MORPHOLOGICAL DIFFERENCES BETWEEN THE TWO EYES OF PATIENTS WITH ASYMMETRICAL CATARACT: A PILOT STUDY

By

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except where assistance was specifically acknowledged. The sources of all references are clearly acknowledged.

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ABSTRAK

Kajian julong kali ini dijalankan dengan matlamat mencari kewujudan perbezaan fizikal antara kedua mata bagi pesakit-pasakit katarak yang tidak seimbang.

Di antara pesakit-pasakit katarak klinik mata USM yang mana mata-mata mereka diukur(Biometri) dan kataraknya digredkan dengan system pengredan katarak yang diubahsuai, 51 pesakit (102 matanya) didapati mempunyai ketidakseimbangan katarak yang ketara. Mata–mata ini dikumpulkan kepada kumpulan teruk (1) dan yang tidak (2).

Analisa purata bacaan biometri kedua kumpulan dibuat menggunakan ujian t berkecuali. Kanta-kanta bagi mata kumpulan 2 didapati adalah lebih tebal dengan ketaranya jika dibandingkan dengan kumpulan 1. (t=2.568, P=0.012) Perbezaan purata panjang biji mata, ruang depan mata dan kecembungan kornea antara kedua kumpulan adalah tidak ketara. Kesimpulannya, peranan biometri mata terhadap kejadian katarak yang tidak seimbang tidak dipastikan. Oleh itu, satu penyelidikan yang lebih mendalam dalam tujuk katarak tak seimbang ini merangkumi kriteria ketara takrifan katarak tidak seimbang; jangka waktu penyelidikan yang lebih panjang melibatkan lebih penyelidik berkecuali dan meneliti aspek lain seperti isipadu biji mata disyorkan.

ABSTRACT

This pilot study was aimed to look for morphological differences between the two eyes of patients with asymmetrical cataract.

Cataract patients visiting the eye clinic USM had their eyes measured (biometry) and cataracts graded with modified cataract grading system of whom fifty-one patients (102 eyes) were found to have the defined significant asymmetrical cataracts between the fellow eyes. The two eyes of these patients were grouped into severe (1) and less severe (2) cataract groups. The ocular biometries were analyzed.

More patients were found to have longer axial length and thinner lens morphology on their more cataractous eyes. Means of biometric readings of the two groups were analyzed using independent t test. The lenses of the group 2 were found to be significantly thicker than that of group 1. ($t=2.568$, $P=0.012$) The mean axial length, anterior chamber depth and the keratometric reading between the two groups were not significantly different statistically

.

In conclusion, axial length, keratometric reading, anterior chamber depth and lens thickness; their role for the occurrence of the cataract asymmetry is uncertain, a more detailed study taking more obvious cataract asymmetry as the criteria; longer study period involving more blinded observers and including other ocular feature like the volume of the eye is recommended for the future study on cataract asymmetry.

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1. INTRODUCTION

1. INTRODUCTION

Cataract is a major public health problem. The World Health Organization estimated that 45 million people in the world (The world health report 1998) are blind, about half of them are due to cataract, mainly by age related cataract. In Malaysia the overall prevalence of the cataract is 2.54% with estimated population involved of about 490,000. (National Eye Survey 1996)

Surgical extraction is the only treatment available until now. About 1.5 million cataract surgeries are performed each year in the United States alone. (The world health report 1998) It is the most frequently done surgery in the US among people 65 years and above, with estimated cost to medicare of $3.4 billion in 1997. This increasing need for surgical resources are even more critical in the developing countries. (Steiberg EA, Javitt JC, Sharkey D et al 1993)

Because of the impact on the health system all over the world, many studies were done mainly with the aim to delay, to prevent and to treat the cataract. These studies involved identifying the environmental risk factors and genetic factor. Studies were also done to find the non-surgical way of treating cataract. Many were also done looking on ways to cut the cost of treatment and to improve the outcome of treatment. Apart from surgical technique, the correct biometry of the eye is also important in order to calculate the intraocular lens power.

