Web-based system for outcome analysis and modification in laser vision correction.

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DECLARATION

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ABSTRACT

Refractive laser eye surgery is a specialised field in ophthalmology which aims to correct the refractive disorder of an eye. The most established technique is LASIK, which has shown good results for the treatment of simple myopia. Complex refractive disorders, such as compound myopic astigmatism, have shown less predictable refractive outcomes, and in some cases the severe over- or under-correction can even worsen the preoperative situation and damage the eye.

In its first stage, this research aimed to develop a software system able to present and analyse refractive outcomes. Over 2 prototype stages, this research has led to an operational system named IBRA (Internet Based Refractive Analysis), offering web-based data collection and refractive and vector analysis.

In a second stage, Nomogram calculation formulas were developed and integrated into IBRA. These formulas were created from linear regression and best-fit analyses of spherical and cylindrical outcome data stored in IBRA. The purpose of the nomogram calculations was to provide surgeons with adjustment factors that could be used to improve the refractive outcome of patients with complex refractive disorders.

Two extensive clinical audits and a randomized controlled trial were performed at Moorfields Eye Hospital to evaluate the IBRA nomogram adjustments. This research showed that IBRA was able to achieve a positive health change. In addition, results from the audits and trial contributed to the knowledge of nomogram adjustments and provided a framework in which future investigations on nomogram and treatment modifications could be performed.

In addition to the above clinical studies, two evaluations were performed with the use of IBRA and data logging techniques to investigate users' behaviour relating to the management of data entry processes and the use of analysis functions. This research revealed the best method for entering refractive data, and was able to identify the most important analysis methods.

Finally, the use of IBRA and its user-interface were investigated with a user satisfaction survey. The results from this questionnaire based study showed a high acceptance of the web-based platform of IBRA and indicated points for improvement (Documentation).

ABBREVIATIONS

AE	Angle of Error
Ax	Axis
BCVA	Best-corrected Visual Acuity
BZ	Bruno Zuberbuhler
CHI	Centre for Health Informatics, CU
CI	Correction Index
CU	City University London
Cyl	Cylinder (Astigmatism)
D	Diopters
DBMS	Database Management System
DE	Defocus Equivalent
DSG	David S. Gartry
DV	Difference Vector
EHR	Electronic Health Record
Femto	Femtosecond (fs)
HID	Hospital Identification Number
HTML	Hypertext Markup Language
IBRA	Internet Based Refractive Analysis
IOP	Intraocular Pressure
IOS	Index of Success
ISO	International Organization for Standardization
LASIK	Laser-Assisted In-situ Keratomileusis
LASEK	Laser-Assisted Sub-Epithelial Keratomileusis
LogMAR	Scale expressing angle of resolution
MEH	Moorfields Eye Hospital
NID	National Health Service Identification Number
OD	Right eye (oculus dexter)
OS	Left eye (oculus sinister)
PHP	Hypertext Preprocessor
PID	Patient Identification Number
QUIS	Questionnaire for User Interface
RCO	The Royal College of Ophthalmologist
RMS	Root Mean Square
RSB	Residual Stromal Bed
SD	Standard Deviation
SE	Spherical Equivalent
SIA	Surgically Induced Astigmatism Vector
Snellen	Eye chart (Dutch ophthalmologist H. Snellen)
Sph	Sphere Value
SUMI	Software Usability Measurement Inventory
TIA	Target Induced Astigmatism Vector
UCVA	Uncorrected Visual Acuity

Chapter 1

INTRODUCTION

1. INTRODUCTION

1.1. Background

Refractive vision disorders such as myopia (short-sightedness) and astigmatism (abnormality in the shape of the cornea) can be corrected with refractive laser eye surgery.

A refractive laser unit consists of a laser source, a system of optical instruments and controller software. The algorithm that describes the relation between the laser power and the amount of surface ablation (removal of corneal tissue) necessary to achieve the refractive change bases mainly on empirical data. Although mechanically perfected over the last 10 years, the treatment algorithm of the controller software has not kept up and suffers from optimisation. Imprecision in the treatment can result in an outcome that is over- or undercorrected, and may even worsen the preoperative situation and damage the patient's eye. As a consequence, intensive care and re-treatments are necessary.

The collection and analysis of refractive outcome data has become an increasingly important requirement of refractive surgery practice. Not surprisingly, the forthcoming Quality Standard and Revalidation initiatives of The Royal College of Ophthalmologists underpin this importance in the provision of auditable outcomes of surgery.

One of the most critical factors that can affect the outcome after laser vision correction is the nomogram that the surgeon uses. A nomogram is a unique group of detailed treatment settings that is programmed into the laser. The best results are achieved when the treatment is tailored for each person based on age, gender, prescription, and other factors.

Although there are software systems on the market that can analyse refractive data and perform nomogram optimisation, such systems use an unspecific general approach. A system that performs both general and patient-individual nomogram modifications, using 2-3 different calculation technologies, has not yet been developed. In addition, the use of modified nomograms has never been evaluated scientifically with controlled randomised trials or audit cycles.

1.2. Aim of the research

The aim of the research is to record, analyse and improve the health outcome in patients undergoing laser vision correction.

1.3. Objectives of the research

Basic objectives:

- To perform an extensive literature and software review.
- To establish requirements in the area of refractive eye laser surgery.
- To analyse the management of data entry processes.
- To evaluate user preferences and user satisfaction.
- To present and publish the results of this research.

Main clinical objectives of the research:

1. To develop a system that can combine data collection and analysis and offer tools for standardised outcome presentation.
2. To make the system easily accessible, secure, safe, flexible and capable of future developments.
3. To develop and integrate means (algorithms, formula) that can provide information on how refractive laser treatments could be improved.
4. To test the system in a clinical (private practice) environment with real patient treatments.
5. To evaluate the system impact on patient's health.
6. To improve the understanding of nomogram adjustments.

1.4. Administrative organisation and settings

A prototype of the system and a functional successor were developed and clinically tested at the Eye Clinic, Cantonal Hospital, Lucerne, Switzerland, and further revised in accordance to the needs.

Additional system development, methodological support and system evaluations were performed at the Centre for Health Informatics, City University London, United Kingdom.

New treatment algorithms with formulas for individual nomogram calculations were created and implemented in collaboration with the Refractive Laser Unit at Moorfields Eye Hospital NHS Foundation Trust, London.

The clinical evaluation included a randomised controlled trial, which was performed in accordance with National Ethical Commission guidelines and the Research & Development Department at Moorfields Eye Hospital. A user-centred system evaluation was performed at the Centre for Health Informatics, City University London.

The analysis of the results was performed at the Centre for Health Informatics, London. Statistical support was provided by medical statisticians at Moorfields Eye Hospital.

Summary of participating organizations:

- Centre for Health Informatics, School of Informatics, City University London.
- Refractive Surgery Unit, Moorfields Eye Hospital, London.
- Department of Research and Development, Moorfields Eye Hospital
- Department of Corneal and External Eye Disease, Moorfields Eye Hospital
- Statistical Advice Unit, Moorfields Eye Hospital, London
- Health and Safety Executive's Research Ethics Committee

1.5. Opportunities

This was the first research that had integrated different refractive outcome analysis techniques in one system, and which undertook extensive user-centred and patient-related system evaluations.

The main promises of this research were:

- To create a calculation formula which can improve the patient's health outcome.
- To improve the understanding of laser treatments for refractive disorders.
- To have a major impact on the surgeon's management of eye laser surgery.
- To contribute to the knowledge of refractive data collection, data analysis and nomogram adjustment.
- To increase the cost-effectiveness of current treatments in reducing the re-treatment rate and additional follow-ups.

1.6. Organisation of the Thesis

This thesis is organised in 8 chapters. The first chapter states the background, aim and objectives of the investigation.

Chapter 2 describes the domain of laser vision correction and provides important information on refractive disorders, principles of laser treatments and refractive outcome analyses.

Chapter 3 reports the results from the literature review on refractive analysis and nomogram adjustments, presents the different refractive analysis software currently available, and outlines the reviewed program languages evaluated for the system development.

In Chapter 4 the thesis continues by discussing the initial needs for the analysis system and presents the development of a prototype system called 'Proexcimer'.

Chapter 5 describes the range of new needs that led to the development of the research system called 'IBRA' (Internet Based Refractive Analysis). All parts of IBRA are presented with screenshots and are discussed.

Chapter 6 reports on 5 evolutions performed to test the IBRA system from both a clinical and a user point of view. The results of clinical audits, randomised clinical trial, survey and data logging processes are presented in scientific format.

In Chapter 7 the results of system development and evaluation are discussed, and compared with the aims and objectives of the research.

Chapter 8 provides a conclusion of the work carried out in this study and the results achieved.

Chapter 2

DOMAIN OF REFRACTIVE LASER EYE SURGERY

2. DOMAIN OF REFRACTIVE LASER EYE SURGERY

Refractive laser eye surgery is a specialised field of eye surgery which focuses on improving the optical state of the eye using an excimer laser beam to reshape the surface of the cornea. This change in the cornea compensates the ocular disease.

This chapter will provide basic information on topics from the field of refractive laser eye surgery which were used in this research, including:

- Refractive disorders (Section 2.1.)
- Principles and techniques of laser vision correction (Section 2.2.)
- Range of refractive data and refractive analysis (Section 2.3.)

2.1. Refractive disorders

Typical indications for laser treatment are refractive vision disorders such as myopia (short-sightedness), hyperopia (long-sightedness) and astigmatism (an abnormality in the shape of the surface of the cornea).

