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Refractive and Visual Outcomes of Femtosecond Laser-AssistedCataract Surgery

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A thesis submitted in fulfilment of the requirements for the degree of Master of Philosophy in Medicine at the University of Sydney

2015

Dedications

To my beloved family – Viktor, Katyusha and Joe

Acknowledgements

I would like to thank my supervisor, Associate Professor John Grigg, for his guidance and support during this project. Dr. Grigg has contributed much of his time facilitating data collection, proof-reading manuscripts and this thesis. I am very grateful.

Dr. Geoffrey Painter, my associate supervisor, has also contributed greatly towards the project by reviewing data analysis and manuscripts. I would like to express my gratitude.

Ms. Natalie Duffy, at Gordon Eye Surgery, contributed significantly to the collection of the large patient databases used in this project. I am very thankful for all her work.

Dr. Yi-Chiao Li has rendered great assistance in the analysis and presentation of the data. I thank him for his contributions.

Finally, thanks must go to the staff at Gordon Eye Surgery who have welcomed me during the data collection and helped me whenever they can. Thank you.

Declaration

This thesis is the result of study during the years 2012 to 2014. The work is my own and has not been submitted for the award of any other degree at any other university.

I gratefully acknowledge the following colleagues and collaborators for their contribution to this research project:

Ms. N. Duffy, for her assistance with part of the data collection and entry;

Dr. Y-C. Li, for his assistance with statistical analysis.

Abstract

Background: Femtosecond laser-assisted cataract surgery (FLACS) has been postulated to produce better refractive outcomes. However, refractive and visual outcomes of FLACS compared to conventional phacoemulsification cataract surgery are currently still lacking.

Objective: To compare the refractive and visual acuity outcomes of FLACS to manual cataract surgery.

Design: Comparative case series.

Participants and Controls: Consecutive series of patients in a private ophthalmic practice in Sydney, Australia, with 337 eyes undergoing femtosecond laser assisted cataract surgery and 230 eyes manual cataract surgery.

Intervention: The Alcon LenSx femtosecond laser was used to create the corneal wounds, anterior capsulotomy and fragment the lens in the femtosecond laser group before phacoemulsification. The manual group underwent standard manual phacoemulsification surgery.

Main Outcome Measures: Residual astigmatism, surgically-induced corneal astigmatism, achievement of target refraction and best-corrected and uncorrected distance visual acuity.

Results: The femtosecond laser group had statistically less mean residual post-operative astigmatism (0.74 vs 0.92 Dioptre cylinder, improvement of 0.18 D, $p<0.001$, 95% C.I. 0.09-0.26) than the manual group. The femtosecond laser produced equivalent mean magnitude (0.53 vs 0.56 Dioptre, $p=0.281$) and variability (standard deviation 0.31 vs 0.33, $p=0.239$) of surgically-induced corneal astigmatism compared to manual cataract surgery. Both surgical methods had equivalent achievement of target spherical equivalent (69% within 0.5 D of target refraction in each group, $p=0.911$) despite higher rates of axial lengths < 22 mm or > 26 mm in the femtosecond group. In eyes with good visual potential and an emmetropic target refraction, post-operative uncorrected distance visual acuity was statistically better in the femtosecond group with an average logMAR 0.0933 compared to 0.1393 (improvement of 2.4 logMAR letters, p=0.020) and with 23% vs 10% of eyes achieving 6/5 or better (p=0.008) and 60% vs 36% of eyes achieving 6/6 or better (p<0.001).

Conclusions: Femtosecond laser-assisted cataract surgery produced less residual post-operative refractive astigmatism and better unaided distance visual acuity compared to manual cataract surgery in this case series. Improved lens centration, tilt and positioning might account for this reduction in astigmatism, as there was no statistically significant difference in surgically-induced corneal astigmatism. This study does not support the hypothesis that femtosecond laser improved the predictability of target post-operative manifest refraction. We did demonstrate a small improvement in best-corrected as well as unaided visual acuity in the femtosecond group, but future randomised control studies with equal baseline characteristics are needed to minimise the effect of confounding variables.

Abbreviations

AL	Axial length
BCDVA	Best-corrected distance visual acuity
CCC	Continuous Curvilinear Capsulorrhexis
CCI	Clear corneal incision
ECCE	Extra-capsular cataract extraction
ELP	Effective lens position
FLACS	Femtosecond laser-assisted cataract surgery
ICCE	Intra-capsular cataract extraction
IOL	Intraocular lens
IOP	Intraocular pressure
LASIK	laser *in situ* keratomilieusis
logMAR	logarithm of minimal angle of resolution
RCT	Randomised control trial
SIA	Surgically-induced astigmatism
SRK	Sanders-Retzlaff-Kraff
UCDVA	Unaided distance visual acuity

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Chapter 1. Introduction

1.1 Cataract Surgery – An Overview

1.1.1 Cataract – A Major Cause of Vision Impairment

Cataract is a major cause of visual impairment. Worldwide it is the leading cause of blindness, accounting for 47.8% of blindness in the world in 2002(1). Although effective surgical services have reduced the rate of blindness due to cataract in developed countries, it remains the leading cause of low vision(1).

In Australia, cataract is the leading principal diagnosis of ophthalmic disorders, accounting for 60.3% of all encounters(2). Cataract extraction accounts for 70% of hospitalisation for eye problems: Altogether, there were 172,224 lens operations carried out in financial year 2005-06 alone (the majority, 165,397, by phacoemulsification) (2). Lens procedures cost the public hospital system over $127 million in 2005-06 (2). However, as private hospitals accounted for more than twice the number of lens procedures carried out in the public hospital system, the monetary cost of cataract surgery in 2005-06 was in excess of $500 million nation-wide(2). Cataract is a significant public health burden indeed.

1.1.2 History of Cataract Surgery

The earliest form of cataract surgery is couching (3). It is said that couching originated in India more than 2,500 years ago and spread through the Roman empire, mediaeval Europe and even sub-Saharan Africa. The method involves puncturing the eye somewhere posterior to the limbus with a needle or knife and pushing the lens to displace it into the vitreous. Complications such as endophthalmitis and lens-induced inflammation limited the results of couching.

After gaining better understanding of the anatomy of the eye in the renaissance period, Jacques Daviel (1696-1762) revolutionalised cataract surgery by developing extracapsular cataract extraction

(ECCE)(4). His method was to make a large inferior corneal wound, incise the anterior capsule, express the nucleus and curette remaining cortex. His “success” rate was 50%, limited by endophthalmitis, loss of vitreous/uveal/retinal content, inflammation from retained lens material and corneal wound healing. Although limited by the technology available at his time, Jacques Daviel propelled cataract surgery into the modern era and ECCE was the standard of care for over a century until the late 1800’s.

The desire to eliminate lens-induced inflammation and posterior capsular opacification led to the development of intracapsular cataract extraction (ICCE) (5), whereby the lens and capsule are removed together. The main barrier in ICCE compared to ECCE is breakage of zonules, and various methods had been devised, such as mechanical breakage by muscle hook, direct grasping of lens by forceps, suction cups and later on cryotherapy probes, and usage of α-chemotrypsin. With the advent of the operating microscope, suture material and sterilisation, ICCE developed into a successful procedure and is still used today in the developed world in limited circumstances, such as dense cataracts with weak zonular support due to trauma or pseudoexfoliation syndrome. However, ICCE is complicated by large corneal incisions and consequent induced astigmatism, corneal endothelial touch by cryotherapy probe or lens, vitreous loss leading to retinal detachment and cystoid macular oedema as well as lack of remnant capsular support for posterior chamber intraocular lens (IOL).

In the middle of the 20th century, the pendulum swung back to ECCE to avoid the complications of ICCE listed above. Double lumen irrigation/aspiration cannulas were developed for removal of cortex material from the capsular bag after the nucleus was expressed. This avoids the problems of inflammation and posterior capsular opacification due to retained cortex experience in earlier ECCE, while the capsule retains vitreous and provides support for posterior chamber IOL. ECCE was the main technique used in the 1970s and ‘80s century until the wide-spread adoption of phacoemulsification in the developed world.

1.1.3 Phacoemulsification Surgery

All methods of cataract extraction described in the previous section required expression of the nucleus. This has the disadvantage of damaging the corneal endothelium and necessitating large corneal wounds and consequent induced astigmatism. In 1967, Charles Kelman pioneered phacoemulsification that revolutionalised cataract surgery (6). This technique utilises a small tip to deliver ultrasound energy to emulsify and break up the nucleus. The nuclear fragments are then aspirated through a small port.

The small corneal wound delivers several advantages. The small wound allows maintenance of the anterior chamber during the operation, reducing vitreous pressure and risks of choroidal haemorrhage. Surgically induced corneal astigmatism from the small phacoemulsification wound is much less compared to the large wounds required for ICCE and ECCE. Furthermore, foldable IOLs made of silicone or acrylic were developed and can be delivered through a corneal incision as small as 2.3 mm. Today, the majority of corneal wounds do not require suturing and the wound healing is much faster. The rapid visual rehabilitation and superior refractive results have propelled wide-spread adoption of phacoemulsification in the developed world since the 1990s.

There are many variants of phacoemulsification surgery and each surgeon develops his/her own preferred style of operating. A basic phacoemulsification procedure involves:

- Ocular anaesthesia: Either peribulbar, sub-Tenon's, retrobulbar, topical or rarely general anaesthesia.
- Globe exposure: Application of antiseptic on the eye, placement of sterile drape and exposure of the eye with a speculum.
- Paracentesis: With a small sharp blade. This is followed by the installation of an ocular viscoelastic device.
- Corneal wound: Clear corneal incision or scleral tunnel is made with a keratome knife of pre-set width, often 2.4 mm.

- Anterior capsulotomy: Most often performed by continuous curvilinear capsulorrhexis (CCC). CCC resists radial capsular tears, stabilises the nucleus inside the capsular bag to allow nuclear disassembly away from corneal endothelium and transfers haptic forces to promote IOL centration. The optimal shape and size of CCC is central and just overlapping the IOL optic, minimising anterior capsular phimosis, preventing anterior dislocation of IOL and facilitating IOL centration.
- Hydrodissection: Separates peripheral cortex from capsule to promote nuclear rotation and cortex removal.
- Lens disassembly: Two main methods are used. Phaco fracturing techniques ("divide-and-conquer") involve sculpting grooves in the nucleus, cracking the nucleus manually and emulsifying lens fragments. Chopping techniques involve grasping the nucleus firmly with high vacuum and using a sharp instrument (chopper) to break the nucleus into fragments. The chopping technique is less applicable to soft nuclei which are difficult to grasp by vacuum.
- Removal of cortex: By aspiration.
- Implantation of IOL: With the aid of an ocular viscoelastic device and through the corneal incision.
- Wound hydration: This usually seals the corneal wounds without the need for suturing.

1.1.4 Intraocular Lens

Before the advent of intraocular lenses (IOLs), cataract surgery resulted in aphakia and attendant optical problems of aphakia correction by spectacles. Harold Ridley was the first ophthalmologist to implant a lens made of polymethylmethacrylate into an eye for aphakic optical correction in 1949. This proved to be revolutionary, as IOLs are far superior to spectacles or contact lenses in optical correction of aphakia, as it eliminates the problems of aniseikonia and various aberrations (7).

The optical advantages of an IOL as correction for aphakia has driven successive waves of innovations in IOL design (8). Various materials have been used to make IOLs, with acrylic being the most common material today. A large number of designs enable IOL support in the anterior chamber angle, on the iris, in the ciliary sulcus or in the capsular bag. Foldable IOLs allows implantation through a small corneal incision without wound enlargement, avoiding the need for wound suturing in the majority of cases, minimising induced corneal astigmatism and promoting rapid healing and visual rehabilitation. The posterior IOL surface and edge have been improved to reduce posterior capsular opacification. Aspheric IOL shapes have reduced spherical aberrations. Finally, multifocal IOLs of various designs have been developed to reduce dependence on spectacles post cataract surgery.

Sophisticated IOL designs, combined with phacoemulsification surgery, have vastly improved safety and refractive results of cataract surgery. In the developed world today, cataract surgery is the safest and most successful operation in medicine. The low rate of complications and rapid visual rehabilitation have raised patient expectations. Cataract surgery today aims not only to treat a blinding pathology but also to provide desirable refractive results for the patient. The refractive aspect of cataract surgery has grown ever more important.

1.2 Determinants of Refraction Post Cataract Surgery

In the early stages of intraocular lens (IOL) implantation in the absence of biometry and IOL power calculation, the standard practice was to implant standard power IOLs of 19D, the average lens power of Gullstrand’s average human eye (7). This resulted in significant residual refractive errors. Improvement of surgical safety has prompted investigations into biometry measurements and IOL power formulae in order to achieve desired refractive outcome. Today, a number of advances have improved accuracy of IOL power calculation, but errors and refractive surprises still occur not infrequently.

1.2.1 Optics of Intraocular Lens Power Calculation

After cataract surgery, there are essentially six refractive media light must travel through to reach the retina: air, tear film, cornea, aqueous humor, IOL and vitreous. Due to the similarities in refractive index between the tear film, cornea, aqueous humor and vitreous, the important refractive interfaces are the air/tear film and the anterior and posterior surfaces of the IOL (7). Therefore, there are essentially two refractive elements in the eye: cornea and IOL, if one regards the IOL as a thin lens. These two elements focus light onto the retina over the length of the eye, which is represented by axial length. Using a thin lens vergence formula, the power of the IOL can be calculated using the following formula:

$P_{IOL} = \frac{n_{vitreous}}{(AL-ELP)} - \frac{1}{\left(\frac{1}{K} - \frac{ELP}{n_{aqueous}}\right)}$, where:

P_{IOL} is the calculated IOL power;

$n_{aqueous}$ is the refractive index of the aqueous;

$n_{vitreous}$ is the refractive index of the vitreous. The refractive indices of the aqueous and vitreous cannot be measured clinically, but is assumed to be about 1.336 by Gullstrand with slight variation for different wavelengths of light (9).

