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CLINICAL METHOD OF CALCULATING OPTICAL NERVE HEAD VERTICAL DISC HEIGHT

Farah Razack Moti

A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, in the fulfillment of the requirements for the degree of Master of Medicine in Ophthalmology

Johannesburg, September 2013

DECLARATION

I hereby declare that this dissertation is my own unaided work. It is being submitted for the degree of Master of Medicine in the branch of Ophthalmology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other University.

Signed *F R Moti* 

This _ 01 _day of __September__2013

The work reported in this dissertation was carried out in the Department of Ophthalmology, St John Eye Hospital (Chris Hani Baragwanath Hospital Complex), Johannesburg, South Africa.

The project was approved by the Ethics Committee of the University of the Witwatersrand (Appendix A)

For Uzayr,
Who made me strive for perfection

To my parents, Razack and Amina
My sisters, Rabia and Nooren-Nisa
My brother, Mohamed
For their endless, loving, unwavering support

PRESENTATIONS ARISING FROM THIS STUDY

Registrar presentation at the Ophthalmological Society of South Africa (OSSA) Congress in Cape Town, South Africa, March 2013

TITLE: CLINICAL METHOD OF CALCULATING OPTIC NERVE HEAD VERTICAL DISC HEIGHT

PRESENTER: Farah Razack Moti

ABSTRACT

OBJECTIVES: There is large variability between individuals on many measurable parameters of the optic disc. The retinal fundus is most commonly measured indirectly via slit-lamp biomicroscopic examination with a fundus spherical lens.
Three optical methods of measuring the vertical disc height were compared:

- Optical Coherence Tomographic (OCT) method
- Calculation using a modified Littman's equation: t = pqs
- Measurement using five different double aspheric Volk fundus lenses on two different slit lamps (Haag-Streit and CSO)

The aims of the study were:

- To calculate a conversion equation of optic disc height measurement by clinical assessment using any one of five double aspheric fundus lenses at the slit-lamp
- To compare the control mechanism of optic disc height measurement on OCT versus calculation using a modified Littman's equation
- To compare measurements between the Haag-Streit BM900 and CSO SL990 slit lamps
- To compare accuracy and agreement of Volk conversion factors based on manufacturer magnification values to the control mechanism

DESIGN & METHOD: A cross-sectional study was performed on patients presenting to the St John Eye Hospital from August '11 to July '12. 100 eyes were measured for:

- The optic nerve head vertical disc height on OCT
- Vertical disc height (VDH) on Haag-Streit and CSO slit lamps with Volk super 66D, 78D, Superfield, Digital Wide Field, Digital High Magnification lenses
- Axial length
- Refraction

Subsequently, 44 new eyes were measured and used to test agreement of the formulated equations.

RESULTS:

- Axial length was not found to have a correlation with VDH (p=0.64).
- The modified Littman's equation: t=pqs where p varies for each lens and q = 0.01306(axial length – 1.82), had very low correlation and poor agreement
- Comparing formulated equations to the OCT VDH, the formulated Digital High Magnification and super 66D lenses were found to have the most accuracy
- Measurements with the Volk Digital Wide Field lens were highly inaccurate and are therefore not recommended for vertical disc height measurement in future
- Comparison of the fundus lens measurements using the two slit lamps showed alarmingly different results. There was no agreement between slit lamp measurements using four of the lenses

CONCLUSIONS:

- The use of axial length and other quantitative factors attained by measures of a schematic eye cannot be used accurately in clinical practice to determine fundus object sizes.
- The slit lamp technique of measuring optic disc size with application of a simple equation yields useful results in close agreement to those yielded by expensive technology. It cannot replace accurate analysis using an OCT but is sufficient in aiding clinical decisions
- Two important factors need to be taken into account when applying slit lamp fundus measurements: the type of lens used, and the slit lamp being used – as measurement standards are inconsistent between slip lamps

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2. Professor Elena Libhaber for her patience and statistical guidance.

3. My colleagues at St John Eye Hospital for supporting me during my process of data collection

4. Dr Antonio dos Ramos for planting the begins of the idea

PERSONAL CONTRIBUTIONS

I, Dr Farah Moti, designed, obtained ethics clearance for and executed this study.

I performed the slit-lamp examinations with the five different fundus lenses.

I performed the Ultrasound axial length measurements.

I performed the Ocular Coherence Tomography (OCT) measurements and analysis.

Statistical contribution: Statistical advice was sought from Professor Elena Libhaber and Dr Nabiha Tayob, however I performed all data capture and statistical analysis myself using Microsoft Excel for Mac 2011, and the statistical programme STATA12.

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LIST OF ABBREVIATIONS

HS	Haag-Streit BM 900 slit lamp
CSO	Construzione Strumenti Oftalmici SL990 slit lamp
AL	Axial length
OCT	Optical Coherence Tomographer
VDH	Vertical Disc Height
OCT VDH	OCT vertical disc height
OCT VDH2	Optical coherence tomography vertical disc height for replication data set
D66	Volk Super 66D lens
D78	Volk 78D lens
SF	Volk Superfield NC lens
DHM	Volk Digital High Mag lens
DWF	Volk Digital Wide Field lens
Eqn	Formulated equation for respective lenses
Rho_C	Lin's concordance correlation coefficient
C_b	Rho_C/Pearson's r (measure of accuracy)

CHAPTER 1

1.1 INTRODUCTION

The optic nerve head, or optic disc, is the terminal part of the optic nerve that is visible on fundoscopic examination. There is much normal inter-individual variability in the many measurable parameters of the optic disc, for example the vertical and horizontal diameters and total area. The optic cup is a whitish central area within the optic disc, so-named because of its cup-like shape. The area between the optic cup and the optic disc margin is the neuroretinal rim. Further parameters of the optic disc include the cup: disc ratio (calculated using the diameters of each part respectively), the cup area and neuroretinal rim area. The cup: disc ratio is the most commonly used clinical finding in the screening of glaucoma as the appearance and size of the optic cup are altered by glaucomatous optic neuropathy.

The measure of actual optic disc diameter is valuable in supporting an array of ophthalmological pathogenetic processes as well as part of pre-emptive screening techniques for other diseases. Whilst many new modern techniques facilitate measurement of optic disc parameters, these are expensive, time-consuming and not readily available in all clinical settings.

1.2 RATIONALE

The optic disc is an important part of routine fundus examination. The commonest method of examining the retinal fundus by ophthalmologists is indirectly via slit-lamp biomicroscopic examination with the aid of a fundus spherical lens. An important part of the examination is a determination of the optic disc size.

There are two key factors:

- Different lenses are manufactured with differing magnification properties, which result in different recorded measurements of optic nerve vertical disc height (vertical diameter) with each lens
- Recordable differences are also impacted by the slit-lamp used, its calibration of ruler measurement, and its magnification properties

This study will attempt to calculate correction factors for the most commonly used double-aspheric fundus lenses by registrars at the St John Eye Hospital, as well as whether or not correction factors differ for the Haag-Streit and Construzione Strumenti Oftalmici (CSO) slit-lamps that are used at the hospital.

There is no literature on measurement of the optic nerve vertical disc height with the Volk Digital High Mag and Volk Digital Wide Field lenses; nor has there been comparison of measures using two different slit-lamps.

1.3 LITERATURE REVIEW

1.3.1 Demographic differences in optic nerve head size

There is large physiological variability of the cup: disc ratio because of the large variation in optic disc size. In a normal Caucasian population, inter-individual variability of optic disc area ranges between 0.8mm^2 and 6mm^2 [1]. Other biologic and demographic factors correlating to variability in disc size include race, height, gender, axial length and refractive error[2].

1.3.1.1 Race

People of African descent have been shown to have larger average optic disc size[3]. The ADAGES study demonstrated that optic disc area is 12% larger in the African-American population[3]. The mean disc area, cup area, and vertical and horizontal cup: disc ratios were found to be significantly greater and the neuroretinal rim area: disc ratio significantly smaller in black compared with white patients[4]. Due to their greater optic disc area, larger cup: disc ratios, cup areas, cup depths and cup volumes, racial differences need to be addressed when creating control variables in techniques used to discriminate between normal and abnormal discs[3].

1.3.1.2 Height

Disc area has been shown to increase by 0.02mm^2 with every 10cm increase in height, excluding very tall and very short people as cited by Jonas et al[1].

1.3.1.3 Gender

Gender factors are still uncertain, as some investigators have found no correlation between gender and disc size, whereas others have found males to have a 3.2% larger optic disc than females[1]. In a population based study, Varma *et al* found black males to have larger disc area, cup area, and cup: disc ratios. Amongst the white patients in their study however, there were no consistent differences except for disc area[4]. The ADAGES study found no differences in gender and optic disc parameters[3].

1.3.1.4 Age

In a large population based study of individuals 40 years or older, no statistically significant age-related difference in optic disc parameters was shown[4].

1.3.1.5 Refractive error

Longer axial lengths have a weakly independent correlation with larger disc size ($p<0.035$) [5]. However, the optic nerve head is abnormally large in eyes exhibiting high myopia, therefore longer axial length taken in conjunction with a myopic refractive error of greater than -8 dioptres shows a significant correlation[6]. Optic disc size is also significantly smaller in highly hyperopic individuals of greater than +4 dioptres, leading to the conclusion that optic disc size is mostly independent of refractive error in the range of -8 to +4 diopters[6].

1.3.2 Relevance of the optic nerve head size

The analysis of the optic nerve head and specifically the assessment of the optic nerve head size is an important one in a spectrum of pathologies.

1.3.2.1.1 Glaucoma and optic nerve head

Glaucoma is the leading cause of irreversible blindness worldwide. Open angle glaucoma is an optic neuropathy that is characterised by optic disc cupping and corresponding VF loss, independent of intraocular pressure (IOP). In glaucomatous screening and monitoring of progression of disease, the extent of cupping is determined by relating the size of the optic cup to the size of the optic disc (the cup to disc ratio), and similarly the area of the neuroretinal rim is related to optic disc size[7]. Optic disc cupping typically occurs before VF loss[8]. Up to 40% of optic nerve axons could be lost before a visual field defect develops on Goldmann perimetry. Therefore the optic nerve head cup: disc ratio is an important sign of glaucomatous damage[2].

Intraocular pressure is an established risk factor for glaucoma, but approximately 50% of open angle glaucoma (OAG) patients have an IOP in normal range[10,11,12]. This requires better evaluation of the optic disc and peripapillary retinal nerve fibre layer. IOP cannot therefore be reliably used to detect glaucoma and a thorough evaluation of the optic disc and peripapillary retinal nerve fibre layer are a necessity.

The Ocular Hypertension treatment study and the Rotterdam population-based study have identified a larger vertical cup: disc ratio as a significant predictive factor in the development of primary open angle glaucoma (POAG) [14,15]. The vertical cup: disc ratio is

the most frequently performed clinical assessment of the optic disc. The simplicity of the technique and lack of expense also make it ideal for screening large populations. The highest level of evidence for glaucoma is fulfilled when the vertical cup: disc ratio falls outside the 97.5th percentile or has a rim width reduced to <0.1. The optic cup size is however related to the optic disc size and size is thus an imperative factor to take into consideration every time that the cup to disc ratio is assessed[16]. Subtypes of glaucoma have been correlated to optic disc size. The disc size of subjects with normal-tension glaucoma is significantly larger than primary open angle glaucoma eyes whilst pseudoexfoliative glaucoma subjects had smaller discs though not significantly smaller than primary open angle glaucoma counterparts[2].

1.3.2.1.2 Disc Damage Likelihood Scale (DDLS)

The estimation of cup: disc ratio detects only about 60% of patients suffering from glaucoma whereas nerve fibre layer assessment has been shown to have far higher sensitivity and specificity for early detection of the disease[17].

In many clinical settings, cost factors do not allow for the equipment that is needed to assess nerve fibre layer thinning accurately hence the development of the disc damage likelihood scale (DDLS) (Figure 1) [19]. It is based on the appearance of the neuroretinal rim of the optic disc corrected for disc size. The DDLS has shown better reproducibility than cup: disc ratio for estimating the amount of disc damage[19]. It also correlates very strongly with the degree of glaucomatous visual field damage[20], and systematic evaluations using this scale are at least as specific and sensitive as Heidelberg retina tomography II confocal scanning laser imaging, but at a much lower cost[21]. This

evaluation is only possible if the examination includes a measurement of vertical optic disc diameter.

	The Thinnest Width of the Rim (Rim/Disk Ratio)			Examples		
Stage	Small Disk < 1.5 mm	Average Size Disk 1.5 – 2.0 mm	Large Disk > 2.0 mm	Small Disk	Average Size Disk	Large Disk
0a	0.5	0.4 or more	0.3 or more			
0b	0.4 up to 0.5	0.3 – 0.4	0.2 – 0.3			
1	0.3 up to 0.4	0.2 – 0.3	0.1 – 0.2			
2	0.2 up to 0.3	0.1 – 0.2	0.05 – 0.1			
3	0.1 up to 0.2	0.01 – 0.1	0.01 – 0.05			
4	0.01 – 0.1	no rim < 45 degrees	no rim < 45 degrees			
5	no rim < 45 degrees	no rim 45 – 90 degrees	no rim 45 – 90 degrees			
6	no rim 45 – 90 degrees	no rim 91 – 180 degrees	no rim 91–180 degrees			
7	no rim > 90 degrees	no rim > 180 degrees	no rim > 180 degrees			

Figure 1. The Disc Damage Likelihood Scale (DDLS)[19]

1.3.2.2 Other ocular pathologies

Pathologies such as optic disc drusen, pseudopapilloedema and nonarteritic anterior ischaemic optic neuropathy occur more commonly in smaller optic discs[7]. Larger optic discs are usually associated with optic pits and the morning glory syndrome[7] and are also thought to be more susceptible to glaucomatous optic nerve damage[17].

1.3.4 Measuring optic disc size

All measurements of the optic disc rely on analysis of images of the disc because in vivo, the only direct measurement possible is through vitreoretinal surgery[22].

1.3.4.1 Slit-lamp measurements of vertical disc height

The slit-lamp observation system is focused at a finite, short distance. Light from the fundus exits parallel in the emmetropic eye; hence the slit-lamp cannot focus on the fundus. With the use of an accessory lens, a fundus image is formed in front of the slit-lamp bio-microscope upon which it can be focused[23]. The slit length beam is adjusted using a knob on the mm measuring scale on the illumination head to correspond with the optic nerve head vertical disc height, and the measurement read off the scale. Other subjective measurements of the optic nerve head include horizontal disc diameter, and corresponding vertical and horizontal cup size measurements in millimetres.

The neuroretinal rim of the optic disc is an indirect measure of the optic nerve fibres. The rim is calculated by disc area minus cup area. Usually determined by sophisticated

and expensive equipment, Jonas and Montgomery[7] measured the area of the neuroretinal rim using planimetrically measured horizontal and vertical disc diameters. They concluded that simple linear measurements of disc and cup diameters are sufficient to reliably estimate the neuroretinal rim for clinical purposes[7].

Slit lamp biomicroscopic measurements of optic disc height show an acceptable degree of interobserver variability. Pharmacological mydriasis of eyes prior to measurements has shown to improve interobserver agreement[24]. Discrepancies occur as a result of the slit-lamp used as well as the double aspheric fundus lens used.

The European Glaucoma Society has devised a table, based on the European Optic Disc Assessment trial, assessing the grading of optic discs into small, medium or large dependent on the fundus lens used (Table 1) [25].

Table 1. Grading of optic disc into small, medium or large

	SMALL	MEDIUM	LARGE
Disc Area	<1.6mm^2	1.6 – 2.8mm^2	>2.8mm^2
Volk 60D	<1.65mm	1.65 – 2.2mm	>2.2mm
Volk 78D	<1.3mm	1.3 – 1.75mm	>1.75mm
Volk 90D	<1.1mm	1.1 - 1.45mm	>1.45mm
Superfield	<1.15mm	1.15 -1.50mm	>1.5mm
Super 66D	<1.45mm	1.45 -1.9mm	>1.9mm

(*Adapted from European Glaucoma Society: Terminology and Guidelines for Glaucoma 3rd Edition*[25])

Ruben[26] has calculated a conversion factor for measurement of optic disc height at the slit lamp using the 90D lens (manufacturer not stated): Y = 1.17X + 0.24, where x is the slit lamp measurement and y the actual disc size. Thirty-seven eyes of thirty-seven patients were used and compared to planimetric disc diameter measurements using optic disc photographs. Reproducibility was established by measuring only ten further optic discs[26].

