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”Repeatability and reproducibility of macular thickness with the Huvitz Optical Coherence Tomography HOCT-1F/1 and Auto Tracking program”

”Repeterbarheten och reproducerbarheten av makulas tjocklek med Huvitz Optical Coherence Tomography HOCT- 1F/1 och Auto Tracking program”

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Abstract

Background: Optical coherence tomography is a technology that produces cross-sectional images of the retina and is used to detect and monitor retinal pathologies. One important parameter is retinal thickness in the macular area. The purpose of this study is to investigate the repeatability, reproducibility, and reliability of the Huvitz HOCT-1F/1 measurement of retinal thickness using the ETDRS macular grid.

Methods: Macular thickness of the subjects' right eye was obtained at the Open Clinic at the Unit of Optometry, St Erik Eye Hospital in, Stockholm, Sweden. All the measurements were done with the Macular 3D protocol (A-scan 512 x B-scan 96). For repeatability, two separate manual measurements were performed by Examiner 1. To evaluate the reproducibility, Examiner 2 took one manual measurement, and this was compared with one of the measurements made by Examiner 1. Examiner 2 also performed one more measurement with Auto Shoot program. The Huvitz HOCT-1F/1 Auto Shoot program reliability was evaluated by comparing Auto Tracking (manual measurement made by Examiner 1) and the Auto Shoot program (automatic measurement made by Examiner 2). Intra-class correlation coefficients (ICCs) were calculated to evaluate machine repeatability.

Results: A total of 65 normal eyes were analysed. The ICC values for repeatability range from 0.88 (outer superior) to 0.99 (inner temporal). The ICC values for reproducibility range from 0.94 (outer superior) to 0.99 (inner nasal, inner temporal and outer nasal). Meanwhile, for reliability of the Auto Shoot program, the ICC values range from 0.93 (outer superior) to 0.99 (inner nasal and inner temporal). In summary the ICCs are greater than 0.88 in all the total macular thickness which indicates good reliability of Huvitz HOCT-1F/1.

Conclusions: Huvitz HOCT-1F/1 has high repeatability, reproducibility and reliability in measuring all macular thickness areas on healthy eyes.

Keywords

Optical coherence tomography, Repeatability, Reproducibility, Reliability, Huvitz HOCT-1F/1, Spectral domain optical coherence tomography, Macular thickness, Intra class correlation coefficient, Healthy eyes, Auto Shoot program

Sammanfattning

Bakgrund: Optisk koherenstomografi är en teknik som tar tvärsnittsbilder av näthinnan för att upptäcka, diagnostisera och följa upp retinala ögonsjukdomar. En viktig parameter är tjockleken i makulaområdet. Syftet med studien är att utvärdera repeterbarheten, reproducerbarheten och tillförlitligheten hos Huvitz HOCT-1F/1 avseende mätningar av den retinala tjockleken med ETDRS makulakarta.

Metod: Makulas tjocklek från patienternas högra öga undersöktes på öppna mottagningen vid enheten för optometri vid S:t Eriks Ögonsjukhus i Stockholm, Sverige. Samtliga mätningar utfördes med utrustningens protokoll Macular 3D (A-scan 512 x B-scan 96). Repeterbarheten utvärderades genom två separata manuella mätningar utförda av undersökare 1. För reproducerbarheten utfördes en manuell mätning av undersökare 2 och denna jämfördes med en av mätningarna från undersökare 1. Undersökare 2 genomförde en ytterligare mätning med Auto Shoot-programmet. Tillförlitligheten hos mätinställningen Auto Shoot utvärderades genom att jämföra inställningarna Auto Tracking (manuell mätning gjord av undersökare 2) och Auto Shoot (automatisk mätning gjord av undersökare 2). Intra Class-korrelationskoefficienten (ICC) användes för att analysera utrustningens tillförlitlighet.

Resultat: Totalt analyserades 65 normala ögon. ICC-värden för repeterbarheten visade ett intervall från 0,88 (yttre superiora) till 0,99 (inre temporala). Gällande reproducerbarheten visade ICC-analysen ett intervall mellan 0,94 (yttre superiora) till 0,99 (inre nasala, inre temporala och yttre nasala). Tillförlitligheten för Auto Shoot-intervallets värden varierade från 0,93 (yttre superiora) till 0,99 (inre nasala och inre temporala). Sammanfattningsvis gav ICC-analysen, i sin helhet, värden över 0,88 för hela makulas tjocklek, vilket indikerar god tillförlitlighet gällande Huvitz HOCT-1F/1.

Slutsats: Huvitz HOCT-1F/1 har god repeterbarhet, reproducerbarhet och tillförlitlighet vid mätning av alla områden på makulas tjocklek hos friska ögon.

