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COMPARISON OF INTRAOCULAR PRESSURE MEASUREMENT WITH GOLDMANN APPLANATION TONOMETRY AND WITH ICARE

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Populärvetenskaplig sammanfattning

Grön starr, eller glaukom, är en ögonsjukdom som ger miljoner människor runt om i världen synnedsättning eller blindhet. Ett förhöjt tryck i ögat är en riskfaktor och en sänkning av det den enda bevisade metoden att bromsa sjukdomen. Ögontryck mäts hos dessa patienter för att följa den trycksänkande behandlingen och Icare är en snabb mätmetod som används mer och mer. Det verkar dock som att mätvärdena skiljer sig från de man får med Goldmanns mätmetod som anses vara den gyllene standarden för mätningar. Därför är det av intresse att undersöka om båda metoderna är tillförlitliga och användbara i kliniskt arbete.

I studien gjordes upprepade mätningar med endera mätmetoden varefter variation och mätfel jämfördes, med målsättningen att ta redan på om mätfelet var detsamma för de båda metoderna och att utvärdera om metoderna var kalibrerade till varandra. Totalt gjordes 120 mätningar fördelade på 20 försökspersoner. Tre mätningar gjordes två dagar efter varandra på varje försöksperson med en av metoderna. För att få oberoende mätningar var det två separata grupper.

Mätvärdena med Icare var något högre och mer spridda än de med Goldmanns mätmetod. Den uppskattade variansen för mättillfällen var sju gånger högre med Icare och för mätfelet tre gånger högre, och skillnaden mellan metodernas medelvärde var 2,4 mmHg.

Slutsatsen blev att variationen och mätfelet inom metoden var högre för Icare och att tillförlitligheten i mätningar därmed inte var lika hög som med Goldmanns mätmetod. Mätmetoderna var inte heller helt kalibrerade till varandra.

Abstract

Background/introduction

Glaucoma affects millions of patients around the world and causes blindness and visual impairment. Elevated intraocular pressure is a risk factor and a reduction can slow progression down. Thus, measurements are important to surveil glaucoma patients. Icare is increasingly being used to determine eye pressure and it is desirable to know whether Icare is reliable.

Purpose

The purpose of the study was to evaluate whether the variation due to measurement occasion and measurement errors was the same for both methods, and if the methods were calibrated against each other.

First time mentioned in abstract

Method

This study was conducted on healthy humans as a prospective observational study with 20 participants in a hierarchical model.

Results

The estimated variation in measurements were three times lower with Goldmann application tonometry than with Icare, and seven times lower among occasions. The difference between the means was 2.4±0.9 mmHg, with the Icare value higher than the GAT value.

Conclusion

The variance in measurement error and the variance due to occasion was lower with Goldmann application tonometry, and therefore the reliability was different between the methods and lower in Icare. The methods were not calibrated to each other.

Abbreviations

GAT – Goldmann applanation tonometry, IOP – Intraocular pressure, NCT – Non-contact tonometry

Background

Intraocular pressure

The eye can be seen as an approximate sphere surrounded by the strong sclera of connective tissue. The intraocular pressure (IOP) is built up by the fluids inside the eye, as the force on the inner surface of the anterior eye. Since other structures such as the vitreous and the lens, have a relatively constant volume, the IOP varies with the volume of aqueous humor produced by the ciliary body in the posterior chamber of the eye and the level of outflow. The production of aqueous humor follows the circadian rhythm, with the peak production rate in the morning, then lower in the afternoon and lowest at night (Koskela & Brubaker, 1991). IOP is not constant, but varies along with hemodynamics and cardiac pulse with a median ocular pulse amplitude of 3 mmHg (Kaufmann et al., 2006). The aqueous humor flows between the lens and the iris into the anterior chamber. The major part drains through the trabecular meshwork, Schlemm's canal, the aqueous veins and the episcleral veins back to the hemodynamic system (Johnson, 2006). If the IOP is elevated it expands the trabecular meshwork and Schlemm's canal collapses with increased outflow resistance (Johnstone & Grant, 1973). Aside from the trabecular outflow a smaller amount of aqueous humor drains through uveoscleral outflow (Bill & Phillips, 1971). The human body changes over time and in the aging human eye there is a decrease in the production and drainage of aqueous humor (Toris et al., 1999). Among individuals with elevated IOP the use of topical ocular hypotensive medication can reduce the IOP (Kass et al., 2002). Different microinvasive, classical and laser, surgery treatments can be done to different parts of the physiological drainage system to reduce IOP (Andrew et al., 2019). Trabeculectomy as a surgical procedure had been evaluated over a time span of 20 years and found to be a good solution to reduce IOP over time (Landers et al., 2012).