Lim, O'Brien and Bolton[27] did a similar study to work out conversion equations for five lenses namely: Volk 60D, 78D, 90D and Nikon 60D and 90D, using simple regression analysis. Only twenty-five eyes were used and their study control were measurements from the Heidelberg Retina Tomograph[27] that gives slightly smaller optic disc height measurements than stereophotographs, optical coherence tomography or Discam values[16]. No further mechanisms to ascertain accuracy or reproducibility of their equations were performed. Their best-fit equations are as follows:

Volk 60D: Y = 0.85X + 0.06 Nikon 60D: Y = 0.74X + 0.51

Volk 78D: Y = 0.86X + 0.41 Nikon 90D: Y = 0.98X + 0.73

Volk 90D: Y = 0.89X + 0.59

Papastathopoulos and Jonas[28] ascertained simplified conversion factors for the Volk 60D and Volk Superfield lenses as factors of 1.0 and 1.5 respectively. They also found that the refractive error of the eyes does not need to be taken into account as long as it does not exceed a myopic error of -8D. Their study used 125 eyes of 65 patients however their statistical method of calculating the conversion factor was not described and only 10 optic discs were measured thereafter to ascertain reproducibility[28].

Spencer and Vernon[29] compared the absolute measurement of optic disc height with Volk 78D lens and compared it to the optic disc biometer and planimetric results. Twenty-nine eyes of twenty-nine patients were used and simple regression analysis performed. The 78D lens showed better correlation but poor agreement with planimetric measurements, however they suspect that eliminating the manufacturer's magnification factor in their calculations may have attained better agreement. They concluded that for Volk 78D: Y = X/0.86 – 0.41. No further methods were applied to determine reproducibility of the equation[29].

None of the above studies compared measures with different slit-lamps, nor did they use the 5 specified lenses that will be used in the current study.

Based on the Volk manufacturer magnification factors, conversion factors have been concluded for each fundus lens. For the Volk super 66D lens, the magnification factor is 1, hence no conversion necessary; Volk 78D lens magnification factor of 0.93 results in conversion factor of x1.1; Volk Superfield NC lens magnification of 0.76 results in conversion of x1.3; Volk Digital High Mag magnification of 1.3 results in conversion of x0.77; Volk Digital Wide Field magnification of 0.72 results in conversion of x1.4.

1.3.4.2 Quantitative measurements

There have been many technological advances in glaucoma imaging devices used for screening of patients at risk of disease and of increased progression rates. Many new

technologies are available but comparison to subjective stereo-photograph evaluation remains the gold standard[30].

1.3.4.2.1 Confocal Scanning laser Ophthalmoscopy

The baseline stereometric parameters of the Heidelberg Retina Tomograph (HRT) and additional measurements of the Moorfields Regression Analysis (MRA) are as follows:

- The dependence of neuroretinal rim area on optic disc size
- Probability that neuroretinal rim may decline with age
- Thickness of RNFL

In the HRT 3.0, the Glaucoma Probability Score is also available which uses a geometric model to describe the shape of the optic disc; cup size; and cup depth amongst other measurements[30].

1.3.4.2.2 Discam digital optic disc stereocamera

The Discam is a computer-assisted planimetric system that acquires sequential disc photographs in a semiautomatic fashion. The operator dependent part of the process is drawing the definition of the optic nerve head and cup, where after quantitative parameters are calculated[31]. The Discam results, especially for optic disc vertical height, compare favourably with stereo-photographic methods[32].

1.3.4.2.3 Optical Coherence Tomography

Optical Coherence Tomography (OCT), an optical analogue of B-scan ultrasonography, is based on low-coherence light in the near-infrared spectrum (840 nm) and creates sagittal optical tissue sections. OCT provides quantitative measurements of the optic

nerve head and retinal nerve fibre layer (RNFL) via topographic imaging. Very large optic discs have a decreased sensitivity. The best performing disc parameters are cup diameter, cup: disc vertical ratio and cup area. As cited by Li *et al*, other studies consistently confirm cup: disc vertical ratio to be of the best performing parameters. OCT specificity is as high as 96% but sensitivity is moderate for detecting probability of glaucoma disease[33].

As each different ONH imaging modality is based on different technology and different definitions used for locating anatomic sites on the optic disc, significant differences have been found when comparing specific topographic markers. Reproducibility of optic nerve parameters by OCT has however been displayed[34]. Most published studies on ONH topology analysis have been oriented around HRT, with less attention focused on assessing the capability of analysing the optic disc changes in glaucoma using OCT.

Theoretically, OCT is more advantageous over HRT as it offers a higher axial resolution, automated outlining of optic disc margin, and a consistent reference plane for delineation of the neuroretinal rim boundary. The determination of the position of the reference plane is the most essential element in ONH topographic analysis, because accurate calculations of ONH parameters depend heavily on the appropriate choosing and marking of a reference plane. OCT determines the level of the reference plane in relation to the cut-off ends of the retinal pigment epithelium (RPE) around the optic cup, a fixed anatomic landmark, and thus allows a consistent and reproducible estimation of cup–disc boundary and neuroretinal rim area (Figure 7). By default, the reference plane is located 150 μm above the level of RPE, found to be optimal in terms of diagnostic

performance in glaucoma detection and correlation with visual function. Because the reference plane and ONH margin lie at constant positions, subsequent ONH measurements can therefore be analysed with low variability[35]. Inappropriate automated disc recognition can however occur even under 'ideal' examination conditions and manual adjustments need to be made[34].

OCT has become an effective tool in the analysis of retinal nerve fibre layer and optic disc parameters, with theoretical advantages over the HRT.

1.3.4.3 Calculated measurements using specific optical formulae

Aside from imaging, one can obtain a control value of optic disc size for comparison using calculations applying specific formulae. Optic disc area measured planimetrically does not differ from values of the optic disc using the formula of an ellipse[7]. However, the use of spherical error for magnification is less accurate than formulae that use the axial length[16].

There were three key developments in the creation of a formula based approach:

- First, in 1982, Littman developed a formula to determine the size of retinal features by fundus photography: t = pqs where t is the true size of the retinal feature, p is a numerical constant based on the lens or telecentric model used, q is a factor dependent on optical dimensions of a given eye and s is the size of the retinal image measured[36]

- Second, in 1993, Bennet, Rudnicka and Edgar[36] demonstrated that factor q can be determined very simply using the axial length of the eye by an equation: q = 0.01306 (x – 1.82), where x is the measured axial length of the eye[36]. The correction factor q can be used with great accuracy within 20 degrees of the optical axis[37]. It must be noted that contact ultrasound measurements of the axial length underestimate optical measurements by 0.16 to 0.30mm due to shallowing of the anterior chamber by the probe, and it is suggested that a correction for true axial length be made by adding 0.25mm to measurements by this mechanism[22]

- Third, in 2003, Ansari-Shahrezaei *et al*[37] compared the magnification properties of four indirect double aspheric fundus lenses, namely Volk 60D lens, 66 stereo fundus lens, 78D lens, and Superfield NC lens. The total change in magnification is greatest for the 60D lens as p for this lens does not increase from myopia to hyperopia. Factor p calculated in their analyses is 3.04 for Volk 60D lens; 3.56 for Volk 66 stereo fundus lens; 3.69 for Volk 78D lens, and 4.61 for Volk Superfield NC lens[37]

The modified Littman equation is therefore: : t = pqs where

q = 0.01306(axial length – 1.82) and p = 3.56; 3.69; 4.61 for

Volk super 66D; Volk 78D and Volk Superfield NC lenses respectively

1.4 RESEARCH HYPOTHESIS

The were three key thrusts to the research hypothesis:

a) The optic nerve vertical disc height can be measured accurately using indirect fundus lenses at the slit lamp by means of a conversion equation.

b) The optic nerve vertical disc height can be accurately measured by means of an equation incorporating the axial length of the eye, in this case the modified Littman equation.

c) The formulated conversion equation from a) is more accurate than Volk conversion factors based on manufacturer magnification values

1.5 RESEARCH OBJECTIVES

Based on the three research hypotheses, there were four key research objectives:

a. To compare the similarity or dissimilarity between the control mechanism of optic disc height measurement - Optical Coherence Tomography (OCT) versus calculation using a modified formula of Littman's equation

{t = pqs; where q = 0.01306 x (axial length – 1.82) }

b. To calculate a conversion equation of optic disc height measurement by clinical assessment using any one of five double aspheric fundus lenses at the slit-lamp

c. To compare the interchangeability of the two different slit lamps – Haag-Streit BM900 and CSO slit lamp

d. To compare accuracy and agreement of Volk conversion factors based on manufacturer magnification values to the control mechanism of optic disc height measurement with Optical Coherence Tomography (OCT), and agreement of Volk conversion factors to research objective a) conversion equations

CHAPTER 2

2.1 STUDY DESIGN

A cross-sectional study was performed on patients presenting to the St John Eye Hospital between August 2011 and July 2012.

2.2 EXPERIMENTAL METHOD

Prior to this research project being carried out, a protocol was submitted to the Human Research Ethics Committee (Medical) at the University of the Witwatersrand. Ethics was approved and a clearance certificate was issued: Ethics number M110619. (Appendix A)

Patients who qualified for inclusion were approached. Informed consent was obtained from all willing and voluntary participants. A data-capturing sheet was completed and no further follow-up required (Appendix B).

2.2.1 Technique of examination

One hundred eyes of fifty patients were used.

2.2.1.1 Refraction

The patient's visual acuity was measured using a standard Snellen chart and refraction was then measured on all patients by the primary researcher with the Nikon Handheld Auto refractor (Figure 2). All patients had a Visual Acuity between 6/4 and 6/18 and refraction of between -3.00DS and +2.25DS.



Figure 2. Nikon Handheld Autorefractor

2.2.1.2 *Pupil dilatation*

All patients had their pupils dilated with 1% topical tropicamide drops (Figure 3).



Figure 3. Tropicamide 1% topical drops

2.2.1.3 *Axial Length measurement*

Contact ultrasound measurements of the axial lengths of participant eyes were recorded by the primary researcher with the Alcon OcuScan (Figure 4). An additive correction factor of 0.25mm corrected for the underestimations made by contact ultrasound mechanisms of measuring axial length.

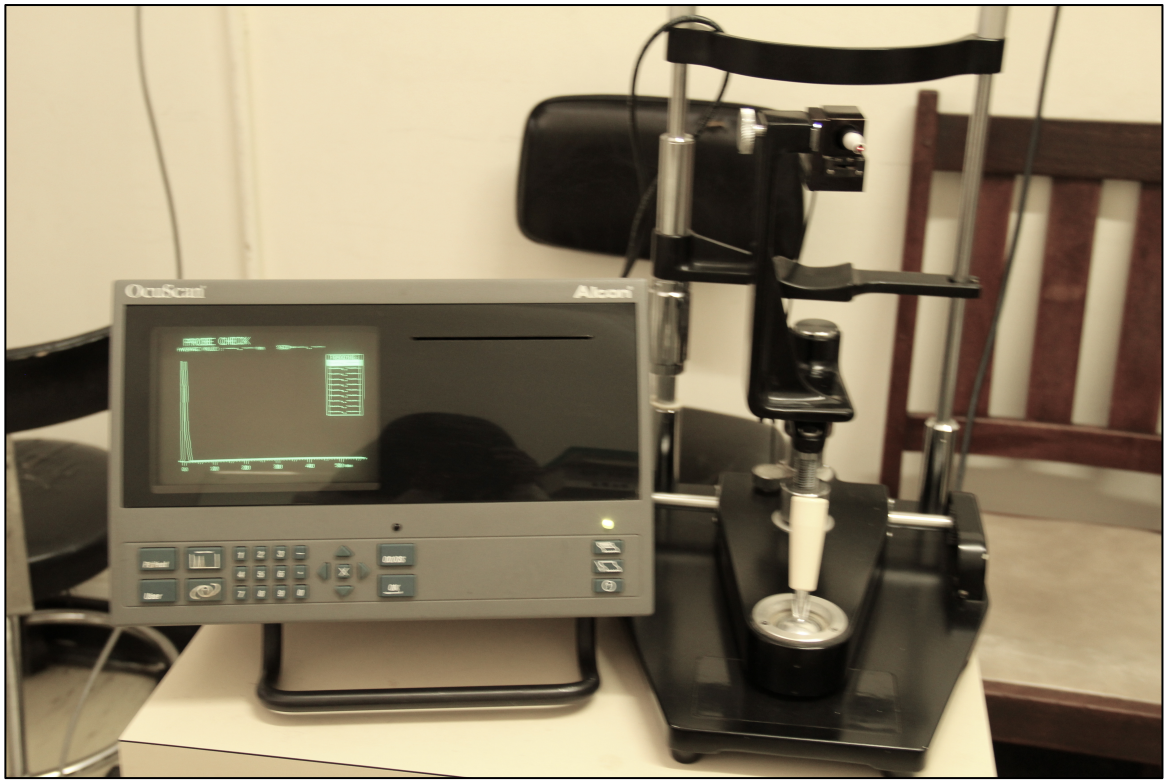


Figure 4. Alcon Ocuscan

2.2.1.4 Optical Coherence tomography measure of vertical disc height

Two measurements using the Optopol Copernicus Stratus High Resolution Optical Coherence Tomographer (OCT) (Figure 5) were taken of each eye by the primary researcher. The mean of the two separate measurements of vertical disc height was used as the gold standard vertical disc height measure. Good quality images were ensured with all Q values > 4. The optical Q is equal to the ratio of the resonant frequency to the bandwidth of the cavity resonance. Higher Q values indicate a lower rate of energy loss of frequency per bandwidth.

In some cases automatic determination of ONH borders (Figure 6) resulted in discs of irregular and unnatural shape and size. In a separate session, all discs and scans per disc were studied and manually redrawn when appropriate. Cup-offset was left unchanged. indicates correct OCT evaluation of the optic disc height as the distance between the ends of the retinal pigment epithelium on either side of the disc.