2.1.1. Myopia

If one thinks of the eye as camera, then the retina would be the film and the cornea the lens (objective). The camera is able to produce a sharp image when the lens is able to focus the light rays on the film plane. The eye works in a similar way. If the light rays are focused on the retina the image is sharp.

Myopia is a vision disorder in which the light rays are focused on a single point that lies in front of the retina (within the globe). The image is blurred. This can occur in 2 situations. Firstly, the axial length of the eye is too big; the eye “is too long”. This situation is called axial myopia (Figure 2.1.1.). Secondly, the cornea is focusing the light rays too strongly. This situation is called refractive myopia.

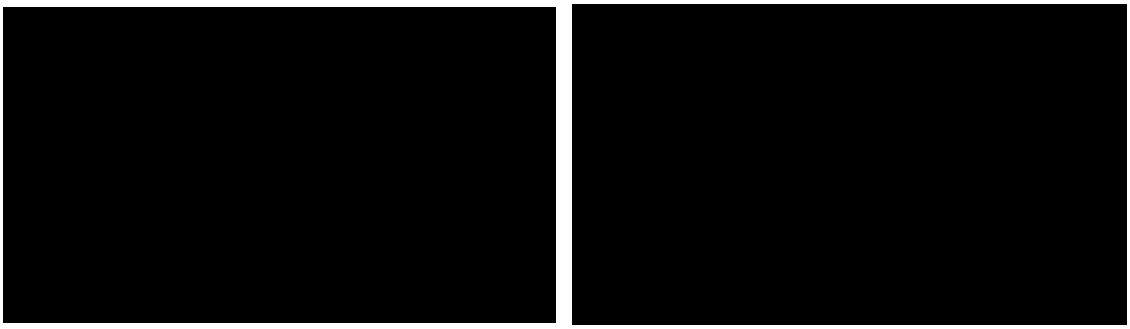


Figure 2.1.1. Left image: In myopia, the light rays are focused on a single point that lies in front of the retina (within the globe). Images from distant objects are blurred. Right image: Correction of myopia with a (biconcave) minus lens.

Mild to moderate myopia can be corrected with spectacles. The spectacles have to move the point of focus further back so it can reach the retina. The types of lenses used for this purpose have a biconcave curvature and are called minus (diverging) lenses.

The degree of myopia is measured in diopters [D] by the strength (or optical power) of a corrective minus lens. Low myopia usually describes myopia of -3.00 D or less. Myopia is common and is regarded as physiological if less than -6.00 D.

The incidence of myopia varies with age, country, sex, race, ethnicity, occupation, environment, and other factors (Verma 2005 and Fredrick 2002). In Western Europe a review found that 26.6% aged 40 or over have at least -1.00 D of myopia and 4.6% have at least -5.00 D (Kempen 2004).

Of those with high myopia (-6.00 D or more) there is a subset who are at risk of degenerative changes with increased prevalence of retinal detachment, choroidal neovascularisation and open angle glaucoma (Oxford Handbook of Ophthalmology). Myopia has also been found in association with genetic disorders like Down's syndrome, Marfan’s syndrome or albinism.

2.1.2. Hyperopia

The focal point of incoming light in the hyperopic eye, which is too “short”, lies behind the retina (Figure 2.1.2.), which means that distant objects are seen fairly clearly, whilst near objects are represented in a distinctly blurred manner.

Figure 2.1.2. In hyperopia the light rays are focused behind the retina (outside the globe).

2.1.3. Astigmatism

Astigmatism is a refractive disorder that results from a common abnormality in the shape of the cornea. The human cornea is usually dome-shaped, like part of a football, but with astigmatism, the cornea has an ellipsoidal shape, more like part of a rugby ball. This will cause blurred and distorted vision.

Similar to an ellipse being described by 2 axes (a major and minor axis) the ellipsoid cornea is described by 2 radii. The meridian with the smaller radius is also called the steeper axis, which lies perpendicular to the meridian with the bigger radius, which is called the flatter axis. Each radius has a different refraction and all the light that passes through an astigmatic cornea will therefore produce two focal planes, instead of one. Usually, one of the focal planes is in front of the retina, with the other one behind (Figure 2.1.3.). This situation is called mixed astigmatism. In simple astigmatism one of the two focal points is focused on the retina.

Astigmatism can be combined with myopia. This situation is called myopic astigmatism. Simple myopic astigmatism is a situation with one focal point in front of the retina and one focal point on the retinal plane (Alio 1995).

Astigmatism is mainly hereditary and the prevalence increases with age (Robert 2003 and Asano 2005). Astigmatism is not a rare condition and remains lifelong. Approximately 17% of eyes of a normal population have at least 2 diopters of

astigmatism, but only 1% of eyes have more than 4 diopters. Higher amounts, especially irregular forms of astigmatism, may cause blurred vision, squinting or headaches, and occasionally can be very difficult to correct with spectacles or contact lenses.

The diagnosis of astigmatism is made by subjective refraction (the process to determine the best corrective lenses) and corneal topography (a procedure that scans the shape of the cornea, Figure 2.1.4.).

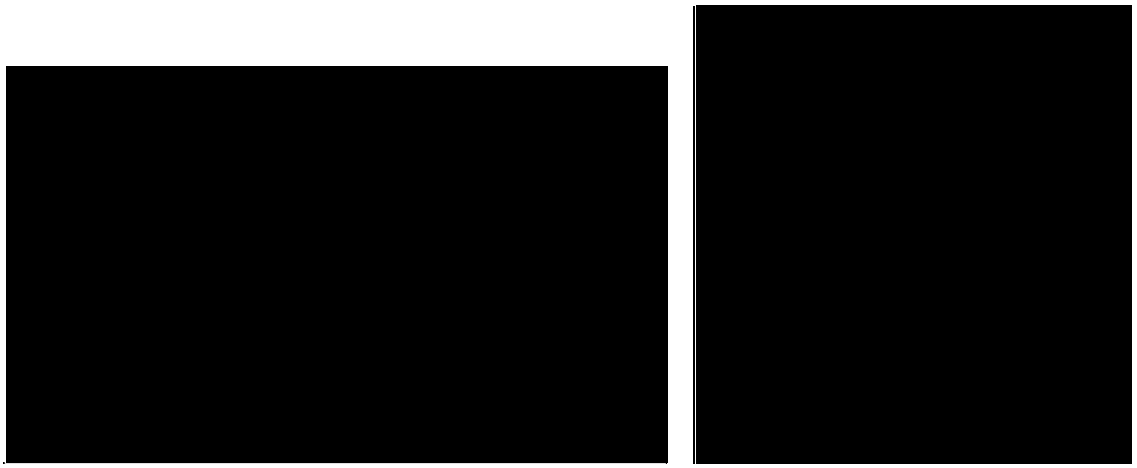


Figure 2.1.3. The "rugby ball" shaped cornea of an eye with astigmatism produces 2 focal planes. Left image: Both planes are in front of the retina in simple myopic astigmatism. Right image: The planes are in front and behind the retina in mixed astigmatism (red and blue lines).

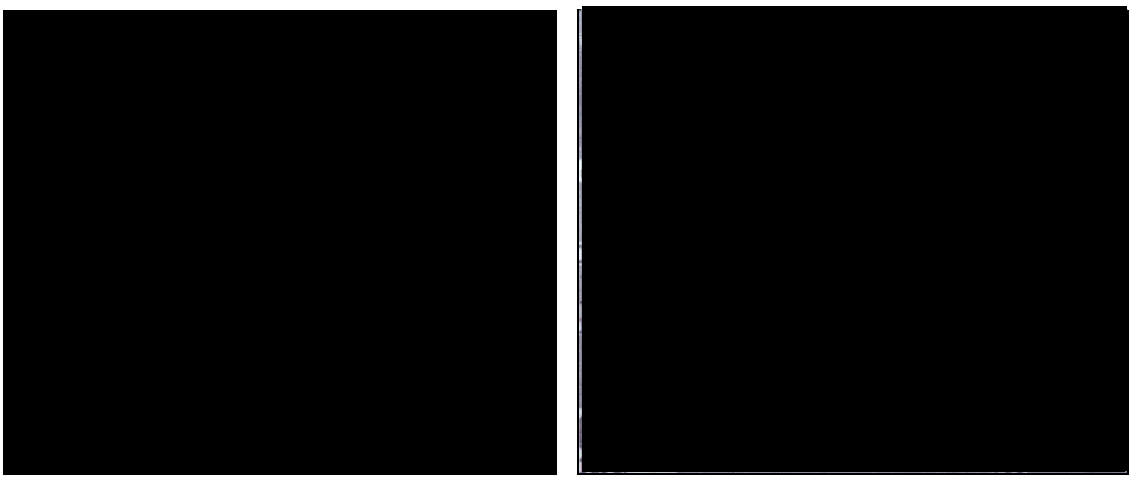


Figure 2.1.4. Topographic image of an eye with corneal astigmatism (bow tie figure). Left image: before laser surgery; Right image: same eye 3 months after LASIK showing flattening of the central cornea (greener=flatter) and disappearing of the bow tie figure.

Astigmatic corrections are more challenging than purely spherical corrections. Astigmatism can be corrected by spectacles with a cylindrical lens, a lens that has different radii of curvature. Such lenses are more complex to prescribe and more expensive to produce. Patients with higher amounts of astigmatism may require contact lenses to achieve good visual acuity.