Works on biometry were aimed mainly at improving the intraocular lens calculation. Hoffer K. J had found that the patients with axial myopia are more likely to develop cataracts at an earlier age than those with shorter axial lengths. This conclusion was drawn from the data in which young cataract patients were having longer axial length when compared to the older cataract patients. However, there was no mention about the difference in the axial lengths between the eyes of those myopic patients. (Hoffer et al 1993)

Age related cataracts are usually bilateral but may be of different density or severity (asymmetry) between the two eyes of the same patient at the time of presentation. No work had been done looking at the intrinsic ocular parameters in relation to asymmetrical cataract. Yu and associates measured mean difference of axial length. They found an average difference between fellow eyes of 0.42mm. However no study was done relating this biometrical asymmetry to the development of the cataract. Kenneth J. Hoffer (1980) in his famous biometry of 7500 cataractous eyes, in which he compared the biometric values of both eyes for 1800 patients to determine the need to measure the axial length of the fellow eye in order to calculate intraocular lens power for one eye and to determine the consistency of these measurements between fellow eyes. The mean of the difference in axial length between fellow eyes was 0.34mm. However the standard deviation of 0.7mm indicated that there was no predictable trend in axial length symmetry between fellow eyes. Comparison of the average keratometric values for fellow eyes disclosed a mean difference of 0.87 $\pm$ 0.83 diopter. This indicated that 66% of the patients showed a difference in average keratometric values of 0.04 to 1.7 diopters. However, the series did not answer the question whether the biometric differences between fellow eyes relate to asymmetry in cataracts.

Patient with age related cataract of different severity between the two fellow eyes is a common finding in the routine ophthalmic clinic. However, what actually cause the asymmetrical cataract appearance in these apparently identical eyes that are exposed to the same environment, same systemic effect of the same host and developed out of same genetic make up remains to be answered. This query had triggered us to find the answer. So, this study was designed to find out the difference in the morphological aspects between two eyes of a same subject possessing age related cataract of differing severity.

Subject with considerable difference (significant asymmetry defined in this study) in the density of the age related cataracts between two eyes were studied. Cataract grading system was used to grade the severity of the individual eye and compared to confirm with the defined asymmetry in order to be included in this study.

It that hoped that the result of this study would enable a pre-measurement judgment about the biometry of the eyes be made before making the measurement when confronted with a patient with asymmetrical cataracts. Hence, biometrical difference between two eyes of a patient with asymmetrical cataract would not be taken with surprise and any non-specific difference between two eyes due to technical error would be identified. In other words biometry would be easier and devoid of uncertainties as it was already predicted the way it would behave.

In summary, this study was designed to determine the morphological difference between 2 eyes of patients having asymmetrical cataracts.

1.1. OBJECTIVES

1.1.1. GENERAL OBJECTIVE

The general objective is to determine the morphological difference between the two eyes of patient with asymmetrical cataract.

1.1.2. SPECIFIC OBJECTIVES

i. To measure and compare the axial lengths of fellow eyes of patients with asymmetrical cataracts using A scan.

ii. To measure and compare the keratometric readings of fellow eyes of patients with asymmetrical cataracts using autokeratometer.

iii. To measure and compare the anterior chamber depths of fellow eyes of patients with asymmetrical cataracts using A scan.

iv. To measure and compare the lens thickness of fellow eyes of patients with asymmetrical cataracts using A scan.

2. BACKGROUND

2.1.Background information

Cataract is defined as opacity within clear lens of the eye. It can occur in the nucleus of the lens, the cortex or the subcapsular region of the lens. Constantinus Africanus (AD1018), an Arabic ocularist, introduced the term; it means "waterfall" or "blockage of flow". By the different presentations they are divided into age related, traumatic, toxic, secondary and congenital cataracts. The cataractogenesis is not well understood but oxidative damage from photochemically or nonphotochemically generated oxygen radicals is the accepted mechanism. (Gerster 1989)

Age related cataract is so named because it is seen in aging patient. Studies had found age is the most important risk factor for the development of age related cataract. However the cutoff age has never been included in defining age related cataract. The national eye survey (1996) had found that there was a marked increment in the prevalence of cataract in population aged 40 and above. Many epidemiological studies on age related cataracts had taken varying minimum age limit as the inclusion criteria of sampling. It ranged from 40 to 50 years. (Matthew Burton et al 1997; Leske MC 1991; J M Teikari et al 1997; Lyle BJ et al 1999) For this study the lower age limit was 45 years adopting the age limit used in the major cataract studies done by the Italian-American Cataract Study Group 1991 and The Linxian Cataract Studies. (Sperduto RD 1993) This was done as an extra precaution of avoiding possible erroneous inclusion of the secondary cataract in the study.