AL is the axial length;

K is keratometry;

ELP is the post-operative effective lens position, ie. the distance between the anterior corneal surface and the principal plane of the implanted IOL.

The thin lens formula above ignores the thickness of the cornea and the intraocular lens and is therefore imperfect. However, thick lens formulae are considerably more complex and not in wide-spread use (10). The pioneering Russian ophthalmologist S. N. Fyodorov was the first in applying the thin lens formula in calculation of IOL power (11). It has stood the test of time ever since and forms the basis of IOL power calculation in all subsequent efforts. The formula above appears simple enough – the power of IOL can be calculated by knowing three variables – axial length, keratometry and effective lens position. The axial length and keratometry can be measured clinically. However, the post-operative ELP cannot be measured but must be predicted from pre-operative parameters. This prediction introduces the largest source of error and contributes to the majority of refractive surprises post cataract surgery today (12). The remainder of this section will review the advances in biometry measurements and calculations of IOL power.

1.2.2 Early Intraocular Lens Power Formulae: SRK-I and SRK-II

In the early years of IOL power calculation, the predictive results of theoretical formulae based on the thin lens formula in Chapter 1.2.1 were poor. Instead, regression analysis based on a large number of cases was shown to be more accurate. The Sanders-Retzlaff-Kraff-I (SRK-I) formula (13) was the most successful linear regression formula at the time and states:

$P_{IOL} = A - 0.9K - 2.5AL$, where:

A is a numerical constant, the “A-Constant”, which incorporates variation in IOL design and ELP;

P_{IOL} is the calculated IOL power;

K is dioptric keratometry measurement, assuming corneal refractive index of 1.3375;

AL is the axial length in mm.

From the SRK-I equation above, axial length is the most important determinant of IOL power calculation and a 1 mm of error in axial length error results in 2.5 D of shift in IOL power. Keratometry has a smaller effect on IOL power calculation. The A-constant depends on the shape and design of the IOL implanted. Manufacturers of IOLs today specify an average A-constant for their IOLs. However, surgical techniques and patient cohort also impact on the A-constant.

Therefore, for each surgeon using a specific biometry, surgical technique and IOL, the A-constant needs to be optimised.

The SRK-I formula was found to be adequate for eyes with average axial length between 22 and 24.5 mm. However, if axial length is outside this range (especially in long eyes), the formula was found to be inaccurate due to variable ELP in these eyes. The SRK-II formula (14) attempted to ameliorate the predictions by introducing a correction factor for the length of the eye. SRK-II improved predictive power. However, the empirical regression formulae were quickly superseded by theoretical formulae. Today, the regression formulae are no longer in widespread use.

1.2.3 Axial Length Measurement

Measurement of axial length is a crucial step in biometry. It is estimated that a 0.1 mm error in axial length measurement results in approximately 0.27 D of error in the spectacle plane in an eye with normal dimensions (10). Axial length error used to be the largest contributor to inaccuracy in biometry. Therefore, accurate measurement of axial length to within 0.1mm is necessary.

Initially, the only available instrument to measure axial length was A-scan ultrasound, which measures the time ultrasound waves travel through ocular media while reflected by refractive surfaces. A-scan ultrasounds are prone to a large number of errors. Since the velocity of sound waves in the aqueous, vitreous and lens are different, the optical path of the ultrasound determines the average velocity and therefore impacts on axial length measurement (15). Furthermore, the ultrasound needs to be placed exactly on the visual axis, which is difficult to achieve especially in eyes with dense cataracts or posterior staphylomata. Indentation of the cornea by the ultrasound probe in contact methods changes the axial length of the eye, and therefore immersion methods are preferred to reduce this error.

The imperfections of A-scan ultrasound led to the development of optical biometry using the principle of coherence interferometry (16). Optical biometry has many advantages over ultrasound. It is a non-contact method, eliminating errors from indentation. The patient fixates on the target while measurements are taken, ensuring the measurements are as close to the visual axis as possible. Optical biometry does have limitations. It cannot be used to measure eyes with dense cataracts. It is still dependent on assumptions made of refractive indices of various optical media. Moreover, the axial length measurements are from corneal surface to retinal pigment epithelium rather than to the internal limiting membrane as in ultrasound measurements, requiring conversion between the two. However, optical biometry has vastly improved the accuracy of axial length measurements (17, 18). Today, optical biometry is the standard method of axial length measurement unless patients have dense cataracts or cannot comply with measurement. The accuracy is so high that axial length measurement is now no longer the largest contributing factor to refractive error (12). Optical biometry is commercially available as IOLMaster (Carl Zeiss Meditec) and Lenstar (Haag-Streit).

1.2.4 Keratometry

The cornea is the major refractive element in the eye, accounting for about 2/3 of the eye's refractive power (7). Furthermore, errors in measurement of corneal refractive power will impact on measurement and calculation of IOL power. Therefore, accurate measurement of corneal refractive power is pivotal. Unfortunately, measuring the cornea's refractive power is not simplistic.

Keratometers estimate corneal refractive power indirectly by measuring the size of an image reflected by the anterior tear film. This is used to estimate the radius of the corneal curvature, which was then used in thin lens formula to estimate dioptric refractive power of the cornea assuming an average refractive index. However, this ignores the refractive power of the posterior surface of the cornea, which is difficult to measure directly (19). Most methods assume the posterior corneal curvature is related to the anterior curvature (20, 21). However, how the two curvatures are related is still a subject of debate and refinement (22-24).

The estimation of dioptric power of the cornea is further complicated by spherical aberration. Spherical aberration adds to the dioptric power of the cornea, and this depends on the size of the pupil: the larger the pupil, the larger the spherical aberration (10). Therefore, measurement of pupil size is important. Furthermore, the cornea has a prolate configuration to reduce spherical aberration, and the asphericity of both anterior and posterior surfaces of the cornea changes with age (23, 24), further changing corneal dioptric power.

Taking the above together, measuring only anterior corneal curvature without refining the estimation of posterior curvature or spherical aberration will introduce errors in keratometric power estimation. Modern IOL power formulae attempt to take these factors into account.

1.2.5 Prediction of Effective Lens Position in Modern Theoretical Formulae

While axial length and keratometry can be measured clinically, the ELP must be estimated. Furthermore, ELP depends on IOL design. The early empirical formulae such as SRK-I inherently incorporated some estimation of ELP in regression, but this was crude and induced large errors. The adjustment factor introduced in SRK-II was largely a crude attempt to adjust for ELP, which varies with axial length.

Early theoretical formulae such as Binkhorst I (25) assumed fixed ELP regardless of eye configuration, which resulted in larger prediction errors than the regression formulae which at least had some inherent estimation of ELP. The “second generation” theoretical formulae started to attempt estimation of ELP. Binkhorst found an association between axial length and ELP and incorporated this correction in the Binkhorst II formula (26). Fyodorov found the corneal height to be associated with ELP (27). Both these measures improved accuracy of IOL power calculation. This lead to “third generation” theoretical formulae, including SRK/T (28), Hoffer-Q (29) and Holladay I (30), which used two parameters to estimate ELP and achieve more accurate estimation of IOL power. More than twenty years later, these third generation formulae are still in widespread use. The parameters used in various formulae are summarised in Table 1.

Table 1 Predictors of effective lens position used by theoretical formulae for calculation of intraocular lens power. ACD – pre-operative anterior chamber depth; AL – axial length

Formulae	**Predictors**							**Reference**
	AL	Corneal curvature	ACD	Lens thickness	Age	Refraction	Corneal width	
Binkhorst I								(25)
Binkhorst II	Yes							(26)
Fyodorov		Yes						(27)
SRK/T	Yes	Yes						(28)
Hoffer-Q	Yes	Yes						(29)
Holladay I	Yes	Yes						(30)
Haigis	Yes		Yes					(20)
Olsen	Yes	Yes	Yes	Yes		Yes		(31)
Holladay II	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unpublished

More recently, multiple regression analysis have been developed incorporating more variables. Olsen found that a regression using five variables – axial length, anterior chamber depth, keratometry, lens thickness and refraction – gave a more accurate prediction of ELP (31). Holladay incorporated seven variables in the Holladay II formula and also claimed superior predictive results, but did not publish the results of the regression analysis. These modern theoretical formulae, incorporating more variables to achieve more accurate ELP prediction, perform better than SRK/T across the spectrum of axial lengths (32). However, their use has not been widespread due to inertia from clinicians and commercial reasons. Continued refinement of ELP prediction in modern formulae should further improve refractive outcomes post cataract surgery.

1.2.6 Manufacturing of Intraocular Lens

The manufacturing and testing of intraocular lens is regulated by the International Organisation for Standardisation (ISO) standard 11979-2.2 (33). The standard stipulates the manufacturing error tolerance at 0.4 D, which represents a source of refractive error. Traditionally, IOLs are supplied in 0.5 D increments due to manufacturing error. However, some manufacturers of IOLs have conscientiously improved error tolerance below 0.11 D. This lead to a manufacturer providing IOLs with 0.25 D increments which was shown to reduce post-operative refractive error (34). Unfortunately, the technical specification and performance of IOLs are difficult to find as suppliers guard them as commercial secrets. It is incumbent upon individual surgeons to seek these details from IOL suppliers in order to choose IOLs that reduce post-operative refractive error.

1.2.7 Benchmark Standards of Refractive Outcome Post Cataract Surgery

In 2009, the refractive outcomes of a large series of cataract operation in the National Health Service of the United Kingdom was published (35). The authors found that 55% of eyes were within 0.5D and 85% eyes were within 1.0D of calculated target refraction. This paper is regarded as the benchmark standard for refractive outcomes after cataract surgery.

However, as patient expectations continue to grow, this level of refractive accuracy is now regarded as unacceptable by many patients and ophthalmologists. There is a constant drive within the ophthalmology community to continue to improve refractive outcomes post cataract surgery. Since refinements in the measurements of axial length and keratometry have decreased the amount of error these two variables contribute, the focus is now on improving the ELP, which is the largest source of refractive error today. Besides optimising IOL power formula, attention is now turned to optimising surgical techniques. Femtosecond laser assisted cataract surgery represents such an attempt to improve refractive outcome, as will be further discuss in Chapter 1.3 below.

1.3 Femtosecond Laser-Assisted Cataract Surgery

1.3.1 Laser in Cataract Surgery

The idea of using laser in cataract surgery is not new. Krasnov used a Q-switched ruby laser to create small perforations on the anterior capsule to allow release of soft lens material (36). The neodymium-doped yttrium aluminium garnet (Nd:YAG) laser was used by some investigators to create anterior capsulotomy, (37). Lasers such as Erbium:YAG were focused directly on the nucleus to break down lens material to delay the need for cataract surgery (38). The Nd:YAG laser was coupled to a phacoemulsification probe to aid breakage of nuclear fragments (39) and was shown to reduce ultrasound energy (40). However, due to either complications or clinician preference for non-laser-based techniques, these applications of laser never gained wide-spread acceptance in the management of cataracts. Prior to femtosecond laser, the only laser in routine use for cataract management was the Nd:YAG in breaking posterior capsular opacification after cataract surgery (41).

1.3.2 Femtosecond Laser: Physical Properties

The femtosecond laser employs Nd:glass as the active medium, which generates laser light with a wavelength of 1053 nm delivered in pulses of 10^{-15} second. The wavelength of the femtosecond laser means it has little absorption by the cornea, which allows precise focusing of 3 µm spots within 5 µm of accuracy within the anterior chamber (42). The femtosecond laser's ultrafast pulse time of

10^{-15} second allows delivery of very small amounts of energy to target tissues, minimising collateral damage. The femtosecond laser's effect on the target tissue is that of photodisruption, turning target tissue into plasma and creating rapidly expanding and collapsing small gas bubbles (43). The bubbles and acoustic shock waves separate tissue. By creating a plane of bubbles, the femtosecond laser can achieve extremely precise cuts of intraocular tissue with little collateral damage to adjacent structures.

1.3.3 Application of Femtosecond Laser in Corneal Refractive Surgery

Femtosecond laser was first introduced in corneal refractive surgery in 2001 (44). It is used to create flaps in laser *in situ* keratomilieusis (LASIK) surgery, with more than two million procedures performed worldwide (45). The flaps created by femtosecond laser are more accurate and predictable than possible with a manual keratome, which enables improved safety and outcome in LASIK surgery (46). Today, femtosecond laser flap creation is the gold standard in LASIK surgery and is being increasingly applied to many other aspects of corneal surgery where extreme precision results in better outcome and safety.

1.3.4 Application of Femtosecond Laser in Cataract Surgery

As discussed in Chapter 1.2.7, precise refractive outcomes after cataract surgery have become more and more important. Since femtosecond laser can perform cuts in the anterior segment with a level of precision unattainable with manual methods, it has been applied to cataract surgery to improve its precision. In cataract surgery, three steps require separation or cutting of ocular tissue: corneal wound creation, anterior capsulotomy and lens fragmentation. Femtosecond laser has been applied to all three steps in what is now termed femtosecond laser-assisted cataract surgery (FLACS).