Nyckelord

Optisk koherenstomografi, Repeterbarhet, Reproducerbarhet, Reliabilitet, Huvitz HOCT-1F/1, Spektral-domän optisk koherenstomografi, Makulatjocklek, Intra Class-korrelationskoefficient, Friska ögon, Auto Shoot-program

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Background

Optical coherence tomography (OCT) is a non-invasive, and non-contact technology that produces in-vivo cross-sectional images of the transparent layers in the retina with micron resolution (Huang et al., 1991). In clinical practice, it is used for looking at retinal structure changes and gives quantitative (thickness and volume) data (Molnar et al., 2015). The technique has been proven to be very useful for the detection and follow up of macular pathologies. Conditions included are macular degeneration, macula edema and glaucoma (Huang et al., 1991). In the macula, it can detect pathological changes e.g., epiretinal membrane, vitreomacular traction, and macular holes (Chatziralli et al., 2017; Wilkins et al., 1996; Steel et al., 2016; Goldberg et al., 2014). The spectral-domain OCT's ability to clarify the status of the outer retina has great clinical importance (Hunter et al, 2013). By visualising the outer retina, many cases of visual loss have been explained. The status of the photoreceptor inner and outer segment junction (IS/OS) and external limiting membrane is helpful in predicting the outcome in macular edema. The machine has sensitivity for detecting cystoid macular edema in its early stages (Hunter et al, 2013). Fleckenstein et al. (2010) affirmed that a reduction in retinal thickness is a hallmark of geographic atrophy (GA), a disease progression with loss of photoreceptor cells and retinal pigment epithelium (RPE).

The macula is divided into the anatomical areas; fovea, parafovea, perifovea. The area is five to six millimeters in diameter and the center is called the fovea. The center of the fovea is termed foveola centralis. In this central area, the retinal layers are very thin due to the absence of the ganglion cell layer (GCL) and the inner nuclear layer (INL). This zone is also avascular. Due to the displacement of the inner retinal layers, there is a foveal slope, i.e., the foveal pit, surrounded by the foveal wall. At this wall, there is a high density of ganglion cell layers and a shift from in density from mainly cones to mainly rods. The outermost region, perifovea has a similar retinal profile, but is thinner. The thickness of the peripheral retina is one-third thinner than the parafovea (Provis et al, 2005). There are four retinal vascular networks in the macula. One superficial supply the GCL and below and under the inner nuclear layer (INL) there are two deeper capillary networks. The fourth network runs with nerve fiber layer (NFL) axons. The superficial blood vessel can cause artifact of shadows and affect the thickness profile (Cambell et al., 2017).

On every new machine, the repeatability must be evaluated to separate a true clinical change from noise (Mansouri et al., 2014). Because OCT is used as a guidance regarding diagnosis and follow up, it is important examine at the individual OCT system's repeatability, reproducibility, and reliability (Ctori & Huntjens, 2015). Repeatability is the variation in data when one examiner performs the scanning, while reproducibility is the variation in data measured by two different examiners. The machine's reliability is of interest when using different scan programs. All these factors must be established to optimise the use of OCT as a clinical tool. A feature of OCTs that improves the accuracy and reliability of the system is automatic tracking systems (Kita et al., 2015). The instrument follows eye movements and performs an automatic rescan if the patient loses fixation during measurement. Studies have shown that the repeatability of the retinal nerve fibre layers thickness significantly improved with automatic tracking (Langenegger et al., 2011; Brautaset et al, 2016). Factors that affect the repeatability of OCT are media opacities, machine resolution, capture speed, auto-segmentation software, and patient cooperation (Hong el al., 2019). Several studies have established repeatability and reproducibility of total retinal thickness, in healthy individuals and those with ocular pathology (Hong et al., 2019; Liu et al., 2014; Ctori & Hutjens, 2015; Parravano et al., 2010; Brautaset et al., 2014). High repeatability has been demonstrated on GCL-IPL with several spectral domain optical coherence tomographs (Lee et al., 2018) Molnar et al. (2015) demonstrated good repeatability and reproducibility of macular thickness measurements in a study of children performed with SD-OCT Cirrus version 6.0.2.81.

The second generation of OCT is spectral domain optical coherence tomography (SD-OCT). The technology has a faster scan speed, a higher resolution and greater depth penetration compared to the first generation of OCTs. It gives 3D retinal images and uses a coherent light source of a superluminsecent diode to capture echoes of the backscattering light from the biological tissue (Yaqoob et al., 2005). The Huvitz Optical Coherence Tomography HOCT-1F/1 (Huvitz HOCT-1F/1) is a new SD-OCT device, with improved availability for optometrists. The instrument combines an OCT, full fundus camera and PC in one device (Huvitz HOCT-1F/1 manual, 2017). No studies have yet been performed and the instrument needs validation.

The purpose of this study is to investigate the repeatability, reproducibility and reliability of the Huvitz HOCT-1F/1 measurement of the retinal thickness using the Early Treatment Diabetic Retinopathy Study (ETDRS) macular grid.