Glaucoma

There are millions of patients around the world affected by glaucoma which causes blindness and visual impairment, and although cataract is the leading cause of blindness in the world, glaucoma is the major cause of blindness in most of the developed countries (Resnikoff et al., 2004). The reason for the difference is cataract surgery in the developed countries. Glaucoma is classified into two subtypes, the more common open-angle glaucoma and the less common angle-closure glaucoma, and also divided into primary and secondary, of which the latter results from trauma, inflammation, medications, tumor and other conditions (Weinreb et al., 2014). The subtypes are named after the iridocorneal angle. Open-angle glaucoma is responsible for three quarters of the cases and although

being less common, angle-closure glaucoma causes almost half of the glaucoma related blindness (Quigley & Broman, 2006). Glaucoma can be described as a multifactorial optic neuropathy, where the optic disc is damaged and visual field loss is observed (Mantravadi & Vadhar, 2015). It has a multifactorial etiology and is clinically a group of ocular disorders united by an IOP associated optic neuropathy (Casson et al., 2012). The main risk factor for development and progression, with increased visual field loss, is elevated IOP, which is measured as a clinical parameter (Kass et al., 2002). Although associated, elevated IOP is a risk factor for glaucoma and not the definition of the disease (Anderson, 1989). Reduction of the IOP by topical ocular hypotensive medication, surgery, or laser, is the single proven method to slow glaucoma progression down (Kass et al., 2002). Glaucoma patients with a normal IOP also benefits from hypotensive treatment to slow visual field loss progression down (Oie et al., 2017).

Measurement of eye pressure

IOP is literally the pressure inside the eye that should be measured in some way. The true IOP can be invasively measured with a manometric device, such as a pressure sensitive transducer (Pallikaris et al., 2005). For obvious reasons, this is not practically useful in daily routine work at the clinic and therefore IOP is usually estimated using a non-invasive method. Hence, IOP is measured as an estimate of the difference between the atmospheric pressure and the true pressure inside the eye. The most basic method is manual palpation which is subjective and fairly reliable (Troost et al., 2005). In the mid-19th century, the development of tonometers began, based on the indentation of the eye produced by a load from a weight or a spring, and later in the same century applanation tonometry was developed based on the principle of corneal flattening, although the devices developed were difficult to use and unpopular (Stamper, 2011). The first useful applanation tonometer was the GAT, developed by Goldmann in 1950's (Goldmann & Schmidt, 1957). GAT is still widely used and considered as the "gold standard" for IOP measurements. Some other methods used are the portable Tonopen (Mckay-Marg tonometer), the air-puff tonometry performed with a non-contact tonometer (NCT), and the Icare rebound tonometer (Stamper, 2011). Investigation of the inter-device agreement among GAT, NCT, Icare and Icare PRO rebound tonometers and Tonopen XL shows good agreement among GAT, NCT and rebound tonometers, but lower agreement between Tonopen XL and the other four (Kato et al., 2018). Good intra-device agreement is also found and evaluated with calculation of intraclass correlation coefficients out of three sets of consecutive measurements at one time, but however, all study subjects are investigated with all methods at a single occasion (Kato et al., 2018). A good correlation between measurements with GAT, Icare ONE and Icare HOME is shown, as well

as good correlation between Icare performed by both the patients and by an ophthalmologist (Rosentreter et al., 2011). The methods of interest in this study is GAT and Icare which are described below.

Goldmann applanation tonometry

Goldmann applanation tonometry (GAT), developed in the 1950's, is based on applanation, which refers to the force required to flatten the central part of the cornea and to balance it with the pressure inside the eye. A prism on a sensor arm mechanically transfers the applanation force to the tonometer, the force is adjusted, and a measurement value is read on a scale. The prism has a diameter of 3.06 mm to equalize the effects of corneal elasticity and tear surface tension. The GAT is designed and calibrated to the fixed area of the prism. (Goldmann & Schmidt, 1957).

GAT is with low variability, both inter- and intra-observer, the "gold standard" for intraocular measurement (Choudhari et al., 2009). The downside with GAT is the need of an experienced ophthalmologist, a biomicroscope with a slit-lamp, and a patient that cooperates well. It is also of relevance to use topical fluorescein and anesthesia together with the GAT (Bright et al., 1981). Corneal thickness is a factor that affects the GAT measurements, with underestimation of IOP in thin corneas and overestimation in thick corneas (Ehlers et al., 1975). Calibration errors beyond the manufacturers recommended tolerance is another issue when GAT is used (Choudhari et al., 2009).

Icare rebound tonometry

The Icare is based on rebound, which refers to the motion and impact when a probe launched to the eye collides and bounces back (Kontiola, 1996). When bouncing back the deceleration of the magnetized probe induces voltage in a solenoid, which is measured and then returns a calculated IOP (Kontiola, 1996). Studies show that measurements with Icare correlate well with measurements with GAT (Rosentreter et al., 2011; van der Jagt & Jansonius, 2005). Even inexperienced examiners are shown to get accurate values from measurements with the Icare (Abraham et al., 2008). Corneal thickness affects the Icare measurements, with underestimation of IOP in thin corneas and overestimation in thick corneas (Brusini et al., 2006). The advantages with Icare are that there is no need for topical anesthesia or fluorescein, it is handheld, portable and can be used outside the examination room. There is also an Icare for self-tonometry, developed to be used by the patients themselves (Rosentreter et al., 2011).