There are four main commercial platforms of femtosecond laser delivery system for FLACS: LenSx (Alcon, Alisa Viejo, CA, USA), LensAR (LensAR, Orlando, FL, USA), Catalys (Optimedica, Santa Clara, CA, USA) and Victus (Technolas Perfect Vision, Bausch and Lomb). Although bearing small differences, the basic procedures are similar between all platforms and include the following steps:

1. **Pre-operative assessment:** This involves full ophthalmic and biometric examination of the eye, to assess fitness for femtosecond laser-assisted cataract surgery. The size, shape and position of anterior capsulotomy are determined keeping the intended IOL in mind. The location, structure and depth of corneal wounds are chosen, as well as the nuclear fragmentation pattern.
2. **Docking of the eye:** The eye needs to be immobilised before femtosecond laser can be applied. However, the docking process creates several problems. First, the normal anatomy of the eye is distorted. Secondly, the docking process can raise intraocular pressure (IOP) to ≥ 80 mm Hg (47, 48). This level of IOP could be tolerated by younger patients in corneal refractive surgery, but carries significant risks of central retinal artery occlusion and "snuff-out" of glaucomatous optic neuropathy in typically older cataract patients with more ocular co-morbidities. This has compelled manufacturers of femtosecond laser platforms to devise alternative docking methods to reduce IOP rises. The LenSx platform used to have curved contact lenses which produced IOP rises of 40 mm Hg (49). In 2013, Alcon introduced the Soft-fit contact lens system for the LensX platform which has enabled procedures to be completed with IOP elevations to only the low 20mmHg range. OptiMedia also devised a fluid-filled interface (LiquidOptics) which limited IOP rise to about 8-12 mm Hg (50, 51). Development of no-touch, non-applanating suction system is continuing and may increase acceptability of femtosecond laser-assisted cataract surgery.
3. **Anterior segment imaging:** After the eye is docked, three-dimensional high-resolution imaging of the anterior segment is required to deliver precise femtosecond laser energy to intended target tissues and avoid damage to other ocular structures such as the iris and posterior capsule. The LenSx, Catalys and Victus platforms employ Fourier-domain ocular coherence tomography (FD-OCT) (52) while the LensAR platform uses confocal image system similar to Scheimpflug cameras (53, 54).

4. **Laser treatment:** During the treatment stage, femtosecond laser energy is delivered to the target tissue in a peripheral to central and posterior to anterior direction where possible. Therefore bubbles created first are located posterior to subsequent bubbles. This has two advantages: posterior bubbles scatter subsequent laser energy and reduces transmission to the retina while they do not affect focusing of subsequent laser energy (55). The order in which corneal incisions, capsulotomy and lens fragmentation are carried out varies between different platforms.
5. **Cataract removal and IOL implantation:** The LenSx and Victus platforms require patients to be transported to another room for subsequent surgery, while the LensAR and Catalys platforms allows the patient to remain on the same bed while the femtosecond laser machine is removed. The eye is sterilised, and the corneal incisions are opened by a blunt spatula. The anterior capsulotomy flap created by the laser is removed with a pair of forceps. Lens disassembly on the laser-cracked nucleus and implantation of IOL proceed as in conventional phacoemulsification surgery.

1.3.5 Safety Aspects of Femtosecond Laser-assisted Cataract Surgery

As a new surgical technique, FLACS is said to require a period of adaption. A number of reports in the literature suggest that in the first hundred cases of FLACS, there could be an increased complication rate as surgeons become accustomed to the laser. Bali *et al*. reported a number of complications in the initial introduction of FLACS including suction breaks during treatment, incomplete corneal incisions requiring manual keratome, anterior capsulotomy tags and radial tears, free-floating capsulotomy, capsular blockage syndrome, posterior capsule tears and dropped/dislocated nucleus (56). However, only three of the surgeons had previous experience with femtosecond LASIK surgery and it was unclear what training/instruction they received. With more experience with FLACS, the rate of complications decreased significantly (57).

A specific complication of FLACS is the phenomenon of anterior capsular tags, which probably results from patient movement or optical imperfections (such as corneal folds or scars) during the delivery of the laser energy. The incomplete capsulotomy can result in anterior capsular tags during removal of the capsulotomy. Robin *et al*. reported an incidence of anterior capsular tear of 1.87%, which extended to the posterior capsule and resulted in vitreous loss in some cases (58). Even in complete capsulotomies, scanning electron microscopy revealed the presence of aberrant misplaced laser pits. The occurrence of anterior tears due to capsular tags and bridges was also observed by a number of other reports and the incidence of tears range from 4% (59) to 5.3% (60). Interestingly, another group reported minimal rate of anterior capsular tear of 0.1% (61). Therefore, the incidence of anterior capsulotomy tag leading to tears appears to be highly variable and surgeon/platform-dependent. Meticulous care to avoid patient movement during laser energy delivery such as communication and improved patient comfort would likely to be a factor. Further improvement in the laser delivery systems to recognise and compensate for patient movement would also help to reduce this complication.

There are other FLACS-specific complications reported in the literature. One specific complication of FLACS is capsular block syndrome where the posterior capsule ruptures during hydrodissection, possibly due to gas bubbles created during laser lens fragmentation (62) and prevented by lens decompression or manual division before hydrodissection (63). Another complication was inadvertent delivery of femtosecond laser energy to the cornea due to patient movement and suction breakage (64, 65).

Therefore, adoption of FLACS does require training and modification of surgical techniques (66). With training and preparation, the majority of published studies reported equivalent rates of complication compared to conventional cataract surgery (for example, (67, 68).

One group of investigators reported significantly decreased effective phacoemulsification time after femtosecond laser lens fragmentation compared to conventional phacoemulsification (69, 70).

However, it is not clear whether the surgeons used “divide-and-conquer” or “phaco-chop” techniques and the grade of cataract was not controlled. These findings were replicated by other groups, again without specifying lens disassembly techniques (67, 68). Despite shortcomings in study designs, it is very plausible that lens disassembly by femtosecond laser does decrease ultrasound time and energy.

The decreased ultrasound time and energy could have several benefits, one of which may be decreased corneal oedema and endothelial damage. Palanker *et al*. showed that FLACS resulted in less corneal oedema and this was associated with a slightly increased gain in BCDVA in a non-randomised non-blinded study involving 59 eyes (55). Takacs *et al.* showed that eyes undergoing FLACS had significantly less corneal oedema at day one post-operatively compared to conventional surgery, but the difference disappeared by one week (71). Abell *et al.* published 6-month follow-up data on FLACS (72). In agreement with the previous studies, they found less immediate post-operative corneal oedema in the FLACS group than manual surgery, but there was no difference at 6 months. They also found the FLACS group had less endothelial cell loss at 6 months than manual surgery. Interestingly, a subset of patients in the FLACS group did not undergo laser-assisted wound creation, and they appeared to have less endothelial cell loss at 6 months compared to those with wounds created by laser, raising the possibility that the laser energy used to create corneal wounds is actually more damaging to the endothelium than manual keratome. They concluded the best way to minimise endothelial loss was to create wounds manually and use laser-assisted lens fragmentation to achieve zero effective phaco time.

Another possible benefit of decreased ultrasound energy is decreased cystoid macular oedema. In a small study of 40 eyes, FLACS resulted in a marginally less increase in inner macular thickness measured by ocular coherence tomography (49). However, this difference became non-significant by 1 month post-operatively, and no difference was found for foveal thickness or macular volume. A very small follow-up study was unable to replicate the finding of increased inner macular thickness

(73), and significant criticism of the methodology exists (74). No other reports could demonstrate any difference in the rate of cystoid macular oedema between FLACS and conventional surgery post-operatively (67, 68, 75).

Taken together, FLACS appears just as safe as conventional phacoemulsification surgery. FLACS does employ slightly different techniques and specific complications can develop. However, given appropriate training and adaptation, it appears as safe as conventional phacoemulsification, with the possible benefits of decreased ultrasound energy.

1.3.6 Intraocular Lens Positioning after Femtosecond Laser Anterior Capsulotomy

The creation of anterior capsulotomy by continuous curvilinear capsulorrhexis is one of the most difficult steps in cataract surgery. It is estimated that 1% of manual capsulorrhexis results in an anterior capsular tear, which can extend to the posterior capsule and result in vitreous loss (76).

It has been shown in several studies that the size, circularity and position of the anterior capsulotomy can affect lens positioning. Small anterior capsulotomies may cause phimosis and hypermetropic shift of the IOL (77). Conversely, large or irregular anterior capsulotomies can cause IOL tilt and decentration (78). Size of anterior capsulotomy also affects ELP (79), which is the largest contributing factor to post-operative refractive error and the main focus of IOL power calculations, as discussed in Chapter 1.2.5. All of these changes impact on refractive results post cataract surgery (80). Furthermore, decentred and tilted IOLs induce higher order aberrations (81). These changes are magnified when toric or multifocal IOLs are implanted.

The precision of femtosecond laser allows creation of a precisely circular, centred and sized anterior capsulotomy. Nagy *et al.* were first to demonstrate that anterior capsulotomy created by femtosecond laser in porcine and human eyes has a precision unmatched by manual capsulorrhexis (82). Capsulotomy created by femtosecond laser is unaffected by corneal magnification, anterior chamber depth or pupil size as in the case of manual capsulotomy (83). Furthermore, femtosecond laser capsulotomy appears to reduce the amount of incomplete overlap with the IOL one week post op in a non-blinded study (83). Some studies demonstrated that femtosecond laser capsulotomy may also be more resistant to radial tears (84, 85). The improved precision of laser capsulotomy over manual capsulorrhexis has been replicated in a number of follow-up studies and appears irrefutable (55, 84, 86, 87).

The precise capsulotomy has been found to decrease IOL decentration in a study of digital photographs of 40 eyes post femtosecond capsulotomy and manual CCC (88). The Femtosecond laser capsulotomy group was found to have less IOL decentration, although it was not clear how patients were selected, whether there was blinding, or whether the decentration was associated with refractive error or visual problems. The authors followed up with another non-randomised non-blinded study using a Scheimpflug camera attached to a corneal topographer to measure IOL decentration and tilt in 45 eyes (89). Again, a statistically significant improvement in IOL decentration and tilt was found, but this did not translate into clinically significant improvement in uncorrected visual acuity.

Mihaltz *et al.* used a wavefront aberrometer to study optical aberrations, image quality and IOL tilt following femtosecond and manual capsulotomy in 99 eyes in a non-blinded study (90). They found no difference in optical aberrations but slight improvement in IOL tilt, which was correlated with improved image quality (point spread function and modulation transfer function). There was no difference in the visual acuity between two groups.

The above studies appear to cast little doubt that an anterior capsulotomy created by femtosecond laser has a more precise size, circularity and position than manual capsulotomy. This appears to decrease incomplete IOL overlap, decrease IOL decentration and tilt in a small number of non-randomised non-blinded studies. Whether these results can be replicated by independent groups using better study designs, or how they will translate to a clinical benefit, remains to be seen.

1.3.7 Corneal Incisions with Femtosecond Laser

Femtosecond laser has been used to create clear corneal incisions (CCI) (55). In a study with cadaveric eyes, the multiplanar corneal wounds constructed with femtosecond laser appear to be more resistant to wound leakage (91). Although the uniplanar wounds constructed by keratomes usually self-seal without the need for suturing, femtosecond laser has the potential to construct eve safer wounds.

However, relatively little is known about the refractive effect of femtosecond laser. Serrao *et al*. studied the effect of 2.75 mm femtosecond laser tri-planar CCI and 2.75 mm manual uniplanar CCI on corneal topography on only 14 cadaveric human eyes (92). They found no difference in the surgically induced astigmatism or topographical measurements between two groups. This is a small study on *ex vivo* eyes, taking no account of corneal healing expected in patients. Besides this small *ex vivo* study, no other study on the effect of femtosecond laser CCI on the cornea exists so far.

1.3.8 Refractive Outcome of Femtosecond Laser-assisted Surgery

Given the effect of anterior capsulotomy on ELP and the ability of femtosecond laser to create accurate capsulotomies, it is postulated the femtosecond laser could improve the refractive outcome of cataract surgery. However, the data on refractive outcomes have been sparse so far.

All studies above suffered from small numbers of cases and lack of randomisation and blinding. Therefore, it remains inconclusive whether FLACS improves calculation of IOL power and refractive outcomes. Furthermore, no report of post-operative astigmatism has been made in the literature thus far.

1.3.9 Economic Aspects of Femtosecond Laser-Assisted Cataract Surgery

One of the most controversial aspects of FLACS is the economic impact on patients and health care systems. FLACS requires additional equipment and consumables, training of personnel and in most instances a separate room. Anterior segment imagining, application of the laser and transferring the patient to another operating table also means FLACS takes more time than manual surgery (93).

This translates increased cost, adding to the economic burden borne by patients and the healthcare system. The economic impact and potential erosion of surgical training has prompted heated discussion (74, 94).

Abell and Vote (95) recently published a cost-benefit analysis of FLACS compared to conventional manual surgery. Even with the most optimistic estimate of improvement in visual outcome and excluding all complications, FLACS is not cost-effective currently. The cost of FLACS will need to be lowered dramatically or the results of the technique need to be proven far superior, in order for FLACS to become cost effective.

1.4 Aim of the Study

The excellent safety profile and visual rehabilitation of phacoemulsification has transformed cataract surgery (see Chapter 1.1). The advances in biometry and IOL power calculation have improved post-operative refractive results so greatly that cataract surgery is regarded by some as a refractive procedure today, with heightened patient expectation of spectacle-free sharp vision (see Chapter 1.2). FLACS has been developed in this environment. There is little doubt that FLACS can create anterior capsulotomy and corneal incisions with an accuracy that manual keratomes cannot match, and this might result in marginally better IOL decentration and tilt (see Chapters 1.3.6 and 1.3.7). However, whether this translates to better refractive outcomes is uncertain, since studies in the literature are few in number and showed either no or marginal improvement in refractive outcomes so far (see Chapter 1.3.8). Considering the costs, FLACS is a current topic of intense controversy in ophthalmology and more data regarding the refractive outcomes of FLACS compared to conventional phacoemulsification is need.