Methods

Inclusion criteria

Eighty-one healthy subjects participated in the study and were examined at the Open Clinic at the Unit of Optometry, St Erik Eye Hospital, Stockholm, Sweden. All patients underwent well-segmented OCT images. Subjects were mainly students from the Optometry program at the Karolinska Institute. The mean age is 28.4, with ages ranging from 19 to 58, and the female/male ratio was 51/30. Every measurement of macular thickness was performed by trained examiners and on the same OCT using the Macular 3D protocol (A-scan 512 x B-scan 96) over an area of 9X9 mm. Only the subjects' right eye was measured. The selected mode was horizontal scan direction, the signal level of the OCT sensitivity was set to fine, and the fundus surface imaging OCT enfaced off. The minimum pupil diameter criterion of 2.5 mm was followed according to the Huvitz HOCT-1F/1 manual (2017). No dilating drops were used (Burkholder et al., 2009; Brautaset et al., 2016). This research followed the ethical principles of the Declaration of Helsinki. Before the scans were taken, each patient signed an informed consent form for the study.

OCT examination

Huvitz HOCT-1F/1 is a non-invasive, high-resolution OCT; it has a scan range in the fundus X (vertically): 6-12 mm, Y (horizontally): 6-9 mm, and Z (depth): 2.1 mm. It has a scan rate of 68 kHz and a super luminescent laser diode with a wavelength of 840 nm. The resolution in tissue is 20 μm lateral and 7 μm on the z-axis. It performs segmentation of seven retinal layers. The 3D acquisition time is 1.4 s. The fastest mode on the instrument is composed by 512 A-scans and 96 B-scans (Huvitz HOCT-1F/1 manual, 2016).

Procedure

The same order of measurements was followed throughout the entire study and each subject was measured on the same day. The Huvitz HOCT-1F/1 Auto Tracking program was used for all the measurements. Notably, if artefacts are found, the scan is retaken. Between every measurement, the subject was reseated in front of the device. To ensure comfort, no flash light on fundus was used, only OCT images in OCT mode. Every subject gazed at an internal fixation target in the machine. To optimise OCT signals, the scan examiners instructed the subjects to look at the internal fixation target without blinking and then the optimised button was pressed.

To evaluate Huvitz HOCT-1F/1 repeatability, two separate manual measurements were performed by Examiner 1. To evaluate the reproducibility, Examiner 2 took one manual measurement and compared this with one of the measurements made by Examiner 1. Moreover Examiner 2 performed one more measurement with the Auto Shoot program. When Auto Shoot is on, the machine automatically optimises images when the patient's eye is in position and focusses on the fixation spot. The image is taken automatically when fixation and eye position is right,

without any influence from the examiner. Before the measurement was performed with Auto Shoot, the joystick was pulled back to the default position. The Huvitz HOCT-1F/1 Auto Shoot program reliability was evaluated by comparing Auto Tracking (manual measurement made by Examiner 1) and Auto Shoot program (automatic measurement made by Examiner 2).

Interpretation of the images was made after the scan was taken and after further evaluation, consequently a decision made if the scan is good enough to proceed with. For total macular thickness, the B-scan segmentation was set between inner limiting membrane (ILM) and retinal pigment epithelium (RPE). The exclusion criteria for the B-scan are artefacts, segmentation errors and ocular pathologies. Examples of artefacts include shadows from blinks and floaters, segmentation errors from vitreomacular traction and epiretinal membrane (Hardin et al., 2015). An infrared image of the macular thickness map was studied and artefacts and pupils within the measurements zone were excluded. Signal strength ≤ 5 were also excluded.

The data on macular thickness grid was analyzed. The grid itself is divided in 9 zones as in the ETDRS as shown in Figure 1 (Woijtkowski et al., 2005).

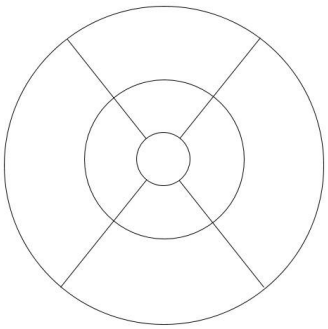

Figure 1: Illustration of ETDRS macular grid

Statistical analysis

All statistical analyses were performed using Matlab, GraphPad Instat3, and Excel. Repeatability, reproducibility, and reliability were evaluated in terms of intra-class correlation coefficients (ICCs). The ICCs come in various forms. For the evaluation of repeatability, a two-way mixed effect, absolute agreement and multiple measurement test was used. Meanwhile, for reproducibility and reliability, a two-way random effect, absolute agreement, and mean of two observers test was used (Koo & Li, 2016) In general, lower variations between measurements generates higher ICC values where ICC values less than 0.5 are indicative of poor reliability. Values between 0.5 and 0.75 indicate moderate reliability; values between 0.75 and 0.9 indicate good reliability; and values greater than 0.9 suggest excellent reliability (Koo & Li, 2016). ICC is a measure of both correlation and agreement between measurements and is therefore better to use when examining the reliability of a new instrument (Koo & Li, 2016).