Much has been studied about the cause of the age related cataracts. M Cristina Leske et al (1991) found the association of cataract with multiple external factors, such as nutritional intake, medical history and environment.

The Italian-American Cataract study group reported that there is an association between the sunlight exposure and the age related cataract. This finding was also noted by Leske et al 1991 in a case-control study of the risk factors for cataract. Cecile Delcourt et al (2000) in the Pathologies Oculaires Liees a l'Age (POLA) study further confirmed the role of sunlight exposure in the pathogenesis of cataract, in particular in its cortical localization. Ultra violet light may play a role in the cataractogenesis. Burton M. 1997 in a cross sectional study in two villages in Pakistan with different levels of ultraviolet radiation had found that ultra violet light exposure is a possible risk factor for cataract formation and he had suggested that there may be a saturation effect, whereby above a certain cut-off point further exposure to ultra violet light would not significantly increase the prevalence of cataract.

Nutrition also has an effect in the pathogenesis of cataract. Regular use of multivitamin supplements decreased risk for all cataract types. (Leske et al 1991, The Linxian Cataract Studies and Robert D 1993) Since Vitamin C, Vitamin E and carotenoids are antioxidants or radicals scavengers, they may influence the process of oxidative damage. This theory was studied by Barbara J. Lyle, Julie A Mares-

Perlman et al in the Beaver Dam Eye Study 1999 with the conclusion of a possible protective effect of vitamins E and C on the development of nuclear cataract.

The risk of nuclear opacities is increased with increasing cigarette smoking and decreased if the subject had quit smoking. (West et al 1989) The risk of cataract among heavy alcohol drinkers was more than non-drinker (odds ratio, 4.6; $p < 0.05$) but light drinkers were not at increased risk. (Munoz et al 1993) The result suggested that heavy alcohol consumption would increase the risk of posterior subcapsular cataract. In another Beaver Dam Eye Study, Ritter et al (1993) noticed that people with history of heavy drinking were related to more severe nuclear sclerosis, cortical, and posterior subcapsular opacities. Participants who drank wine had less severe nuclear sclerosis and cortical opacities. Increased consumption of beer was related to increased risk of cortical opacities.

The genetic etiology of nuclear cataract was studied by Ibrahim M. Heiba et al. (1993) Their results suggested that a single major gene could account for 35% of the total variability of age-sex-adjusted measures of nuclear sclerosis. In a study on 506 pairs of female twins, the proportion of variance explained by genetic factors accounted for 48%; age accounted for 38% of the variance and unique environmental effects for 14% of variance. It proved that genetic effects are so important even in such a clearly age related disease. (Hammond C.J.2000)

With the above risk factors working at equal amount on both eyes, still there is considerable number of patients exhibiting cataract to a varying extent between their fellow eyes. Something else must be at work in patients with this asymmetry. Something intrinsic to the eyes may play a role deciding which eye to develop the cataract first. Report of biometrical difference between both eyes did exist (Hoffer KJ 1980) but whether this difference is present in patients with cataract asymmetry is yet to be studied. The research question to be answered in this study was whether significant morphological difference exists in patients with asymmetrical cataracts.

2.2. Cataract grading and classification

Study on cataract requires a reliable, repeatable and rapid method for grading cataract. In order to meet the demand for epidemiological and clinical study on cataract, the cataract classification and grading had been developed and modified dramatically. It ranges from the simplest and rapid method (V Mehra et al 1988) of grading clinically significant cataract without pupillary dilatation to the most sophisticated ones requiring expensive gadget like slit lamp camera (Lens opacities classification system 1988) or digital camera. Even in one system of classification and grading, it had evolved to the extent picking up a small cataract progression in each cataract type. All these methods quantify cataracts subjectively. One objective method of grading cataract is by using lensometer (LM701). Use of this method had demonstrated that there was significant correlation between the lens opacity meter reading and the visual acuity loss. (SJ Tuft 1990)

V Mehra and D C Minassian in their rapid method of grading utilized the direct ophthalmoscope set at +2D to visualize the red reflex from a distance of 1/3 meter through the undilated pupil. The opacities in the lens that disturbed the red reflex were distinguished from non-lenticular opacities and were graded as follows. 0 being no opacities; 1 being tiny scattered dark spots in the red reflex, maximum area occupied by the dots is 1mm square; 2A obscured area being smaller than area of clear red reflex; 2B the obscured area equal to or larger than area of clear red reflex and 3 red reflex being totally obscured.