Aim

In the ophthalmology department, Icare is increasingly being used as a quick way to determine eye pressure. The measurement is performed by an optician or a nurse when the patient arrives at the eye clinic. This serves as a screening method and GAT can be used if the values are abnormal. Usually eye pressure is measured with one measurement at one occasion. But the measurements done with Icare subjectively appear to be different from those done with GAT. Thus, it is of importance to evaluate whether the variation due to measurement occasion and measurement errors is the same for both methods. Furthermore, it is desirable to find out if the methods are calibrated against each other. It would be of importance to know whether both methods are reliable and therefore could be used at the clinic.

In summary, the primary aim of this study is to compare variations ~~within measurements~~ between GAT and Icare. The secondary aim is to evaluate the measurement values with GAT and Icare, and how they correspond to each other.

Hypothesis

Primary hypothesis: The ~~measurement error is~~ equal for both methods.

Secondary hypothesis: The two methods are calibrated to each other.

Method

Study design

This study was conducted on healthy humans as a prospective observational study. There were two independent study groups, one for each method. The independency between the groups were necessary to enable the measurement errors to be detected within each group, with the assumption that the unobservable random effects and the error term were independently distributed and with the layout $Y_{ijk} = \mu + \alpha_{(i)} + \beta_{j(i)} + \varepsilon_{k(ij)}$ (Oono & Shinozaki, 2006). The number of study objects, occasions and measurements per occasion were chosen to provide sufficient estimates of the causes of variation. Method was a fixed factor, and study object, occasion and measurement were random factors. No cross-examination between the methods were done and no control objects participated.

> ← Purpose to compare methods, no need of control group

Study model

> better to use subjects, try to replace all.

The study was set up as a hierarchical model, originating from the two methods GAT and Icare. The study population was a total of 20 study objects, of which half were assigned to each method. This was done without freedom of choice as every other study object was assigned to either method, in the same order as they signed up for the study.
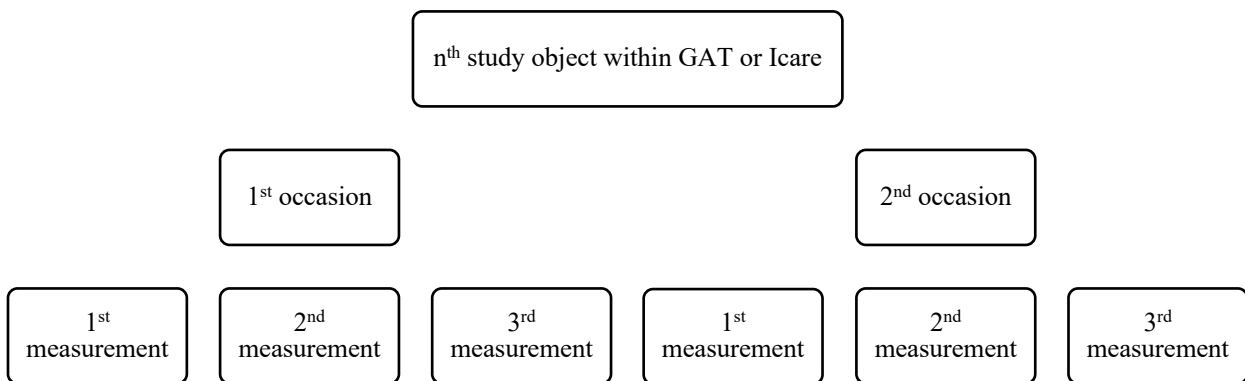
	nth study object within GAT or Icare	

1st occasion		2nd occasion

1st measurement	2nd measurement	3rd measurement	1st measurement	2nd measurement	3rd measurement

Figure 1. The hierarchical model of the study. Structure showed after the assignment of study objects to one of the methods.

Assigned to either GAT or Icare, the study objects were examined twice during two consecutive days, 1st and 2nd occasion, and at each occasion three measurements with one of the two methods were done, 1st, 2nd and 3rd measurement.

Participants

The study population was recruited amongst voluntary and healthy medical students at Uppsala University. The volunteers were asked for known eye diseases and were excluded if there were any that could affect their eye pressure or the measurement of it. Contact lens wearers were also excluded due to practical reasons.

Equipment

The two methods used to collect measurement data were GAT and Icare rebound based tonometry.

To perform the GAT a BM 900 biomicroscope with a slit-lamp, an attached AT 900 applanation tonometer (Haag-Streit AG), a Tonup sterile single use applanation prism (CSO Srl) and topical fluorescein and anesthesia eye drops (Minims®, fluorescein sodium 0.25 % and lidocaine hydrochloride 4 %, Bausch & Lomb) were used.