The aim of this study is to compare refractive and visual acuity results between FLACS and conventional cataract surgery. Refractive and visual outcomes are measured by:

- Post-operative manifest refraction and how this relates to IOL power calculation

- Post-operative residual astigmatism
- Visual acuity, corrected and uncorrected

Chapter 2. Materials and Methods

2.1 Study Design

This study is a prospective non-randomised comparative case series comparing FLACS to conventional phacoemulsification surgery. Although double-blinded randomised control trials are the gold standard in interventional studies, this is not feasible at the current moment as FLACS is only available in the private sector in Australia at a considerable cost to the patient.

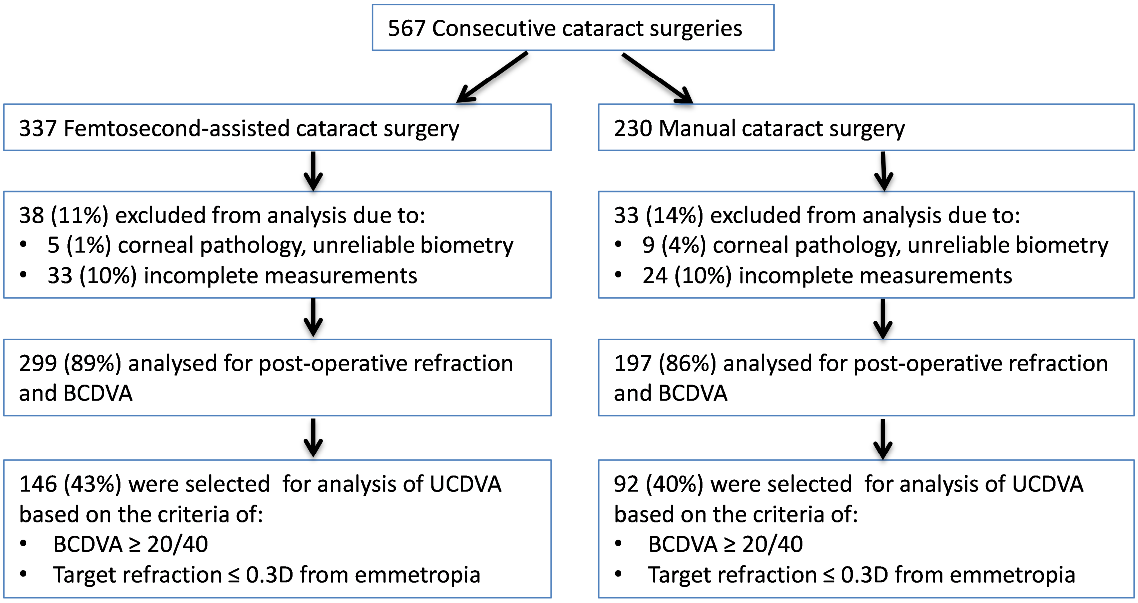
2.2 Participants

Three ophthalmic surgeons (Drs. J. Grigg, G. Painter and S. Booth-Mason) at Gordon Eye Surgery, Sydney were the first in Australia to implement the LenSx platform (Alcon LenSx Lasers Inc., Aliso Viejo, CA) in a freely accessible hospital setting at Dalcross Adventist Hospital, Sydney. From September 2011 to November 2012, these three surgeons performed 337 FLACS at the hospital (femtosecond group). During the same period of time, 230 eyes underwent conventional phacoemulsification cataract surgery by the same surgeons and were used as the control group (manual group).

Ten percent (33/337) of the femtosecond group and 10% of the manual group (24/230) had incomplete post-operative biometry, refraction or visual acuity results. In addition, 5/337 (1%) of the femtosecond group and 9/230 (4%) of the manual group had significant corneal and external diseases or an inability to co-operate with biometry or refraction post-operatively. These eyes were excluded from this study. Altogether, 299/337 (89%) eyes in the femtosecond group and 197/230 (86%) of eyes were available for analysis. This represents a satisfactory follow-up rate. The flow of patients is presented in Figure 1.

Visual acuity depends on post-operative refraction as well as the organic health of the eye. Furthermore, a subset of patients prefered to aim for myopia post-operatively in order to decrease

Figure 1 Flow chart of patient numbers analysed in this study. Abbreviations: BCDVA – best-corrected distance visual acuity; UCDVA – uncorrected distance visual acuity.



dependence on spectacles. In order to make valid comparisons of unaided visual acuity, eyes with post-operative best-corrected distance visual acuity (BCDVA) of worse than 6/12 and planned monovision defined as target refraction of more than 0.3D from emmetropia were excluded from analysis of uncorrected distance visual acuity (UCDVA). Altogether, 146/337 (46%) eyes in the femtosecond group and 90/230 (40%) met the criteria for analysis of UCDVA (see Figure 1).

Detailed discussions about the risks and potential benefits of the procedure were held and informed written consent was obtained from all patients. All patients who were suitable for laser-assisted surgery were offered the procedure and patients chose according to their freewill. The following exclusion criteria for femtosecond laser stipulated by the manufacturer were applied:

- Corneal disease that precludes applanation of the cornea or transmission of laser light at 1030 nm wavelength
- Descemetocele with impending corneal rupture
- Corneal opacity that would interfere with the laser beam
- Presence of blood or other material in the anterior chamber
- Hypotony, glaucoma, or the presence of a corneal implant
- Poorly dilating pupil, such that the iris is not peripheral to the intended diameter for the capsulotomy
- Conditions which would cause inadequate clearance between the intended capsulotomy depth and the endothelium
- Residual, recurrent, active ocular or eyelid disease, including any corneal abnormality (for example, recurrent corneal erosion, severe basement membrane disease)
- A history of lens or zonular instability
- Any contraindications to cataract or keratoplasty surgery
- Previous corneal incisions that might provide a potential space into which the gas produced by the procedure can escape

- Corneal thickness requirements that are beyond the range of the system
- Paediatric surgery

The study conforms to the tenets of the Declaration of Helsinki. Ethics approval was obtained from the University of Sydney Human Research Ethics Committee for the evaluation of the safety and refractive outcomes of the two surgical methods.

2.3 Pre-operative Evaluation

Patients underwent detailed ophthalmic examination before surgery, including automated refraction, keratometry, biometry, uncorrected distance visual acuity and best corrected distance visual acuity using Snellen visual acuity measurement, slit-lamp biomicroscopy and Goldman applanation tonometry to measure intraocular pressure (IOP). Automated refraction was obtained with a TopCon RM8900 autorefractor (TopCon, Tokyo, Japan). Biometry was recorded with an IOL Master optical biometer (Carl Zeiss Meditec, Dublin, CA) where possible or with immersion A-Scan using an OcuScan (Alcon, Fort Worth, TX) where not. In addition, corneal topography was measured with a Pentacam (Oculus, Germany) in some patients.

The patients' visual requirements were elicited and target manifest refraction was determined. The intraocular lens was chosen according to calculations from biometry using predominantly the SRK-T formula, but occasionally other third generation formulae were used where significant axial length aberration existed. Where significant corneal astigmatism existed, toric IOLs were chosen.

2.4 Surgical Intervention

All three surgeons in this study attended training courses on femtosecond laser in cataract surgery with pioneer cataract surgeons in the United States. Introductions were facilitated by Alcon Laboratories (Fort Worth, TX) in the USA.

The LenSx laser system was used to perform all the laser-assisted cataract procedures. A mixture of topical, peribulbar and sub-Tenon's anaesthesia was used. Chloramphenicol 0.5% (Chauvin

Pharmaceuticals, England) and Voltaren Ophtha (Novartis, NJ) eye drops were administered pre-operatively as per the hospital protocl. Pupillary dilation was achieved with 3 doses of phenylephrine 2.5% and cyclopentolate 1% eye drops (Chauvin Pharmaceuticals, England) with a supplemental dose of phenylephrine 2.5% at the completion of every laser procedure.

In the femtosecond group, docking of the laser delivery system was achieved by applanating the cornea with a sterile single-use patient interface under video microscope guidance and applying suction to stabilise the eye. The capsulotomy, lens fragmentation and corneal wound size and position were determined in the pre-operative planning phase, and laser energy was applied to the eye to create anterior capsulotomy, lens fragmentation and primary and secondary corneal incisions. One 2.4-2.5 mm trapezoid three-plane main wound and one 1.0-1.1 mm single-plane side port were constructed.

After the laser procedure, the patient was transferred to the operating suite where the eye was anaesthetised, prepared with a solution of 5% betadine and draped in a sterile fashion. Adrenaline was added to the Balanced Salt Solution Plus (Alcon Laboratories, Fort Worth, TX) irrigation solution at 1 mg / 1,000 mL and additional intracameral lidocaine and/or adrenaline was used when necessary. The corneal incisions were opened bluntly with a Slade spatula (Ascico, Westmont, IL), a viscoelastic device was instilled and the anterior capsulotomy flap was removed with capsulorhexis forceps. Gentle hydrodissection and nuclear rotation was carried out, if appropriate, after decompression of the anterior chamber. The nucleus was then divided manually by the surgeons' preferred technique following the path of the laser cuts and removed by phacoemulsification in segments. The Infiniti phacoemulsification system (Alcon Laboratories, Fort Worth, TX) with Ozil and IP technology was used with similar parameters between the three surgeons and between the two groups. Remaining cortical material was removed with standard irrigation and aspiration and a folded intraocular lens (IOL) was inserted into the capsular bag, followed by minimal hydration of the wounds and instillation of intracameral cefuroxime if the patient was not allergic. None of the wounds in this study required suturing.

Patients who underwent standard phacoemulsification surgery had identical pupil dilation, anaesthesia, preparation and sterile draping. The main corneal wound was constructed with a 2.4 mm keratome and a side port with a 15° blade. After the installation of viscoelastic, anterior capsulotomy was commenced with a cystotome needle and completed with capsulorrhexis forceps. Gentle hydrodissection and nuclear rotation, if appropriate, was carried out and the nucleus then divided with phacoemulsification by nuclear grooving and cracking. The remainder of the technique was identical to the laser-assisted technique described above.

2.5 Post-operative Evaluation

Patients were instructed to instil chloramphenicol 0.5% (Aspen, South Africa) and either dexamethasone 0.1% (Alcon Laboratories, Fort Worth, TX) or prednisolone 1%/phenylephrine 0.12% (Allergan, Irvine, CA) eye drops four times daily in the operated eye in a reducing schedule, determined by surgeon preference. Some patients also received ketorolac 0.5% (Allergan, Irvine, CA) eye drops in a similar schedule. Follow-up was at one day, one week and one-month.

Post-operative keratometry and refraction were measured at one month post-operatively. Auto-refractor readings were used to determine the post-operative residual astigmatism and spherical equivalent. Surgically induced astigmatism was calculated using the double angle vector analysis method (96).

2.6 Statistical Analyses

Statistical analysis (descriptive statistics, T-tests, Pearson's χ-square tests and generalised linear models) was performed with SPSS software version 21 (IBM/SPSS Inc., Chicago, IL).

Chapter 3. Results

3.1 Pre-operative Patient's Characteristics

Between September 2011 and November 2012, 299 eyes which had undergone femtosecond laser-assisted cataract surgery (femtosecond group) and 197 eyes which had undergone manual cataract surgery (manual group) were available for analysis (see Figure 1).

Their demographic and pre-operative refractive characteristics are summarised in Table 2. The femtosecond group was on average slightly younger by 4.7 years (p<0.001), more myopic by 0.47 D (p=0.099) and had better pre-operative best-corrected visual acuity by 0.0777 logMAR (logarithm of minimal angle of resolution, equivalent to 3.9 logMAR letters, p=0.007). There was no statistically significant difference in the amount of pre-operative corneal astigmatism and the two groups had equivalent rates of toric lens implantation. Notably, the femtosecond group had a significantly higher rate of high ammetropia greater than 4 Dioptres (D) (18% vs 9%) and axial length < 22 mm or > 26 mm (12% vs 4%). Patients with younger ages tend to have higher rate of high refractive error, especially high myopia (Table 2 Demographic and refractive characteristics of eyes undergoing femtosecond laser-assisted cataract extraction and manual phacoemusification cataract surgeries. Numbers displayed are mean ± standard deviation. P-values are derived from independent two-sample T-tests for averages and Pearson's X-square tests for percentages. logMAR – logarithm of the minimal angle of resolution.

	Femtosecond	Manual	p-value
Number of eyes	299	197	
Female eyes	64%	64%	0.925
Average age of eye at operation (years)	72.7 ± 9.2	77.3 ± 9.3	<0.001
Average pre-operative manifest refraction (D)	-0.15 D ± 3.45	+0.32D ± 2.91	0.099
Myopia -4 D or greater	13%	7%	0.036
Hypermetropia +4 D or greater	5%	2%	0.042
Axial length < 22 mm	7%	1%	0.001
Axial Length > 26 mm	5%	3%	0.222

Average pre-operative corneal astigmatism (dioptres cylinder)	0.88 D ± 0.64	1.00 D ± 0.67	0.059
Best-corrected visual acuity (logMAR)	0.2871 ± 0.2829	0.3648 ± 0.3284	0.007
Intraocular lens type	66% Monofocal 38% Toric 1% Multifocal	65% Monofocal 35% Toric	0.454

Figure 2), as well as unusual axial lengths, especially > 26 mm (Figure 3).