Lens opacities classification system (LOCS I) (Chylack LT 1988) was developed for use in the lens opacities case control study (Leske MC 1991) in which the system was used to separate "cases" of cataract from "controls" without cataract. The LOCS I grades the presence or absence of opacification in each of three lenticular zones: Nuclear (N), posterior subcapsular (P) and cortical (C). The grading follows an ordinal scale ranging from 0 (no opacification) to 2 (definite opacification). A grading of 0 implies the absence lens opacities; a grade of 1 implies the presence of early opacification and grade 2 implies definite cataract. Some examples of such gradings are as follows: N0P0C0 for clear lens, N0P0C2 for a cortical cataract, and N0P1C0 for an early posterior subcapsular cataract. The boundaries between the gradings are defined by a set of standard photographs. The set consists of one color slit-lamp photograph that is used to grade nuclear opalescence as well as nuclear color, and three black and white Neitz CTR retroillumination photographs that are used for the posterior subcapsular and cortical classifications.

The nuclear zone as seen in slit lamp

The nuclear zone comprises the entire lens within the zones of enhanced supranuclear scatter; even in a clear lens the supranuclear zones appear as areas of enhanced scatter and therefore, are useful landmarks. (Chylack LT 1988)

Nuclear Color

The nuclear color is determined by the degree of yellowing of the brightest portion of the posterior cortical-posterior subcapsular reflex. The color of the nucleus is graded by comparison with the color of standard photograph N. (Chylack LT 1988).

Nuclear opalescence

The nuclear opalescence is graded by comparing the average opalescence of the nuclear region with that in the same area of the standard photograph. The color in this region is ignored in making this decision. The average density or opalescence of the nuclear zone must be envisioned and compared with the average opalescence of the standard. (Chylack LT 1988)

Cortical zone of a lens as seen in slit-lamp

The C or cortical zone includes the subcapsular anterior, cortical anterior, cortical equatorial, cortical posterior, and supranuclear zones of the original American Cooperative Cataract Research Group classification scheme. (Figure 2.1) (Chylack LT 1988)

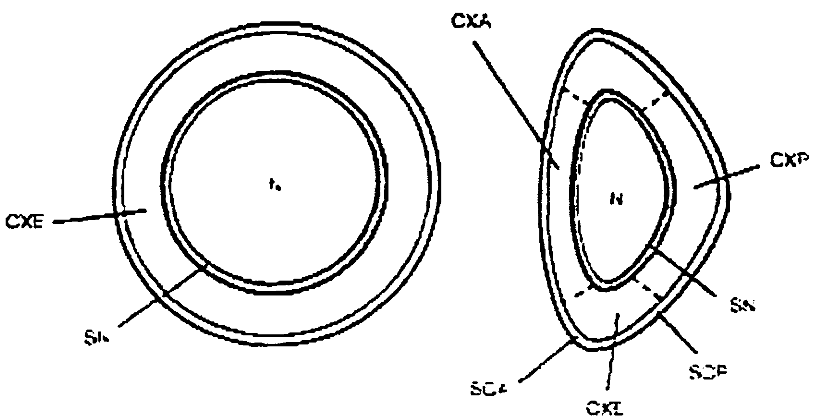

Figure 2.1. –Diagrammatic representation of anatomic zones of human crystalline lens used in American Cooperative Cataract Research Group. SCA= Subcapsular anterior; SCP= Subcapsular posterior; CXA= Anterior cortical; CXE= Equatorial cortical; CXP= Posterior cortical; SN=Supranuclear and N= Nuclear.