2.2. Principles and techniques of laser vision correction

Glasses and contact lenses have drawbacks: they are a hindrance in certain professions and activities (e.g. chef, actor, sports). Reducing the dependence on spectacles or contacts promises an improvement in quality of life. For many people, the prospect of going through life without glasses or contact lenses is reason enough to consider intervention of this kind. Intolerance to contact lenses can be a further incentive for wanting refractive surgery.

Over the past 20 years, refractive surgery has undergone a turbulent development. Despite intensive scientific monitoring there is no long-term experience reaching back more than 10-15 years of more recent procedures.

A wide range of corrective methods is available in refractive surgery. A basic distinction is made between corneal procedures and lens procedures. In corneal procedures (Table 2.2.1.) the refractive strength of the cornea can be modified using the excimer laser. Most common procedures are Femto-LASIK (Laser Assisted In-Situ Keratomileusis) and LASEK (Laser Assisted Sub-Epithelium Keratomileusis). Lens procedures correct the vision disorder through an additional lens which is implanted into the eye, or through a lens replacement.

	Myopia	**Hyperopia**	**Astigmatism**
LASIK	up to -8.0 D	up to +3.0 D	up to 4.0 D
LASEK	up to -6.0 D	up to +1.0 D	up to 3.0 D

Table 2.2.1. Indications for corneal procedures

2.2.1. LASIK (Laser assisted in-situ keratomileusis)

Laser assisted in-situ keratomileusis (LASIK) is one of the most frequently performed elective procedures to correct myopia. Around 100,000 LASIK procedures are performed per year in the United Kingdom, and over 12 million procedures have been performed worldwide since the introduction in 1993 (Maurino 2008). It is a highly effective (private) outpatient procedure.

The majority of people with focusing errors of the eye are able to have LASIK. However, some people are not able to have laser eye correction. Possible reasons for this include ocular surface diseases, thin corneas, early cataract or focusing errors outside the range that can be corrected by laser.

Generally, suitable patients for LASIK have:

- An age of 21 or more (the eye is still growing until this age).
- Myopia up to -8 dioptres and hyperopia up to +3 dioptres.
- Regular astigmatism (up to 4 dioptres).
- A stable spectacle or contact lens prescription for at least 12 months.
- Good vision in both eyes with glasses or contact lenses.

A typical LASIK procedure consists of multiple steps. The whole intervention takes place using anaesthetic eye drops and lasts about 10-15 minutes per eye.

Flap creation

First of all, a thin flap of corneal tissue is prepared. For this procedure two different techniques can be used: a mechanical microkeratome or a Femto laser. A microkeratome is a precision surgical instrument with an oscillating blade designed for creating a flap. The hand piece (Figure 2.2.1.) mainly consists of an engine connected to a controller unit, which analyses the resistance of the oscillation of the blade with the aim to prevent blockage. The head of the microkeratome contains the single use blade. It can be mounted on a disposable holder unit for flap creation. During the cut, the eye is temporarily fixed using a suction ring, which is felt as a slight pressure in the eye. A negative pressure of up to 80 mmHg is used for this fixation, rarely leading to conjunctival or choroidal haemorrhages. The blade of the microkeratome smoothly moves forward and cuts a corneal flap with a specific depth. After the cut, the holder is removed and the flap lifted (Figure 2.2.2.).

Figure 2.2.1. Microkeratome hand piece (AMO) and head with holder and support unit, fixed to the cornea by a vacuum.

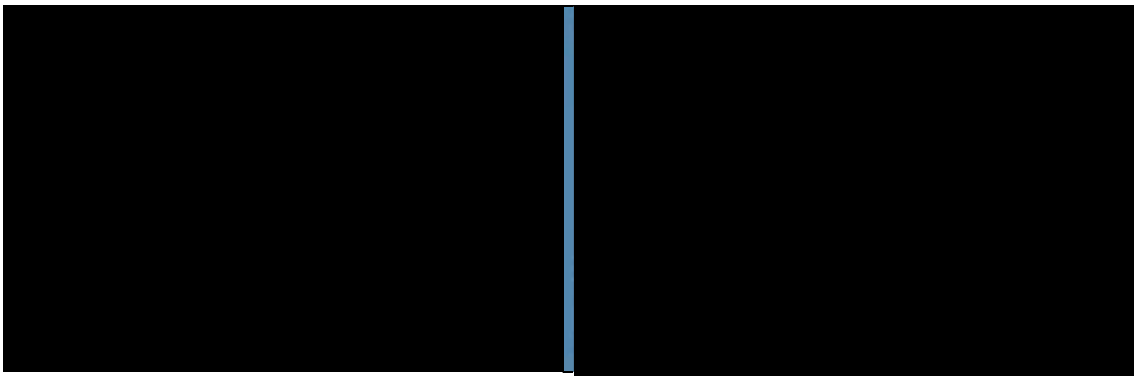


Figure 2.2.2. Creating a corneal flap with a microkeratome.

In recent years, the "bladeless" technique has gained popularity, mainly for hygienic reasons. This method uses a Femto laser (Figure 2.2.3.) to create a corneal flap. A Femto laser is an expensive piece of equipment (approximately £250,000 per unit) and operates with a high energy laser with a wavelength of 1050nm.

The beam of the Femto laser is focused to create a micro air bubble (explosion) in the corneal stroma. The bubble naturally expands and separates the corneal fibres and layers. If multiple air bubbles are placed next to each other, two corneal planes can be separated. The anterior plane can be used as the corneal flap. With this technique the

surgeon can customize the corneal flap for every individual patient. The term ‘Femto-LASIK’ is used for LASIK treatments with Femto laser flap creation.

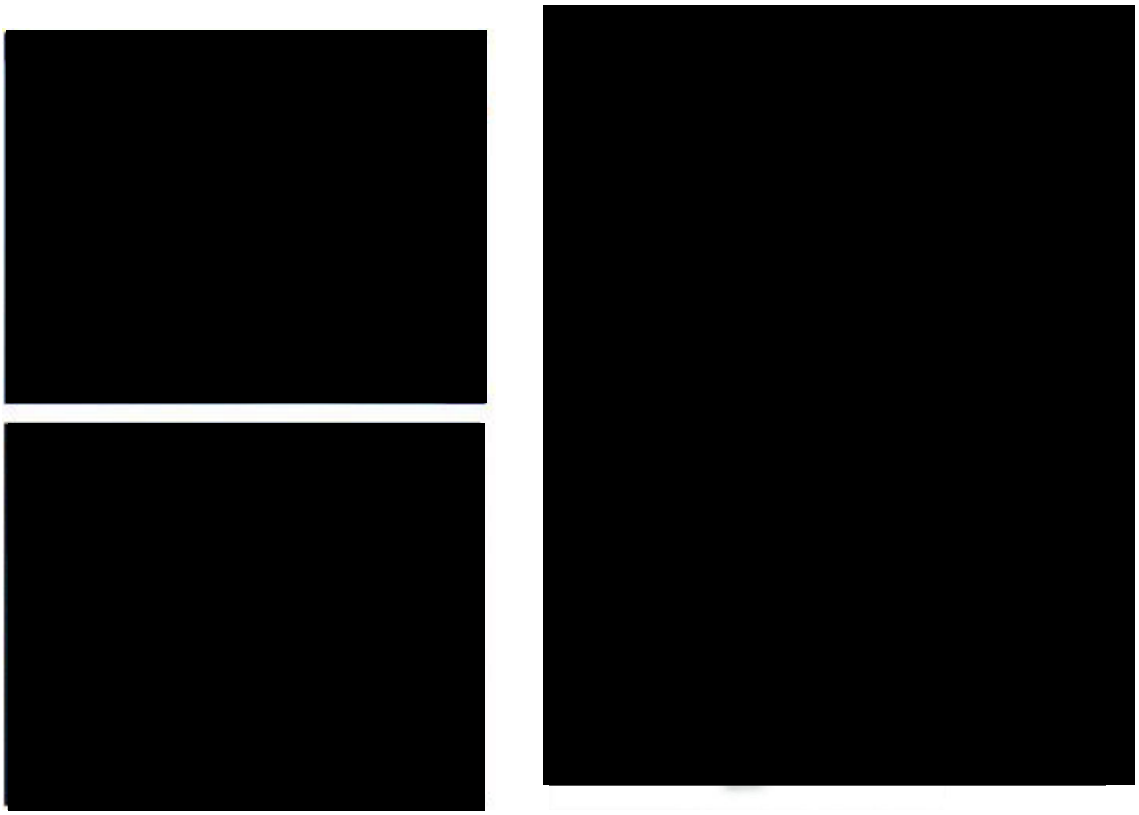


Figure 2.2.3. Creation of a corneal flap with a Femto laser (Ziemer).

Corneal ablation with the Excimer laser

To reshape the cornea an excimer laser is used. Computer-controlled pulses of excimer laser light are applied to the inner layers of the cornea (also called corneal stroma). This removal of corneal stromal tissue (also called ablation) reshapes the cornea and changes the refractive power of the cornea (Figure 2.2.4.). This procedure takes between 30 and 90 seconds. In this process the smallest, unintentional eye movements are also registered by the laser and automatically corrected.