The ocular comorbidities of patients undergoing surgery in both groups are summarised in Table 3. A wide variety of ocular pathology encountered in ophthalmic practice is encountered in the patient population. Notably, there is a high prevalence of glaucoma in both groups with 8% in the femtosecond group and 21% in the manual group.

3.2 Achievement of Calculating Target Refraction

The achievement of target manifest refraction was measured by computing the absolute difference between target refraction (calculated according to biometry measurements and IOL power formulae) and the post-operative spherical equivalent. A boxplot of absolute refractive error is displayed in Figure 4. The distributions are right-skewed as most eyes were within 0.5 D of target refraction.

Table 2 Demographic and refractive characteristics of eyes undergoing femtosecond laser-assisted cataract extraction and manual phacoemusification cataract surgeries. Numbers displayed are mean ± standard deviation. P-values are derived from independent two-sample T-tests for averages and Pearson's X-square tests for percentages. logMAR – logarithm of the minimal angle of resolution.

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Intraocular lens type	66% Monofocal 38% Toric 1% Multifocal	65% Monofocal 35% Toric	0.454

Figure 2 Scatterplot of pre-operative refraction vs age at date of operation.

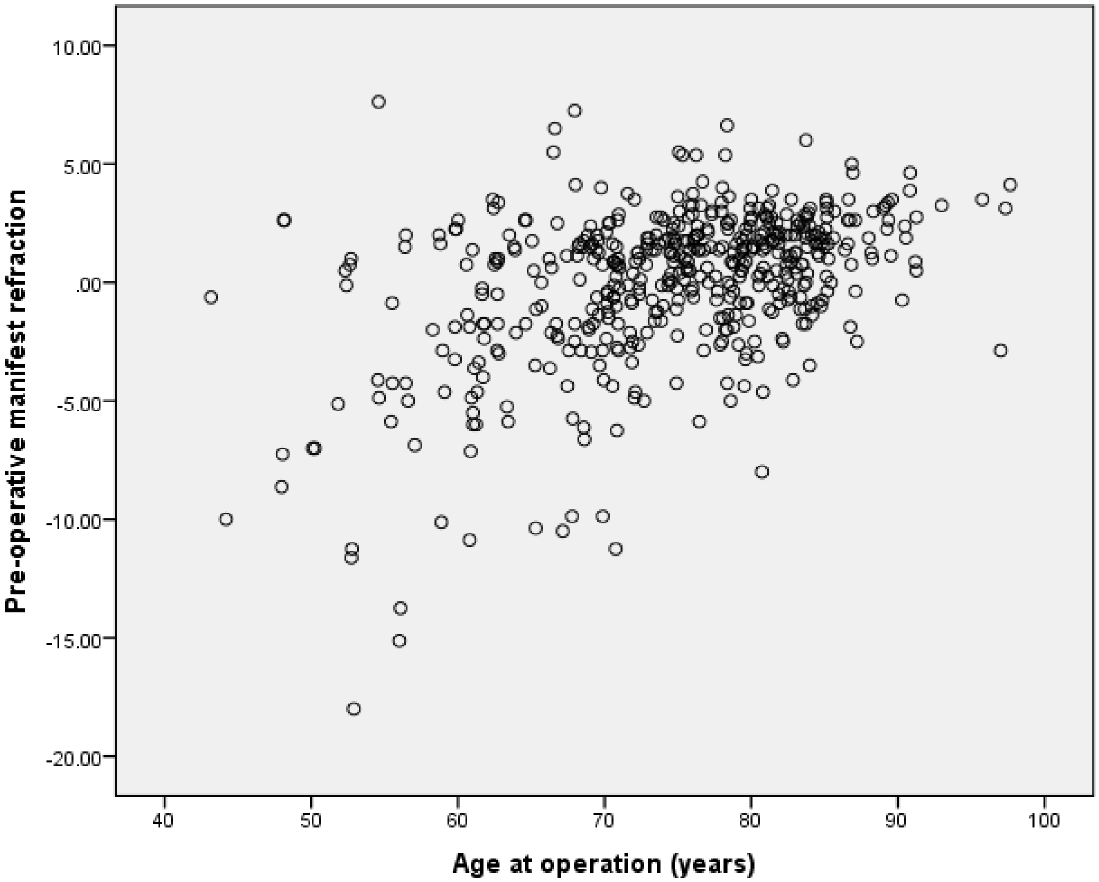


Figure 3 Scatterplot of axial length vs age on the date of operation

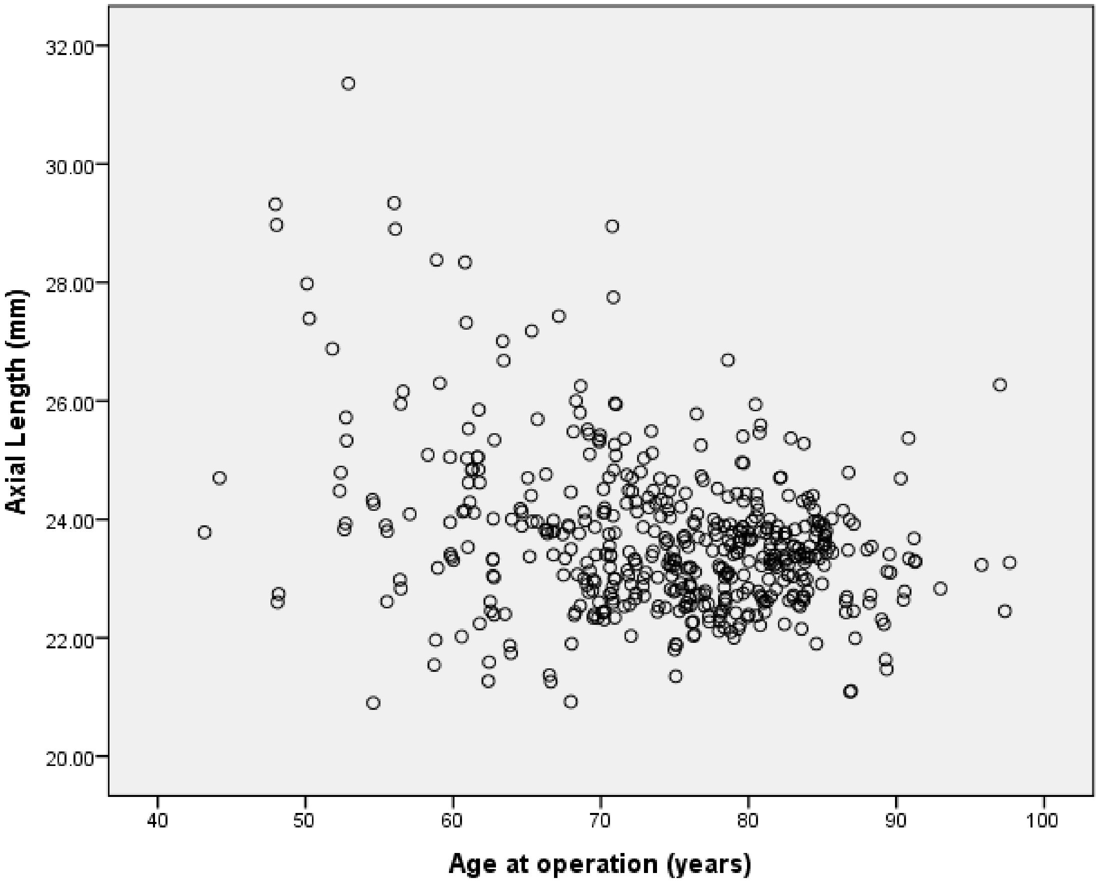
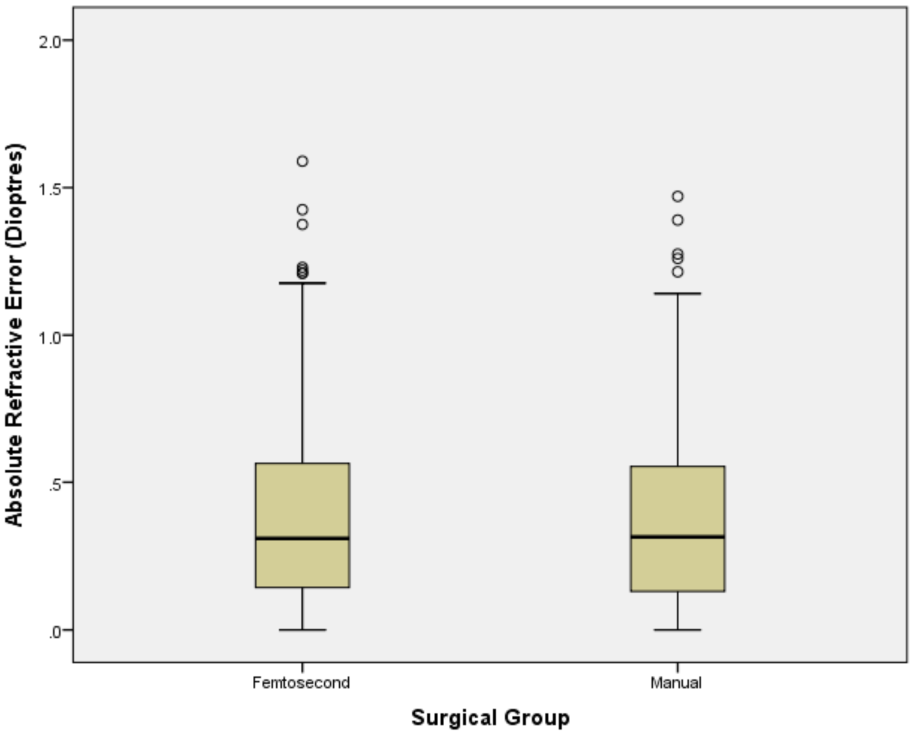


Table 3. Percentage and number (in brackets) of eyes with ocular comorbidities undergoing femtosecond-assisted and manual cataract surgeries. AMD – aged-related macular degeneration

	Femtosecond	**Manual**
Number of eyes	299	197
Corneal conditions	1% (3) Fuch's endothelial dystrophy 2% (6) Contact lens wear 1% (2) Pterygium excision 1% (2) Vortex keratopathy <1% (1) Corneal scarring	<1% (1) Fuch's endothelial dystrophy <1% (1) Contact lens wear <1% (1) Herpes simplex keratitis
Glaucoma	8% (25) Glaucoma of any type 1% (2) Trabeculectomy	21% (42) Glaucoma of any type <1% (1) Trabeculectomy
Retinal Conditions	4% (11) Significant AMD 3% (8) Epiretinal membrane 1% (4) Vitreo-mac traction 1% (3) Previous retinal detachment 1% (2) Macular hole <1% (1) Macular telangiectasia 1% (2) Myopic degeneration 2% (5) Retinoschisis	3% (6) Significant AMD <1% (1) Diabetic retinopathy <1% (1) Epiretinal membrane <1% (1) Vitreo-mac traction <1% (1) Retinal vein occlusion <1% (1) Vitelliform dystrophy
Other Conditions	1% (2) Strabismus <1% (1) Floppy iris syndrome <1% (1) Thyroid eye disease <1% (1) Uveitis <1% (1) Hemianopia	1% (3) Pseudo-exfoliation syndrome <1% (1) Amblyopia <1% (1) Uveitis

Figure 4 Boxplot of absolute refractive error (difference between calculated and actual post-operative manifest refraction) by surgical group



However, normality of distribution is a minor assumption in t-tests and would not grossly invalidate results, especially when variances are similar between the two surgical groups. The femtosecond and manual groups had mean absolute error of 0.39 D (±0.31) and 0.39 D (±0.32) respectively, with a p-value of 0.990 for difference between the means and 0.778 for Levene's test for equality of variance. Therefore, there is no difference in the calculation or variability in target refraction between the groups. A cumulative frequency graph is displayed in Figure 5, which showed 43% in the femtosecond group compared to 41% in the manual group achieved ≤0.25 D from the target refraction (p=0.576), 69% in each group achieved ≤ 0.5 D difference (p=0.911), 87% (cf. 86%) achieved ≤ 0.75 D difference (p=0.748), 95% (cf. 94%) achieved ≤ 1.0D difference (p=0.606), while 5% (cf. 6%) of patients had >1.0 D of difference from target refraction (p=0.606). Both surgical groups were equally successful in achieving target refraction.

Subgroup analysis on patients with axial length < 22 mm or > 26 mm (n = 36 in femtosecond group and n = 7 only in the manual group) showed similar results, with a difference of 0.05 D between two groups, p = 0.819, and 95% C.I. of -0.39 to +0.49 D. This is reflected in the scatterplots of mean absolute error vs axial length (

Figure 6) which showed a paucity of abnormal axial lengths in the manual group. Although no difference in the absolute error in the group of extreme axial length was demonstrated, the sample size is small and there is probably not enough statistical power to detect a difference.