In Instat3, all the data passed normality test and a paired t-test was performed. Two-tail p-values were calculated. For all statistical analyses, the significance threshold was set to $p < 0.05$. In Excel the mean difference, standard deviation and maximum difference in macular thickness within the 9 zones were calculated. Maximum difference is the largest single difference between the measurements that stood out in one zone.

Results

This study analyzed data from 65 eyes. A total of 16 were excluded. 12 were excluded after the first data compilation due to tabulation errors. The remaining other four, were excluded due to segmentation error, artifacts, pathological change and one subject could not attend all measurements. The mean of signal strengths on all measurements is 7, with values ranging from 5 to 8. The following tables present the mean value, the mean difference and standard deviation and maximum difference, and the p-value and ICC of macular thickness. Table 1 shows results regarding (i.e. only one examiner); Table 2 outlines results regarding reproducibility in Table 2 (i.e. with two examiners); while Table 3 presents the result regarding reliability in Table 3 (i.e. with two examiners).

Table 1. repeatability of macular thickness

	MeanE11	MeanE12	Mean difference	Max difference	P-value (two-tail)	ICC
Central (µm)	230.22±16.74	229.25±16.52	0.97±4.58	29	0.10	0.96
Inner inferior (µm)	306.89±12.84	307.82±12.88	-0.92±3.41	12	0.03	0.96
Inner nasal (µm)	308.51±14.38	308.80±14.36	-0.29±2.77	11	0.40	0.98
Inner superior (µm)	311.86±13.21	312.29±13.75	-0.43±4.19	26	0.67	0.95
Inner temporal (µm)	296.94±12.29	297.05±12.66	-0.11±2.04	7	0.59	0.99
Outer inferior(µm)	262.29±12.67	262.54±12.75	-0.25±4.38	26	0.65	0.94
Outer nasal (µm)	293.15±13.74	293.00±14.08	0.15±3.17	22	0.70	0.97
Outer superior (µm)	271.92±13.52	271.71±12.48	0.22±6.32	29	0.79	0.88
Outer temporal (µm)	252.23±11.90	253.32±11.82	-1.09±4.00	24	0.03	0.94

P < 0.05 indicates statistically significant difference

ICC = intraclass correlation coefficient

E11 = examiner 1, measurement 1 E12 = examiner 1, measurement 2

As shown in Table 1, for repeatability, the overall mean difference in macular thickness, ranged from 0.11 µm (inner temporal) to 1.09 µm (outer temporal). The maximum difference for repeatability varied from 7 µm (inner temporal) to 29 µm (central and outer superior). Significant difference was found in the outer temporal and inner inferior sectors. Meanwhile, ICC ranged from 0.88 (outer superior) to 0.99 (inner temporal).

Table 2. reproducibility of macular thickness						
	MeanE2	**MeanE11**	**Mean difference**	**Max difference**	**P-value (two-tail)**	**ICC**
Central (µm)	229.65±16.35	230.22±16.74	0.57±4.91	32	0.36	0.98
Inner inferior (µm)	308.06±13.27	306.89±12.84	-1.17±3.95	22	0.02	0.98
Inner nasal (µm)	309.40±14.53	308.51±14.38	-0.89±3.27	13	0.03	0.99
Inner superior (µm)	312.52±13.73	311.86±13.21	-0.66±4.97	25	0.29	0.97
Inner temporal (µm)	297.49±12.80	296.94±12.29	-0.55±2.99	16	0.14	0.99
Outer inferior (µm)	262.74±12.27	262.29±12.67	-0.45±4.03	12	0.38	0.97
Outer nasal (µm)	293.59±13.79	293.15±13.74	-0.43±2.55	12	0.18	0.99
Outer superior (µm)	271.75±12.63	271.92±13.52	0.17±6.34	29	0.83	0.94
Outer temporal (µm)	252.71±12.03	252.23±11.90	-0.48±3.32	15	0.26	0.98
P < 0.05 indicates statistically significant difference						
ICC = intraclass correlation coefficient						
E2 = examiner 2, measurement 1 E11 = examiner 1, measurement 1						

Table 2 on reproducibility shows that the overall mean difference in macular thickness ranged from 0.17 µm (outer superior) to 1.17 µm (inner inferior). The maximum difference for reproducibility varied from 12 µm (outer inferior and outer nasal) to 32 µm (central). There is significant difference in the inner inferior sector and in the inner nasal sector. Notably, ICC ranged from 0.94 (outer superior) to 0.99 (inner nasal, inner temporal and outer nasal).