Cortical and Subcapsular cataract grading

The classification of cortical and posterior subcapsular opacities must be done only when viewing the opacity against a red reflex created by a narrow, short slit beam directed into the eye exactly along the visual axis. If cortical changes are seen in the obliquely oriented slit beam but disappear in the retroillumination image, they are not graded as cataract. (Chylack LT 1988)

In grading cortical opacity, the concept of "aggregate opacification" must be understood. The cortical spokes and other changes may appear in several noncontiguous locations in the cortex. The classifier must envision an aggregate opacity that is an opacity in which all of the individual cortical opacities are lumped into one zone. In this mental reconstruction the size of the opaque zone, relative to the size of the opaque zone in the cortical standard determines the class. (Figure 2.2)

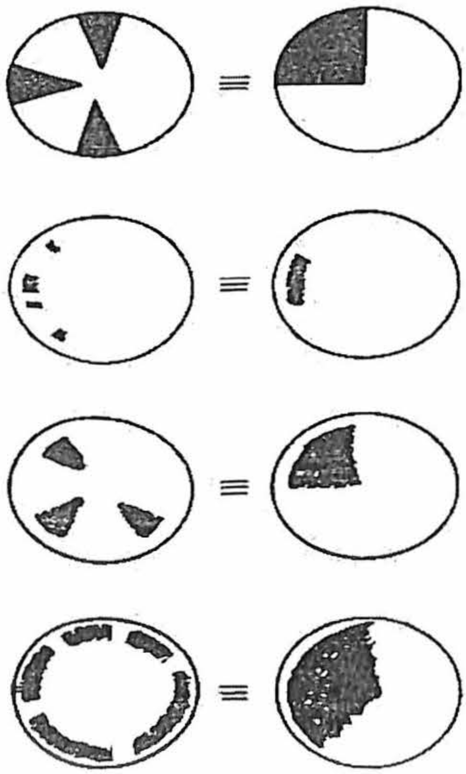

Figure 2.2. –Diagram indicating the method of estimating " aggregate " area of opacity if several separate opacities are present in crystalline lens. Mentally combine separate opacities into aggregate.

Selection Of the standard photographs

From hundreds of color slit-lamp photographs, one photograph (N) was selected to represent an intermediate range of color change and an intermediate amount of opalescence. In the similar manner the standard photographs for the cortical and subcapsular were selected from hundreds of retroillumination photographs of patients with cortical and subcapsular cataracts independently. (Lens opacities classification system 1988) Evaluation of the LOCS indicates an overall good to excellent reproducibility, either when used at slit lamp or to grade lens photographs. (Cristina Leske et al 1988)

Lens Opacities Classification System II (Chylack LT et al 1989) is the improved version of LOCS I. It uses a set of colored slit lamp and retroillumination transparencies to grade different degrees of nuclear, cortical and subcapsular cataract. The system uses 4 nuclear standards (NO, NI, NII, NIII) slit lamp photographs for grading nuclear opalescence (N), one of these nuclear standards (NI) is used to grade the nuclear color (NC); 5 cortical standards retroillumination photographs ("Ctr", "CI", "CII", "CIII" and "CIV") to grade the cortical cataract and 3 subcapsular standards retroillumination photographs ("PI", PII" and "PIII") to grade the subcapsular cataract. These standards represent boundaries between grades. It is easy to learn and can be applied consistently by different observers. It can be used to grade patients' cataracts at slit lamp or to grade the slit lamp or retroillumination photographs.

It is useful for both cross sectional and longitudinal studies of cataract. Maraini et al (1989) had independently validated this system. The authors found excellent inter- and intraobserver reproducibility. There was a tendency to underestimate posterior subcapsular cataracts on photographic gradings compared with slit lamp gradings.

John M. Sparrow (1990) had compared the LOCS II to the Oxford Clinical Cataract Classification showed that it had better intraobserver repeatability for all cataract type with the kappa value being higher. The interobserver repeatability was also better for all type of cataract except for posterior subcapsular cataract.

Lens opacities classification system III was developed to improve the limitation of unequal interval between the standards. (Chylack LT 1993). However, the even grading distribution was created in the immature spectrum of cataract maturity. No grading was given for the mature side of the spectrum that is relevant in a study such as this wherein difference between an early and a mature cataract do occur in a patient. Therefore modification to meet the demand of the study had been made.

2.3. Asymmetrical cataract

Age related cataract presenting simultaneously in both eyes but of differing severity is not an uncommon finding in ophthalmic clinic. The reason for asymmetry and the extent of it had never been studied. Hoffer in his famous study on biometry of 7500 eyes with cataract selected 1800 patients for a comparison of fellow eyes to determine the need to measure the axial length of the fellow eye in order to calculate the intraocular lens power for one eye and to determine the consistency of these measurements between fellow eyes. The mean of the difference in axial length between fellow eyes was 0.34mm. But this was not correlated with the asymmetry of cataract between the eyes. In a separate biometric study involving patients with no cataract in both the eyes, there were no significant differences in corneal curvature, intraocular pressure or refraction between right and left eyes. (Patrick Joi et al 1993) Comparison between right and left eyes could not determine whether there is any significant difference in the keratometric reading between severely cataractous and the less cataractous eyes.