3.3 Surgically-induced Astigmatism

The magnitude of surgically-induced corneal astigmatism (SIA) was calculated from pre- and post-operative keratometry readings using the standard double-angle vector subtraction formula (96) which states:

Figure 5 Cumulative frequency of absolute refractive error (difference between calculated and actual post-operative manifest refraction) by surgical group

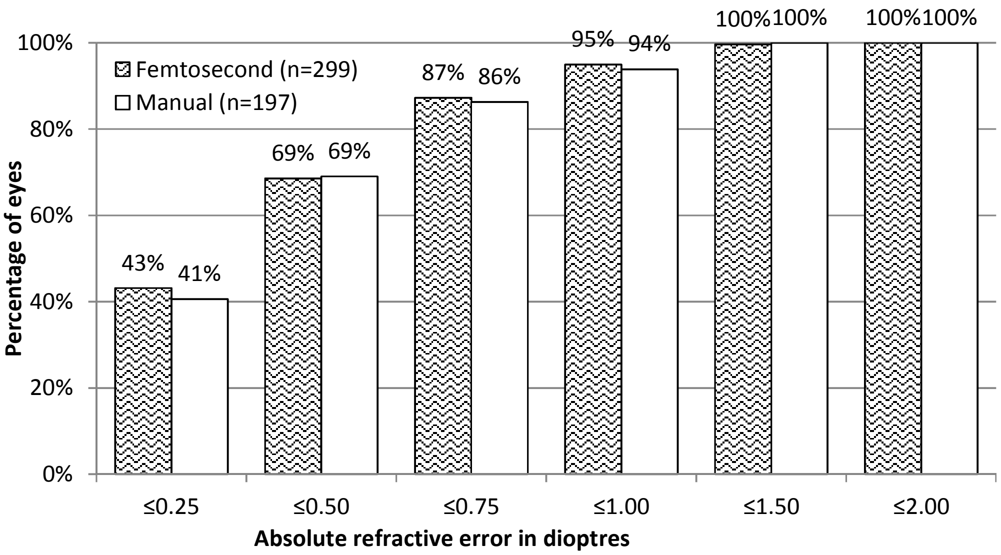
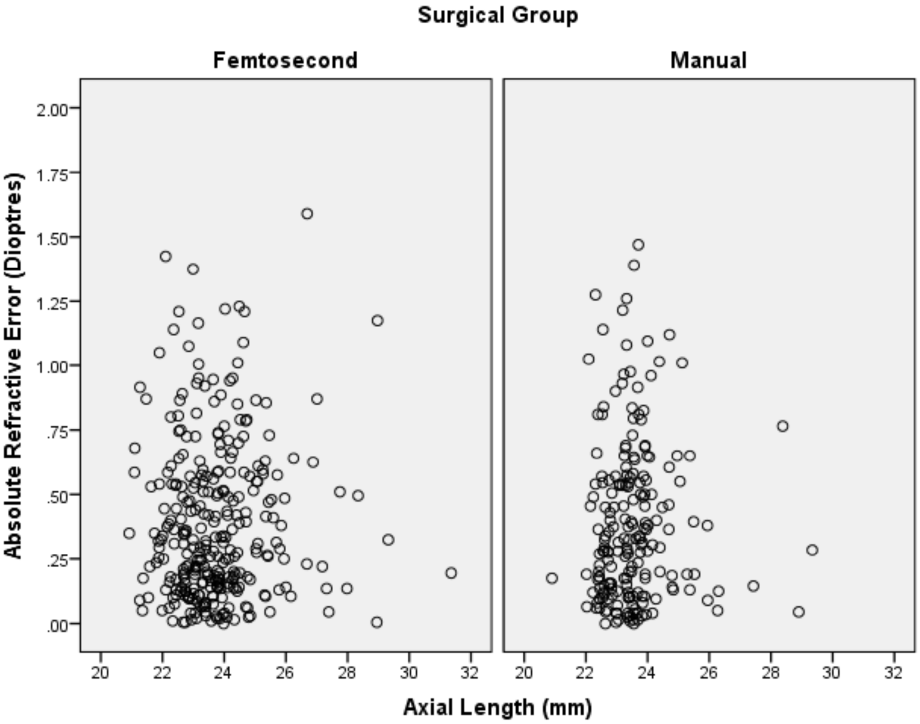


Figure 6 Scatterplot of absolute refractive error against axial length by surgical group.



$SIA = \left[K_{pre}{}^{2} + K_{post}{}^{2} - 2K_{pre}K_{post}\cos 2\left(\theta_{pre} - \theta_{post}\right)\right]^{0.5}$, where:

SIA = magnitude of surgically-induced corneal astigmatism;

K_{pre} = magnitude of pre-operative corneal astigmatism;

K_{post} = magnitude of pre-operative corneal astigmatism;

Θ_{pre} = angle of the pre-operative steepest meridian;

Θ_{post} = angle of the post-operative steepest meridian.

A boxplot of SIA distribution is displayed in Figure 7 and a cumulative frequency graph is displayed in Figure 8. The mean SIA was 0.53 for the femtosecond group and 0.56 for the manual group, and the difference of 0.03 D was not statistically significant (p=0.281, 95% C.I. -0.09 to 0.03). In the femtosecond group, there were slightly greater number of eyes with lower degrees of astigmatism but this was not statistically significant: 20% (cf. 19% in the manual group) of eyes had ≤ 0.25D of SIA (p=0.724), 51% (cf. 48%) had ≤ 0.50D (p=0.521) and 79% (cf. 75%) achieved ≤ 0.75D (p=0.263), while 8% (cf. 12%) of the femtosecond group having a SIA > 1.00 D (p=0.163). The standard deviations for the femtosecond and manual groups are 0.31 and 0.33 respectively (p=0.239, Levene's test of equal variance). Therefore, no statistically significant difference in the magnitude and variability of SIA between the femtosecond and manual groups was found.

3.4 Residual Post-operative Astigmatism

A boxplot of residual post-operative astigmatism is displayed in Figure 9 and a cumulative frequency graph is displayed in Figure 10. The femtosecond group has less residual refractive astigmatism than the manual group. The average residual astigmatism in the femtosecond group was 0.74 D (±0.45) compared to the manual group's 0.92 D (±0.54). The difference of 0.18 D had a p-value of < 0.001 and 95% C.I. of 0.09 to 0.26. In the femtosecond group, 19% (compared to 11% in the manual group)

Figure 7 Boxplot of surgically-induced corneal astigmatism by surgical group.

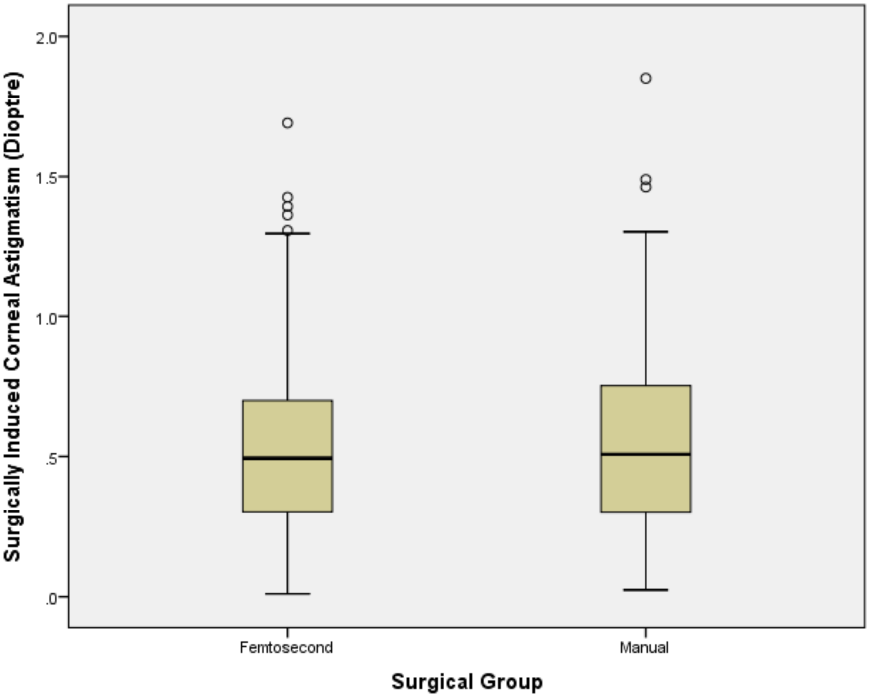


Figure 8. Cumulative frequency of surgically induced astigmatism in femtosecond and manual groups.

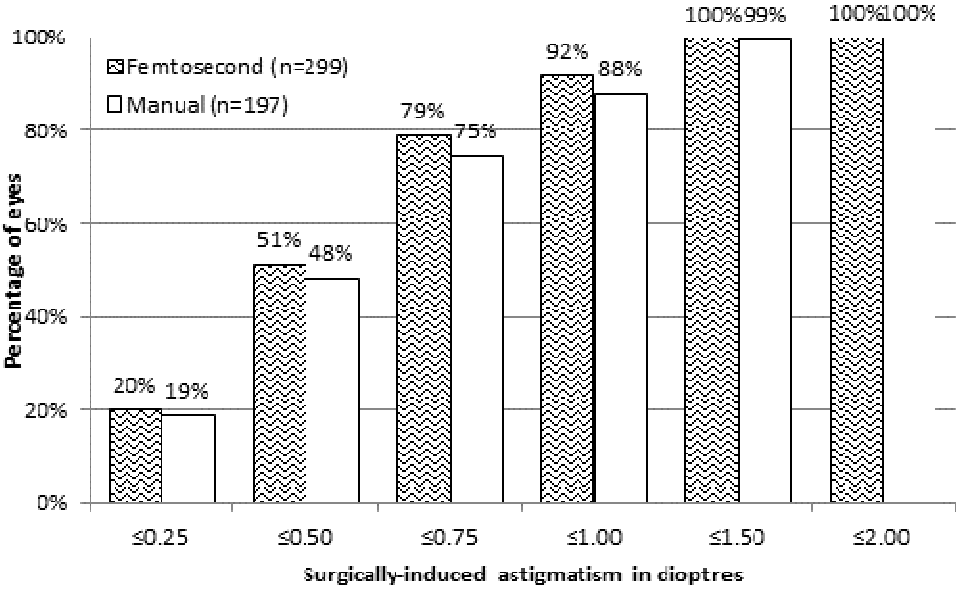


Figure 9 Boxplot of residual post-operative astigmatism by surgical groups

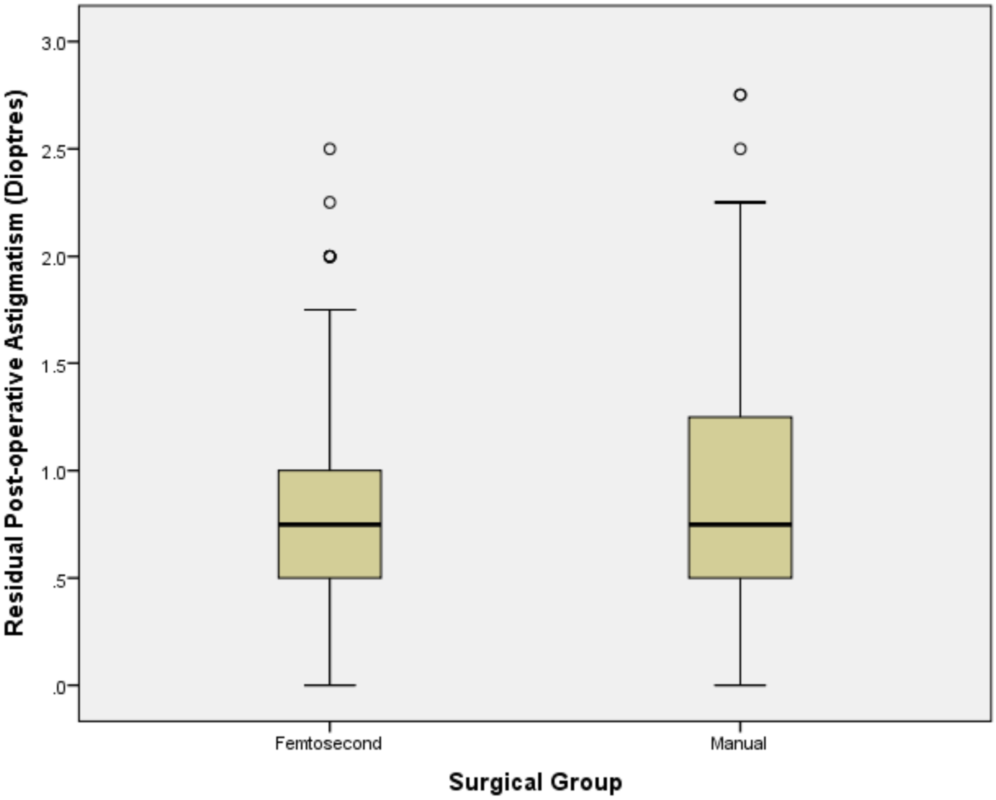
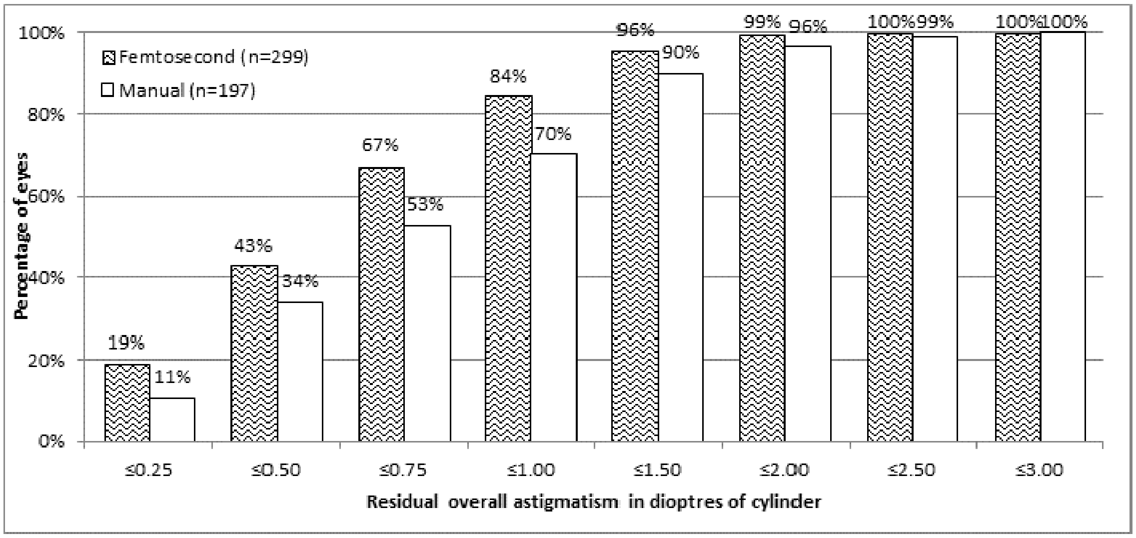


Figure 10 Cumulative relative frequency of residual post-operative astigmatism in femtosecond and manual groups.



had ≤ 0.25 D of post-operative astigmatism (p=0.012), 43% (cf. 34%) had ≤ 0.5 D of post-operative astigmatism (p=0.050), 67% (cf. 53%) had ≤ 0.75 D (p=0.001), while 16% (cf. 30%) had > 1.0 D (p<0.001). Therefore, the femtosecond group had less residual post-operative astigmatism.