Figure 5. SOCT Copernicus HR by Optopol

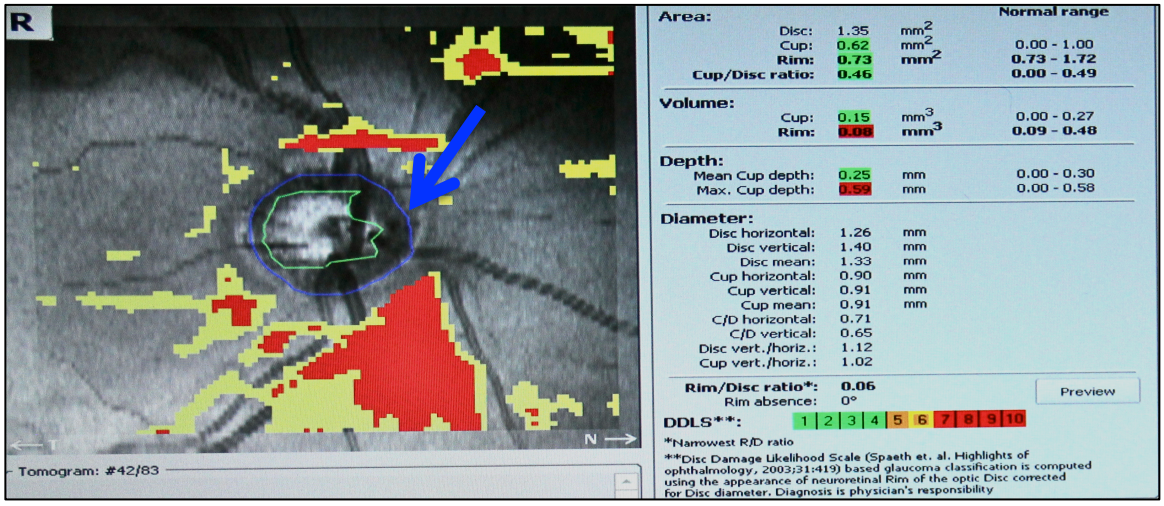


Figure 6. OCT analysis of optic disc

The area on the left shows automatic delineation of the optic disc rim (blue ring, arrow) and cup rim (green circle)
The area on the right shows calculated values of area, volume, depth and diameters of the optic disc components as well as DDLS score based on in-built analysis

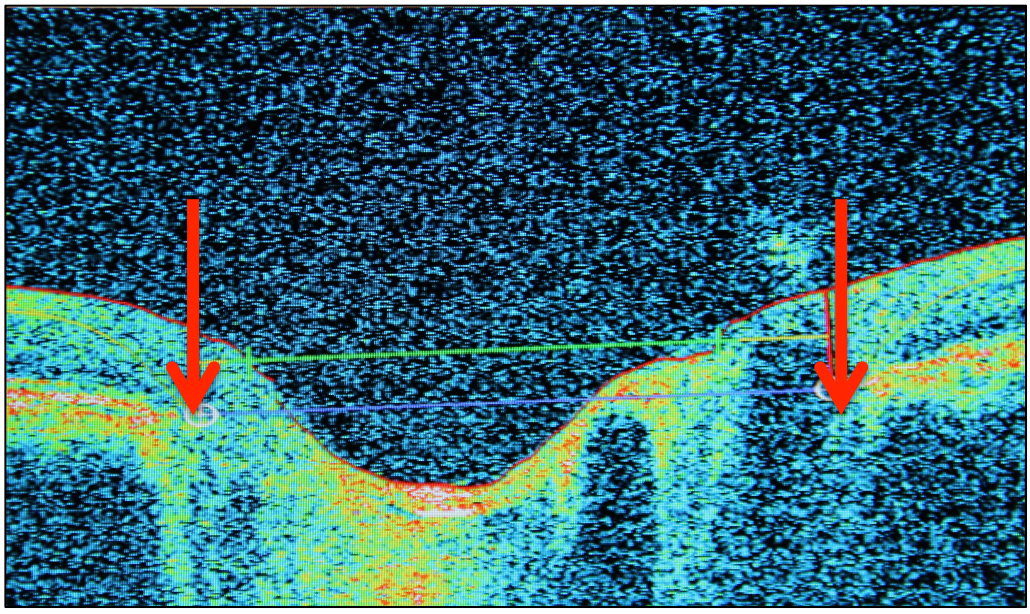


Figure 7. OCT imagery

indicating that the OCT evaluation of optic disc is not the distance of the image 'pit' (green upper line), but the distance from where the retinal pigment epithelium (RPE) end (blue lower line, between the two vertical red lines, in between arrowheads)

2.2.1.5 Slit lamp measurements

Lastly, consecutive measurements using five different fundus lenses – namely the Volk super 66D, Volk 78D, Volk Superfield NC, Volk Digital Wide Field and Volk Digital High Mag (Figure 7) were taken of each eye, using a Haag-Streit BM900 slit lamp (Figure 8) and Costruzione Strumenti Oftalmici (CSO) SL990 slit lamp (Figure 10), both at magnification of X16. The Volk super66, Digital Wide Field and Digital High Mag were loaned from Volk Optical through the intermediary company Surgical Ophthalmic Supplies (SOS).

The optic disc was viewed with each lens as in a normal fundus examination. The lens was held in front of the patient's eye and the optic disc brought into focus by moving the slit lamp away from the lens. A narrow vertical slit beam of light was progressively reduced in size (from 8mm on the Haag-Streit and 10mm on the CSO) until it was judged to correspond to the size of the disc. The inner border of the scleral canal was taken to be the optic disc height. The disc height was then read off the scale on the slit lamp illuminator head (Figure 10 and Figure 12). The scale was then reset to 10mm or 8mm depending on which slit lamp was used and the next lens measurement recorded. The Haag-Streit slit-length beam is calibrated in 0.1mm increments, readings were estimated to the nearest 0.05mm. For the CSO, the beam is calibrated in 0.2mm increments and thus the readings were judged to the nearest 0.1mm.



Figure 7. Volk super 66 D; 78 D; Superfield NC; Digital Wide Field; Digital High Mag



Figure 8. Haag-Streit slit lamp

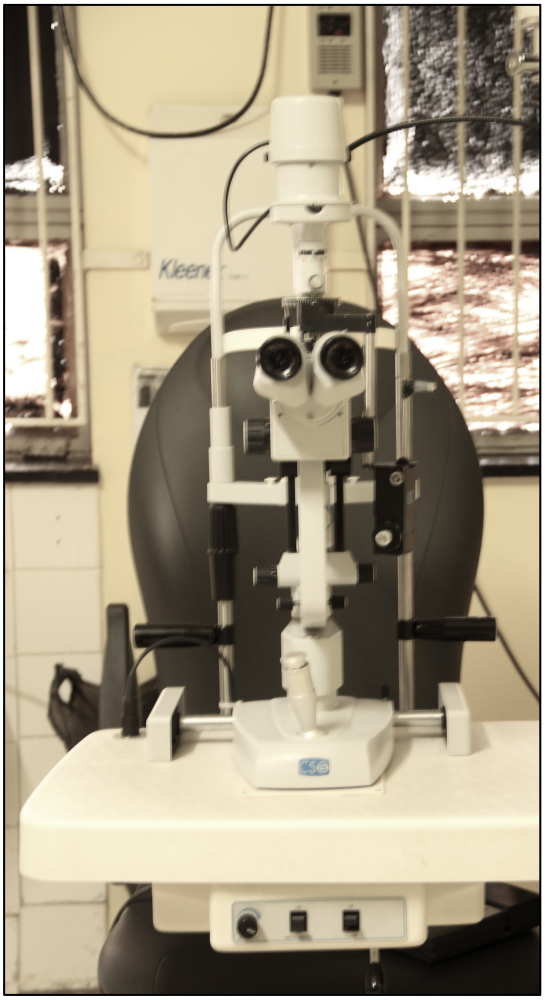


Figure 9. CSO slit lamp

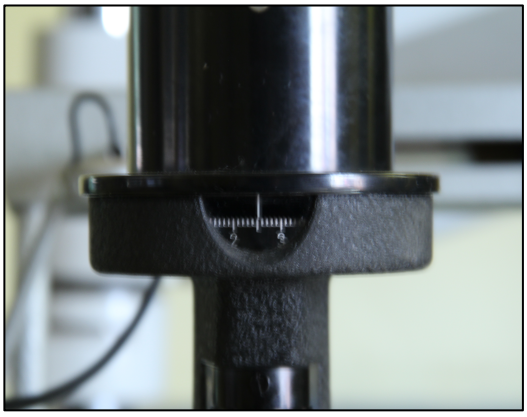


Figure 10. Haag-Streit slit length ruler

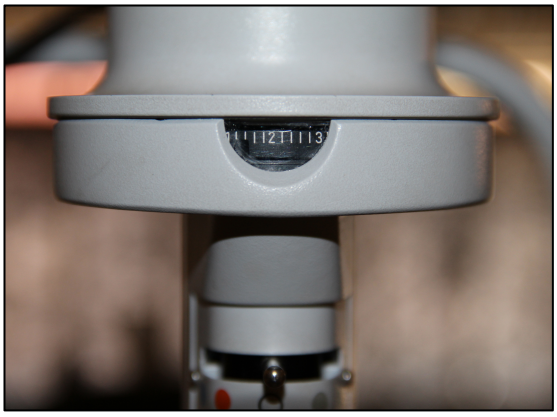


Figure 11. CSO slit length ruler

2.2.2 Inclusion Criteria

Adult patients attending the St John's Eye Hospital out-patient clinic were invited to participate. Patients agreeable to participation were given an information leaflet (Appendix C) and then asked to sign a patient consent form (Appendix D).

2.2.3 Exclusion criteria

Four basic exclusion criteria were utilised in the study:

- Patients with a refractive error less than -8 dioptres or greater than +4 dioptres
- Patients with swollen discs
- Patients with opaque media or other pathology precluding dilated fundoscopic examination of the optic nerve head
- Pseudophakic patients (patients having undergone cataract surgery)

2.2.4 Study sample

Based on the literature, between 20 and 40 eyes deemed an adequate sample size. Statistically there was no accurate way of working out the exact required sample size as there was no data available on specific standard deviations. As there was very little limitation to my population pool, a total of 100 eyes were analysed according to the experimental design. Once the data had been analysed and conversion equations formulated, a further 44 eyes were analysed in order to test the newly formed hypothesis on conversion equations.

2.2.5 Data collection

Each patient was assigned a unique number to ensure anonymity. All patient information collected during the course of the research was kept strictly confidential. Data from the data capture sheets (Appendix B) was recorded in Microsoft Excel for Mac 2011 by the primary researcher.

2.2.6 Data management and statistics

2.2.6.1 Littman's modified formula

The measured axial length with the Alcon OcuScan was corrected for by adding a factor of 0.25 to the measured value in millimetres to account for inaccuracies of ultrasound guided axial length measurements[22].

The calculated optic nerve head vertical disc height measurements for the Volk super 66D, 78D and Superfield were then captured using the formula:

$t = pqs$ where $q = 0.01306(\text{axial length} - 1.82)$ and $p = 3.56; 3.69; 4.61$

for Volk super 66D; Volk 78D and Volk Superfield NC lenses respectively

2.2.6.2 Statistics

Data was analysed using STATA 12 software by the primary researcher. Generalised linear mixed model analysis (Multilevel mixed effects linear regression analysis) was performed on data from 100 eyes to formulate conversion equations. As data was used from two eyes per patient, this resulted in paired data due to their high correlation. For accurate analysis the data was therefore analysed with a Generalised linear mixed

model that allows for correlation between observations, including random effects that explain the origin of the correlations.

The conversion equations were then calculated by regression of the relevant lens.

VDH = coefficient constant + coefficient of lens variable

Bland-Altman agreement plots and Lin concordance correlation were then performed on 44 new eyes to ascertain agreement of equations to gold standard values. Good correlation does not mean good agreement. Perfect correlation is indicated by points lying along any straight line, however perfect agreement is only if the points lie along the line of equality[38]. Good agreement via Lin's concordance correlation is indicated by a rho_c value close to 1. Bland-Altman agreement is calculated by plotting the difference between variables against the mean of the variables. Most points should lie between the 95% limits of agreement which alone does not indicate good agreement if the limits are very far apart[38]. It is useful to analyse both Lin's concordance and Bland-Altman agreement, as these two statistical methods are complimentary in most cases.

2.2.7 Staff and administration

The study was carried out by Dr F. R. Moti (registrar) at the St John Eye Hospital and supervised by a consultant (Dr Susan Williams) from the Division of Ophthalmology.

2.2.8 Ethical considerations

The protocol has attained ethical clearance by the Wits Human Research Ethics Committee. The ethics protocol number is M110619 (Appendix A).

CHAPTER 3: RESULTS

3.1 PATIENT BASELINE VARIABLES

One hundred and forty-four eyes of 72 patients were included in this study.

One hundred eyes were used in the initial phase of the study to perform the research objectives (see section 1.5). Forty-four eyes were then used to test the conversion equation formulated. The baseline factors of the first 100 eyes are summarised in Table 2. Patient co-morbidities not affecting results are deferred to Appendix D.

Table 2. Summary of baseline factors of sample population

CONTINUOUS VARIABLE	*OBS*	*MEAN*	*STD DEV*	*MIN*	*MAX*
Age	*50*	*47.7*	*13.122296*	*21*	*72*
AL	*100*	*23.3831*	*0.9436537*	*20.24*	*25.84*
OCT VDH	*100*	*1.735*	*0.1489119*	*1.4*	*2.15*

CATEGORICAL VARIABLE	*FREQ*	*PERC*
GENDER	*50*	
F	*33*	*66.00*
M	*17*	*34.00*

AL = axial length
OCT VDH = OCT vertical disc height
F = female M = male

3.1.1 Gender

Thirty-three (66%) of the patients were female and the remaining seventeen (34%) were male.

Gender was not found to be a significant factor affecting optic nerve head vertical disc height, with a p value of 0.41 on linear regression using a mixed model. Significance was regarded as a p value < 0.05.

3.1.2 Age

The mean age of patients was 47.7 years with a standard deviation of 13.10 years i.e. 67 of the patients were between the ages of 44 and 61 years. Figure 12 below depicts the age distribution from youngest age 21 to oldest age 72 years. The distribution is uniform. When age was regressed against the gold standard measure for purposes of this study i.e. OCT vertical disc height measurements, no correlation was found with a p value of 0.09.

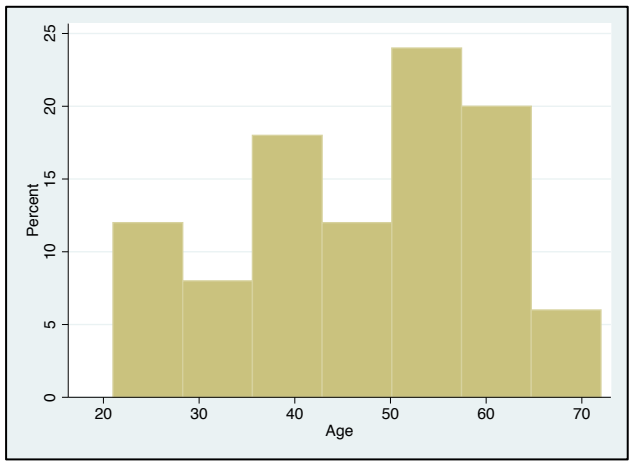


Figure 12. Age distribution of patients

3.1.3 Axial Length

The mean axial length of all eyes measure was 23.38mm. The mean for females was 23.13mm and for males was 23.88mm. As depicted in Figure 13 below, the distribution of axial lengths is relatively uniform within a tightly bound range, as would be expected due to the exclusion restrictions of refractive errors of <-8 dioptres and >+4 dioptres.

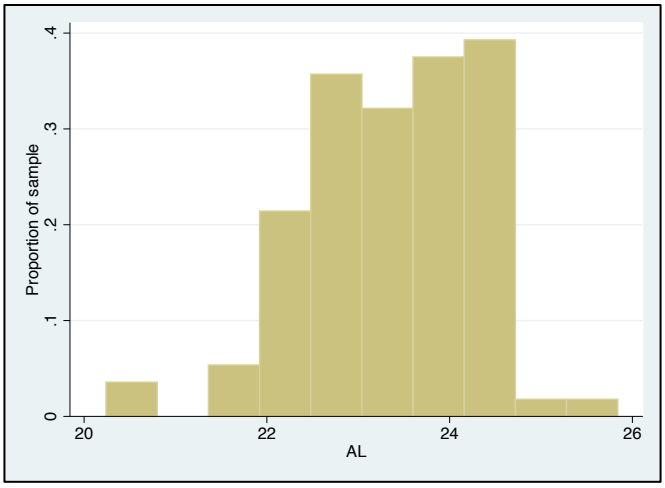


Figure 13. Patient range of axial length in millimetre

3.1.4 Optic nerve head vertical disc height with OCT

The OCT value of vertical disc height (VDH) was used as the gold standard measurement in this study.

The mean vertical disc height for 100 eyes was 1.74mm with a standard deviation of 0.15mm with minimum value of 1.4mm and maximum of 2.15mm. Figure 14 shows the histogram range of values across the population sample.

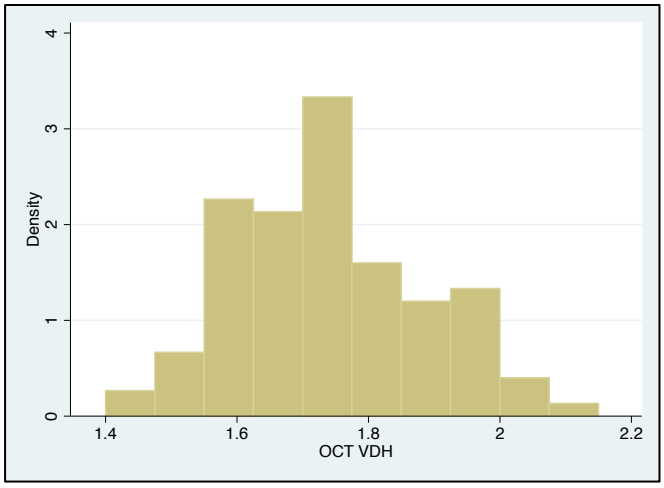


Figure 14. Range of OCT vertical disc height (mm)

Table 3 shows the variation in OCT average values for males vs females and left vs right eyes. Pearson's correlation coefficient for right versus left OCT VDH values is 0.88 – the high correlation supports the data being paired rather than independent variables.