To perform the Icare rebound based tonometry an Icare TA01i Tonometer and single use probes (Icare Oy) were used.

Measurements

Goldmann applanation tonometry

The GAT was used and handled according to the instructions of professor Per Söderberg. First the study object was seated, and eye drops with lidocaine and fluorescein was applied in the eye of interest for measurements without pressure on the eye. The study object was told to twinkle, and excess of the eye drops was wiped away. Then the slit-lamp of the biomicroscope was turned on with the cobalt blue filter applied and the diaphragm fully opened at an angle of 45 degrees, and the oculars were adjusted to match my visual impairment. The single use prism was put in the correct position. The study objects head was set in position with the jaw and forehead placed in correct position. The biomicroscope was moved to get the prism into correct position straight in front of the center of the study objects cornea, and then slowly applied onto the cornea. The adjustment knob was turned clock- and counterclockwise until the green semicircles' inner edges matched. Then the biomicroscope was removed and the measurement value recorded.

Icare

The device was turned on, loaded, and handled according to the instructions in the manual. The measurements with the Icare were done as explained hereafter. First the measuring button was pressed to start the device and then the single use/disposable probe was carefully inserted into the probe base.

The measuring button was pressed to complete the loading, and the Icare tonometer was ready for use when '00' appeared on the display. To obtain adequate measurement values the study object was seated in an upright relaxed position and told to look straight forward at a certain point to keep the eye steady. The forehead support knob was adjusted to obtain the correct distance, 4 – 8 mm between the cornea and the probe, with the central groove in a horizontal position. The Icare tonometer was held in position in front of the patient's eye, with the probe in front of the central part of the cornea, as central as possible. The measuring button was lightly pressed, and the probe bounced at the cornea. The device indicated each rebounding probe, disregarded those considered as incorrect, and calculated a mean after six successful measurements discarding the highest and lowest. When the IOP was shown in the display the mean value could be seen and recorded. (Icare Finland Oy, 2015)

Procedure and data collection

The voluntary study objects came to the ophthalmology clinic at Uppsala University Hospital, where they were informed about the study and then signed the written informed consent. The study objects were assigned to one of the two methods, every other following the order in which they signed up for the study. After the participants came to the examination, measurements of eye pressure were performed on one eye, three times in a row, with a short break of four to five minutes between the measurements. The next day at about the same time of the day, the study objects returned, and a new set of measurements was made. GAT and Icare were used as described in the previous section, and eye pressure measurement data was recorded in a Microsoft Excel spreadsheet.

Statistical analysis

The age of the study objects was processed with descriptive statistics, as maximum, minimum, median and mode. The age distribution was also checked for outliers according to Tukey's fences. The distribution between right and left of the eyes examined was described and the distribution between the sexes was checked. The measurement values collected were showed in a table and described with the distribution for the both occasions, and as a boxplot for the two methods and occasions separated, described with maximum, minimum, mean, sample standard deviation, median and mode. The measurement data was also checked for outliers according to Tukey's fences.

The model was hierarchical, and a factorial analysis of variance was performed. The obtained values were used to further calculate variance components which were presented in a table. Comparison between the estimated measurement errors of the two methods and the variation between occasions between the two methods was done.

The calibration between the methods was investigated by estimating confidence intervals for each method and for the mean difference between the methods. The α-value was set to 0.05.

Analysis was made through manually performed calculations in Microsoft Excel office 365 version 16.33 and thereafter controlled with the IBM SPSS Statistics version 25 software.

Ethical approval

This degree project was accomplished as a student project, no patient journals were required, and no publication was planned. Both methods were non-invasive, harmless to the study objects, and clinical routine methods and all study objects also signed a written informed consent. The project was therefore not sent for approval by the Swedish Ethical Review Authority.

Results

Descriptive results

Study objects

The 20 study objects were all recruited amongst medical students at Uppsala University and they were distributed within the methods as follows. In the GAT group 7/10 were female, and in the Icare group they were equally distributed between the sexes. The right eye was examined in all cases, except one in the GAT group in which case the left eye was examined as the study object felt more comfortable with that.
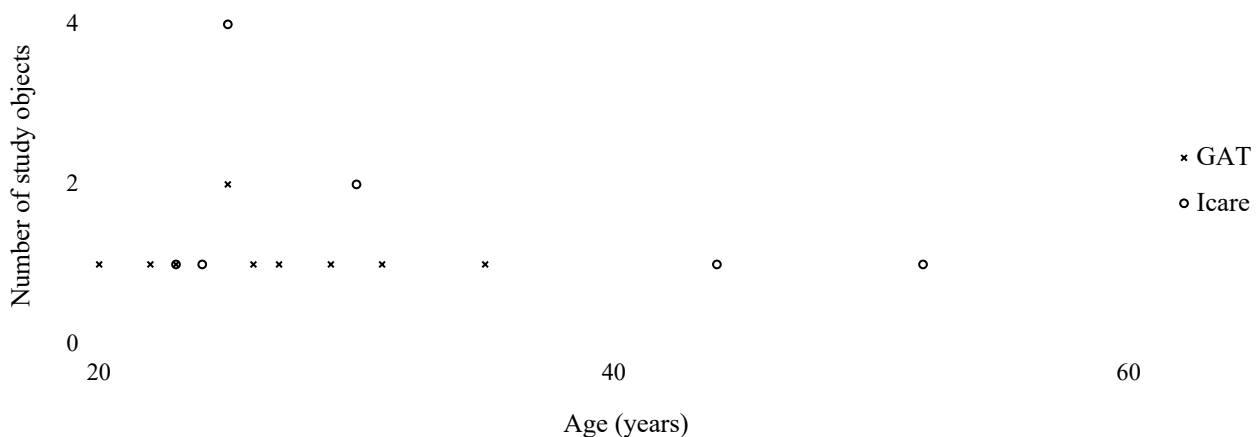