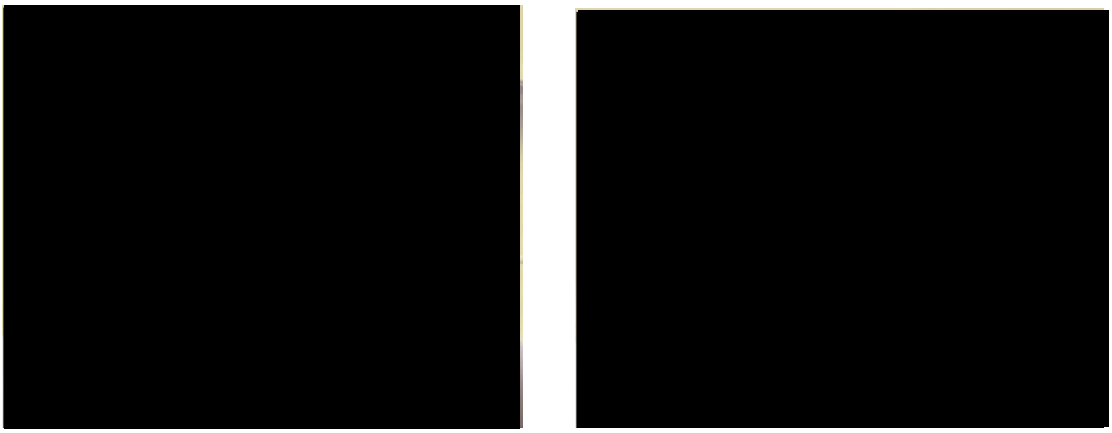


Figure 2.2.4. The laser beam removes corneal stromal tissue to change the refraction.

Once the ablation has been completed the corneal flap is replaced and positioned, and antibiotic and anti-inflammatory eye drops are applied. Further fixation, e.g. with sutures, is not necessary. Slightly blurred vision and slight watering of the eye are both normal following the intervention. After just a few hours, sufficient visual acuity is achieved so that glasses or contact lenses are no longer required. The vision stabilises after 4-8 weeks.

Most new generation Excimer laser units offer wavefront (customised) treatments. Using wavefront measurements (Figure 2.2.5.) the unique imperfections of each individual eye, just like a fingerprint, can be determined. The wavefront data then is used to calculate an individual treatment profile, allowing higher ablation precision.

Figure 2.2.5. Wavefront measurements of an eye

From a technical and engineering point of view, the Excimer laser unit (Figure 2.2.6.) is a highly expensive treatment unit (£350,000) and consists of hardware and software.

The hardware is the part that produces a laser beam with 192nm wavelength. This beam is directed via a system of highly precise optical instruments (mirrors and lenses) to a binocular microscope where it finally is focused on the patient's eye.

Figure 2.2.6. Excimer laser unit for laser vision correction used for this research (VISX S4).

The software part controls the mirrors, the lens positions and the laser power that is needed for the refractive treatment. A calculation algorithm (nomogram) describes the relation between the laser power and the surface ablation. The nomograms mainly base on empirical data.

Risks and complications of LASIK

No surgical procedure is ever risk-free. Fortunately, sight-threatening complications from laser vision correction are rare. Serious complications occur in less than 1% and many LASIK complications can be resolved with additional surgery or medical treatment. A list of possible complications is shown in Table 2.2.2. Visual aberrations summarise symptoms such as glare, double vision, ghosting, halos, starbursts, loss of contrast sensitivity, and problems with low-light or night vision.

Complications	Symptoms	Treatments
Incomplete corrections	Blurry, less-than-perfect vision	Glasses or contact lenses; eye drops; re-treatment
Decentred ablations	Visual aberrations	Eye drops; re-treatment
Oversize pupils (pupils > treatment zone)	Visual aberrations	Eye drops; re-treatment
Haze	Visual aberrations	Eye drops; re-treatment
Irregular flap (folds, wrinkles, striae)	Visual aberrations	Surgical correction; second laser procedure
Dry eye	Dry, itchy or scratchy eyes, often with redness and sense of foreign object in eye, and sometimes pain	Prescription dry eye medication; artificial tears; punctal occlusion (blockage of tear ducts in order to retain tear film on eye)
Diffuse lamellar keratitis (eye inflammation)	Visual aberrations	Eye drops; surgical rinsing of cells
Epithelial ingrowth	Visual aberrations	Surgical removal of epithelium
Infection	Redness, oozing of eyes, sometimes pain	Eye drops; oral medications

Table 2.2.2. Complications, symptoms and treatments in LASIK (Keith Croes).

2.2.2. LASEK (Laser assisted in-situ keratomileusis)

LASEK is an alternative laser refractive procedure. LASEK is known as a 'surface procedure' and may be safer if the cornea is relatively thin, or if any other medical conditions mean that LASIK is not the best option.

Instead of creating a corneal 'flap' on the surface of the cornea, the very superficial layer of corneal epithelial cells is treated with alcohol and moved to the side, allowing the underlying cornea to be re-shaped by the refractive laser with wavefront technology (Figure 2.2.7.). Afterwards, the epithelium can be smoothed over the lasered corneal surface. The surface cells then grow back across the cornea within a few days. Finally, a bandage contact lens protects the surface layer that has not yet grown together securely until it has completely healed, and is then removed.

Generally, the recovery period is longer than for LASIK, and in the first days following treatment, patients may experience a foreign body sensation and may suffer from eye pain and photophobia. The improved vision is not appreciated until the epithelium has fully healed, usually after about a week. The long-term results for low to moderate short-sightedness are very similar to LASIK.

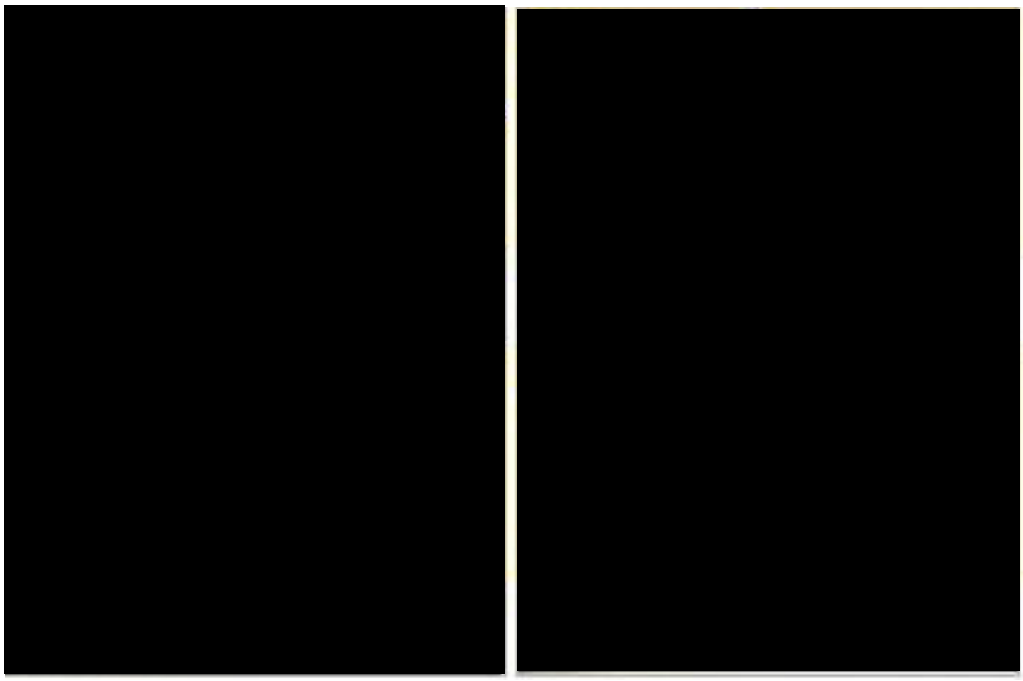


Figure 2.2.7. LASEK procedure.

2.2.3. Planning and programming laser treatments

Refractive eye laser surgery requires careful preoperative assessment and an extensive planning of the treatment (Figure 2.2.8.).

A typical procedure of a Femto-LASIK treatment consists of the following steps:

- Pre-assessment and consenting
- Deciding on a treatment plan, ablation pattern and target refraction.
- Programming the Femto laser for flap creation
- Programming the Excimer laser for corneal ablation
- Follow-up visits

Pre-assessment and consenting

The pre-assessment for laser surgery comprises a comprehensive examination of the eyes and a discussion of visual needs with a Consultant Ophthalmic Surgeon. The examination includes an exact determination of best-corrected and uncorrected visual acuity with refraction, measurement of intraocular pressure and nocturnal pupil diameter, slit lamp examination of the eye lids, cornea, lens, optic nerve and retina, and testing of the extraocular muscles. A laser scan of the corneal surface (topography) is also carried out routinely and sometimes wavefront measurements are added.

At the end of the assessment, the surgeon discusses the findings with the patient and determines the suitability for laser vision correction. Sometimes the surgeon has to advise against undergoing laser surgery. Additional information is provided on the benefits, risks and possible complications (Table 2.2.2.) of laser vision correction, on the predictability of visual and refractive outcomes, and on the cost of the treatment. Finally, once the patient agrees to go ahead, a consent form is signed by the patient acknowledging being informed completely and with understanding.

Deciding on a treatment plan, ablation pattern and target refraction

At this stage the surgeon can suggest a certain method of correction (LASIK or LASEK) and has the chance to discuss treatment targets with the patient. In most cases, patients request emmetropia, enabling them to see distant objects clearly without the need for glasses. The spherical equivalent of emmetropia is zero.

Depending on the vision disorder, different patterns of ablation (the way the corneal tissue is removed by the laser) are applied. For example, myopia is treated with a spherical ablation. This is a straightforward treatment process with a uniform, disc-like ablation of the corneal stroma.