Table 3. Average OCT vertical disc height values for males and females and left versus right eyes

	Average OCT vertical disc height value (mm)		
	LEFT EYE	RIGHT EYE	TOTAL
Females	1.72	1.72	1.723
Males	1.77	1.74	1.758
Grand Total	1.74	1.73	1.735

3.1.5 Replication data set

Forty-four new eyes were analysed and the Vertical Disc Height formulated equations above, applied to them. Only four lenses were used as the Volk Digital Wide Field was shown to be completely unreliable. The replication data set OCT VDH values will be labelled OCT VDH2.

The new sample had a strong gender skew, with seventy-two percent (72%) of patients being female and just twenty-three percent (23%) of patients being male.

The mean age of patients in the sample was 47.7 years with a standard deviation 13.1,

Table 4. Mean values of Continuous variables

CHARACTERISTIC	*MEAN ± STD DEV*
OCT VDH2	*1.68 ± 0.20*
D66 CSO	*1.56 ± 0.25*
D66 HS	*1.52 ± 0.22*
D78 CSO	*1.23 ± 0.21*
D78 HS	*2.08 ± 0.28*
SFCSO	*2.07 ± 0.29*
SFHS	*2.00 ± 0.27*
DHMCSO	*1.73 ± 0.27*
DHMHS	*2.57 ± 0.32*

OCT VDH2 = Optical coherence tomography vertical disc height for replication data set
HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens

3.2 RESULTS FOR RESEARCH OBJECTIVE A

To compare, using correlation coefficients, and then agreement, the similarity or dissimilarity between two control mechanisms of optic disc height measurements: Optical Coherence Tomography (OCT) versus calculation using a modified formula of Littman's equation

{t = pqs; where t is the true size of the retinal feature, p is a numerical constant based on the lens or telecentric model, q is a factor dependent on optical dimensions of a given eye and s is the size of the retinal image measured q = 0.01306 x (axial length – 1.82) }

The values of 'p' are constants depending on the fundus lens used, as calculated by Ansari-Shahrezaei *et al*[37]:

- *p = 3.56 for Volk super 66D lens*
- *p = 3.69 for Volk 78D lens*
- *p = 4.61 for Volk Superfield NC lens*

The component of the 'q' value requiring assessment is the value of the axial length. As shown in Figure 15 there is little correlation between axial length value and OCT vertical disc height with a very low R^2 of 0.00218. Further more, univariate regression reveals a p-value of 0.85 for Axial length and Pearson's correlation coefficient of 0.05. This data indicate that axial length has very little correlation with optic disc size.

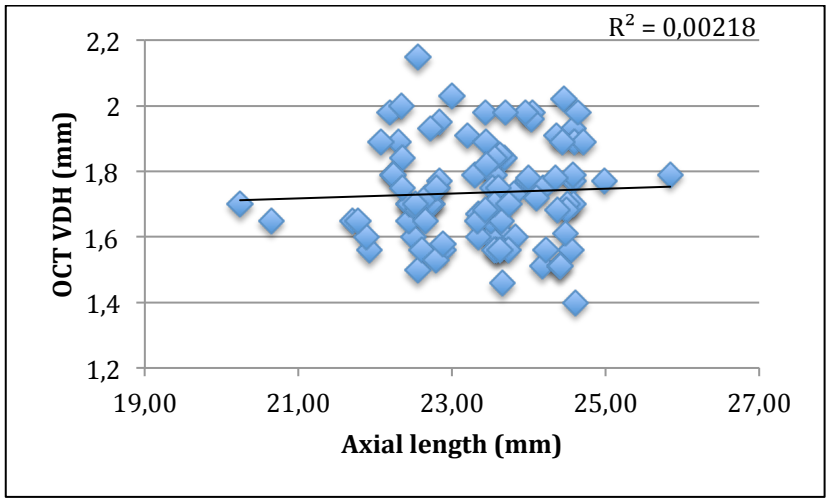


Figure 15. Scatter plot comparing axial length in mm (x-axis) to OCT vertical disc height (y-axis)

Table 6 below shows the mean value of population sample of vertical disc height measured with OCT, and values 't' from the modified Littman equation.

Table 5. Values of disc height gold standard OCT and Value 't'

CHARACTERISTIC	*MEAN ± STD DEV*	*VARIANCE FROM OCT MEAN*	*VARIANCE STD DEV*
OCT VDH	*1.74 ± 0.15*		
't' VALUES FOR:			
SUPER 66 CSO	*2.15 ± 0.31*	*0.55*	*0.26*
78 D CSO	*2.19 ± 0.32*	*0.63*	*0.27*
SUPERFIELD CSO	*2.41 ± 0.37*	*0.73*	*0.37*
SUPER 66 HS	*1.76 ± 0.23*	*0.02*	*0.13*
78 D HS	*1.82 ± 0.25*	*0.08*	*0.18*
SUPERFIELD HS	*1.95 ± 0.35*	*0.21*	*0.23*

HS = Haag-Streit slit lamp

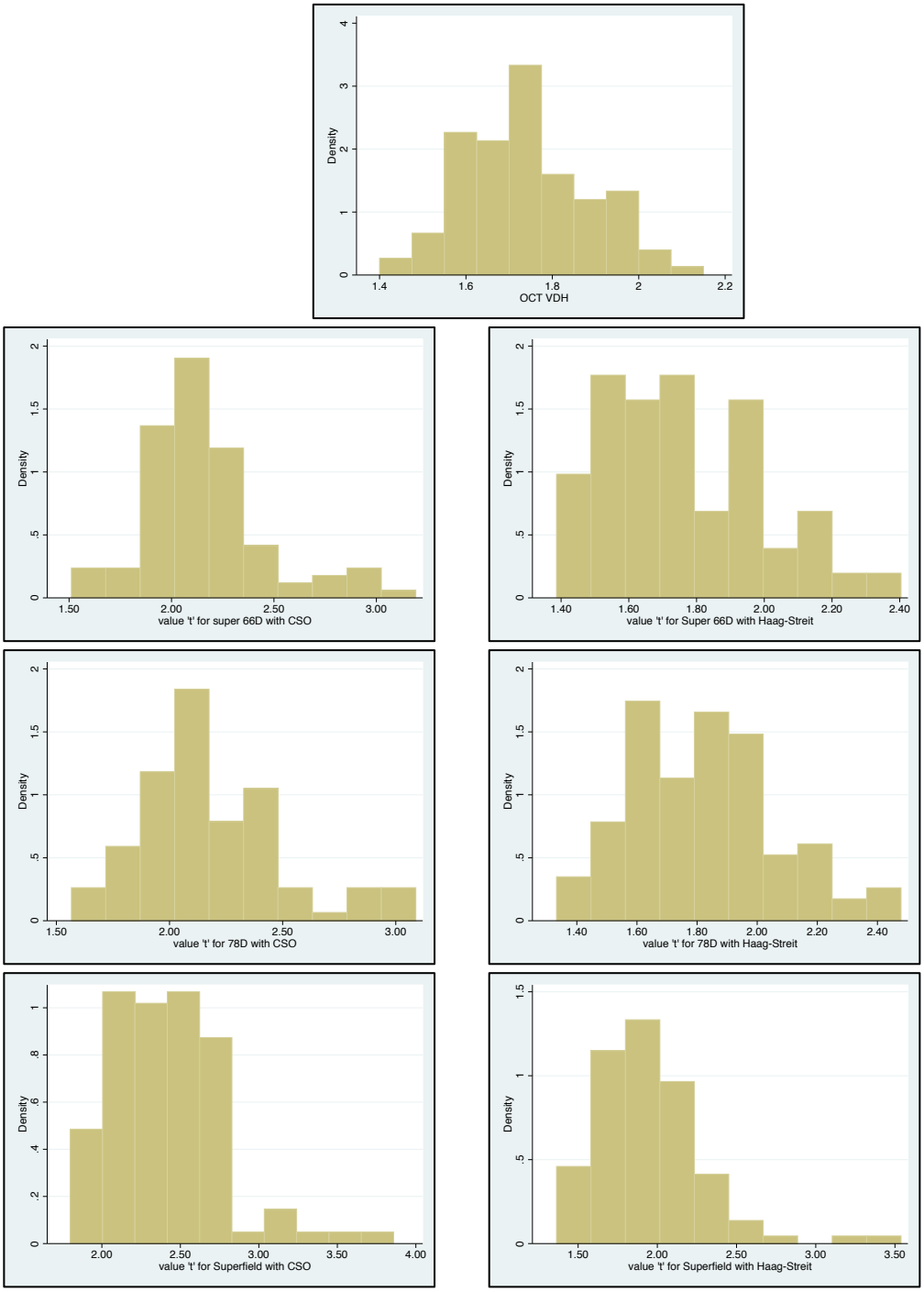


Figure 16. Series of histogram plots comparing OCT vertical disc height density plot (top graph) with plots of calculated 't' value for respective Volk super 66, 78D and Superfield lenses using the Haag-Streit (HS) and CSO slit lamps

As can be seen from Table 5 above, the best result attained is using the equation t = pqs for the Volk Super 66 dioptre lens on the Haag-Streit slit lamp. However, the shapes of the histograms in Figure 16 do not support this, correlation does not mean agreement. Table 6 below indicates little difference in Pearson's correlation coefficient of direct slit lamp measurements and values calculated with Littman's modified equation, with direct slit lamps measurements actually having better correlation. The highest correlation both with direct measurement and Littman's equation are shown with the Volk 78D lens.

Table 6. Pearson's correlation of direct slit lamp measurements and value 't' with OCT vertical disc height

	Pearson's correlation coefficient with OCT VDH	
	Direct slit lamp lens measurement	Value 't' of modified Littman equation
Super 66D lens with HS	0.82	0.77
Super 66D lens with CSO	0.66	0.65
78D lens with HS	0.84	0.82
78D lens with CSO	0.72	0.71
Superfield lens with HS	0.77	0.78
Superfield lens with CSO	0.69	0.67

HS = Haag-Streit slit lamp

3.3 RESULTS FOR RESEARCH OBJECTIVE B

Conversion equation of optic disc height measurement by clinical assessment using any one of five double aspheric fundus lenses at the slit-lamp

The five different fundus lenses used were:

- Volk Super 66 D
- Volk 78 D
- Volk Superfield NC
- Volk Digital Wide Field
- Volk Digital High Mag

All lenses showed a high correlation ($p<0.00001$) to the gold standard OCT vertical disc height (VDH).

Table 7 depicts the values of clinically measured optic nerve head vertical disc height and variances thereof from OCT VDH.

Table 7. Mean of slit lamp values and gold standard OCT VDH and variances

CHARACTERISTIC	*MEAN ± STD DEV*
OCT VDH	*1.74 ± 0.15*
D66 CSO	*2.12 ± 0.29*
D66 HS	*1.74 ± 0.21*
D78 CSO	*2.09 ± 0.29*
D78 H	*1.74 ± 0.23*
SF CSO	*1.83 ± 0.26*
SFHS	*1.48 ± 0.26*
DHMCSO	*2.64 ± 0.28*
DHMHS	*2.23 ± 0.26*
DWFCSO	*1.47 ± 0.33*
DWFHS	*1.17 ± 0.19*

OCT VDH = Optical coherence tomography vertical disc height
HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens

Table 8 below shows the results of multilevel mixed-effects linear regression with OCT VDH. All lens measurements with the Haag-Streit slit lamp have a much higher Wald chi^2 value (test for significance of individual variables and the whole model based on the chi-squared distribution).

Table 8. Multilevel mixed-effects Linear Regression Analysis with OCT VDH

MULTILEVEL MIXED EFFECTS LINEAR REGRESSION WITH OCT VDH				
CHARACTERISTIC	*B COEF ± SE*	*95% CI*	*p-VALUE*	*Wald chi^2*
AGE	*-0.003 ± 0.001*	*-0.005 +0.004*	*0.10*	*2.92*
GENDER	*-0.035 ± 0.042*	*-0.048 - 0.118*	*0.41*	*0.69*
Axial Length	*-0.004 ± 0.020*	*-0.043 - 0.351*	*0.64*	*0.04*
D66 CSO	*0.332 ± 0.049*	*0.235 - 0.428*	*<0.001*	*45.37*
D66 HS	*0.570 ± 0.049*	*0.474 - 0.666*	*<0.001*	*134.46*
D78 CSO	*0.368 ± 0.036*	*0.296 - 0.440*	*<0.001*	*61.13*
D78 HS	*0.544 ± 0.044*	*0.458 - 0.631*	*<0.001*	*152.78*
SFCSO	*0.368 ± 0.051*	*0.268 - 0.467*	*<0.001*	*52.62*
SFHS	*0.417 ± 0.045*	*0.309 - 0.504*	*<0.001*	*87.74*
DHMCSO	*0.349 ± 0.048*	*0.254 - 0.444*	*<0.001*	*51.93*
DHMHS	*0.439 ± 0.043*	*0.356 - 0.523*	*<0.001*	*105.76*
DWFCSO	*0.317 ± 0.043*	*0.232 - 0.402*	*<0.001*	*53.85*
DWFHS	*0.505 ± 0.065*	*0.378 - 0.633*	*<0.001*	*60.80*

HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens

Table 9 shows results of univariate linear regression analysis using one randomly selected eye per patient. In this analysis, age becomes statistically significant with a p-value < 0.02. Beta coefficient values are only slightly different. Analysis of right eyes only or left eyes only yield similar results with age still producing a p value <0.02 and coefficient values differing again only slightly.

Table 9. Univariate linear regression analysis of OCT Vertical disc height (VDH)

UNIVARIATE LINEAR REGRESSION WITH OCT VDH			
CHARACTERISTIC	*B COEF ± SE*	*95% CI*	*p-VALUE*
AGE	*-0.003 ± 0.001*	*-0.005 + 0.0004*	*0.02*
GENDER	*-0.035 ± 0.031*	*-0.098 - 0.027*	*0.27*
Axial Length	*0.007 ± 0.016*	*-0.024 - 0.390*	*0.64*
D66 CSO	*0.336 ± 0.390*	*0.258 - 0.413*	*<0.001*
D66 HS	*0.588 ± 0.041*	*0.506 - 0.669*	*<0.001*
D78 CSO	*0.368 ± 0.036*	*0.296 - 0.440*	*<0.001*
D78 HS	*0.551 ± 0.036*	*0.478 - 0.623*	*<0.001*
SFCSO	*0.393 ± 0.041*	*0.311 - 0.475*	*<0.001*
SFHS	*0.432 ± 0.036*	*0.359 - 0.504*	*<0.001*
DHMCSO	*0.372 ± 0.039*	*0.296 - 0.449*	*<0.001*
DHMHS	*0.459 ± 0.035*	*0.389 - 0.529*	*<0.001*
DWFCSO	*0.312 ± 0.034*	*0.245 - 0.379*	*<0.001*
DWFHS	*0.548 ± 0.054*	*0.441 - 0.654*	*<0.001*

HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens

The conversion equations were calculated by regression of the relevant variables using multilevel mixed-effects linear regression.

The equation for VDH for each lens at each slit lamp was:

VDH = coefficient constant + coefficient of lens variable

Table 10 below depicts the equations formulated from the regression model. The Volk 78D lens measured with the Haag-Streit has the highest log likelihood value indicating highest statistical significance in terms of supporting null hypothesis.

Table 10. Summary of formulated conversion equations

LENS	*EQUATION*	*Log likelihood*	*p value*
D66 CSO	*VDH = 1.03 + 0.33D66CSO*	*99.46*	*< 0.0001*
D66 HS	*VDH = 0.75 + 0.57D66HS*	*116.46*	*< 0.0001*
D78 CSO	*VDH = 1.00 + 0.35D78CSO*	*102.65*	*< 0.0001*
D78 HS	*VDH = 0.79 + 0.54D78HS*	*121.50*	*< 0.0001*
SFCSO	*VDH = 1.06 + 0.37SFCSO*	*100.66*	*< 0.0001*
SFHS	*VDH = 1.12 + 0.42SFHS*	*109.15*	*< 0.0001*
DHMCSO	*VDH = 0.81 + 0.35DHMCSO*	*99.41*	*< 0.0001*
DHMHS	*VDH = 0.76 + 0.44DHMHS*	*111.37*	*< 0.0001*
DWFCSO	*VDH = 1.27 + 0.32DWFCSO*	*102.06*	*< 0.0001*
DWFHS	*VDH = 1.14 + 0.51DWFHS*	*102.51*	*< 0.0001*

HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens

The results of each lens will be discussed separately.