Table 3. reliability of macular thickness						
	MeanE2auto	**MeanE11**	**Mean difference**	**Max difference**	**P-value (two-tail)**	**ICC**
Central (µm)	229.51±16.22	230.22±16.74	0.71±5.14	33	0.80	0.98
Inner inferior (µm)	307.95±12.68	306.89±12.84	-1.06±4.10	18	0.04	0.97
Inner nasal (µm)	309.03±14.43	308.51±14.38	-0.52±3.24	11	0.20	0.99
Inner superior (µm)	312.60±13.96	311.86±13.21	-0.74±5.19	24	0.26	0.96
Inner temporal (µm)	297.34±12.74	296.94±12.29	-0.40±3.09	15	0.30	0.99
Outer inferior (µm)	262.59±12.82	262.29±12.67	-0.29±5.00	23	0.64	0.96
Outer nasal (µm)	293.52±14.02	293.15±13.74	-0.37±4.57	22	0.52	0.97
Outer superior (µm)	272.40±12.28	271.92±13.52	-0.48±6.65	29	0.57	0.93
Outer temporal (µm)	253.23±11.66	252.23±11.90	-1.00±4.46	21	0.08	0.96
P < 0.05 indicates statistically significant difference						
ICC = intraclass correlation coefficient						
E2auto = examiner 2, measurement with Auto Shoot program E11 = examiner 1, measurement 1						

Table 3 on reliability reveals that the overall mean difference in macular thickness ranged from 0.29 µm (outer inferior) to 1.06 µm (inner inferior). The maximum

difference for reliability varied from 11 μm (inner nasal) to 33 μm (central). A significant difference was noted in the inner inferior sector. Meanwhile, ICC ranged from 0.93 (outer superior) to 0.99 (inner nasal and inner temporal).

Discussion and conclusions

The purpose of this study is to evaluate the new Huvitz HOCT-1F/1 for macular thickness measurement. We found that the machine has high repeatability, reproducibility and reliability based on the measurements of all macular thickness areas. On average, the mean difference between repeated measurements is within 1.2 μm for all parameters. In some areas, the differences in values show statistical significance for repeatability, reproducibility, and reliability. Conversely, p-values are highly affected by outliers in the measurement data in all patients, while ICC values are not (Koo & Li, 2016). For this reason, ICCs are of more interest in our study for the validation of the machine. The data values of ICC should ideally range between 0.75 and 0.9. In summary, the ICC for repeatability, reproducibility and reliability are greater than 0.88 in all the total macular thickness values. The lowest ICC value (0.88) is found on repeatability.

Our study demonstrated that when the same investigator takes repeated measurements, the values are comparable. Hong et al. (2019) showed high repeatability for normal eyes on average macular thickness. Hong et al. (2019) also compared repeatability between SS-OCT and SD-OCT in eyes with different retinal diseases and normal eyes with measurement of central macular, RNFL and GC-IPL thickness. The ICC values for macular thickness in the study exceeded 0.99 for SD-OCT. Our values are not completely in line with this; nonetheless, it still shows low variation, ranging from 0.88 to 0.99, which is a good starting point when evaluating a new machine. This can be compared to a previous study by Brautaset et al. (2016) who showed that the automatic tracking function generated higher repeatability.

The results for reproducibility show excellent reliability with values over 0.9, which indicates high accuracy and precision. This is important as in a clinical setting, different examiners use the same machine, and patients undergo longitudinal follow-up. The study of Liu et al. (2014) compared SD-OCT instruments in normal eyes a custom-built Ultrahigh-resolution OCT and RTVue100 OCT. The ICC value of reproducibility was high i.e., 1 and 0.99. Values from our data follows the same trend of good reproducibility ranging from 0.94 to 0.99.

A fundamental question is whether measurements are more reliable when an examiner makes the measurement or when the automatic software program has been used. The ICC values show that the Auto Shoot program performs against the Auto Tracking program used for all the other measurements; both obtained ICC values of 0.99. Auto Shoot has an ergonomic and time saving advantage and is therefore recommended. Moreover, the measurement is more rapid, the examiner spends less time with the joystick looking for good focus.

The aim of the current study is to evaluate the instrument and not every individual measurement of the participants. However, it is important to remember that when clinically evaluating a change in thickness, the overall thickness of the individual must be assessed. A thickness change of 23 μm can be of greater importance to a patient with a thinner macular thickness of <250 μm than to one with a thickness between 250-400 μm (Krzytolik et al., 2007). The maximum difference for repeatability is 29 μm; for reproducibility 32 μm; and for reliability, 33 μm. The resolution of Huvitz HOCT-1F/1 is 7 μm and values below this should be considered with caution. Repeatability for Huvitz HOCT-1F/1 is good; the differences that depend on the machine are, in clinical practice, not significant. The measurements can be replicated.

The anatomy and topography of a normal macula must be known to recognize pathological changes. This study shows that Huvitz H-OCT-1F/1 was able to confirm normal anatomy of macular thickness. The thinnest part of the macula is the fovea (central ring of EDTRS grid). Next zone including the foveal wall (middle ring of the ETDRS grid) also match the fact that the GCL layers is extra thick and then thins out in the periphery (outer ring of the ETDRS grid). Other factors that matter when measuring macular thickness include the difference between the retinas structure avascular zone and vascular zone. Conversely, this does not seem to have affected the result because of the low variability between each measurement.