Figure 2. Age distribution of study objects at the first occasion.

The age of the study objects ranged from 20 to 35 years in the GAT group and from 23 to 52 years in the Icare group. The medians were similar with 25.5 years and 25 years, respectively, and both groups had the same mode of 25 years. The few older study objects skewed the age distribution, although only the oldest study object qualified as an outlier.

Description of data

All data were collected as integers and entered in an Excel spreadsheet. Measurements with GAT were read and estimated to the nearest integer from the scale with only even numbers, and readings from the Icare were displayed and read as integers. The measurement values were processed and visualized in Table 1 and Figure 3 to 5.

Table 1. IOP values by method, study object, occasion and measurement.

	Occasion	1			2		
	Measurement	1	2	3	1	2	3
Method	Study object within methods						(mmHg)
GAT	1	14	14	13	15	13	13
	2	8	10	11	11	12	10
	3	10	12	11	14	15	13
	4	13	12	12	14	12	11
	5	9	10	9	9	9	10
	6	15	13	13	14	13	14
	7	14	14	14	13	12	11
	8	13	11	12	13	10	12
	9	14	12	12	13	12	11
	10	10	10	9	11	9	10
Icare	1	15	17	14	23	19	17
	2	20	16	16	13	15	17
	3	13	9	10	13	9	11
	4	18	17	14	13	14	13
	5	16	13	15	12	12	13
	6	16	18	15	11	11	11
	7	15	16	14	10	11	12
	8	11	11	11	13	12	9
	9	19	13	15	17	15	18
	10	17	15	16	14	15	16

Three measurements were made within each of the two occasions, within each of the ten study objects, within each of the two methods which gave 120 values. Each study object belonged to only one method according to the hierarchical study design and therefore the measurements were independent.
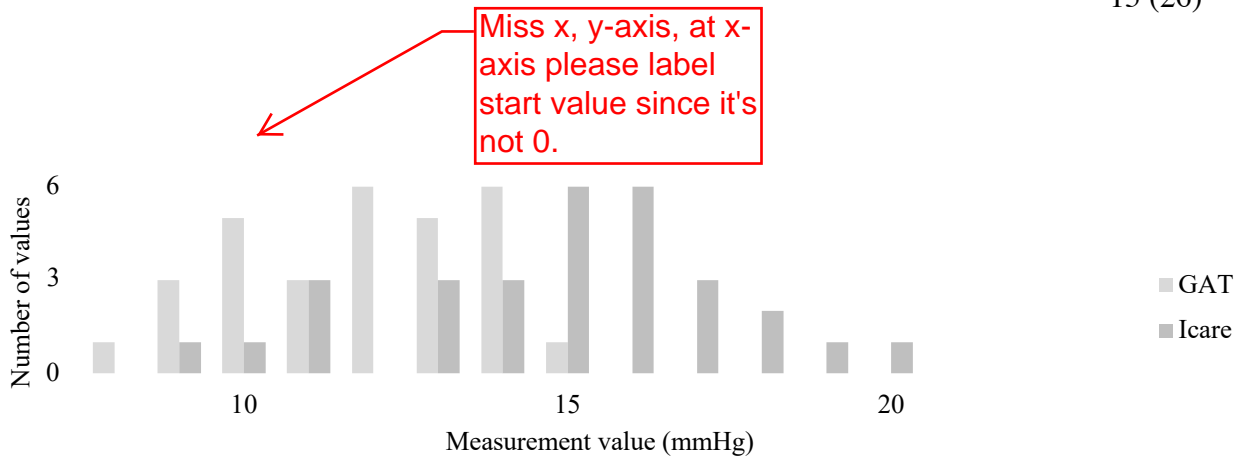
Miss x, y-axis, at x-axis please label start value since it's not 0.