3.3.1 RESULTS OF VOLK SUPER 66D LENS

The mean value of the super 66 lens with CSO slit lamp was 2.12 ± 0.29mm (min 1.5mm; max 3mm). For the super 66 lens with HS slit lamp it was 1.74 ± 0.21 (min 1.35mm; max 2.3mm).

Histogram analysis of the Super 66 lens with Haag-Streit slit lamp displays slightly better correlation than the CSO slit lamp (Figure 17).

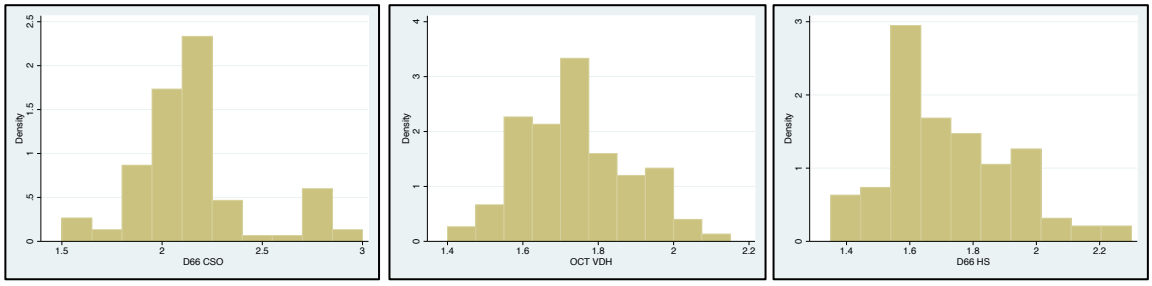
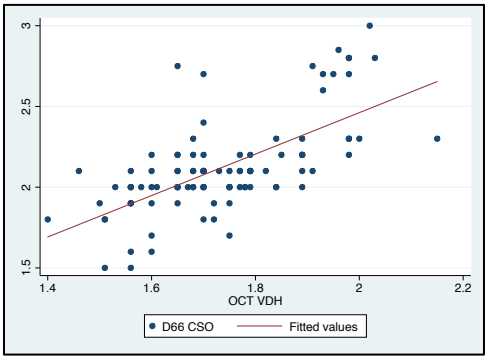


Figure 17. Histogram comparison of Volk super 66D with CSO slit lamp; OCT vertical disc height; Volk super 66D with Haag-Streit slit lamp

The two-way plots (Figure 18) also show that there is significant correlation between OCT VDH and the super 66D lens, with regression line almost through zero in Figure 18A of Super 66D CSO and through zero in Figure 18B of Super 66D HS.

A. 

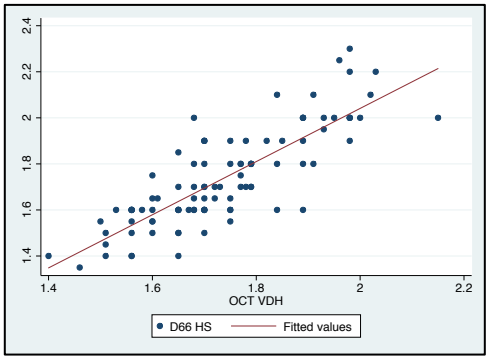
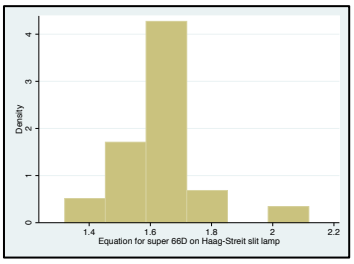
B. 

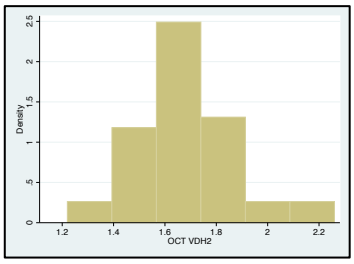
Figure 18. Two-way plots of: A. Super 66D on CSO slit lamp with OCT VDH and B. Super 66D on Haag-Streit slit lamp with OCT VDH

Regression analysis revealed two different equations for the super 66 lens, depending on the slit lamp being used.

VDH = 1.03 + 0.33D66CSO
VDH = 0.75 + 0.58D66HS

In the replication data set, histogram analysis shows a fair comparison of equation super 66 HS to OCT Vertical disc height of replication data set (VDH2) (Figure 19A and Figure 19B) and a slightly better comparison of equation super 66 CSO (Figure 19C).

A. 

B. 

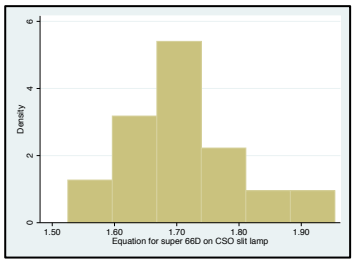
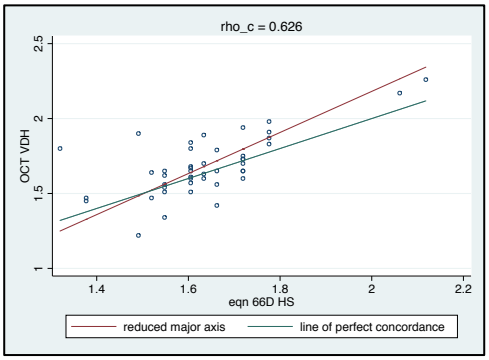
C. 

Figure 19. Histogram comparisons of A. Equation for super 66D lens on Haag-Streit slit lamp; B. OCT vertical disc height of replication data set (VDH2); C. Equation for super 66D lens on CSO slit lamp

Lin's correlation coefficient for super 66 HS (rho_c = 0.626, higher correlation are values closer to 1) shows a good association of reduced major axis (SD line) to the line of perfect concordance. It is evident from Figure 20A that for larger optic nerve vertical disc height, there is poorer agreement with the super 66D lens on Haag-Streit underestimating disc size. Lin's correlation coefficient for super 66D with CSO, has a value rho_c = 0.639. The super 66 D with CSO tends to overestimate the size of small discs, and underestimate the size of medium and large discs (Figure 20B).

A.



B.

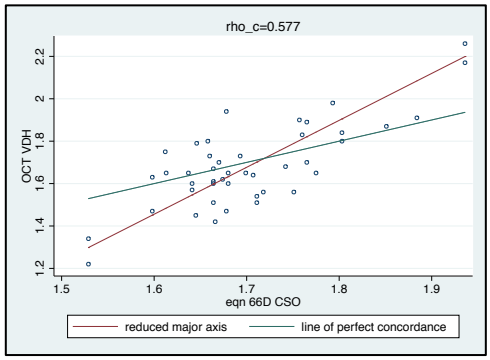
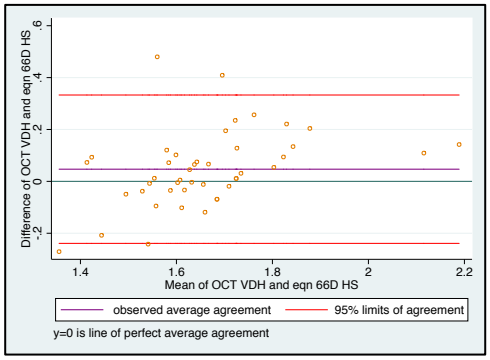


Figure 20. Lin's concordance correlation for A. Super 66D lens on Haag-Streit to OCT VDH2 and B. Super 66D lens on CSO slit lamp to OCT VDH2

A.



B.

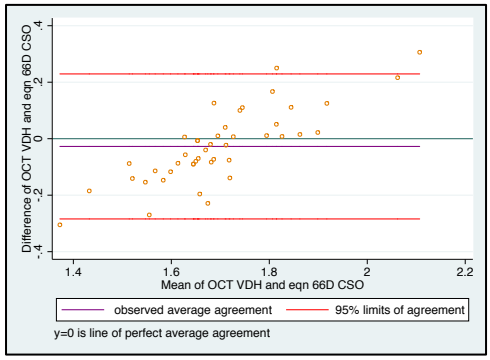


Figure 21. Bland-Altman plot of agreement between OCT VDH2 and A. Equation for super 66D on Haag-Streit slit lamp AND B. Equation for super 66D on CSO slit lamp

Figure 21A shows a good level of agreement for the Super 66D lens on Haag-Streit slit lamp using the Bland-Altman method with the observed average agreement line in very close proximity to the line of perfect agreement. On the Bland-Altman agreement plot for Super 66D on CSO slit lamp (Figure 21B), the observed average agreement line is in very close proximity to the line of perfect agreement as well.

3.3.2 RESULTS FOR VOLK 78D LENS

The mean value of the 78D lens with CSO slit lamp was 2.09 ± 0.29mm (min 1.5mm; max 2.8mm). For the 78D lens with HS slit lamp it was 1.74 ± 0.23 (min 1.2mm; max 2.4mm).

Histogram analysis shows excellent comparison of 78D HS to OCT VDH and a poorer comparison of 78D CSO.

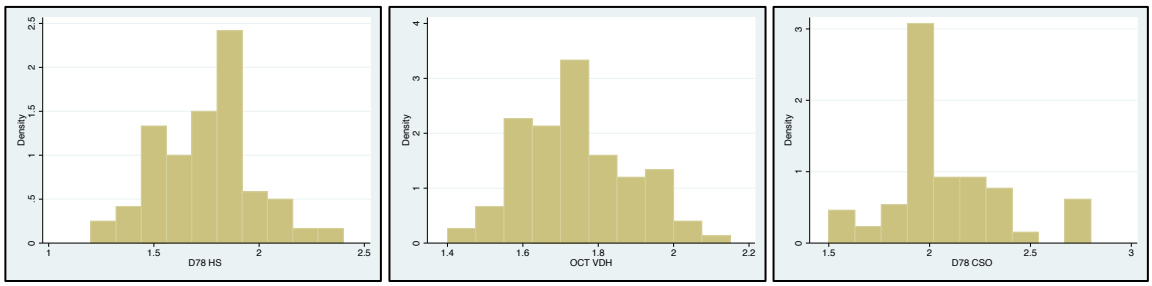
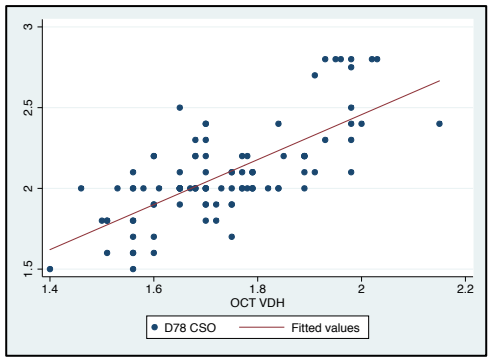


Figure 22. Histogram comparisons of 78D lens on Haag-Streit slit lamp; OCT VDH; and 78D lens on CSO slit lamp

The two-way plot of 78D HS (Figure 23B) shows very tight correlation of the points around the best-fit line compared to the 78D lens with CSO slit lamp (Figure 23A).

A.



B.

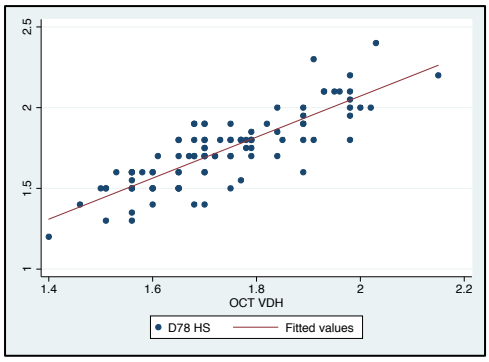
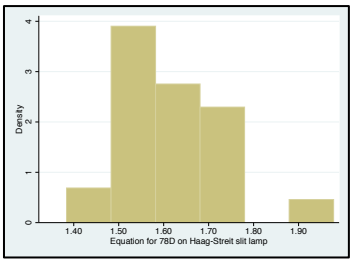


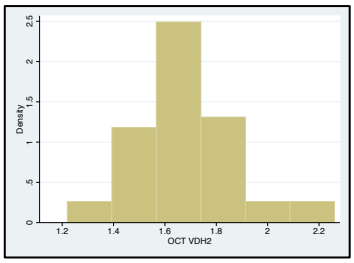
Figure 23. Two-way plot of A. Volk 78D lens on CSO slit lamp with OCT VDH and B. Volk 78D lens on Haag-Streit slit lamp with OCT VDH

Regression analysis revealed two different equations for the 78D lens, depending on the slit lamp being used.

VDH = 1.00 + 0.35 D78CSO
VDH = 0.79 + 0.54 D78HS

On analysis of the replication data set, histogram analysis shows a skewed deviation of equation 78D HS (Figure 24A) with a marginally better comparison of equation 78D CSO (Figure 24C) to OCT VDH2 (Figure 24C).

A. 

B. 

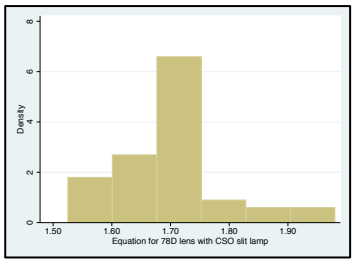
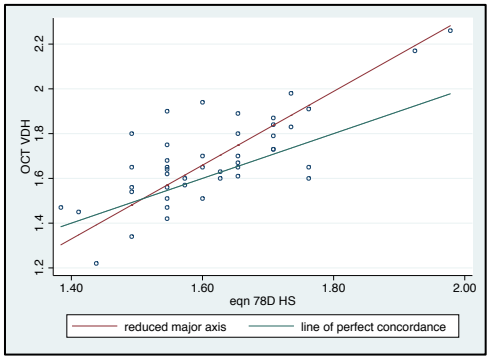
C. 

Figure 24. Histogram comparisons of A. Equation for 78D lens on Haag-Streit slit lamp; B. OCT VDH2; C. Equation for 78D lens on CSO slit lamp

Lin's correlation coefficient for 78D HS (rho_c = 0.615) shows a close association of reduced major axis (SD line) to the line of perfect concordance. It is evident from Figure 25A that for larger optic nerve vertical disc height, there is poorer concordance with the 78D lens on Haag-Streit underestimating disc size. Lin's correlation coefficient for equation 78D with CSO, has a value rho_c = 0.642. The 78D with CSO equation tends to overestimate the size of small discs, and underestimate the size of large discs (Figure 25B).

A.



B.

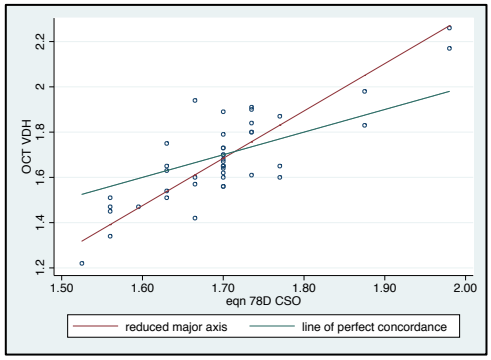
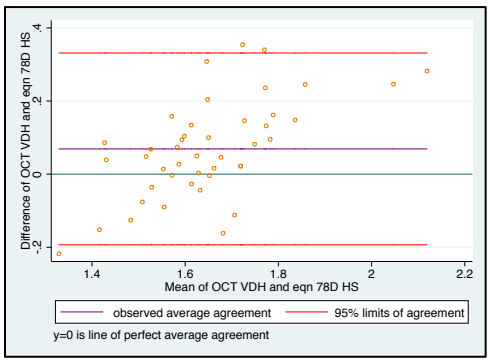


Figure 25. Lin's concordance correlation for A. Equation for Volk 78D lens on Haag-Streit slit lamp to OCT VDH2 and B. Equation for Volk 78D lens on CSO slit lamp to OCT VDH2

The Bland-Altman plot for equation 78D HS (Figure 26A), shows poor agreement of the observed average to line of perfect agreement. The observed average line lies slightly above the line of perfect agreement, indicating an overestimation of optic disc height values. On the Bland-Altman agreement plot for 78D lens on CSO slit lamp (Figure 26), the observed average agreement line is almost exactly over the line of perfect agreement.

A.



B.

