette 3 were significantly higher than those from all other techniques ($P < 0.001$). All other techniques were not significantly different from each other. All P values were determined by a mixed effects linear regression model. *$P < 0.05$. **$P < 0.01$, ***$P < 0.001$.

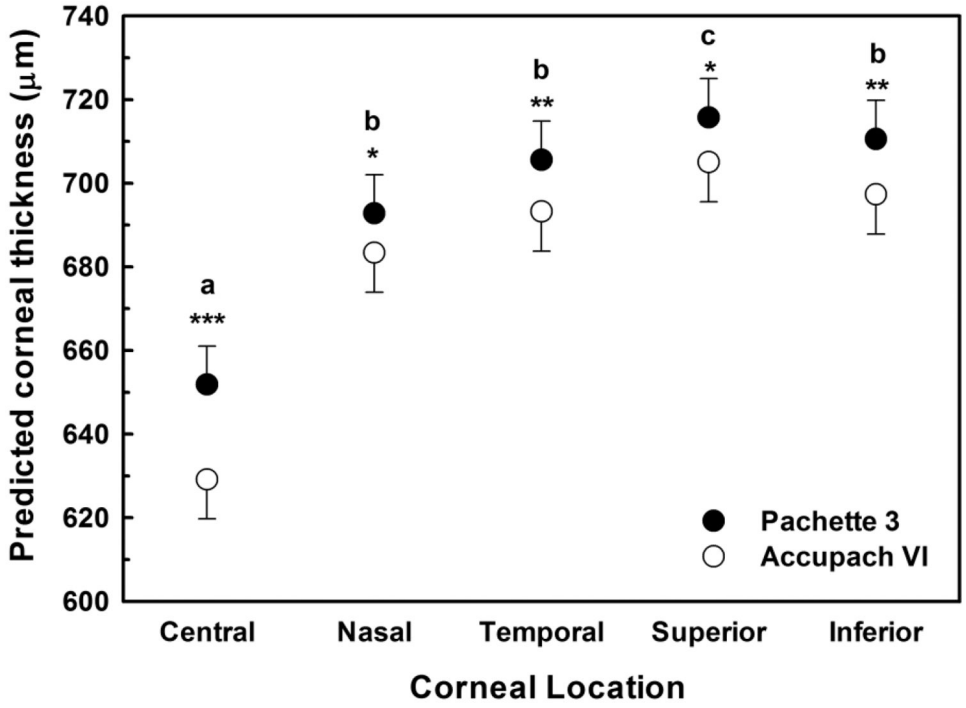


Fig. 3.

Predicted mean ± standard error corneal thickness at five different locations as measured by ultrasonic pachymetry (USP) devices, Pachette 3 and Accupach VI excluding data >999 µm in 99 dogs with or without corneal disease. At all locations, Pachette 3 generated significantly greater corneal thickness measurements than the Accupach VI ($P < 0.05$). In normal dogs, central corneal thickness (CTT) was significantly less than the other four regions for both USP devices; superior perilimbal corneal thickness was significantly greater than inferior, nasal and temporal perilimbal thickness and CCT ($P < 0.05$). The P values were determined by mixed effects linear regression with a Bonferroni test for post-hoc analysis. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ for technique. ^{a,b,c} $P < 0.05$ for location.