Since toric lenses are used in this study, analysis of post-operative astigmatism by lens type was carried out. In eyes with monofocal lens implants, the residual astigmatism for femtosecond and conventional groups was 0.73 (±0.44) and 0.87 (±0.53) respectively (p-value 0.012). In eyes with toric lens implants, the residual astigmatism for femtosecond and conventional groups was 0.77 (±0.48) and 1.00 (±0.56) respectively (p-value 0.004). This is further demonstrated by a two-way analysis of variance whereby both the Lens Type term as well as Lens Type * Surgical Group interaction term had non-significant p-value (p=0.180 and p=564 respectively). Therefore, the improvement in astigmatism was not influenced by the type of intraocular lens implanted.

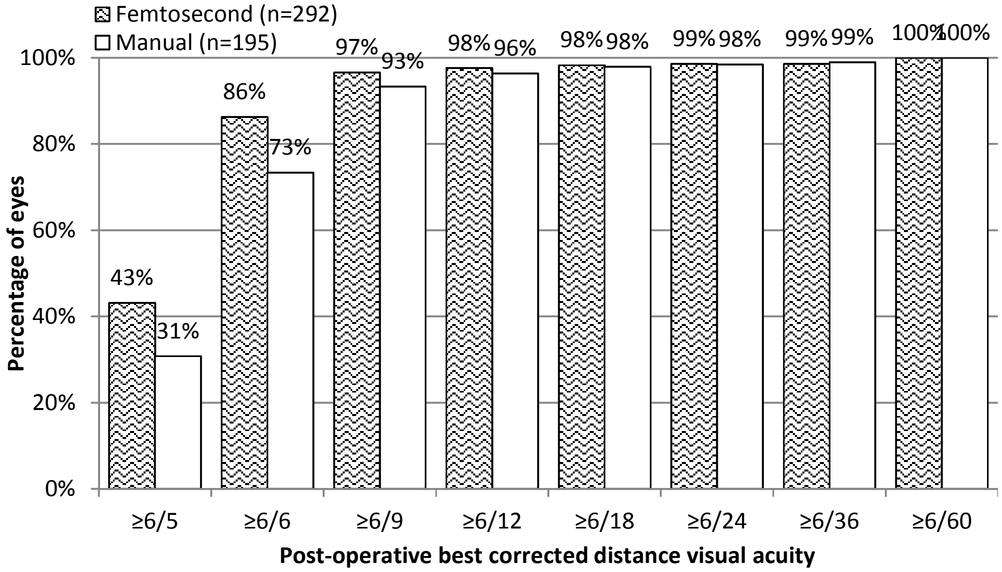
3.5 Best-corrected Distance Visual Acuity

The best-corrected distance visual acuity (BCDVA) was measured on a Snellen visual acuity chart and converted into logMAR (logarithm of minimal angle of resolution). A cumulative relative frequency graph of BCDVA by surgical group is shown in Figure 11. Both groups achieved good corrected distance visual acuity, with 39% overall achieving 6/5 or better, 82% achieving 6/6 or better and 95% achieving 6/9 or better.

3.6 Unaided Distance Visual Acuity

Post-operative uncorrected visual acuity (UCDVA) is influenced by refraction as well as the organic health of the eye. A number of patients prefer myopia as a refractive end-point in order to decrease spectacle dependence for near vision; these eyes are not expected to have good uncorrected distance visual acuity. Some eyes have ocular pathology that limits visual potential (see Table 3). In order to compare UCDVA, patients with non-emmetropic refractive aims (defined as target refraction of more than 0.3 D away from emmetropia) and limited visual potential (defined as

Figure 11 Cumulative relative frequency of best-corrected distance visual acuity in femtosecond and manual groups.



achieving a post-operative BCDVA of worse than 6/12) are excluded from UCDVA analysis. Overall, 143 and 92 patients met the above inclusion criteria in the femtosecond and manual groups, respectively (see Figure 1).

A boxplot of the distribution of UCDVA by surgical group is shown in Figure 12, and a relative frequency diagram of the distribution is shown in Figure 13. The UCDVA was statistically better in the femtosecond group. The mean UCDVA for the femtosecond group was 0.0933 logMAR ± 0.1581 (equivalent Snellen 20/30+3) compared to 0.1404 logMAR ± 0.1393 (equivalent Snellen 20/30+1) in the manual group. The difference was 0.0472 logMAR or 2.4 logMAR letters with a p-value of 0.020. In the femtosecond group 23% (compared to 10% in the manual group) of eyes achieved 20/17 or better (p=0.008) and 60% (cf. 36%) achieved 20/20 or better (p<0.001). Therefore, the femtosecond group achieved statistically significantly better UCDVA post-operatively in the subgroup of eyes with good visual potential in which emmetropia was the target refraction.

The post-operative refractive outcomes of this subset selected for UCDVA analysis closely mirrored the whole group. As in the initial group, the femtosecond subgroup was found to have better post-operative refractive astigmatism than the manual subgroup with the average residual astigmatism in the femtosecond subgroup being 0.72 D (±0.46) compared to the manual subgroup's 0.96 D (±0.58) with a difference of 0.25 D of cylinder (p=0.001, 95% C.I. 0.10 to 0.39). Similarly to the initial group, the mean SIA for the femtosecond subgroup at 0.51 D, was slightly lower than the manual subgroup at 0.55, but difference of 0.03 D was not statistically significant (p=0.409, 95% C.I. -0.11 to 0.04). The standard deviations for both femtosecond and manual subgroups are the same at 0.29 (p= 0.976). Both subgroups were also equally successful in achieving target refraction with no statistically significant differences between the subgroups. 40 % in the femtosecond subgroup compared to 39% in the manual subgroup achieved ≤0.25 D from the target refraction (p=0.927), 67% (cf. 75%) achieved ≤ 0.5 D difference (p=0.196), 86% (cf. 90%) achieved ≤ 0.75 D difference (p=0.368), while

Figure 12 Boxplot of residual post-operative uncorrected distance vision (UCDVA) by surgical group. logMAR – logarithm of minimal angle of resolution.

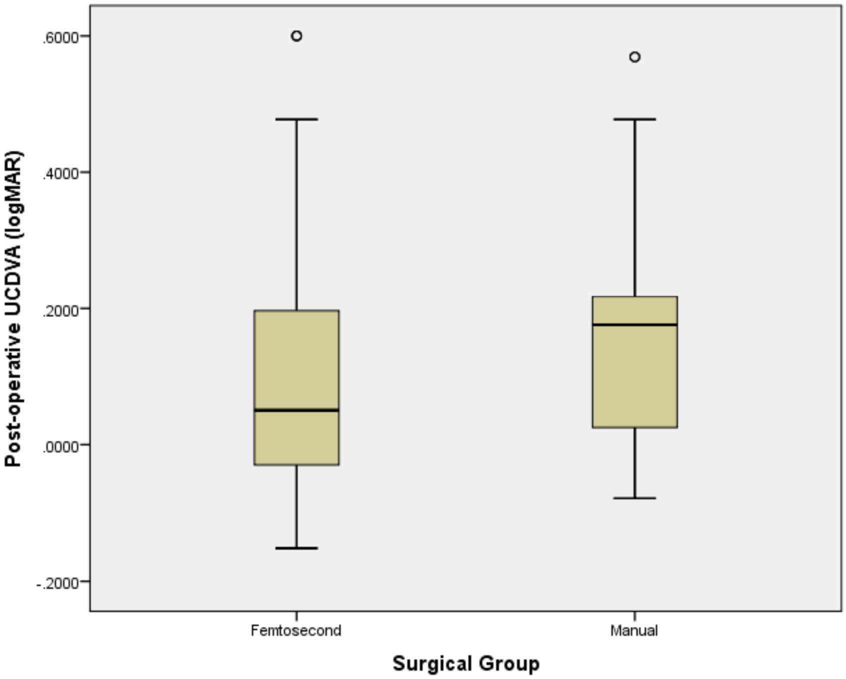
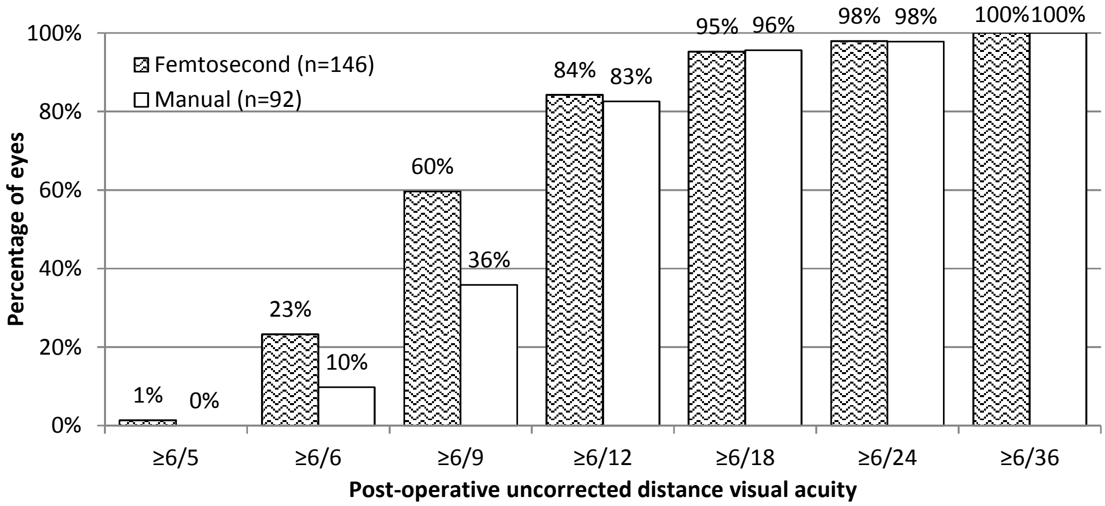


Figure 13 Relative cumulative frequency of post-operative distance unaided visual acuity in femtosecond and manual groups

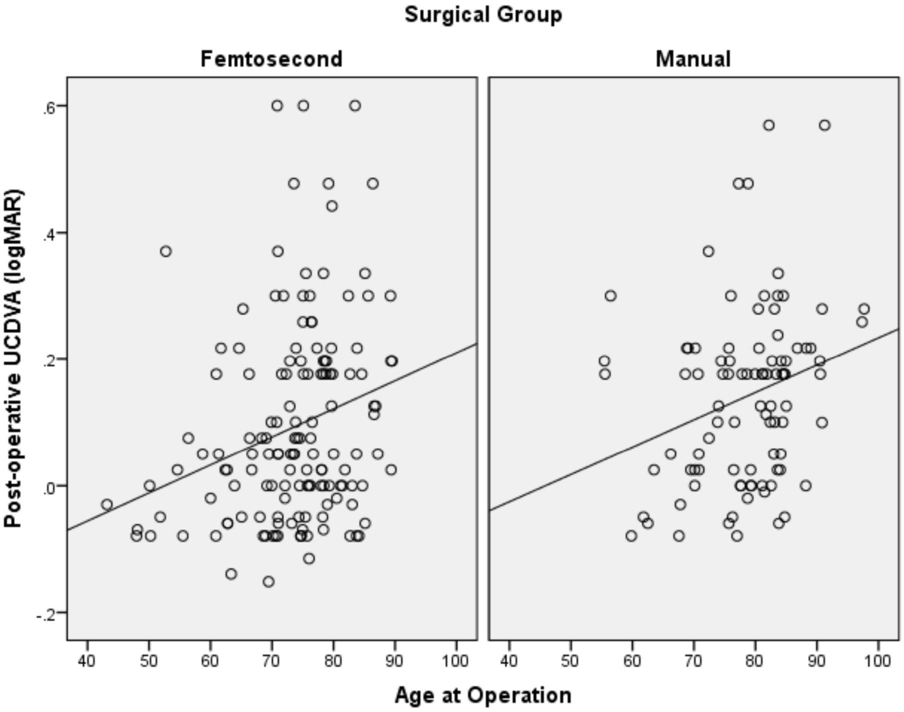


7% in each subgroup had >1.0 D of difference from target refraction (p=0.922). The femtosecond and manual subgroups had mean gap from target refraction of 0.09 D (±0.50) and 0.09 D (±0.48) respectively, with a p-value of 0.966 for difference between the means and 0.524 for Levene's test for equality of variance. Altogether, the outcomes of the subgroup selected for UCDVA analysis reflected the main group closely. It is not likely that there is inherent bias in the selection of the subgroup for UCDVA analysis.