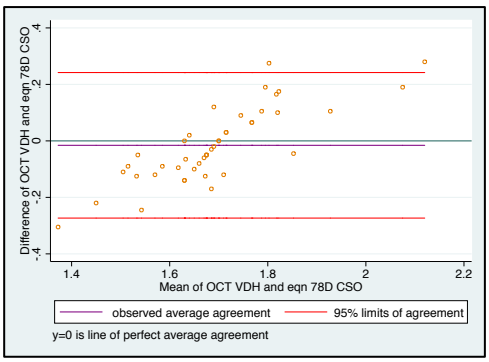


Figure 26. Bland-Altman plot of agreement between OCT VDH2 and A. Equation for 78D on Haag-Streit slit lamp AND B. Equation for 78D on CSO slit lamp

3.3.3 RESULTS FOR VOLK SUPERFIELD LENS

The mean value of the Superfield (SF) lens with CSO slit lamp was 1.83 +- 0.26mm (min 1.3mm; max 2.8mm). For the Superfield lens with HS slit lamp it was 1.48 +- 0.26 (min 1.0mm; max 2.8mm).

Histogram analysis shows good bell curve formation of SF HS (Figure 27) though taller peak than OCT comparative graph, and a very different formation of SF CSO histogram.

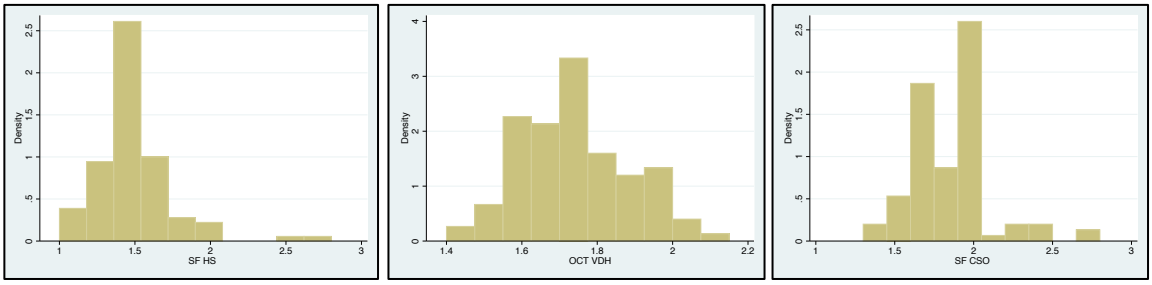
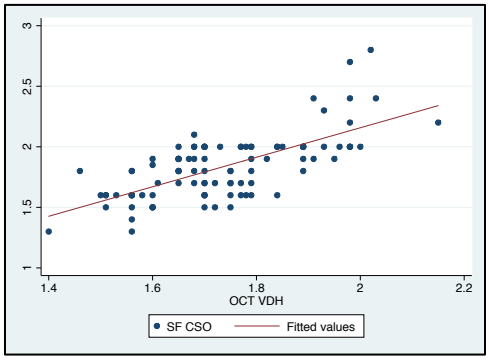


Figure 27. Histogram comparison of Superfield lens on Haag-Streit slit lamp; OCT VDH2; and Superfield lens on CSO slit lamp

Both two-way scatter plots showed tight correlation around the best-fit line, with SF CSO (Figure 28A) very far from zero y-axis and SF HS plot (Figure 28B) almost going through zero.

A. 

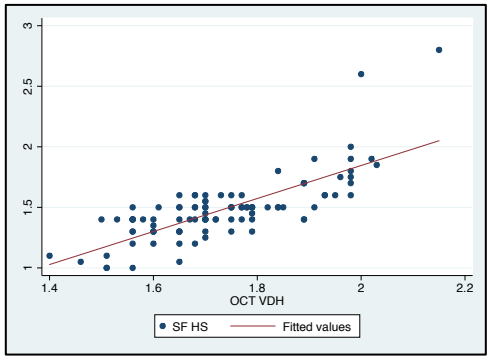
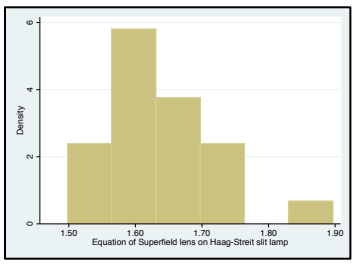
B. 

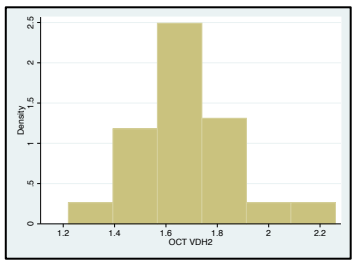
Figure 28. Two-way plot of A. Superfield (SF) lens on CSO slit lamp with OCT VDH and B. Superfield lens on Haag-Streit slit lamp with OCT VDH

Regression analysis revealed two different equations for the Superfield lens, depending on the slit lamp being used.

VDH = 1.06 + 0.37 SFCSO
VDH = 1.12 + 0.42 SFHS

On analysis of the replication data set, histogram analysis shows a skewed deviation to the left of equation Superfield HS (Figure 29A) and also a lesser left skewed deviation of equation Superfield CSO (Figure 29C) to OCT VDH2 (Figure 29B).

A. 

B. 

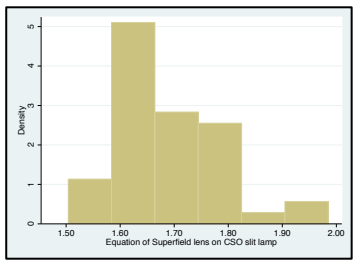
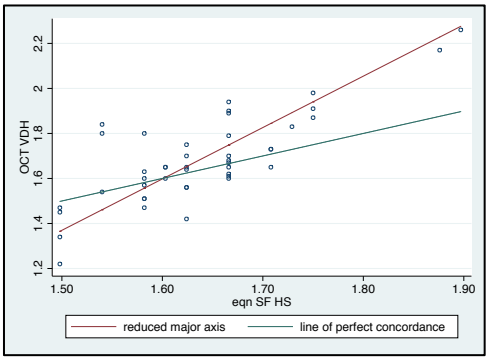
C. 

Figure 29. Histogram comparison of A. Equation for Superfield lens on Haag-Streit slit lamp; B. OCT VDH2; C. Equation for Superfield lens on CSO slit lamp

Lin's correlation coefficient for equation SF HS (rho_c = 0.556) is the lowest and as indicated in Figure 30A, the reduced major axis does not correlate well with the line of concordance. Lin's correlation coefficient for equation SF CSO (rho_c = 0.694) is very high (Figure 30B).

A.



B.

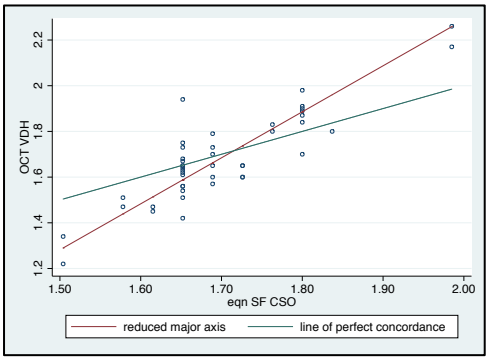
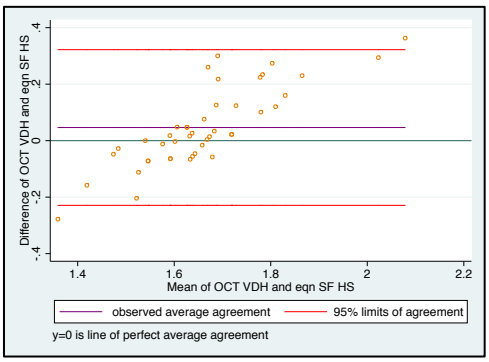


Figure 30. Lin's concordance correlation for A. Equation for superfield lens on Haag-Streit slit lamp to OCT VDH2 and B. Equations for superfield lens on CSO slit lamp to OCT VDH2

In the Bland-Altman plot for the Superfield lens on Haag-Streit slit lamp (Figure 31A) more plots are scattered above y = 0 line (line of perfect agreement) indicating the tendency to overestimate larger discs. The Bland-Altman plot for Superfield lens on CSO slit lamp (Figure 31B) shows a high degree of agreement.

A.



B.

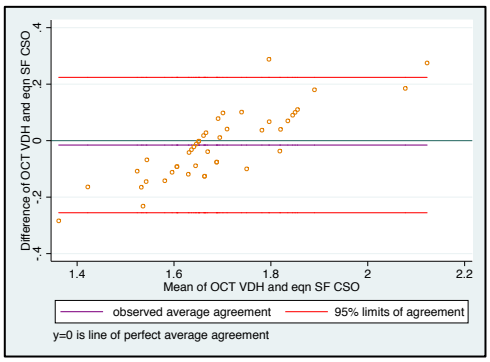


Figure 31. Bland-Altman plots of agreement to OCT VDH2 for A. Equation for superfield lens on Haag-Streit slit lamp; B. Equation for superfield lens on CSO slit lamp

3.3.4 RESULTS FOR VOLK DIGITAL HIGH MAG

The mean value of the Digital High Mag (DHM) lens with CSO slit lamp was 2.64 +- 0.28 (min 1.8mm; max 3.0mm). For the Digital High Mag lens with HS slit lamp it was 2.23 +- 0.26 (min 1.7mm; max 2.8mm).

Histogram analysis shows a very rightly skewed deviation of DHM CSO than OCT comparative graph; and very boxed central formation of DHM HS histogram (Figure 32).

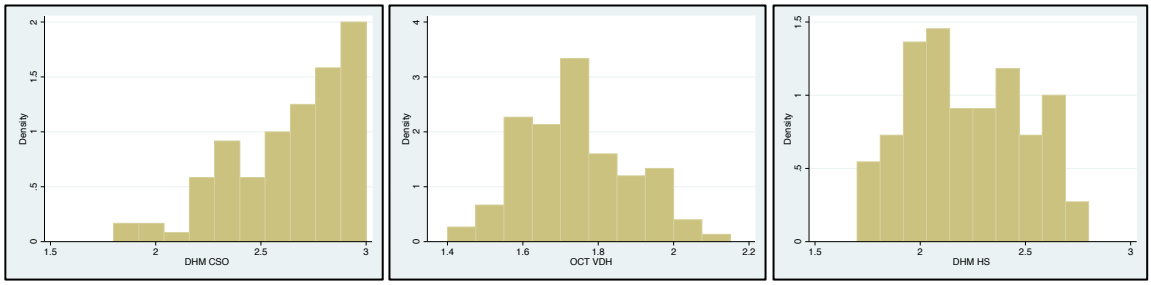
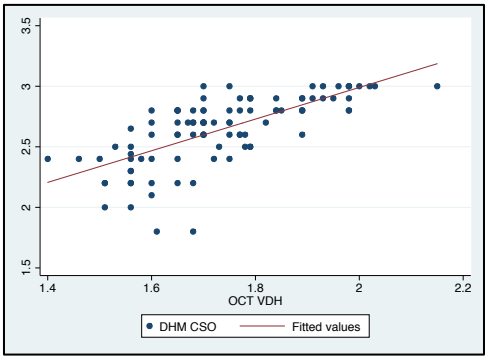


Figure 32. Histogram comparison of Volk Digital High Magnification lens on CSO slit lamp; OCT VDH; and Digital High Magnification lens on Haag-Streit slit lamp

Two-way plot of DHM CSO shows fair correlation of scatter to best-fit line (Figure 33A), however where x = 0, y > 2 therefore not going through zero. Figure 33B depicts DHM HS two-way scatter shows better correlation and line formation closer to 0.

A. 

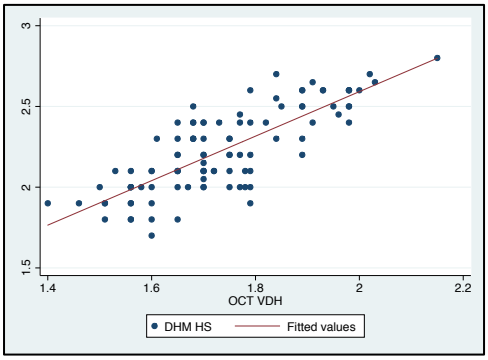
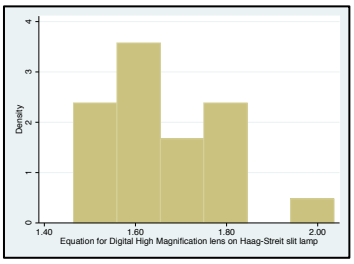
B. 

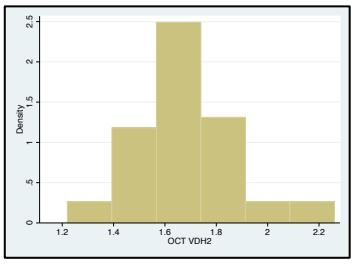
Figure 33. Two-way plot of A. Digital High Magnification (DHM) lens on CSO slit lamp with OCT VDH and B. DHM lens on Haag-Streit slit lamp with OCT VDH

Regression analysis revealed two different equations for the DHM lens, depending on the slit lamp being used.

VDH = 0.81 + 0.35 DHMCSO
VDH = 0.76 + 0.44 DHMHS

Histogram analysis shows a skewed deviation to the left of equation DHM HS (Figure 34A) and also a right skewed deviation of equation DHM CSO (Figure 34C) to OCT VDH2 (Figure 34B).

A. 

B. 

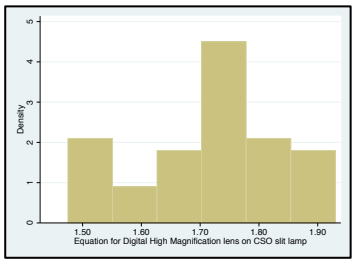
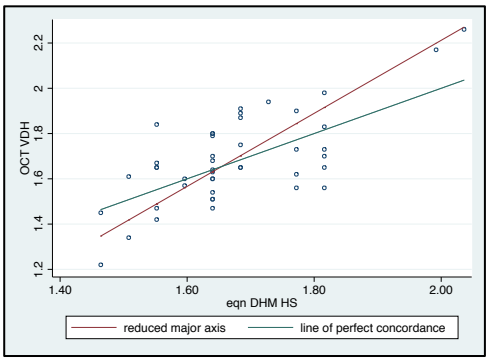
C. 

Figure 34. Histogram analysis of A. Equation for Digital High Magnification lens on Haag-Streit slit lamp; B. OCT VDH2; and C. Equation for Digital High Magnification lens on CSO slit lamp

Lin's concordance correlation for DHM HS (rho_c = 0.627) shows mild underestimation of very large discs (Figure 35A). Lin's concordance for DHM CSO has a rho_c = 0.693 (Figure 35B). It shows some overestimation of disc size.

A.



B.

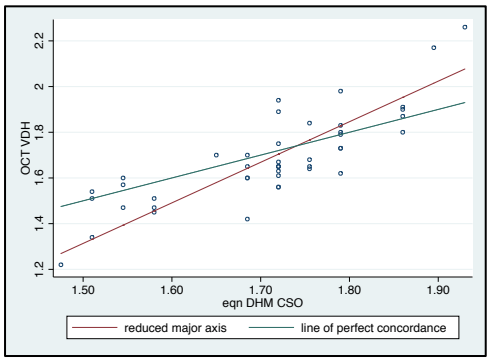
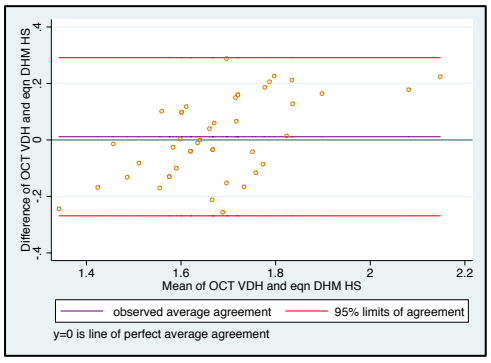


Figure 35. Lin's concordance correlation for A. Equation for digital high mag on Haag-Streit slit lamp with OCT VDH2 and B. Equation for digital high mag lens on CSO slit lamp with OCT VDH2

Bland-Altman on the Digital High Magnification lens on Haag-Streit slit lamp (Figure 36A) shows excellent agreement with the line of observed agreement superimposed on the y = 0 line. The equation for digital high magnification on CSO slit lamp Bland-Altman plot (Figure 36B) has more points below the y = 0 line, and fair agreement as points are not diffusely scattered.