Various factors that may have affected our results could be patient dependent (dry eye), examiner error (incorrect image alignment), or machine dependent (Hardin et al., 2015). Stein et al.'s (2016) study showed that dryness can affect the scan quality. Therefore, artificial tears were used in cases of excessive blinking, dry eye problem, and difficulty taking a good scan. When measurements were performed, the normative database was not installed in the OCT. Notably, the study was performed on a prototype of Huvitz HOCT-1F/1, and this may have affected the outcome. All data collected in the machine were constantly used to improve the segmentation algorithm and generate changed limit values, which could have influenced the result in a positive direction if the data had been collected after updating of the database. In our study we chose a B-scan of 96. The machine has B-scan values up to 128. We do not believe our results had been different by choosing a denser B-scan. This is confirmed by Velaga et al.'s (2017) study, showing that only B-scan values below 16 affects the retinal thickness measurements. Presumably the study's ICC values had been better, with a scan protocol of 6X6 mm area. This is only speculative, and no study has been found to support this. It is possible that an area of 6X6 mm can generate a higher resolution and a greater depth penetration, with the same number scan but in a smaller area. Interestingly, 6X6 mm area seems to be the standard protocol in many studies.

Low signal strength can mask preexisting pathological thinning of the retinal nerve fiber layer and is also an important indicator of good quality OCT images (Hardin et al., 2015). The mean of signal strengths on all measurements in the current study is 7, with strengths ranging from 5 to 8, which indicates that our measurements are of good quality. According to the Huvitz HOCT-1F/1 manual (2017),

signal strength between 5 and 8 is normal. A theory is that a signal strength of 5 in Huvitz HOCT-1F/1 can correspond to a higher signal strength in another machine and that the manufacturer has a more generous limit for signal strength compared to several other manufacturers.

The current study was performed on healthy eyes, but it would be interesting to learn whether the ICC values would still high on subjects with retinal disease. Consequently, it determines whether the machine could be a tool for monitoring disease progression and explore how well the segmentation algorithm works. We therefore recommend further research with the Huvitz HOCT-1F/1 segmentation on GC-IPL and RNFL layers because they are used as biomarkers for retinal disease (Hong et al., 2019). Patel et al.'s (2009) study of patients with neovascular age-related macular degeneration showed segmentation errors in 90% of the patients and recommended manual measurements of central macular thickness. Several other studies also found that pathological change can compromise measurements (Chen & Kardon., 2016; Hong et al., 2019). In future studies on Huvitz HOCT-1F/1, we would like to see a repeatability study on the Auto Shoot program, which would further increase the reliability of the setting of the machine.

We have the following general recommendations for use of OCT it is important that the person measuring knows how a good and normal OCT image should look like and what is needed to achieve this. The interpretation requires a good image and an experienced assessor. Hence patient should not leave the clinic until the image quality has been assessed. It is always up to the investigator to assess the quality. Use the fundus image to get an overview of the eye and consider the quality of the fundus image. Always compare the right and left eyes, to detect abnormal differences. Anyone who carries out the assessment of the image should be familiar with potential pitfalls. For diseases that can cause segmentation error, always go through segmentation and see that the lines behave normally. If not, use manual segmentation. Look at the overall picture when you value the image.

About guidelines for future use of Huvitz HOCT-1F/1, we recommend that anyone who performs measurements should receive sufficient instruction. The Auto Shoot program particularly requires some training. Always have the joystick pulled back before starting the Auto Shoot scan. When measured values deviate from normal range, start by taking another scan and then go through the segmentation. Determine if this value is reasonable and compare it with total macular thickness. Remember that the version of the program affects the values, and this should be considered when recording values. Always compare the measurement values in the machine instead of in the journal.

Is Huvitz HOCT-1F/1 adequate for detection, diagnosis, and follow up?

We found a high intra class correlation between intra- and inter individual measurements, as well as measurements with different settings when measuring the macular thickness in nine macular areas in healthy subjects. The Huvitz HOCT-1F/1 should be further investigated for detection and follow up of macular disorders and pathological eyes in regular clinic.

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Appendix

Appendix 1 Research plan

Appendix 2 Information about participation in research studies

Appendix 3 Consent to participation in research study

Appendix 4 Huvitz Optical Coherence Tomography HOCT-1F / 1, user manual, Revision A

All appendixes are in Swedish.

Appendix I

Forskningsplan/Projektplan

Hur är repeterbarheten och reproducerbarhet i macula med Huvitz Optical Coherence Tomography -1F/1 med autotracking program?

Frågeställning:

Har Huvitz OCT en bra repeterbarhet (på maculas tjocklek)?

Hur är reproducerbarheten på Huvitz OCT (maculas tjocklek)?