The effect of age on UCDVA was investigated by plotting a scatterplot of UCDVA against age by surgical group in Figure 14. In both groups, there is a positive association between UCDVA in logMAR and age. The higher the eye's age, the higher the logMAR. Generalised linear regression modelling confirmed findings in the scatterplot, with p<0.001 for the association between age and UCDVA but p=0.196 for the surgical group term. Residual plots did not show any evidence of non-normality or unequal variance (data not shown). Therefore, UCDVA results are confounded with the age. In other words, the improvement in UCDVA in the femtosecond laser group could be explained by the group's younger age.

To investigate whether improved refraction affected UCDVA, general linear modelling of UCDVA with surgical method, age, post-operative manifest refraction and astigmatism. Except surgical method (p=0.557), all other variables were found to be correlated with UCDVA (p=0.009 for age, p<0.001 for post-operative refraction and p<0.001 for post-operative astigmatism). Therefore, the improved UCDVA results in the femtosecond group could be explained by the younger age and improved astigmatism.

Figure 14 Scatterplot of uncorrected distance visual acuity (UCDVA) in logarithm of minimal angle of resolution (logMAR) against age by surgical group. Best-fit linear regression lines were added to the plot.



Chapter 4. Discussion

4.1 Introduction

Femtosecond laser-assisted cataract surgery (FLACS) is a new surgical technique that exploits the precision of femtosecond laser in the creation of corneal wounds, anterior capsulotomy and nuclear fragmentation in phacoemulsification surgery. It is generally accepted that the corneal wounds and capsulotomy created by femtosecond laser have a precision that is unmatched by manual methods (see Chapters 1.3.6 and 1.3.7), and its proponents speculate that FLACS may lead to improved refractive results due to improved prediction of surgically-induced corneal astigmatism (SIA) and intraocular lens placement (97). However, the superiority of refractive outcomes in femtosecond laser has not been proven, with small existing studies showing either no or little improvement in post-operative refraction (see Chapter 1.3.8). Given the expense and logistical issues, whether FLACS generates significantly superior results is a current issue of intense controversy in ophthalmology (74, 98). More comparison of refractive outcomes between FLACS and manual cataract surgery is needed.

This study aims to compare the refractive outcomes between FLACS and manual cataract surgery. The study is a prospective non-randomised non-blinded comparative case-control series of FLACS (since its introduction in an ophthalmic practice) versus manual cataract surgery by a group of three experienced cataract surgeons in a private practice in Sydney, Australia. The number of eyes analysed was 496, which is the largest database published by far and this lends to the strength of the conclusions.

The main criticism of the study design is its non-randomised non-blinded nature. Randomised clinical trials (RCTs) are the gold standard in interventional studies since they have the tendency to balance known and unknown confounder variables which may render biased outcomes. However, due to the current cost of FLACS and the lack of necessary research funding and infrastructure, RCTs on FLACS are not feasible at present. The study design in this study represents the next best level of evidence. Furthermore, RCTs are conducted in artificial trial environments with rigid inclusion and exclusion criteria and may not reflect everyday practice. This post-marketing study could reflect real clinical practice more closely, where clinicians are faced with issues such as ocular pathologies, inaccuracies in biometry and refraction on a daily basis. Therefore, data from this study have important merits and represent a significant landmark study on refractive outcomes of FLACS.

The lack of blinding is another potential criticism of this study. Blinding of surgeons administering the operations would be difficult or impossible to achieve. Blinding of subjects would require placebo femtosecond laser treatment, for which there was no funding. Blinding of observers is a possible source of bias and could have been instituted had there been funding and infrastructure specifically allocated to this study, such as a dedicated orthoptist who would assess all post-operative patients. Unfortunately this study did not have the resources to perform blinding and this could be a source of bias and criticism. Further studies would benefit from blinding if the funding and infrastructure are available.

4.2 Patient Characteristics

As could be expected in a non-randomised study, the baseline patient characteristics were not identical in both groups. The femtosecond group were slightly younger (by 4.6 years, p<0.001). It had a higher proportion of high ammetropia > 4 D (18% vs 9%) and atypical axial length > 26mm or < 22 mm (12% vs 4%), which renders the calculation of IOL power and prediction of refractive outcome less precise. The number of eyes with high ammetropia and atypical axial length was even more marked in the UCDVA subset. The mean difference in the preoperative corneal astigmatism between the two groups was borderline non-significant (difference of 0.11 D, p= 0.059) in the initial group and non-significant in the UCDVA subset (difference of 0.12 D, p= 0.202). A larger proportion of eyes with glaucoma were in the manual group (21%) than in the femtosecond group (8%).

The unequal baseline patient characteristics predispose this study to selection biases. Multivariate analysis showed glaucoma had no effect on post-operative astigmatism and refraction. Nor did glaucoma have an effect on visual acuity. Therefore, the high proportion of glaucoma patients, especially in the manual group, had no impact on the results of this study. This is not unexpected, as there is no obvious link between glaucoma and refractive outcomes, and unless glaucoma is advanced, central vision is usually not affected.

The most significant confounder in this study is patient age. The femtosecond group is younger on average, and younger patients are likely to have fewer ocular comorbidities that can limit their visual acuity. Multivariate analysis confirmed that age is confounded with best-corrected as well as unaided visual acuity results. The younger age of the femtosecond group could potentially explain the slightly improved visual acuity found in the group.

The femtosecond group as also found to contain eyes with unusual axial lengths (especially > 26 mm) as well as high refractive error (especially high myopia). Both of these variables are correlated with age, with the younger eyes having more unusual axial lengths and refractive errors. This could potentially make prediction of IOL power less accurate and impact on post-operative refraction, disadvantaging the femtosecond group. However, this was not shown to be the case in our study in subgroup and multivariate analysis. This could be due to the relatively low numbers of cases in each group.

In summary, several confounding variables have been identified in this study. They interact with each other and may impact on the outcomes in this study. Randomised control studies in the future will minimise confounding variables at selection and provide higher level of evidence than this study.

4.3 Achievement of Calculated Target Refraction

The initial femtosecond laser and manual groups both achieved a high degree of post-operative spherical equivalent refractive predictability. In the femtosecond group, 43% of patients achieved ≤0.25 D of absolute refractive error compared to 41% in the manual group (p=0.576), 69% in each group achieved ≤ 0.5 D (p=0.911), 87% (cf. 86%) achieved ≤ 0.75 D (p=0.748), 95% (cf. 94%) achieved

≤ 1.0D (p=0.606), while 5% (cf. 6%) of patients had >1.0 D of error from target refraction (p=0.606). The mean absolute error was identical in both groups at 0.39 D (p=0.990). Levene's test for equality of variance had a p-value of 0.778, indicating the two groups had equal variability. Therefore, the two groups had equivalent achievement of manifest refraction. Both groups compare well with published refractive benchmarks(35).

The femtosecond group did have two inherent disadvantages in IOL power calculation. First, it had greater numbers of eyes with higher degrees of ammetropia and atypical axial length, which cause refractive unpredictability. Second, the manual group had the advantage of surgeon-optimised A-constants from the beginning while the femtosecond group had to develop these during the course of the study. However, subgroup and multivariate analysis did not show a significant effect of axial length on refractive error.

To date, there were three studies published in the literature comparing refractive errors after FLACS to manual surgery. Two studies found no statistically significant difference between the surgical methods (90, 99) while one study found a small difference of 0.13 D, which was statistically significant but clinically not significant. The sample size of our study far exceeds any of the other studies in the literature. We were unable to find any difference between the two surgical groups. Therefore, there is little evidence to support the hypothesis that a capsulotomy constructed by femtosecond laser can lead to a more precise effective lens position (ELP) and therefore more predictable postoperative refraction.

The three surgeons involved in this study are experienced anterior segment surgeons. The capsulorrhexis they constructed probably differed little from those made by femtosecond laser. This study cannot exclude the possibility that in circumstances where capsulotomies are more irregular, femtosecond might reduce post-operative refractive error.

4.4 Surgically-induced Astigmatism

In this study, the mean SIA was 0.53 for the femtosecond laser-constructed corneal wounds and 0.56 for the manual keratome (p=0.281). There was no statistically significant difference between the cumulative frequencies of SIA magnitude either. The standard deviations for the femtosecond and manual groups were also not significantly different. Therefore, the magnitude and variability of SIA were not different between the femtosecond and manual groups.

To our knowledge, this is the only study comparing SIA between femtosecond laser and keratome wounds in the literature. Although femtosecond laser is capable of constructing precise multiplanar wounds that may be more secure against post-operative wound leakage, a statistically significant difference in SIA between femtosecond laser- and keratome-constructed wounds could not be demonstrated. It seemed that differences in the shape and size of the wounds did not result in significant differences in the way cornea shape changed. Therefore, femtosecond laser did not improve the prediction of corneal shape and calculation of toric lens.

4.5 Residual Post-operative Astigmatism

In this study, a statistically significant reduction in residual refractive astigmatism at one month post-operatively was found comparing femtosecond laser to the manual group. The mean residual refractive astigmatism was 0.74 D (±0.45) in the femtosecond group compared to the manual group of 0.92 D (±0.54). The difference of 0.18 D was statistically significant with a p-value of 0.001 and 95% confidence interval of 0.09 to 0.27 D. There were also a statistically significant number of eyes with lower degrees of refractive astigmatism in the femtosecond group than in the manual group. Whether an improvement of 0.18 D is clinically significant is questionable. This improvement in astigmatism did not seem to be affected by type of lens implanted, whether monofocal or toric.

Post-operative astigmatism is affected by an interaction of three factors: post-operative corneal astigmatism, type of IOL implanted as well as positioning of the IOL (tilt and decentration). In the previous section, surgically-induced corneal astigmatism was shown to be equivalent between the two surgical methods. Therefore, femtosecond laser conferred no advantage in predicting post-operative corneal astigmatism. Toric lenses were used for 37% of the eyes overall and the rate of implantation is not different between the two surgical groups. The use of toric lens had no impact on post-operative astigmatism, indicating that lens choice was not the cause of improved astigmatism results. It has been hypothesised that femtosecond laser anterior capsulotomy could improve IOL tilt and decentration (88). These parameters were not measured directly in this study, but results from this study could support this hypothesis. Again, the magnitude of any improvement is small and its clinical significance yet to be determined.

4.6 Uncorrected Distance Visual Acuity

The most significant finding in this study was that the femtosecond subgroup achieved better UCDVA, which is a measure of spectacle-free long distance vision. The femtosecond subgroup achieved an average post-operative UCDVA of 0.0933 logMAR (equivalent to Snellen 6/9+3, ±0.1581) compared to the manual subgroup of 0.1404 logMAR (equivalent to Snellen 6/9+1, ±0.1393). This represents 0.0472 logMAR (2.4 logMAR letters) of improvement (p=0.020). Comparing the two subgroups, 23% of eyes in the femtosecond group achieved 6/5 or better compared to 10% in the manual group (p=0.008), and 60% achieved 6/6 or better (cf. 36%, p<0.001). In reverse, only 34% of the femtosecond group achieved 6/9 or worse compared to 52% in the manual group (p=0.006).

Multivariate analysis showed both age and post-operative astigmatism to be associated with improved UCDVA results. A randomised control trial equalising these baseline parameters would be ideal to exclude bias from baseline patient characteristics such as age. However, after adjustment for age, the improvement in UCDVA was still correlated with residual astigmatism, which was less in the femtosecond group. Therefore, it is still plausible that femtosecond laser improved UCDVA through decreased residual astigmatism. The magnitude of the improvement is small, only 2.4 logMAR letters. Again, this is a small change which in itself may have minimal clinical significance. Yet when added to the other small changes there may be a clinically significant effect.

4.7 Conclusion

In this study, we demonstrated that the femtosecond group achieved the same post-operative manifest refraction as the manual group but slightly better residual astigmatism by 0.18 D. Surgically-induced corneal astigmatism was the same in both groups. Post-operative UCDVA was better in the femtosecond group by 2.4 logMAR letters. This, however, was confounded by the younger age in the femtosecond group. This study is the largest database of FLACS compared to manual surgery in the literature, and the results represent strong evidence for non-inferiority of refractive results after FLACS compared to manual phacoemulsification. However, the study failed to demonstrate clinically significant superiority of refractive results over existing manual methods.

Once again, the interpretation of the clinical results is clouded by confounding variables. This is due to the lack of randomisation which can introduce selection bias. A randomised control trial (RCT) is the best study design for interventional studies such as this one. However, the artificial structure and exclusion criteria of RCTs means results are not applicable to all clinical situations. The post-marketing nature of this study sheds important light on the performance of FLACS in real-world clinical practice and the results contributes significantly to the development and acceptance of FLACS.

Effective lens position is an important source of error in IOL power calculation. However, there are a large number of other variables at play in determining post-operative refraction (see Chapter 1.2.5). Therefore, improvement in a single parameter such as ELP can only add a small incremental benefit. Any improvement in ELP is likely to have only a small impact on final refraction. Even if there had been an improvement in ELP by FLACS, the difference was likely to be small and difficult to detect.

This study did not address the safety aspect of FLACS. However, no additional complication compared to manual surgery was found, echoing the majority of studies on the safety aspects of FLACS (see Chapter 1.3.5). In 337 consecutive femtosecond laser-assisted operations in this study, there was a low rate of anterior capsular tears (n=3) and no incidence of posterior capsular ruptures or posterior nucleus loss. No significant learning curve was found as suggested in a previous report (56). FLACS appeared to be a safe and predictable technique that had a high level of patient acceptance.

The introduction of FLACS is currently expensive, requires additional training, prolongs surgical time and requires additional space in the operating theatre (98). This study found FLACS to be a safe predictable procedure which has the potential for reducing phacoemulsification energy and possibly complications such as corneal and macular oedema (see Chapter 1.3.5). A reduction in post-operative astigmatism is a significant clinical finding. Further studies will assist in determining the role and place for this technology in cataract surgery.

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