The ablation pattern for the treatment of astigmatism is much more demanding. Basically, the steeper axis of the cylinder is flattened by torical ablation. Flattening of the steeper axis alone, without reshaping the flatter axis, results in hyperopic shift (the eye gets less myopic). This can be a desired side effect in the treatment of myopia, but is usually not desirable because of its unpredictability (McDonnell 1991).

Over the years newer ablation patterns have been developed, notably the bitoric ablation pattern (Chayet 1998, DeOrtueta 2008) and the cross-cylinder ablation pattern (Vinciguerra 2000 and 1999). In the cross-cylinder ablation technique the amount of astigmatism is divided in two: half of the correction is treated on the flatter meridian and half is treated on the steeper meridian. This method does not lead to unpredictable hyperopic shifts. The treatment pattern for combined myopia and astigmatism is a combination of a spherical and cross-cylinder ablation.

Figure 2.2.8. Planning stages of LASIK treatments.

Programming the Femto laser for flap creation

Modern Femto lasers allow programming and modifying of nearly every parameter defining the corneal flap. The flap diameter and thickness are the most important parameters determined for each patient individually. The flap diameter depends on the ablation pattern and is slightly bigger for the treatment of hyperopic eyes. The thickness depends on the surgeon's preference and experience. Thinner flaps allow more corneal tissue to be treated but are more difficult to lift. Further parameters that can be programmed include the shape of the flap (round or oval), the marginal profile (convex, concave, perpendicular) and the position of the flap (centred, off-set). It requires years of experience to find the ideal programming of the flap parameters for each patient (Faktorovich 2008).

Programming the Excimer laser for corneal ablation

In a successful LASIK treatment, the induced refractive change equals the preoperative refractive error. Although the excimer laser's nomogram provides good support in deciding on the best possible amount of ablation and its profile, one particular parameter has to be adjusted patient-individually. This parameter is the diameter of the

ablation, also called the optical zone (OZ). The optical zone has to be increased in eyes with bigger nocturnal pupil diameter, in hyperopic eyes and in eyes that receive a peripheral blend zone. Finally, the amount of ablation can be boosted or decreased, based on the surgeon's preference.

Follow-up visits

Following surgery, patients are seen the next day to check the position of the corneal flap. Additional reviews can be arranged at 1 week and 1 month following surgery. The refractive change of the eye usually stabilises after 4-6 weeks. The final review is undertaken at 3 months, including comprehensive examination with refraction and topography. Most patients are discharged at this time.

2.3. Refractive outcome analysis

Regular postoperative refractive analysis is good medical practice and can identify factors which, together with individual treatment and wound healing factors, could influence the refractive outcome.

The Royal College of Ophthalmologists (2007) and NICE (IPG164, 2006) have published guidelines regarding good medical practice in refractive laser eye surgery. They advise undertaking a careful audit of results following laser in-situ keratomileusis (LASIK), on a regular basis.

Standards have been proposed regarding how refractive outcomes should be calculated and presented (Waring 2000), and commercially available software facilitates this outcome analysis and nomogram changes (see chapter 3).

The basic principle of outcome analysis and nomogram adjustment is a process consisting of 3 stages (Figure 2.3.1.), normally facilitated by the refractive outcome analysis software:

- Refractive data collection: recording of treatment data, preoperative and postoperative refractive and visual data, and data on complications and patient satisfaction.

- Analysis of the data: results from demographics calculations, Waring graphs, vector analysis, and others; more details on methods of analysis are given in Chapter 3 and 5.

- Transformation of the results into nomogram tables and adjustment factors: use of linear and non-linear regression analysis, nomogram graphs and tables.

Other methods include back-calculation to model strategies for pre-treatment adjustment of the ablation sphere to eliminate unpromising new approaches before clinical trials (Arnalich-Montiel 2009).

Figure 2.3.1. Stages of refractive outcome analysis in refractive laser surgery.

2.4. Summary

This chapter provides information on refractive vision disorders, types of laser treatments, benefits and risks of laser vision correction, and the importance of pre-assessment and postoperative outcome analysis.

Typical indications for a refractive eye laser treatment are vision disorders such as myopia (short-sightedness) and astigmatism (an abnormality in the shape of the surface of the cornea). Laser assisted in-situ keratomileusis with Femto laser flap creation (Femto-LASIK) is the most frequently performed elective procedure and has become the standard in laser vision correction.

Postoperative refractive outcome analysis is a complex procedure consisting of 3 main stages: data collection, outcome analysis and nomogram calculation.

The current state of quality of refractive laser surgery has been presented in review articles on LASIK (Sutton 2010) and LASEK (O'Keefe 2010).

Chapter 3

REVIEW OF LITERATURE, SOFTWARE AND PROGRAM LANGUAGES

3. REVIEW OF LITERATURE, SOFTWARE AND PROGRAM LANGUAGES

A review of literature and software was performed extensively at the beginning of the prototype development in 2002, at the beginning of the evaluations in 2008 and following completion of the evaluations in 2010.

3.1. Literature review on refractive analysis

The focus of the thematic literature review was on the handling and analysis of refractive data, on the presentation of refractive outcomes, and on refractive calculation models (nomograms) for treatment optimisation. We were selective in this review focus, and only wanted to include articles that reported on refractive data in laser eye surgery, such as LASIK or LASEK.

Between 2002 and 2008 many articles on laser eye treatments and techniques for their improvement were published. Surprisingly, only a few new articles reporting on this topic were found in a Medline search since 2008. This could be linked to the fact that this field has not seen significant technical changes over the last 2 years, and that the refractive outcomes from LASIK and LASEK have reached a high precision (Sutton 2010 and O'Keefe 2010).

For the search in Medline (PubMed) and Google we have used a range of different key words, and their combination. These search criteria are listed in Table 3.1.1., which also shows the results from the first selection round.

In total, 429 documents were found on refractive data handling, analysis and optimisation. Although this seems to be a high number of publications, in fact, this number is rather low when comparing to other fields of Ophthalmology dealing with refractive outcomes, for example LASIK for myopia (2130 results) or standard cataract surgery (11206 results). This relative shortage of evidence-based literature is mainly a result of circumstances, given that laser vision correction is performed exclusively in private practice. This business field has some distinctive characteristics, some of which are:

- Laser surgery is part of a highly competitive business with a strong view on reputation. Refractive surgeons prefer not to be identified in undertaking

experimental work (research). This bears the risk of damaging reputations. The general tenor is to remain out of studies.

- If the outcome of a study is not good, it may not be published. This may help to reduce the risk of negative news and damage to the prestige that could ultimately bring about a significant cut to revenue.
- If the research results are very good, the journal reviewers may not believe them. Research results could be manipulated to promote private business (marketing issues).
- Research takes time, during which a surgeon could be consulting or operating on patients, again resulting in extra income. Time used for research does not provide earnings; on the contrary, it increases spending.
- Dealing with private practice participants is more complicated than the management of NHS participants in research projects.

We rejected 393 of 429 articles because the link to laser eye surgery was weak or absent. The topics of the excluded articles showed a wide range, including refractive analysis following cataract surgery, corneal grafting, corneal incisional surgery, testing of refractive equipment, reporting on epidemiological findings, intraocular lens power calculation, and refractive treatment of keratoconus.

The remaining 36 documents were marked for full inspection, and graded on their relevance to this research (Table 3.1.1.). The detailed analysis of these articles showed that some of the articles were presenting obsolete technology (e.g. older versions of laser units and ablation profiles), or technology that has become standard in the meantime (we described these articles with the term ‘historic’). Many of the reviewed articles presented results that are valid only for specific equipment, for example laser units Schwind, Technolas, Nidek or Alcon; or the use of a specific (overnight) contact lens called Paragon. Some of the articles presented results that can only be achieved in combination with additional procedures, e.g. LASIK in combination with a cataract operation, and some of the articles with important findings did not describe the methodology well enough for us to repeat the technique or use the calculation algorithm for our research. However, some of the articles graded as partially relevant (+) were used in this thesis and cited in the corresponding sections.

Search criteria / other key words	Res	Exc	Inc	Full inspection Authors (Year)	Relevance
Refractive data / Calculations / Algorithm / Presentation Refractive outcome / Analysis / Reporting / Presentation	207	195	12	Kaye (2002) Naeser (2001) Holladay (2001) Kaye (2001) Calossi (1993) Arbelaez (2009) Feltham (2008) Anderson (2003) Nakano (2003) Waring (2000) Huang (1999) Hefetz (1997)	+ - (very complete) - (very complex) - (very complex) - (historic) - (only Schwind) - (mainly Technolas) - (only Technolas) - (only Nidek) +++ + - (historic)
Vector analysis	125	115	10	Suominen (2003) Thibos (2001) Alpins (2001) Huang (2000) Corones (1999) Alpins (1997) Shah (1997) Naeser (1997) Alpins (1997) Neumann (1989)	+ - (very complex) +++ - (too general) - (historic) - (integrated in 2001) - (historic) - (too theoretical) - (integrated in 2001) - (for AK only)
Nomogram / Outcome / Treatment / Adjustment / Improvement	97	83	14	Arnalich-Montiel (2009) Lapid-Gortzak (2008) De Ortueta (2008) González-Méijome (2007) Mrochen (2006) Zaldivar (2005) Feiz (2005) Caster (2004) Anderson (2004) Ortiz (2003) Moniz (2002) Reviglio (2000) Ditzen (1999) Probst (1998)	+ - (no details provided) - (only Schwind) - (only Paragon) +++ + - (IOL related) - (only Alcon) - (only Technolas) + (but too general) - (too general) - (mainly results) - (historic) - (historic)
Total	429	393	36		

Table 3.1.1. Overview of the selection process for the literature review, with the search criteria, the results (Res) from Medline search, the excluded documents (Exc), the remaining documents (Inc) that were used for inspection, and the relevance.