Hur är reliabilitet (tillförlitligheten) mellan mätningar med autoshot och manuell dvs autotrack?

Syfte:

Syftet med studien är att utvärdera Huvits repeterbarhet och reproducerbarheten på friska ögon, genom att mäta maculas tjocklek, med Huvitz automatiska autotrack-program. Samt även bedöma reliabilitet av autoshot funktionen.

Varför är det relevant att göra denna studie?

Huvitz OCT är en ny maskin på marknaden och därför är det av intresse att utvärdera undersökningens kvalitativa mätdata. Och få svar på frågan ifall om instrumentet är tillförlitligt eller inte.

Det finns just nu ingen färdig databas med normalvärden i maskinen att relatera studiens mätvärden till, men förhoppningsvis är databasen färdig för användning under hösten 2018.

Repeterbarheten av macula har kliniskt betydelse för att tidigt upptäcka, diagnostisera och kunna följa en behandling. Reproducerbarheten syftar till att jämföra olika undersökares mätningar. Reliabiliteten utvärderar tillförlitligheten av mätdatan med olika mätprogram på OCT:n.

Material/Metod:

Insamling av mätdata genomförs tillsammans med fyra andra grupper.

Inklinationskriterier för studien är 30 friska ögon, i ålder 18-50år. Kön noteras.

Försökspersoner får inte ha en tidigare historik av ögonsjukdomar eller systemsjukdomar. Det undviks genom att kontrollera försökspersonernas OCT bilder efter mättillfället. Då utesluts patienter med patologiska förändringar, låg signalstyrka (mindre än 5) och segmentations fel.

Mätningen tas med autotrackprogram två gånger på endast höger öga. Detta av undersökare 1 vid båda mätningarna.

En mätning med autotrackprogram på höger öga utförs av undersökare 1, jämförs med mätningar av båda ögonen av undersökare 2. (Vi behöver endast jämföra höger ögat för statistik mellan två olika undersökare).

Undersökare 2 gör en autoshot på höger öga och jämförs med undersökare 1 autotrack mätning av endast höger öga.

Statistik Analys

ICC-values.

Svårigheter

Huvits är ett nytt instrument, har det utvärderats ordentligt? Finns andra studier på Huvitz?

Finns det studier om maculas tjocklek?

Svårt att jämföra eller hitta studier på maculas tjocklekslager då ett flertal studier fokuserat på ett specifikt lager eller papillen.

På grund av ovana vid hantering av OCT mätningar. Går det då att lita på resultatet? Svårigheten är att exkludera rätt vid tex. segmentations fel (floaters, blink).

Etiska frågor
Under studien noteras födelseår och kön. Patienten får ett kodat namn som sparas för utvärdering av mätdata. Uppgifterna läggs in i en mapp via Spike. Om något patologiskt eller onormalt upptäcks vid mätningstillfället, bokas patienten in för vidare utredning.

Namnuppgifter, telefonnummer, ålder samlas in. Alla personer som är med i studien får innan mätning läsa igenom informationsblankett och skriva på en samtyckesblankett.

Tidsplan:
TID FÖR DISKUSSIONER MED HANDLEDARE OCH ATT SKRIVA FORSKNINGSPLAN

(läsa artiklar, påbörja inledning och metoddel, komma överens med övriga grupper om när vi ska utföra våra mätning)

26/9, 14:20 inplanerad diskussion med Alberto, sammanställa frågor och skicka innan möte.

5/10 Lämna in forskningsplan (maila till handledare)

11/10 Presentation av projektplan - Du berättar din ide, max 5 min

TID FÖR DATASAMLING

22/10 23/10 26/10 inbokat med övriga grupper.

Mål: att utföra alla våra mätningar innan 14/12

14/12 Statistik, hur ska du analysera din data? Workshop Lista de frågeställningar du vill ha svar på.

TID FÖR SAMMANSTÄLLNING AV DATA OCH DATAANALYS

23/1 Presentera dina preliminära resultat, max 5 min.

TID FÖR ATT SKRIVA SAMT FÖRBEREDA PRESENTATION OCH OPPOSITION

4/3 Lämna in ditt skriftliga arbete till handledare och opponent

14-15/3 Muntlig presentation och inlämning av opponering i skriftligt format

16/3-9/4 Planera in tid för återkoppling på det skriva arbetet med handledare

TID FÖR REVIDERING

10/4 Slutgiltig inlämning till handledare

23/4 Slutgiltig inlämning till examinator

Appendix 2

Information inför deltagande i forskningsstudierna

Nedan ger du ditt samtycke till att delta i studierna där vi undersöker främre och bakre segmentet med hjälp av två OCT maskiner (Huvitz HOCT-1F/1 och Cirrus HD-OCT). En mätning av biomikroskopering samt autorefraktor tillkommer. Metoderna är icke invasiva. De kvalitativa resultaten jämförs för bedömning av instrumentens tillförlitlighet.