A.



B.

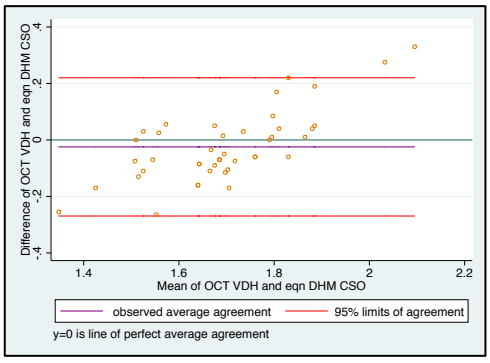


Figure 36. Bland-Altman plots of agreement to OCT VDH2 for A. Equation for Digital High Mag lens on Haag-Streit slit lamp and B. Equation for Digital High Mag lens on CSO slit lamp

3.3.5 RESULTS FOR VOLK DIGITAL WIDEFIELD LENS

Clinical evaluation of disc measurement showed an obvious poor correlation due to the fact that slit lamp rulers do not go below 1.0mm for the CSO and 0.9mm for the Haag-Streit. The mean value of the Digital Wide Field (DWF) lens with CSO slit lamp was 1.47 +- 0.33 (min 0.9mm; max 2.0mm). For the DWF with Haag-Streit it was 1.17 +- 0.19 (min 0.9; max 1.65).

Histogram analysis in Figure 37 confirms the inaccuracies of the lens with numerous optic discs measuring between 0.9mm and 1.2mm. Regression analysis to formulate an equation were not continued for this lens as any further statistical analysis would yield only false results.

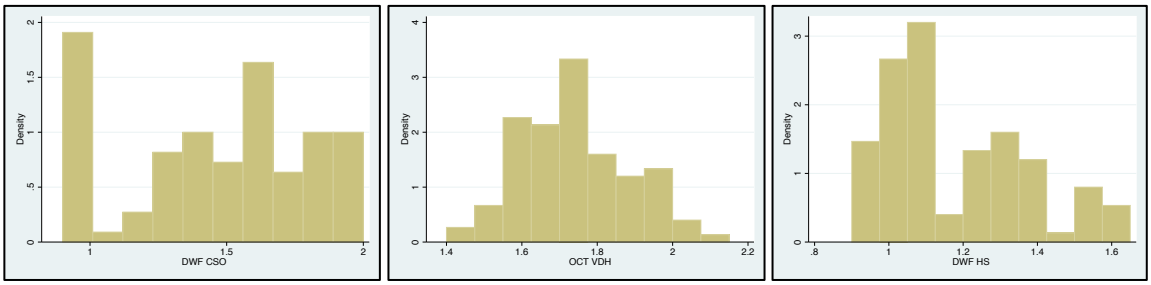


Figure 37. Histogram comparison of Digital Wide Field lens with Haag-Streit slit lamp; OCT VDH; and Digital Wide Field with CSO slit lamp

Table 11 below are the mean values of the equations and their variances from OCT VDH2

Table 11. Mean value and standard deviation of VDH value of equation, and variance from OCT VDH2

CHARACTERISTIC	*MEAN ± STD DEV*	*MEAN VARIANCE FROM OCT VDH2*	*VARIANCE STD DEV*
OCT VDH2	*1.68 ± 0.20*	-	-
Eqn66 HS	*1.65 ± 0.15*	0.02	0.15
Eqn78 HS	*1.62 ± 0.12*	0.06	0.13
EqnSF HS	*1.64 ± 0.09*	0.02	0.14
EqnDHM HS	*1.67 ± 0.12*	0.01	0.14
Eqn 66 CSO	*1.71 ± 0.10*	0.03	0.13
Eqn78 CSO	*1.71 ± 0.10*	0.05	0.13
EqnSF CSO	*1.70 ± 0.12*	0.03	0.12
Eqn DHM CSO	*1.71 ± 0.11*	0.06	0.12

OCT VDH2 = Optical coherence tomography vertical disc height for replication data set
HS = Haag-Streit slit lamp
SF = Superfield lens
DHM = Digital High Mag lens
DWF = Digital Wide Field lens
Eqn = formulated equation for respective lens

Table 12 summarises the concordance and agreement of the formulated equations to the gold standard OCT VDH2 from the replication data set. All rho_c values (concordance correlation coefficients) fall within a small range close to 1.0. All measures evaluated together, show the Digital High Magnification lens to have the highest agreement.

Table 12. Summary of agreement of conversion equations to OCT VDH2

EQUATION	*Rho_C*	*C_b*	*BLAND-ALTMAN*		
			Avg of difference between OCT and equation VDH	*Limits of Agreement (LOA)*	
Eqn 66D HS	*0.626*	*0.918*	*0.047*	*-0.239*	*0.333*
Eqn 78D HS	0.615	0.814	0.069	-0.193	0.331
Eqn SF HS	0.556	0.709	0.046	-0.229	0.322
Eqn DHM HS	0.627	0.896	0.011	-0.269	0.291
Eqn 66 CSO	0.639	0.770	-0.027	-0.284	0.229
Eqn78 CSO	0.642	0.774	-0.016	-0.273	0.242
EqnSF CSO	0.694	0.798	-0.016	-0.255	0.224
Eqn DHM CSO	0.693	0.842	-0.025	-0.269	0.220

Rho_C = Lin's concordance correlation coefficient
C_b = Rho_C/Pearson's r (measure of accuracy)

3.4 RESULTS OF RESEARCH OBJECTIVE C

To compare the interchangeability of the two different slit lamps – Haag-Streit BD900 and CSO slit lamp

Calibration of the slit lamp rulers was compared. A calibration ruler with laser-demarcated graduation marks was not attainable to compare with precision, the accuracy of the slit rulers, so a standard surgical ruler from a ruler/calliper surgical instrumentation set was used. As a result, the graduation marks were thickened beams under microscopic examination, dots as laser beams of micrometre measure would have been more precise.

On comparison of ruler millimetre measurements between slit lamps Figure 39 and Figure 40 show that 1mm on the Haag-Streit, was not 1mm on the CSO slit lamp.

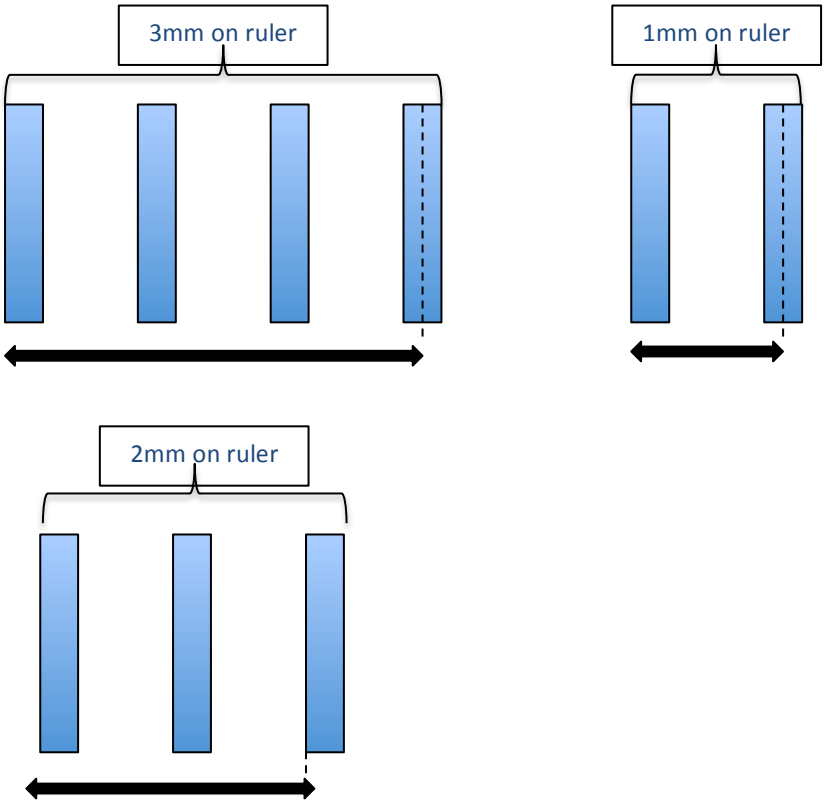


Figure 39. Measurements corresponding to 3mm, 2mm and 1mm on Haag-Streit slit lamp. Haag-Streit measures indicated by black arrows

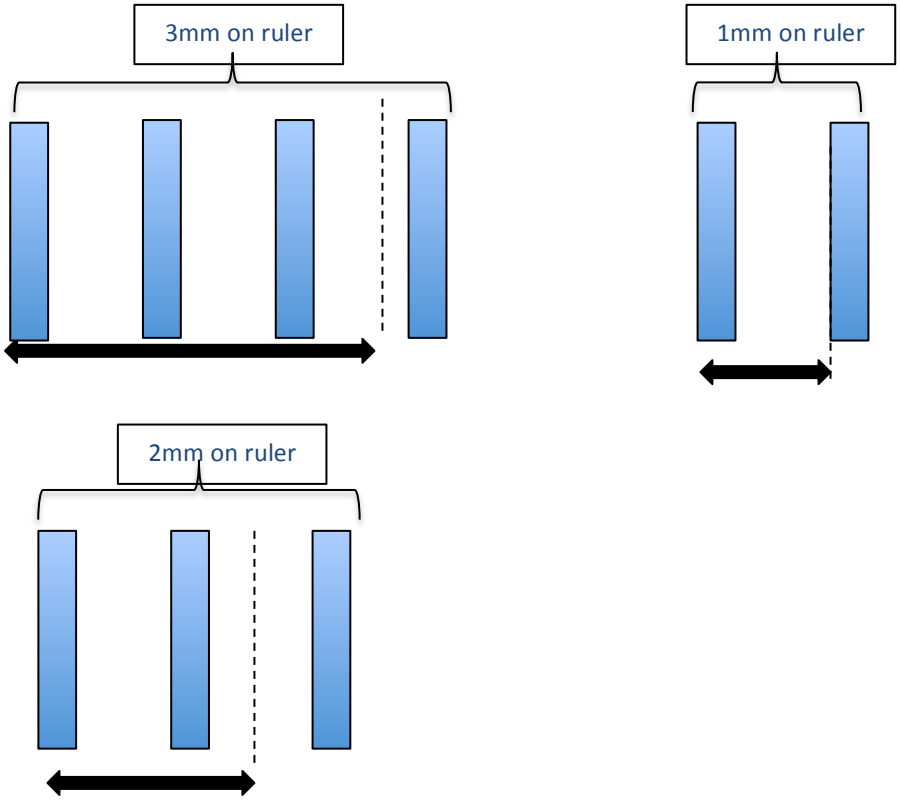


Figure 40. Measurements corresponding to 3mm, 2mm and 1mm on CSO slit lamp. CSO measures indicated by black arrows.

3.5 RESULTS OF RESEARCH OBJECTIVE D

To compare accuracy and agreement of Volk conversion factors based on manufacturer magnification values to the control mechanism of optic disc height measurement with Optical Coherence Tomography (OCT), and agreement of Volk conversion factors to research objective B conversion equations

Table 13 below shows a comparison of mean and standard deviation values for measurements of the four fundus lenses on either the Haag-Streit or CSO slit lamp, when the calculated equation from research objective B was applied, and when the Volk magnification factors were applied. The comparative value is that of the OCT measured vertical disc height measure. The closest Volk magnification factor is for the Superfield fundus lens on the Haag-Streit slit lamp.

Table 13 Comparison of mean and standard deviations of vertical disc height measurements with OCT, calculated equations for respective lenses on two different slit lamps, and Volk magnification factors for lenses

VARIABLE	MEAN	VAR FROM OCT
OCTVDH2	1.68	0
Equation for 66D with HS	1.63	0.05
Volk magnification factor for 66D HS measures	1.56	0.12
Equation for 66D with CSO	1.71	0.03
Volk magnification factor for 66D CSO measures	2.1	0.32
Equation for 78D with HS	1.62	0.06
Volk magnification factor for 78D HS measures	1.83	0.15
Equation for 78D with CSO	1.70	0.02
Volk magnification factor for 78D CSO measures	2.4	0.72
Equation for SF with HS	1.64	0.04
Volk magnification factor for SF HS measures	1.60	0.08
Equation for SF with CSO	1.7	0.02
Volk magnification factor for SF CSO measures	2.25	0.57
Equation for DHM with HS	1.67	0.01
Volk magnification factor for DHM HS measures	1.45	0.23
Equation for DHM with CSO	1.71	0.03
Volk magnification factor for DHM CSO measures	1.80	0.12

CHAPTER 4: DISCUSSION

4.1 STATISTICAL CONSIDERATIONS

When data from both eyes are included, this improves regression coefficient estimates[39]. Using information from one eye is a statistically simple approach, however even if both eyes are higher correlated, this does not mean that the right eye will yield identical results to the left eye[40]. Mixed effects regression models provide flexibility for analysing clustered data with multilevel structures.

The discrepancy between statistical methods can be explained using the example of age as a variable in this study. Varma *et al* conducted a large population based study that found no association between age and optic nerve head size[4]. This study's findings agree when using the robust multilevel mixed effects linear regression analysis ($p < 0.09$), however on univariate linear regression a weak correlation was found between age and optic nerve head vertical disc height ($p < 0.02$). Were age used as a statistically significant variable, that would have required an extra component in each equation accounting for the patient's age. Analysis of such equations yielded less accurate and precise results than the equations concluded in this study.

4.2 AXIAL LENGTH

Oliviera *et al*[5] found a weak correlation between axial length and optic disc area in black patients. White patients screened in their study did not reach statistical significance[5]. This study did not concur with that finding, with a p-value of 0.64.

4.3 LITTMAN'S MODIFIED FORMULA FOR OPTIC NERVE HEAD VERTICAL DISC HEIGHT

The formula t = pqs was applied, where q = 0.01306(axial length – 1.82) and p = 3.56; 3.69; 4.61 for Volk stereo 66D; Volk 78D and Volk Superfield NC lenses respectively.

Due to the poor correlation between axial length and optic disc size the equation seems somewhat flawed.

Furthermore, the results of mean and standard deviation of vertical disc height by these equations had poor correlation to the OCT VDH. There was also no improvement on Pearson's correlation coefficient from baseline, unaltered clinically measured values as compared with the Littman's modified formula values.

Therefore the use of axial length and other factors attained by measures of a schematic eye cannot be used accurately in clinical practice to determine fundus object sizes.

4.4 LENSES

The Volk 66D lens and the Digital High Magnification lens yielded the best results. However the result for the Superfield and Volk 78D lens are not discouraging and may still be considered for clinical use, as their inferiority is not statistically significant.

For the 78D lens, Lim, O'Brien and Bolton formulated an equation based on regression analysis of 25 eyes: Y = 0.86X + 0.41. They also used a Haag-Streit slit lamp. However no

methods to determine agreement of their findings were performed[27]. The central dioptre power of the Superfield lens is equivalent to that of a 90D. Lim, O'Brien and Bolton determined an equation of Y = 0.89X + 0.59 for the Volk 90D lens[27]. Ruben's equation for 90D lens, however differed: Y = 1.17X + 0.24[26]. Again no methods to determine agreement or accuracy were employed. Papastathopoulos and Jonas determined a conversion factor of 1.5 for the Superfield lens[28]. This is a very gross measure and again no methods of agreement were in place. Ten eyes were re-measured five times in order to evaluate reproducibility, but no new eyes on which to test their conversion factor[28]. Due to the large sample size of this study, good correlations and further determinations of agreement, it is fair to conclude these results accurate; and the modified equations derived should be utilised in preference to other previously published work.

The poor correlation of the Volk magnification factors should also be noted. This is in keeping with the findings of Spencer and Vernon[29] who found poor correlation when using the Volk 78D magnification factor. A deterrent to applying this study's equations is the lack of ease with which to recall from memory the equation for a specific lens, applied to a particular slit lamp. However, as shown, the quick conversion of a Volk magnification factor is grossly out of keeping with actual vertical disc height values as measure with OCT. Therefore, when vertical disc height measurement is clinically necessary, these equations should be applied. It should be remembered that measuring the optic disc is not a repetitive examination per patient; therefore a once-off calculation per patient to document an accurate clinical estimation of vertical disc height can reasonably be applied within clinical time constraints.