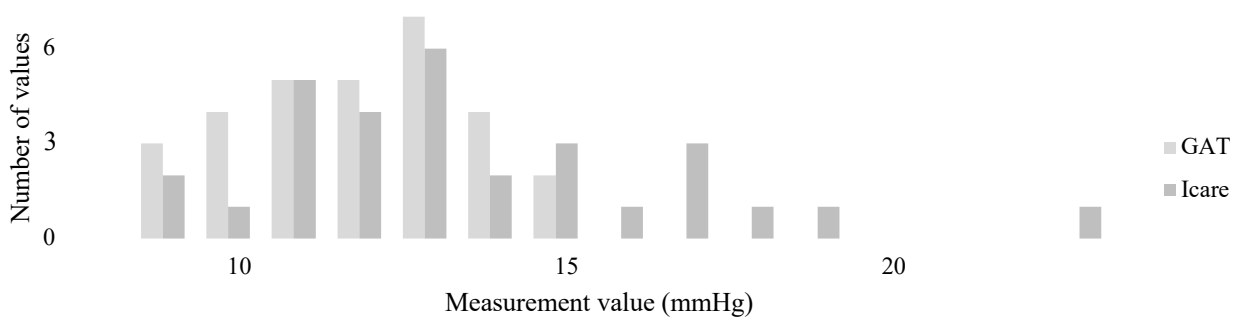**Figure 3.** Distribution of measurement values, first occasion.

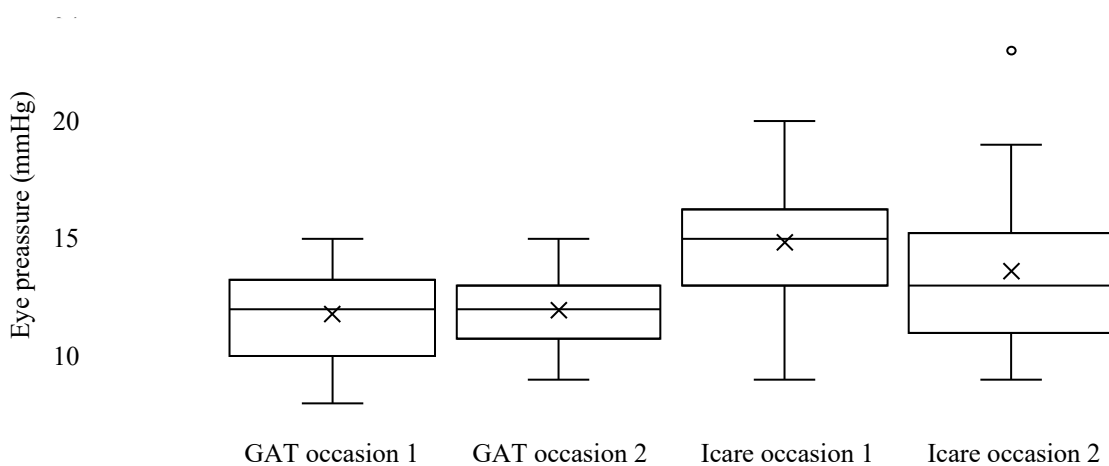**Figure 4.** Distribution of measurement values, second occasion.

Figure 5. Boxplot of measurement values. Methods and occasions separated.

In the GAT group, data ranged from 8 to 15 mmHg and 9 to 15 mmHg and in the Icare group, data ranged from 9 to 20 mmHg and 9 to 23 mmHg, for the first and second occasions. The single Icare value of 23 in the second occasion qualified as an outlier. In the GAT group the mean value and sample standard deviation were 11.9 (1.8) mmHg overall, 11.8 (1.9) mmHg for the first occasion and

12.0 (1.8) mmHg for the second, equivalently in the Icare group the mean value and sample standard deviation were 14.2 (2.9) mmHg overall, 14.8 (2.6) mmHg for the first occasion and 13.6 (3.1) mmHg for the second. The medians were similar with a consistent value of 12 mmHg for GAT, and 14, 15 and 13 mmHg for Icare, overall, first and second occasion. The modes were also in the close range to the means and medians with values of 13, bimodal 12 and 14, and 13 mmHg for GAT, and bimodal 13 and 15, bimodal 15 and 16, and 13 mmHg for Icare, described as overall values, and first and second occasion values. In summary the values of the measurements were more scattered and higher with Icare than with GAT, where they were lower and in a smaller range.

Statistical analysis

Estimated variance components

Study objects, occasions and measurements were random factors and therefore expected to be different, and method was a dependent factor. Since the model was hierarchical a factorial analysis of variance was calculated, and the obtained values were used to further calculate estimated variance components for each method.

Table 2. Estimates of variance components in IOP measurements.

Variance components (mmHg)^2	Methods	
	GAT	Icare
Occasions	0.44	3.28
Measurements	1.00	2.95

The estimated variation among occasions for IOP with GAT was 7 times lower than the estimated variation with Icare. Among measurements the estimated variance was 3 times lower with GAT than with Icare.