Finally, only 3 articles matched the search terms and topic sufficiently, providing specific, significant and generalisable information for this research. We believe that these publications provide essential information on refractive analyses and were therefore used as reference. For many refractive surgeons, these articles have become part of their 'key literature' in reporting refractive outcomes, calculating nomograms and analysing refractive astigmatic data with the method of vector analysis.

3.1.1. Waring Graphs (Reporting refractive outcomes)

The main article linked to the presentation of refractive results is written by George Waring and has the title "Standard graphs for reporting refractive surgery", published in

J Refract Surg, 2000;16:459-466. Mr Waring writes about his experience in refractive analysis, and presents his ideas on how refractive data should be analysed and presented in publications. He proposes a set of six standard graphs (Figure 3.1.1.) which should be included in any paper reporting the results of a series of cases. Generally, the graphs can easily be produced by anyone with widely available software (Microsoft EXCEL). This standardized system of reporting outcomes allows comparison between the results of different publications. The graphs of different articles can be arranged side by side, allowing a direct visual evaluation of the outcomes of surgical procedures. Although originally proposed by Prof Neuhann (Comment: Prof. Neuhann did not publish the concept in a journal, but he spoke about the idea of graphs and refractive outcome reporting at Congresses and in private personal communications), the concept of 6 standard graphs, as presented by Waring, has become a "gold standard" and the concept has been taken on by many surgeons in their routine praxis. Therefore, any software that analyses refractive data and produces outcome graphs has to implement at least some of the Waring recommendations.

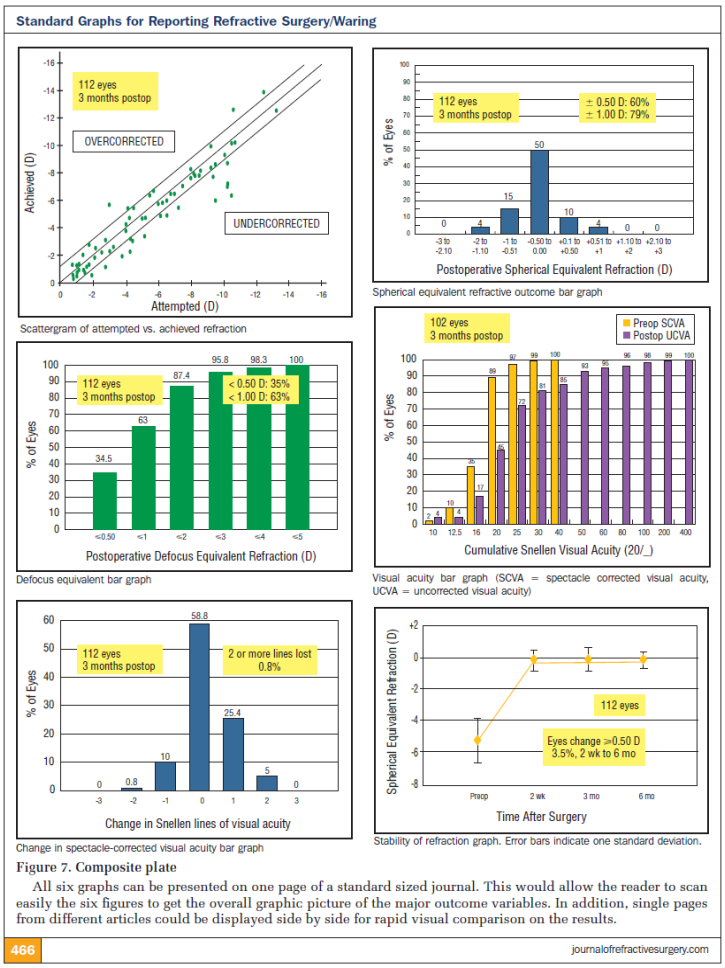


Figure 3.1.1. Set of 6 standard Waring graphs (copy of original publication).

3.1.2. Nomograms adjustments

The key article for nomogram adjustment is authored by Michael Mrochen et al, and has the title "Nomograms for the improvement of refractive outcomes", published in Ophthalmologe 2006;103:331-8. The authors of this study analysed the clinical relevance and limitations of nomograms in case series on a theoretical basis. Their results suggest that the use of individual nomograms can significantly improve the predictability of refractive outcomes. However, the investigations demonstrate that a homogeneous data distribution within cohorts was a key factor for predictable nomogram calculations. The authors concluded that nomograms are helpful for improving refractive outcomes, but are limited to approximately 90% of outcomes within +/-0.5 D of the target.

3.1.3. Vector analysis with the Alpins method

The most important literature on vector analysis is authored by Noel Alpins with the title "Astigmatism analysis by the Alpins method", published in J Cataract Refract Surg, 2001;27(1):31-49. The aim of Mr Alpins's method is to determine the effectiveness of correcting astigmatism by laser refractive surgery by a vectorial astigmatism outcome analysis. For the calculations the method uses 3 fundamental vectors: the target induced astigmatism vector (TIA), the surgically induced astigmatism vector (SIA) and the difference vector (DV). TIA is the astigmatic change (by magnitude and axis) the surgery was intended to induce. This can be seen as a golf scenario where the player intends to hit a ball from a starting point into the hole. SIA represents the amount and axis of astigmatic change the surgery actually induces. In "golf language" this would mean where the ball effectively landed after the hit. Finally, DV is the astigmatic change that would enable the initial surgery to achieve its intended target. This is the required hit of the ball needed to bring it from the (unintended) landing point to the target point (hole). The vectors can be drawn on a double angle vector diagram (Figure 3.1.2.). By examining individual vector relationships to the TIA (e.g. the correction index, index of success, and flattening index), a comprehensive astigmatism analysis is completed. Each index provides information necessary for understanding any astigmatic change.

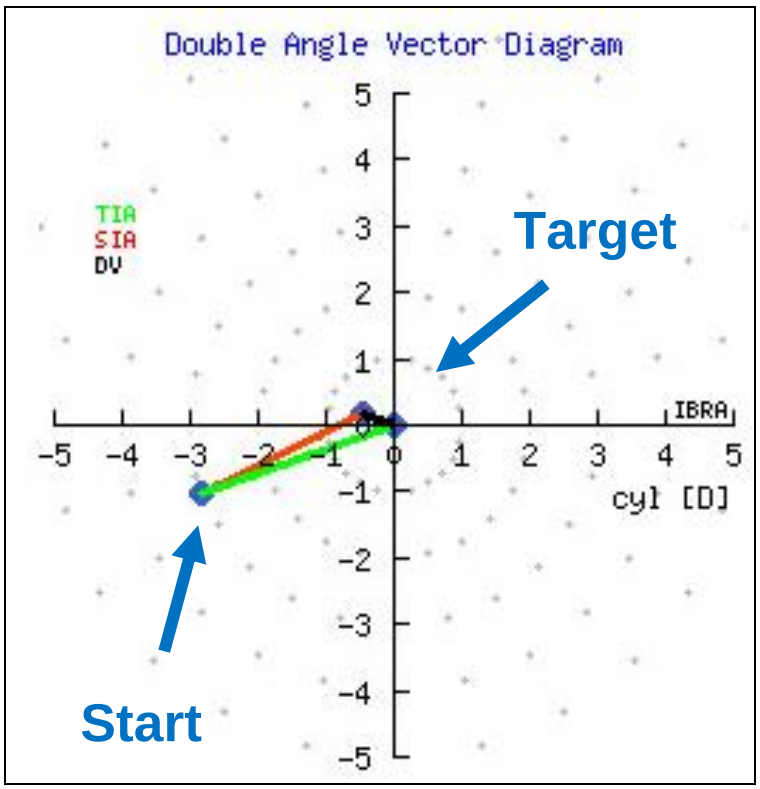


Figure 3.1.2. Double angle vector diagram (produced with the IBRA system) showing TIA (green line), SIA (red line) and DV (black line).

3.2. Review of refractive analysis systems

A review of refractive analysis software over the years showed parallels to the literature review, with minimal changes since 2008. Five different software systems were available on the market in 2008. An April 2010 review showed that 4 of the 5 products are still available, and 3 of 4 products are upgraded on a regular basis (Outcome Analysis, Datagraph-med and ASSORT Software). The Refractive Surgery Outcomes Information System was removed from the market in 2009 and its successor (EUREQUO) has just been introduced, showing a delay of almost 1 year. The most up-to-date review also showed that no other company has invested in the development of outcome software in the field of refractive laser eye surgery.

In the following subsections we will summarise key figures of all 5 software systems that had an influence on refractive surgeons over the last 10 years (Table 3.2.1.); and on the IBRA system development generally. Each system is described with information about the company, the surgeon involved in the development of the system, the features and costs. Images from print screens (where available) show the user interface.

Outcome Analysis and Datagraph-med were available as (case restricted) demo versions and were tested in 2008.

As per 2008/2009, three of the systems offered refractive outcome analysis and were able to produce the set of 6 standard Waring graphs. The main focus of the ASSORT Software was on analysis of refractive data with the method of vector analysis. The RSOIS system was intended to be a refractive database with some (minimal) outcome analysis functions (calculation of mean and standard deviation) without presenting results in graphical form.