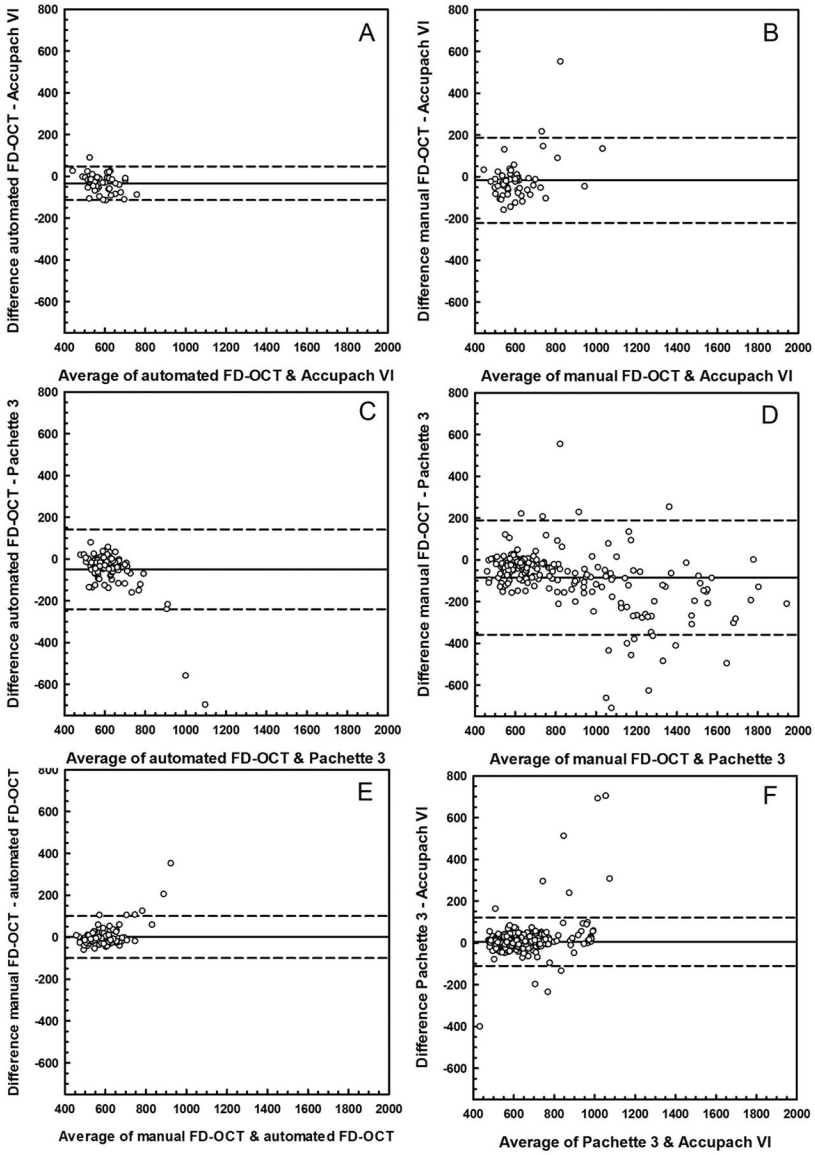


Fig. 4.

Bland-Altman plots displaying corneal thickness measurement differences between automated Fourier-domain optical coherence tomography (FD-OCT) and Accupach (A), manual FD-OCT and Accupach (B), automated FD-OCT and Pachette (C), manual FD-OCT and Pachette (D), automated and manual FD-OCT (E) and Pachette and Accupach (F) in 108 dogs with and without corneal disease. The vertical axis represents the difference between the two techniques, and the horizontal axis plots the mean value for the two techniques. The mean of the differences is represented as the solid horizontal line intersecting the vertical axis and should be close to zero. The dashed lines represent the 95% limits of agreement.

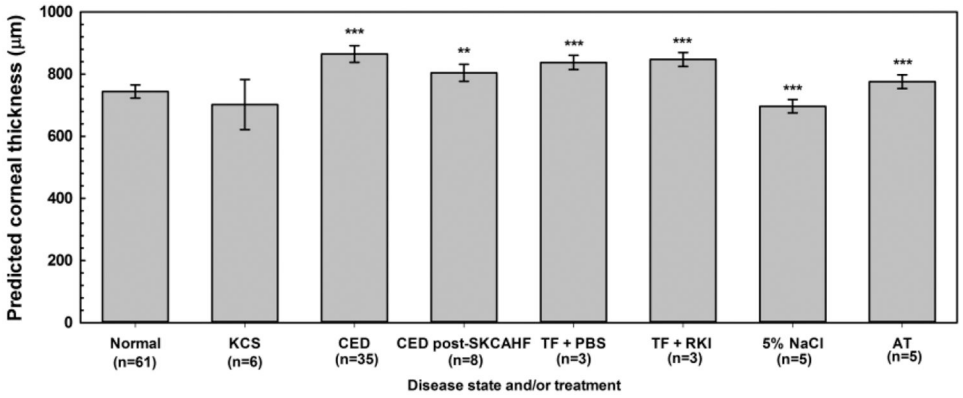


Fig. 5.