Confidence intervals for the methods

Confidence intervals were estimated for each of the methods with the α-value set to 0.05. The study design with independent groups for both methods, gave two independent sets of measurement values, from which the calculations were made. ~~Statistical values were calculated directly from all measurements, and the values were not pooled to neither occasion nor study object.~~
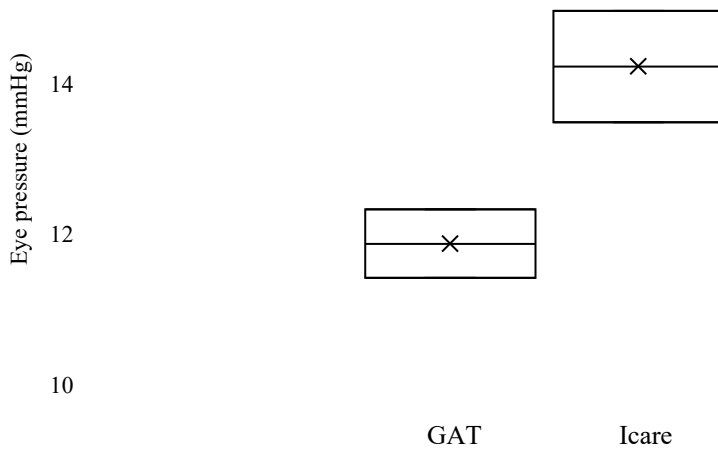
Figure 6. 95 % confidence intervals of the methods. The boxes show the mean values and the upper and lower limits of the 95 % confidence intervals.

The 95 % confidence intervals for each method's mean eye pressures were 11.9±0.5 mmHg for GAT and 14.2±0.7 mmHg for Icare.

Confidence interval of the mean difference between the methods

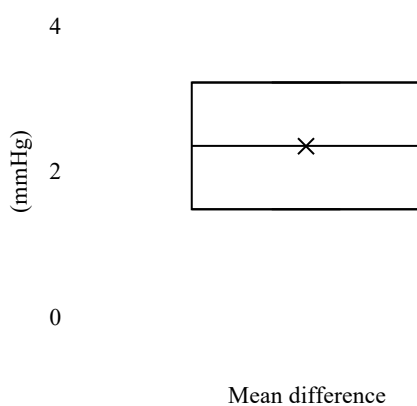A confidence interval was estimated for the mean difference of the methods with the α-value set to 0.05.

Figure 7. 95 % confidence interval of the mean difference between the methods. The box shows the mean value and the upper and lower limit of the 95 % confidence interval.

The difference between the means and the 95 % confidence interval was 2.4±0.9 mmHg.

Discussion

Results

It's better to mention about purposes again since the text is quite long and readers may get lost.
Before discussion about results it usually start with explaining study method (why two independent groups), gender, age. Only normal and most young subjects included, so conclusion only for normal pressure population. Due to time limit, no age groups also. Only one eye included since it didn't aim to compare between eyes. Some texts later can be moved here

Summary of results

The overall mean value and sample standard deviation were 11.9 (1.8) mmHg in the GAT group, and 14.2 (2.9) mmHg in the Icare group. The difference between the mean values of the two occasions were 0.2 mmHg and 1.2 mmHg, GAT and Icare respectively. The measurement values obtained with GAT were less scattered and lower than those obtained with Icare where the measurement values were higher and in a wider range. The estimated variance components in IOP measurements were 7 times lower with GAT than with Icare among occasions and 3 times lower among measurements. The 95 % confidence intervals for the mean eye pressures were 11.9±0.5 mmHg for GAT and 14.2±0.7 mmHg for Icare, and for the difference between the means it was 2.4±0.9 mmHg.

Variance components

The estimated variance components among measurements were 3 times lower with GAT than with Icare. The measurement values were closer together for GAT and therefore the measurement error was smaller. If all the measurement values had been equal, there would have been a variance component of zero and no measurement error in the analysis. The estimated variation components among occasions were 7 times lower with GAT compared to Icare. The model with random factors, independent groups and the variance components implicated that the variance due to occasion was larger in the Icare group.

Agreement of measurements were found to be statistically significant lower in repeated measurements separated by two weeks, with Icare compared to GAT (Davies et al., 2006). In this study the time span between the occasion were one day, but the agreement between the occasions still were lower with the Icare. Since the variation in measurements was analyzed from independent groups corneal thickness or other physiological factors of the examined eyes would not affect the analysis of the estimated variations. The circadian rhythm with differences in aqueous humor production was another factor to consider (Koskela & Brubaker, 1991). Thus, the examinations were performed at about the same time of the day to minimize the impact of diurnal variations. The least contact time of rebound tonometry and the effect of the IOP pulse cycle was suggested as the cause of variation (Stamper, 2011). The hemodynamics has been shown to affect the ocular pulse amplitude by a median of 3 mmHg (Kaufmann et al., 2006). Thus, three measurements were made at each occasion. In a study with 65 examined eyes there were also done three consecutive measurements

with Icare and a 0.3 mmHg difference between the means obtained by two different examiners (Salim et al., 2013). The Icare calculated an average value out of four out of six rebounds for each measurement value and the effect of the IOP pulse cycle should therefore have been small.