Software (Author)	Developed by surgeons	Refractive analysis	Vector analysis	Individual nomogram	Web-based	Eva	Costs
Outcome Analysis (P. Binder)	Yes	Yes	No	No	No	No	$ 4000
Datagraph-med (S. Pieger)	No	Yes	No	No	No	No	€ 1750
Refractive Surgery Cons. (J. Holladay)	Yes	Yes	Yes	No	No	No	$ 8000
ASSORT and Vector (N. Alpins)	Yes	No	Yes	No	No	No	$ 4900
RSOIS (ESCRS)	No	No	No	No	Yes	No	€ 150
IBRA System (B. Zuberbuhler)	Yes	Yes	Yes	Yes	Yes	Yes	£ 400?

Table 3.2.1. Overview of commercially available refractive analysis software systems (up-dated in 2009). For comparison the IBRA system with the aimed features. Eva=Evaluated. The costs are for a single user licence.

3.2.1. Outcomes Analysis Software

This software is produced by Outcomes Analysis Software, Inc., 2500 6th Avenue, Ste. 307 San Diego, CA 92103, USA. The system is developed by Dr Perry Binder, a well known and established American refractive surgeon. The system is a FileMaker Pro Runtime application, and is regularly updated. A single user license (unlimited use) costs USD 4,000.00 and runs on a single computer only. The software has limited server and network operationability (as provide by the FileMaker Pro Server version). The software can record all relevant patient and surgical data via a clear user-interface with multiple data entry pages (Figure 3.2.1.). The system is able to perform complex refractive analysis, to calculate nomograms and to produce a variety of charts, including the set of Waring charts (Figure 3.2.2.). The software does not offer vector analysis

based on the Alpins method. The functionality, user interface satisfaction and clinical effectiveness of the software have not been scientifically evaluated.

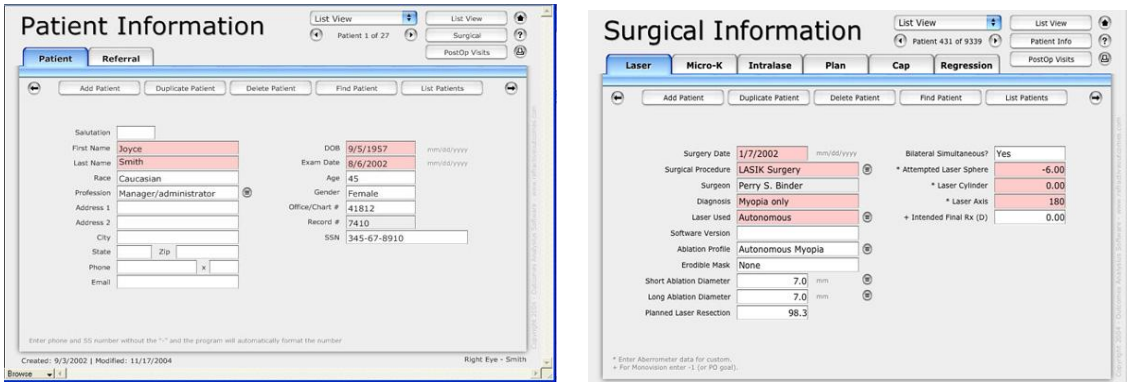


Figure 3.2.1. Two screenshots from the "Outcome Analysis Program Version 4.0", showing the fields for the collection of patient information (left) and surgical information (right).

Figure 3.2.2. Two screenshots from the "Outcome Analysis Software", showing the charts that can be produced by the software (left) and one example of a spherical equivalent histogram (right).

3.2.2. Datagraph-med

This system is produced by Pieger GmbH, Treidelsweg 8, D-90530 Wendelstein, Germany. Behind the company and the programming is the owner Stefan Pieger, who is an electronic engineer. No eye surgeons were involved in the concept or core programming of the system although eye surgeons would surely have tested the system after completion, and provided important feedback. Other than the Outcomes Analysis Software, Datagraph-med is developed in co-operation with ZEISS, one of the global providers of optical and opto-electronic technology. Therefore, the software system is optimised for ZEISS's own refractive laser units, the MEL-80, and offers an interface that can import some of the treatment data (not all of it, and no pre- or postoperative refractive data) directly from the MEL-80 laser into the analysis software. As the market share of ZEISS MEL-80 lasers in the UK is less than 3%, only a minority of refractive

surgeons can take advantage of this. The price for a user license is EUR 1,750.00 for one installation. The software is regularly updated.

Technically, the programming is based on a Microsoft Access and Microsoft Office system, which needs to be (pre-) installed on the PC to run the software application. The system features include a database for the collection of pre- and postoperative data, a refractive analysis tool that can create the Waring graphs, and a (general) nomogram calculation tool (Figure 3.2.3.). The software does not offer vector analysis or complex network functionality. The system has not been evaluated regarding user satisfaction, functionality or effectiveness, although some of the features of the system have been presented by Mirshahi and Kohnen in a German ophthalmological journal (Mirshahi 2002).

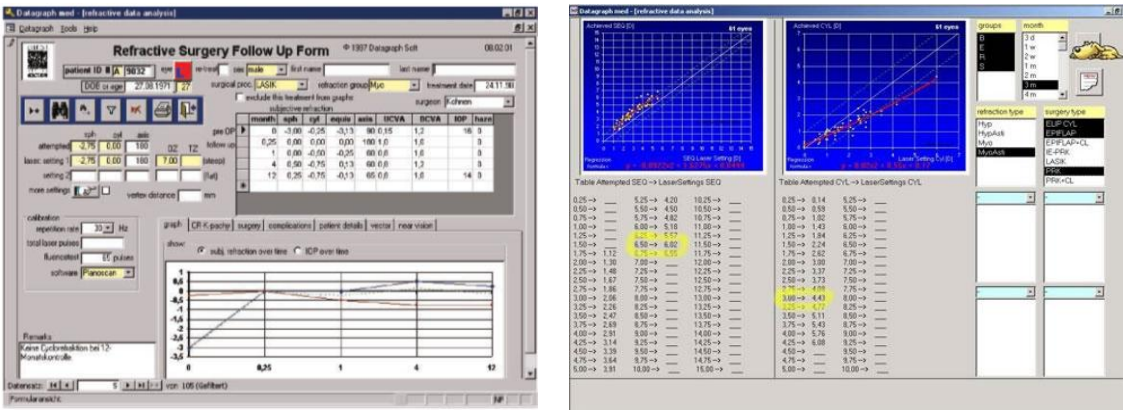


Figure 3.2.3. Two screenshots from the "Datagraph-med Version 3.90", showing a refractive analysis with stability chart (left) and the charts and tables of the nomogram adjustment module (right).

3.2.3. Refractive Surgery Consultant Elite

This product is developed by the Refractive Consulting Group, Inc., 28071 North 90th Way, Scottsdale, Arizona 85262, USA. The programming was performed in conjunction with two established and internationally well known American refractive surgeons: Dr Jack Holladay and Dr Guy Kezirian. These Consultants are also contracted in part by VISX, a global company that produces laser units (VISX S4 laser; used in the controlled trial in this research). This company is owned by Advanced Medical Optics, Inc. (AMO), one of the largest suppliers of ophthalmic equipment. The cost of the software is USD 8,000.00, which includes licenses for 3 computer installations. Version releases are scheduled to occur approximately once yearly. A demo version was not available. The features (taken from the manufacturer's website) include a database with

complex data entry form, laid out in logical order to follow the sequence of a refractive patient pathway (Figure 3.2.4.). The software analyses data and produces Waring graphs. General nomogram calculations are updated constantly as more data is entered. The software includes vector analysis and produces double angle vector diagrams, but the developers do not mention if this method is based on the Alpins method or their own. There is no publication regarding evaluation of the system, although the system has been used for the calculation of results for many publications and presentations performed by Jack Holladay.

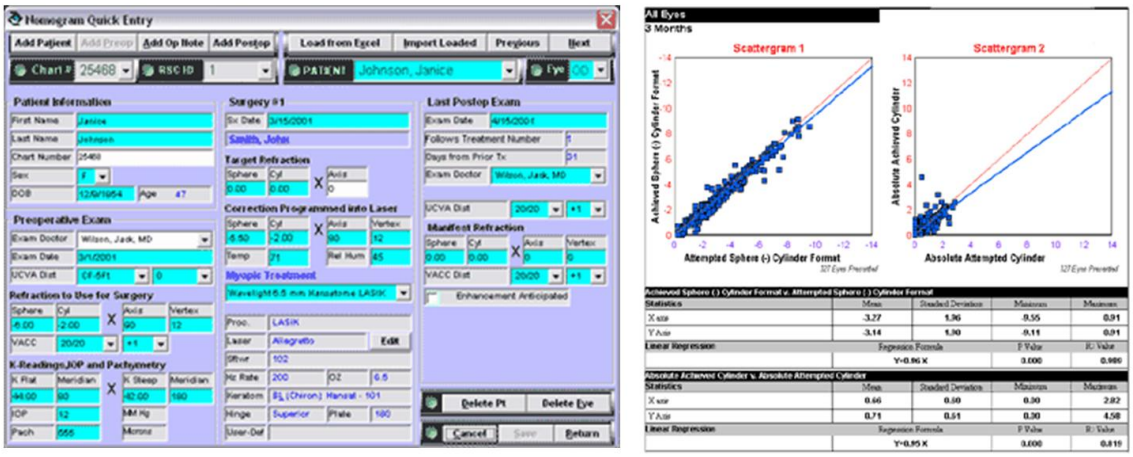


Figure 3.2.4. Two screenshots from the "Refractive Surgery Consultant Elite" Software, showing a data entry form for patient and surgical data (left) and a spherical equivalent and cylinder scattergram in the nomogram calculation module (right).