Predicted mean ± standard error corneal thickness from 108 dogs with or without corneal disease and/or treatment administration. Dogs affected with corneal endothelial degeneration (CED) with or without treatment with a superficial keratectomy and conjunctival advancement hood flap (SKCAHF) had significantly thicker corneas in comparison to normal dogs (P_{CED} <0.001, P_{SKCAHF} < 0.010). Similarly, Beagles treated with transcorneal freezing + phosphate buffer solution (TF + PBS) or TF + rho kinase inhibitor (RKI) also had significantly thicker corneas than normal dogs ($P < 0.001$). Beagles treated with 5% NaCl had significantly thinner corneas, while Beagles treated with artificial tears (AT) had significantly thicker corneas than normal dogs ($P < 0.001$). Predicted corneal thickness did not significantly differ between keratoconjunctivitis sicca (KCS)-affected and normal dogs ($P = 0.615$). **$P < 0.01$, ***$P < 0.001$.

Table 1

Demographic data for study population of 108 dogs.

Breed	Sex	Age, years; median (range)	Bodyweight, kg; median (range)	Disease state and/or treatments performed
BT (*n*=45)	3 FI, 19 FS, 3 MI, 20 MN	11.1 (5–14.6)	9 (3.6–16)	Normal (*n*=28), CED (*n*=16), CED post-SKCAHF (*n*=1)
GSHP (*n*=18)	1 FI, 10 FS, 7 MN	10.6 (7.0–14.5)	26.1, (20–36.2)	Normal (*n*=14), CED (*n*=4)
GWHP (*n*=12)	1 FI, 2 FS, 2 MI, 7 MN	11.2 (0.7–12.6)	29.6, (20.6–38.8)	Normal (*n*=6), CED (*n*=6)
Beagle (*n*=6)	6 FI	1.8 (1.8–1.8)	7.5 (7–8.3)	Normal + 5% NaCl/AT (*n*=5)
		2.5 (2.5–2.5)	8.4 (8.2–8.8)	TF+ PBS (*n*=3)
		2.5 (2.5–2.8)	9 (8–9.4)	TF + RKI (*n*=3)
WHWT (*n*=19)	3 FI, 8 FS, 2 MI, 6 MN	8.6 (3.1–13.7)	8.7 (6.6–12.2)	Normal (*n*=13), KCS (*n*=6)
Other (*n*=8)	5 FS, 3 MN	10.3 (8.2–11.7)	9.7 (2.2–36.3)	CED + 5% NaCl (*n*=1), CED +SKCAHF (*n*=5), corneal endothelial degeneration + SKCAHF (*n*=2)

BT, Boston terrier; GSHP, German shorthaired pointer; GWHP, German wirehaired pointer; WHWT, West highland white terrier; FI, female intact; FS, female spayed; MI, male intact; MN, male neutered; CED, corneal endothelial dysfunction; KCS, keratoconjunctivitis sicca; SKCAHF, superficial keratectomy and conjunctival advancement hood flap; 5% NaCl, sodium chloride 5%; AT, artificial tears; TF, transcorneal freezing; PBS, phosphate buffer solution RKI, rho kinase inhibitor

Table 2

Mean difference in corneal thickness between techniques, including the concordance correlation coefficients (CCC), coefficient of variation (CV) and limits of agreement (LoA) between modalities.

	Mean difference (μm) ± SD	CCC	LoA (μm) width (lower-upper)
Automated FD-OCT – Accupach	−33.2 ± 41.1	0.71	161.1 (−113.7 – 47.4)
Manual FD-OCT – Accupach	−16.9 ± 104	0.61	407.8 (−220.8 – 187)
Automated FD-OCT – Pachette	−49.9 ± 97.2	0.52	381.1 (−240.5 – 140.6)
Manual FD-OCT – Pachette	−84.9 ± 139.8	0.53	548.2 (−359 – 189.2)
Manual FD-OCT – Automated FD-OCT	0.8 ± 51.2	0.81	200.5 (−99.5 – 101)
Pachette – Accupach	5.7 ± 59.1	0.87	231.6 (−110.1 – 121.5)

SD, Standard deviation; FD-OCT, Fourier-domain optical coherence tomography