2.4. General Dimension of the globe

The outer anteroposterior diameter of the globe averages 24.15mm(range, 21.7-28.75), whereas internal anteroposterior diameter averages 22.12mm. These findings were obtained by measuring enucleated eye from cadavers. (Duane's

Ophthalmology) However in vivo measurements were usually done by means of ultrasound. The average anteroposterior diameter from this measurement was in between the outer and the internal diameters; it was 23.65 ± 1.35mm (Kenneth J Hoffer 1980). This is because the measurement was made from the anterior surface of the cornea to the anterior surface of the retina. The signal that was reflected from the inner retina surface was picked up by the transducer forming the posterior most limit of the axial length from the anterior corneal surface.

The anterior chamber depth was measured from the corneal apex to the center of the anterior capsule. There was considerable variability in anterior chamber depth based on age, refractive error, and genetics. The anterior chamber depth decreases with age because of thickening of the lens. Hoffer, in his biometry of 7500 cataractous patients, found that the mean anterior depth was 3.24mm with the range of ± 0.44mm.

Kenneth J. Hoffer measured the lens thickness of cataractous lens of 600 patients. He found that the average lens thickness was 4.63 ± 0.68 mm.

2.5. A-scan ultrasonography

Biometry is a word that does not specifically have to do with ophthalmology. It is merely a term used when discussing biological data and statistics. In ophthalmology A-scan biometry is synonymous to measurement of the axial length of the eye for the estimation of the intraocular lens power prior to cataract surgery. (Kendall CJ 1990) (H R Atta 1999)

A-scan ultrasonography sends a beam of pulsed energy along a fixed line through the organ of interest and displays the echoes reflected back from surfaces intersected by the beam. The ophthalmic ultrasound uses a frequency of 10MHz, the best compromise between resolution and penetration. A piezoelectric crystal transducer generates the ultrasonic waves, which is capable of generating and receiving ultrasonic waves. The amount of time for a transmitted signal to return from a reflected surface can be used to calculate the distance from the transducer to the surface. Different structures transmit the ultrasonic energy at different velocities. However, most A-scan instruments employ a preset an average velocity (1548m/sec in this study) for the entire eye that represent a composite of the different velocities encountered by the beam. (D M. Albert and F A. Jakobiec1994)

In order to get the actual axial length of different structures along the optical axis, remeasurement using specific velocity for a specific tissue could be done. The sound wave travels in different tissue with a different speed, faster through a more solid structure and slower through a less dense structure. The ultrasound travels through the cataractous lens with an average speed of 1641m/sec and with a speed of 1532m/sec through liquid media like the aqueous or vitreous.

The crystalline lens may vary in thickness, density, and average sound velocity. It is difficult to determine the velocity of an individual cataractous lens because cataract changes may increase the liquid content (lower the velocity), create a dense nuclear sclerosis (increase velocity), or both. Therefore in this study we used speed of 1548m/sec for the composite eye. To calculate the corrected lens thickness, the average velocity of 1641m/sec for all lenses was used.

Instead of re-measuring the eye with the correct speed, the actual axial length of a tissue along the optical axis can be calculated mathematically using velocity correction equation. (Kenneth J. Hoffer 1994)

AL (corrected) = AL (measured) X V (corrected)/V (measured)

Where,

AL (corrected)= Axial length of the tissue to be measured.

AL (measured)= Measured axial length of the same tissue using average sound for the whole eye.

V (corrected) =Sound speed in the particular tissue.

V (measured)=Average sound speed for the whole eye. (1548m/sec)

Use of composite ultrasound speed of 1548m/sec. had caused a thin measure of the lens and a deeper anterior chamber than the real depth across the board. The speed 1641m/sec was used to correct the lens thickness. Cataract maturity increases the water content and thus reduces the sound speed. So use of the correction speed on mature cataract will give a thicker measurement whereas use on a mildly cataractous lens will give a thinner lens measurement. Use of specific speed for each cataract was not possible.

3. MATERIALS AND METHODS