Correspondence between the methods

The measurement values obtained with Icare were higher with a wider distribution than those obtained with GAT. The estimated 95 % confidence intervals for mean eye pressures of the two methods did not overlap and the 95% confidence interval of the sample mean difference between the methods did not contain zero, but ranged from 1.5 to 3.2 mmHg, with a mean of 2.4 mmHg. Therefore, the difference between the corresponding means was statistically significant and the mean difference of the population would be in that range. The fact that this study was performed with two independent groups, unlike all previous studies found where all study objects were examined with both methods, made the comparison between the methods difficult. However, in a study with 103 study objects, both healthy and with ocular hypertension or glaucoma, the 95 % confidence interval of the sample mean difference ranged from 0.0 to 1.2 mmHg and a better agreement between the methods was shown (van der Jagt & Jansonius, 2005). A sample mean difference of 0.6 mmHg was found on a study of 126 examined eyes and the agreement was found to be good (Rosentreter et al., 2011). Means out of three consecutive measurements when performed by 2 two examiners on 65 glaucoma patients were 14.5 mmHg for GAT and 16.9 mmHg for Icare, with a mean difference of 2.45 mmHg similar to this study (Salim et al., 2013). The IOP measured with Icare was slightly higher and with a wider distribution than with GAT but not statistically significant among 109 glaucoma patients (Vincent et al., 2012). In a Swedish study there was clinical implications among 18 % of the 45 glaucoma or ocular hypertension patients with a statistically significant mean difference between Icare and GAT of 1,5 mmHg (Rehnman & Martin, 2008). The mean difference between Icare and GAT in a 153 patients sample, was 0.9 mmHg for IOP readings below 21 mmHg and -0.5 mmHg for IOP readings from 21 mmHg and above, and the corneal thickness was 1 mmHg higher for each 100 μm with Icare compared to GAT (Pakrou et al., 2008). Thus, the patients eye pressure and corneal thickness affects the agreement between the methods. Further, thick corneas has been shown to increase the deviation with Icare from GAT, while normal or thin corneas did not (Rao et al., 2014). In another study of 178 glaucoma patients the Icare value was increased by 0.7 mmHg by each 10 μm increase in corneal thickness (Brusini et al., 2006). All study objects in this study were in the normal range of ocular pressure and thus the Icare readings might be slightly overestimated and corneal thickness was not measured and could have affected the correspondence between the methods. Icare was found to be favorable to GAT when used by inexperienced health care workers

with reasonable accuracy (Abraham et al., 2008). Another advantage with the rebound tonometry was that the Icare for self-tonometry also showed good correlation, especially amongst contact lens wearers, to GAT and Icare performed by experienced ophthalmologists (Rosentreter et al., 2011).

Strengths and limitations

The hierarchical model with two independent groups and measurements with only one method in each examined study object minimized the physical impact on the eye and bias of the eye pressure due to manipulation should have been lower than other studies with multiple measurement methods. However, there were three consecutive measurements done at each examination. The study objects were also randomly assigned to either method to limit bias. Since the study objects were healthy without known eye disease the eye pressures were in the normal range and the study did not evaluate any elevated eye pressures. In the aging human eye production and drainage of aqueous humor decrease (Toris et al., 1999). Most of the study object were young adults with only two older than 40 years and the aging effects should have been low on the measurements. Other studies often include glaucoma patients and patients with elevated eye pressure.

Since I performed the measurements after only short training, there should be taken into consideration that the measurements probably differ from those who would have been made by a trained professional. This would possibly affect the GAT more since that method was considered as more difficult to perform for unexperienced health care workers (Abraham et al., 2008). The Icare was considered as easy to use with consistent readings and no learning effect was found throughout a study of almost 300 eyes (Pakrou et al., 2008). Another factor to be taken into consideration was that I did not use the same equipment for GAT or Icare for all measurements. It was not possible to obtain continuity in this aspect throughout the study because of the usual daily work at the ophthalmology clinic. The risk here was if the equipment used were not calibrated and maintained correctly according to the manufacturer's instructions and therefore gave non-correct readings. Frequent calibration errors were found and only 4 % were within the manufacturer's recommended tolerance in a study (Choudhari et al., 2009).

Conclusion

The difference in variance components showed that the primary hypothesis of equal measurement errors was false and that the measurement errors were larger with Icare. The measurement values obtained with Icare were also higher with a wider distribution than those obtained with GAT. The

secondary hypothesis in this study was shown to be false and the methods were not fully calibrated to each other.

Thus, the Icare seemed to be useful as a clinical tool for screening and for monitoring a patient's eye pressure. The method has been shown to be easy to learn, could be used without any fluorescein and anesthesia and together with its portability it could be clinically useful. However, it would be of importance to note in the medical record which measurement method was used when measurements of a patient's eye pressure were done. There must be considered that patients with eye pressure out of the normal range probably should be examined with GAT.

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