4.5 COMPARISON OF SLIT LAMPS

The reason for including two types of slit lamps in this study is because both are routinely used at the St John Eye Hospital. Additionally, it has becoming increasingly obvious in clinical practice that measure values differ significantly between the two slit lamps, not only for fundus measurements of optic disc or well-demarcated masses, but without use of additional lenses, for example when measuring the size of a corneal ulcer.

Some reasons for this were thought to be confusion on where to read off measurements on the illuminator head ruler. The Haag-Streit slit length (as shown in Figure 10) has a demarcated line in the centre indicating where the length should be read off. The CSO has no such demarcation and there has been confusion amongst registrars who have made an assumption that readings are to be read of an estimated centre of the illuminator head ruler. In fact, on the CSO slit lamp, measurements are read off the left margin of the ruler (Figure 12). However once this error was corrected for, there were still significant differences in the results produced. Also, graduation marks on the Haag-Streit are in increments of 0.1mm and for the CSO, 0.2mm, which would limit results to two decimal place measurements for the Haag-Streit (the minimum being 0.05mm estimated increments) and one decimal place measurements for the CSO (the minimum being 0.1mm estimated increments).

The metre is the length of the path travelled by light in vacuum during a time interval of 1 ／ 299,792,458 of a second. A millimetre is one thousandth of a metre. On comparison

of ruler millimetre measurements between slit lamps, it was evident that 1mm on a Haag-Streit, was not 1mm on the CSO slit lamp. In clinical practice it is not practical to calibrate the illuminator head ruler every time a measurement is made and perform an additional calculation to account for calibration deficiencies.

Though the primary outcome of the study design was not to compare accuracy of slit lamp measurements, it is evident that the Haag-Streit slit lamp generated more accurate and for most lenses, more precise measurements. Also of note is that though the Volk magnification factors are unreliable, values for Haag-Streit measures had a closer correlation to actual values than measures on the CSO.

It is plausible to postulate the formulated equations for the Haag-Streit slit lamp could be applied to slit lamps by other manufacturers, that have an equally calibrated illuminator head ruler, and yield equivalent results.

4.5 STUDY LIMITATIONS

For both slit lamp measures and manual OCT measures, it is difficult to locate the margins of the scleral canal. Observer fatigue and observer error are also confounding factors. All lens measurements were performed by one researcher, which also alludes to the possibility of observer bias as there was no masking of measurements or results.

CONCLUSIONS

Clinical application of fundus measurements is useful and practical not only for efficiency and accurate prediction, but also because ophthalmological equipment is expensive and impractical for many clinical centres especially in developing countries.

Two important factors need to be taken into account when applying slit lamp fundus measurements: the type of lens used, and the slit lamp being used. Use of the Haag-Streit slit lamp yields more accurate and reliable results than the CSO.

Equations for five lenses were formulated via multivariate mixed effects regression analysis, and agreement tested for thereafter. The Volk Digital Wide Field proved unreliable with numerous measures of between 0.9 and 1.2 for varying smaller disc sizes. Agreement was therefore not tested for in this lens, as any further statistical analysis would have yielded false and biased results based on poor correlation of raw data. The best results were ascertained using the Volk Digital High Magnification lens followed by the Volk super 66D lens – suggesting that lenses with higher magnification are more accurate.

The slit lamp technique of measuring optic disc size with application of a simple equation yields useful results in close agreement to complicated, expensive technology. It cannot replace accurate analysis by these methods but is sufficient in aiding clinical decisions and diagnoses on patients.

APPENDIX A

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Farah R Moti

CLEARANCE CERTIFICATE	M110619
PROJECT	Clinical Method of Calculating Optic Nerve Vertical Disc Height
INVESTIGATORS	Dr Farah R Moti.
DEPARTMENT	Division of Opthalmology
DATE CONSIDERED	24/06/2011
M1106190DECISION OF THE COMMITTEE*	Approved unconditionally
	24/06/2011

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 03/02/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr Susan Willaims

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX B: Data Information Sheet

PATIENT NUMBER:
AGE: GENDER:

COMORBIDITIES:

RE LE

VA

REFRACTION

ONH (OCT)

AXIAL LENGTH

CALCULATED ONH USING AL

ONH (66D)

ONH (78D)

ONH (SUPERFIELD NC)

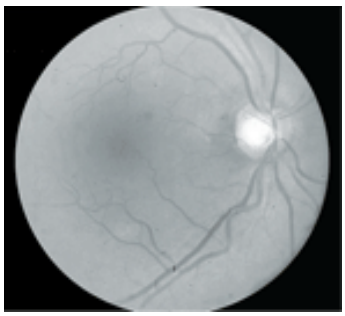
ONH (DIGITAL HIGH MAG)

ONH (DIGITAL WIDEFIELD)

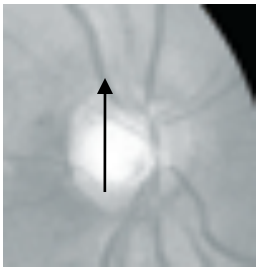
APPENDIX C: Patient Information Sheet

Dear Patient

My name is Dr Farah Moti, I am a registrar (training to become an eye surgeon) in the Division of Ophthalmology at the University of the Witwatersrand. I am conducting research to measure the optic nerve head height. A qualified ophthalmologist in our academic department is supervising this study and the University of the Witwatersrand Human Research Ethics Committee has approved it.
When we look at the back of your eye, picture 1 below is what we see.



PICTURE 1



PICTURE 2

The optic nerve head is shown in the smaller picture. This is the beginning of the nerve (which looks almost like a wire) that connects the eye to the brain. I would like to measure the height of the optic nerve head as shown by the black arrow because it is important to know the height for different diseases and even in normal eyes, not everyone has the same size optic nerve head.

I would like to ask you to be a part of this study. Participation is voluntary and refusing will not affect your medical care. The procedures will not be painful or invasive. In order to participate, I need to instil some drops in your eyes to dilate your pupils. This will make your vision blurry for approximately 4 hours so if you are driving, you cannot drive home immediately. Once you are dilated, I will test your vision and measure your eyes on 3 different pieces of equipment: One will take a picture of the back of your eye like picture 1; two will measure your eye in centimetres from front to back; three will be measuring your eye with different lenses on a slit lamp microscope. This will take about one hour and when we are done you may go home. You may refuse to continue the examination at any point and it will not change your regular management at St John Eye Hospital. The test will have no further consequence on your eyes.

Allowing these tests to be performed will not improve treatment of your eyes nor will it worsen your eye condition, so it will not benefit you in any direct way.
All the information we collect on your eyes will be stored under a number and not your name. I will be the only person who knows your name and will ensure that your personal details remain confidential.

Sincerely, Farah Moti (084 600 6786)

APPENDIX D: CONSENT FORM

Clinical method of calculating optic nerve head vertical disc height

Investigator: Dr F R Moti

Institution: University of the Witwatersrand, Department of Neurosciences, Division of Ophthalmology

To my patient:

This information sheet may contain words that you do not understand. Please ask the doctor to explain any words or information that you do not understand.

I, _____ hereby agree to be part of this study. I understand that this will in no way affect management of the eye problems for which I have presented, nor will it have any long-term adverse effects on my eyes. I have been fully informed as to the procedures to be followed and have been given a description of the discomforts, risks and benefits of joining this study. I will not experience any pain during the measurements of my eye. I understand that if I have any questions at any time, they will be answered. I understand that my confidentiality will be maintained at all times through the use of a numbering system. If I choose not to be a part of this study I will not be treated any differently and this will not affect my regular treatment or medical care in any way.

_____ _____ _____

Name Signature/ thumbprint Date

Study Doctor

I, Farah Moti, herewith confirm that the above mentioned patient has been fully informed about the nature, conduct and risks of this study.

_____ _____ _____

Name Signature/ thumbprint Date

APPENDIX E: Summary of sample population co-morbidities in 3.3.1

CO-MORBIDITY	***TOTAL***
Diabetes mellitus	*5*
Diabetes mellitus & Asthma	*1*
Diabetes mellitus & Hypertension	*6*
Diabetes mellitus, Hypertension & Osteoarthritis	*2*
Gout	*1*
Hypertension	*5*
Hypertension & Asthma	*1*
Hypertension and Rheumatoid arthritis	*1*
Rheumatoid arthritis	*3*
Human Immunodeficiency Virus	*1*
Allergic keratoconjunctivitis	*2*
GRAND TOTAL	*23*

REFERENCES

1. Jonas JB, Budde WM and Panda-Jonas S. Ophthalmoscopic evaluation of the Optic Nerve Head *Surv Ophthalmol* 1999;43(4):293-320
2. Sekhar GC. Optic Disc evaluation in glaucoma *Indian J Ophthalmol* 1996;44:235-239
3. Girkin CA, Sample PA, Liebmann JM *et al*. African Descent and Glaucoma Evaluation Study (ADAGES) II. Ancestry Differences in Optic Disc, Retinal Nerve Fibre Layer, and Macular Structure in Healthy Subjects *Arch Ophthalmol* 2010;128(5):541-550
4. Varma R, Tielsch JM, Quigley HA *et al*. Race-, Age-, Gender-, and Refractive Error-Related Differences in the Normal Optic Disc *Arch Ophthalmol* 1994;112:1068-1076
5. Oliviera C, Harizman N, Girkin CA *et al*. Axial length and optic disc size in normal eyes *Br J Ophthalmol* 2007;91:37-39
6. Jonas JB. Optic disc size correlated with refractive error *Am J Ophthalmol* 2005;139(2):346-348
7. Jonas JB and Montgomery DMI. Determination of the neuroretinal rim area using the horizontal and vertical disc and cup diameters *Graefe's Arch Clin Exp Ophthalmol* 1995;233:690-693
8. Drance SM. What we can learn from the disc appearance about the risk factors in glaucoma? *Can J Ophthalmol* 2008;43:322-327
9. Heijl A, Bengtsson B, Hyman L *et al* for the Early Manifest Glaucoma Trial Group. Natural History of Open-Angle Glaucoma *Ophthalmol* 2009;116:2271-2276

10. Krupin T, Liebmann JM, Greenfield DS *et al*. Low-Pressure Glaucoma Study Group. The Low-Pressure Glaucoma Treatment Study: Study Design and Baseline characteristics of enrolled patients *Ophthalmol* 2005;112:376-385
11. Sommer A, Tielsch JM, Katz J *et al*. Relationship between intraocular pressure and primary open-angle glaucoma among white and black Americans: The Baltimore Eye Survey *Arch Ophthalmol* 1991;109;1090-1095
12. Klein BE, Klein R, Sponsel WE *et al*. Prevalence of Glaucoma: The Beaver Dam Eye Study *Ophthalmol* 1992;99:1499-1504
13. Susanna RJ and Vessani RM New findings in the evaluation of the optic disc in glaucoma diagnosis *Curr Opin Ophthalmol* 2007;18:122-128
14. Gordon MO, Beiser JA, Brandt JD *et al*. The Ocular Hypertension Treatment Study: Baseline factors that predict the onset of primary open-angle glaucoma *Arch Ophthalmol* 2002;120:714-720
15. Czudowska MA, Ramdas WD, Wolfs RC *et al*. Incidence of Glaucomatous Visual Field Loss: A ten-year Follow-up from the Rotterdam Study *Ophthalmol* 2012;117:1705-1712
16. Crowston JG, Hopley CR, Healey PR *et al*. The effect of optic disc diameter on vertical cup to disc ratio percentiles in a population based cohort: the Blue Mountains Eye Study *Br J Ophthalmol* 2004;88:766-770
17. Jonas JB. Size of glaucomatous optic discs *Ger J Ophthalmol* 1992;1(1):41-44
18. Wang FW, Quigley HA and Tielsch JM. Screening for glaucoma in a medical clinic with photographs of the nerve fibre layer *Arch Ophthalmol* 1994;112:796-800

19. Spaeth GL, Henderer J, Lui C *et al*. The Disc Damage Likelihood Scale: Reproducibility of a new method of estimating the amount of optic nerve damage caused by glaucoma *Trans Am Ophthalmol Soc* 2002;100:181-186
20. Bayer A, Henderer JD, Steinmann WG *et al*. Validity of a new disk grading scale for estimating glaucomatous damage: Correlation with visual field damage *Am J Ophthalmol* 2002;133(6):758-764
21. Danesh-Meyer HV, Gaskin BJ, Jayusundera T et al. Comparison of disc damage likelihood scale, cup to disc ratio, and Heidelberg retina tomography in the diagnosis of glaucoma *Br J Ophthalmol* 2006;90:437-441
22. Garway-Heathe DF, Rudnicka A, Lowe T *et al*. Measurement of optic disc size: equivalence of methods to correct for ocular magnification *Br J Ophthalmol* 1998;82:643-649
23. Raasch T. Fundoscopic Systems: A Comparison of Magnification *Am J Optom and Phys Optics* 1982;59(7):595-601
24. Kirwan JF, Gouws P, Linnell AET *et al*. Pharmacological mydriasis and optic disc examination *Br J Ophthalmol* 2000;84:894-898
25. European Glaucoma Society Terminology and Guidelines for Glaucoma[http://www.eugs.org/eng/EGS_guidelines.asp] (website)
3rd edition. Savona, Italy: DOGMA; 2008
26. Ruben S. Estimation of optic disc size using indirect biomicroscopy *Br J Ophthalmol* 1994;78:363-364
27. Lim CS, O'Brien CO and Bolton NM. A simple clinical method to measure the optic disc size in glaucoma *J Glaucoma* 1996;5(4):241-245

28. Papastathopoulos KI and Jonas JB. Ophthalmoscopic Estimation of Optic Disc Size *On J Ophthalmol* http://www.onjoph.com/english/artikel/ophthest.html
29. Spencer AF and Vernon SA. Optic disc measurement: a comparison of indirect ophthalmoscopic methods *Br J Ophthalmol* 1995;79:910-915
30. Weinreb RN, Zangwill LM, Jain S et al. Predicting the Onset of Glaucoma: The Confocal Scanning Laser Ophthalmoscopy Ancillary Study to the Ocular Hypertension Treatment Study. Ophthalmol. 2010;117(9):1674-83
31. Correnti AJ, Wollstein G, Price LL *et al*. Comparison of Optic Nerve Head Assessment with a Digital Stereoscopic Camera (DISCAM), Scanning Laser Ophthalmoscopy, and Stereophotography *Ophthalmol* 2003;110(8):1499-1505
32. Shuttleworth GN, Khong CH and Diamond JP. A new digital optic disc stereo camera: intraobserver and interobserver repeatability of optic disc measurements *Br J Ophthalmol* 2000;84:403-407
33. Li G, Fansi AK, Boivin JF *et al*. Screening for Glaucoma in High-Risk Populations using Optical Coherence Tomography *Ophthalmol* 2010;117:453-461
34. Marsh BC, Cantor BD, WuDunn D *et al*. Optic Nerve Head (ONH) Topographic Analysis by Stratus OCT in Normal Subjects: Correlation to Disc Size, Age, and Ethnicity *J Glaucoma* 2010;19:310–318
35. Leung CK, Chan WM, Hui YL *et al*. Analysis of Retinal Nerve Fiber Layer and Optic Nerve Head in Glaucoma with Different Reference Plane Offsets, Using Optical Coherence Tomography *Invest. Ophthalmol. Vis. Sci.* 2005;46(3):891-899
36. Bennet AG, Rudnicka AR and Edgar DF. Improvements on Littman's method of determining the size of retinal features by fundus photography *Graefe's Arch Clin Exp Ophthalmol* 1994;232:361-367

37. Ansari-Shahrezaei S, Maar N, Biowski R *et al*. Biomicroscopic measurements of the optic disc with a high-power positive lens *Invest ophthalmol Vis Sci* 2001;42(1):153-157

38. Bland JM and Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement *Lancet* 1986;1:307-310

39. Katz JK, Zeger S and Liang KY. Appropriate Statistical Methods to Account for Similarities in Binary Outcomes Between Fellow Eyes *Invest Ophthalmol Vis Sci* 1994:35(5); 2461-2465

40. Fan Q, Teo YY and Saw SM. Application of Advanced Statistics in Ophthalmology *Invest Ophthalmol Vis Sci 2011:52; 6059-6065*