Syfte

Syften är att utvärdera Huvitz OCT repeterbarhet och reproducerbarhet med avseende på maculas och optiska diskens tjocklek samt papillära nervfiberlaget. Utöver detta kommer vi även jämföra med ovan beskrivna mätningarna med Cirrus OCT.
I en av studierna jämförs mätningarna av tårmeniskens storlek med Cirrus OCT samt mätningar utförda med biomikroskop.

Deltagande

Ni har blivit tillfrågade att delta i dessa studier efter att ha varit i kontakt med en av försöksledarna. Att delta i studierna är helt frivilligt.

Genomförande

Deltagandet i studierna innebär ett besök på St. Eriks ögonsjukhus i Stockholm som tar cirka 30 minuter. Vid besöket finns det möjlighet att ställa frågor om undersökningarna.
Det finns inga risker förenade med undersökningsmetoderna. Deltagarna måste komma utan kontaktlinser för att inte påverka resultatet. Ordningsföljden av metoderna är enligt nedan. Efter första mätningen droppas varje patient med ögonsmörjande droppar.

1. Tårmeniskens storlek jämförs mellan biomikroskåpet och Cirrus OCT
2. Jämföra mätningar mellan Huvitz och Cirrus
3. Repeterbarhet, reproducerbarhet samt reliabilitet studeras i Huvitz med avseende på peripapillära nervfiberlagret samt macula och optiska diskens tjocklek.

Ersättning

Efter deltagandet i studierna utgår kompensation i form av fika och godis.

Sekretess

Samtliga svar och resultat behandlas så att inte obehöriga kan ta del av dem. Ansvarig för personuppgifter är Karolinska Institutet. Endast de forskare som är knutna till studierna kommer att ta del av uppgifterna. Original av samtycke, protokoll, formulär och resultat hanteras av försöksledarna vid magisterutbildningen på optikerutbildningen på St. Eriks ögonsjukhus. Resultat sparas och sammanställs elektroniskt i anonymiserad form. Enligt personuppgiftslagen (1998:204) har du rätt att begära ett utdrag på de uppgifter som sammanställts om dig, vid eventuella felaktigheter ska dessa korrigeras.

Frivillighet

Deltagandet i studierna är helt frivilligt och kan närsomhelst avbrytas. Att inte vilja delta eller att avbryta ett deltagande påverkar inte sedvanlig behandling eller omhändertagande. Vid avbrutet deltagande kommer alla ditintills insamlade uppgifter att förstöras.

Resultat

Resultaten från studierna kan komma att publiceras i vetenskapliga tidskrifter. I det som publiceras kommer inte något att finnas med som kan härledas till dig som deltar. I samband med deltagandet kommer ni att tillfrågas om ni önskar att ta del av resultaten.

Ansvar

Forskningshuvudman för studierna är Karolinska Institutet. Ansvarig forskare är Maria Nilsson (maria.nilsson@ki.se) och Alberto Dominguez (alberto.dominguez.vicent@ki.se). Personuppgiftsansvarig är Karolinska Institutet. Deltagande i studierna täcks av patientskadeförsäkringen. Om sjukliga förändringar hittas vid undersökningarna, kontaktas du personligen för vidare bedömning.

Kontakt

Om du har frågor angående studierna och ditt deltagande så kontakta gärna någon av försöksledarna nedan.

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Appendix 3

Samtycke till deltagande i forskningsstudie

Nedan ger du ditt samtycke till att delta i studien där vi undersöker främre och bakre segmentet med hjälp av två olika OCT maskiner. Den kvalitativa mätningen jämförs sedan för bedömning av instrumentens tillförlitlighet. Ytterligare en mätning av biomikroskopering tillkommer. Metoderna är icke invasiva.
Läs igenom detta noggrant. Fyll i mail och telefonnummer och ge ditt medgivande genom att skriva under med din namnteckning längst ned.

Medgivande

- Jag har tagit del av informationen kring studien och är medveten om hur den kommer att gå till och den tid den tar i anspråk.
- Jag har fått tillfälle att få mina frågor angående studien besvarade innan den påbörjas och vet vem jag ska vända mig till med frågor.
- Jag deltar i denna studie helt frivilligt och har blivit informerad om varför jag har blivit tillfrågad och vad syftet med deltagandet är.
- Jag är medveten om att jag när som helst under studiens gång kan avbryta mitt deltagande utan att jag behöver förklara varför.
- Jag ger mitt medgivande till att Karolinska Institutet lagrar och bearbetar den information som insamlas under studien.
- Jag ger detta medgivande förutsatt att inga andra än de forskare som är knutna till studien kommer att ta del av mina personuppgifter.

Stockholm den … / … 2018

…… ……

Telefonnummer	E-post
……	……
Namnteckning	Namnförtydligande

Appendix 4

Huvitz Optical Coherence Tomography HOCT-1F/1, user manual, Revision A, 2017