3.2.4. ASSORT

This system is developed by ASSORT Pty. Ltd., 7 Chesterville Rd., Cheltenham, Victoria 3192, Australia. Responsible for the programming is Noel Alpins, a Melbourne-based ophthalmic surgeon who is the developer of the Alpins Method. His method has been published in many articles and has become the standard for eye surgeons. The price for one license of the ASSORT software is USD 4,900.00. A major feature of the program is the possibility of planning and analyzing astigmatism surgery (Figure 3.2.5.). The Alpins method of astigmatism analysis is displayed both numerically and graphically (Figure 3.2.6.). The software does not produce the standard Waring graphs. A demo version was not available.

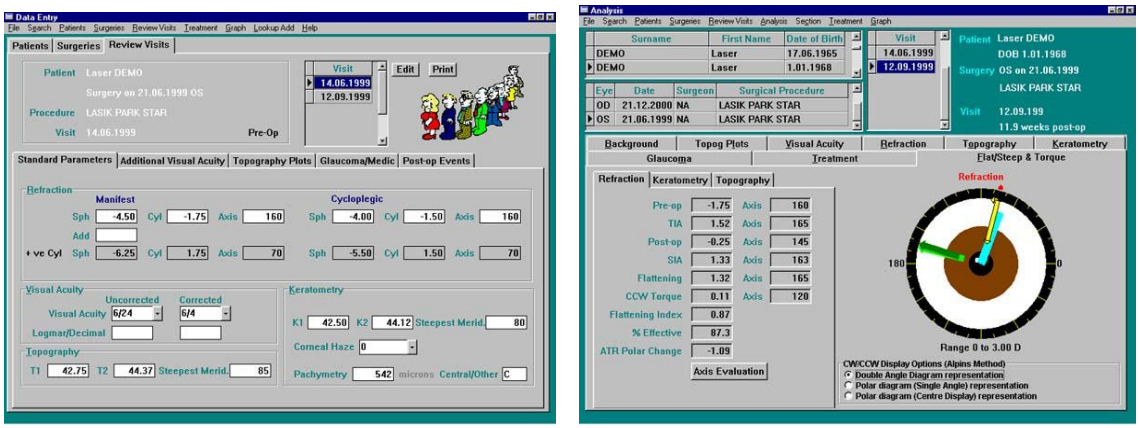


Figure 3.2.5. Two screenshots from the ASSORT Software, showing a data entry form (left) and a vector chart with parameters from vector analysis (right).

Figure 3.2.6. A screenshot of the ASSORT software with a polar diagram (top right), a double angle vector diagram (middle left) with TIA, SIA and DV, and a table with calculated vector parameters (correction index and index of success, in the centre).

3.2.5. Refractive Surgery Outcomes Information System (RSOIS)

This system is no longer in use. It was developed in 2006 for the European Society of Cataract and Refractive Surgeons (ESCRS), Temple House, Temple Road, Blackrock, Co. Dublin, Ireland. The purpose was to collect laser treatment data from patients

treated by the members of the ESCRS. The software was based on web technology and was freely accessible for all members (member fee €150 per year). The RSOIS was mainly a database that offered basic analysis functions (calculations of mean and standard deviation from preoperative and postoperative data). The software did not produce Waring graphs, nor did it calculate nomograms or vector analysis outcomes. Most eye doctors did not like it or use the system, because they understood it as an instrument of controlling from an ophthalmic society. They also criticised that the system did not provide meaningful outcome analysis. Therefore, the members of the ESCRS rejected the system and the Society promised to develop a successor with the name "EUREQUO" (European Registry of Quality Outcomes for Cataract and Refractive Surgery), which has just been made accessible to members.

3.3. Review of program languages for system development

For the development of the prototype and the IBRA system, we reviewed and tested different program languages and developer platforms. Table 3.3.1. provides a summary of the reviewed systems.

Completely different requirements existed at 2 different stages of the system development. Therefore 2 separate reviews of program languages and developer platforms were performed over the years.

The first review focused on the integration of the existing FileMaker database concept into a new system that could also provide graphical output of the results that, so far, had to be performed with EXCEL in a separate step following manual data transfer. The new prototype should combine data collection and analysis in one system, and should present the results in bar charts and scattergrams. As we were given little time for the prototype development, we have omitted the idea of using a 'proper' program language and concentrated instead on 2 commercially available developer platforms, one platform based on FileMaker, the other on Microsoft Office programs, including MS Access, MS EXCEL and Visual Basic. The optional plug-in "xmCHART" from the Austrian company 'X2max Software' FileMaker promised to enable FileMaker to create bar

charts and scattergrams. We decided to continue with the use of FileMaker and started the development of the prototype.

Language / Platform	Description
FileMaker Pro	FileMaker Pro is a relational database application from FileMaker Inc. (Apple Inc.). It can be used simultaneously with a mixed Windows and Mac user base; and can run independently with the 'Runtime Version'. The optional FileMaker plug-in "xmCHART" from the Austrian company X2max Software enables the creation of bar charts and scattergrams. Other plug-ins can produce PDF files and can link FileMaker with web-servers via FTP.
Visual Basic	Visual Basic (VB) is a programming language and a development environment developed by Microsoft. Because of its BASIC heritage and graphical features Visual Basic is considered a relatively easy to learn and use programming language. Microsoft has developed derivatives of Visual Basic, like Visual Basic for Applications (VBA), which is included in many Microsoft applications (Microsoft Office). In order to run Visual Basic applications, the Visual Basic run-time files are required.
C++	C++ (C plus-plus) is a general-purpose, 'middle-level' programming language. C++ is commonly used in the software industry. Some of its application domains include system software, device drivers, embedded software, server and client applications, and entertainment software.
C#	C# (C sharp) builds on the syntax and semantics of C++, allowing C programmers to take advantage of .NET and the common language runtime. It is intended to be a simple, modern, general-purpose, object-oriented, 'higher-level' programming language, developed by Microsoft.
Java	Java is a general-purpose, class-based and object-oriented language developed at Sun Microsystems. The language derives much of its syntax from C++ but has a simpler object model. Java applications can run on any Java Virtual Machine (JVM) regardless of computer architecture.
PHP (HTML)	PHP is a common general-purpose language that was originally designed for web developments. It generally runs on a web server, taking PHP code as its input and creating web pages as output. It can be used free of charge and many 'open source' libraries are freely available. HTML ("HyperText Markup Language") is the predominant language for Web pages. It provides a means to describe the structure of text-based information in a document and to supplement that text with interactive forms, embedded images, and other objects. HTML can include embedded scripting language codes (such as JavaScript, a scripting language widely used for client-side web development) which can affect the behaviour of Web browsers and other HTML processors.

Table 3.3.1. Overview of program languages and developer platforms reviewed for the development of the prototype and the IBRA system.

Three years later, the second review emerged from problems with the use of the FileMaker developer platform (more details on the problems with FileMaker are provided in chapter 4). To get rid of the limitations this platform forced on us, we were searching for an alternative that promised openness and flexibility, which we believed at this stage could only be found in the more complex program languages. The successor of the prototype software should provide a structure that could guarantee integration of any kind of technology in the future. Ideally, the program language should feel comfortable with Internet environments, too. Unfortunately, at this stage, we did not have any knowledge in any of the newer program languages. After a careful review of the languages, we removed C++ and C# from the list as these languages seemed to be too complex for programming amateurs to learn. The race between Java and PHP was very close, and we finally decided to learn and use PHP for the development of the new software system, as we had a couple of good friends who promised to support us in case of problems (more details on our specifications and PHP are presented in Chapter 5).

3.4. Summary

Although there are many publications available on results from laser vision correction, there are few on optimising refractive laser treatments. We have reviewed and summarised the leading publications on presenting refractive outcomes, on nomogram adjustments and on vector analysis in refractive treatments.

We have published details and showed screenshots of the 5 software systems available worldwide on data collection and analysis in laser vision correction. Over the years only 3 of these systems seem to be commonly used and updated. Each software has a different focus and therefore each offers particular benefits. None of the systems includes the functionality we were looking for, i.e. integrating all available analysis methods in one system that can be run over the Internet for an acceptable price.

Finally, this chapter explains the 2 review processes needed to be found, one a developer platform and one a program language for the development of a new analysis system, as aimed in this research.

Chapter 4

PROTOTYPE DESIGN AND DEVELOPMENT

4. PROTOTYPE DESIGN AND DEVELOPMENT

The idea of a software application for the analysis of patient data after refractive laser surgery emerged in 2001 at the private practice laser centre at the Cantonal Eye Hospital in Lucerne, Switzerland. At this time, a simple FileMaker application was used to collect refractive data. The user-interface of this application presented with a single page, containing fields for the data collection of 15 different preoperative and postoperative parameters from visual acuity testing and subjective refraction.

Waring graphs were designed manually in 3 steps. This time-consuming process had to be repeated every time data was extended or changed. The steps were:

1. Data collection with the FileMaker application on an Apple Macintosh computer. (Comment: the refractive surgeons preferred using Macintosh computers, while the Hospital Trust supported only Windows based computer systems.)
2. Data export from FileMaker into Microsoft Excel on a Windows PC. (Comment: the data was transported via 3.5 inch floppy disks.)
3. Manual data processing in Excel included sorting, deletion of empty fields, and grouping of data and results. Bar charts and scattergrams were created and, finally, title, legends and units were applied to the figures (in Excel and PowerPoint).

The Director of the Refractive Laser Centre, Professor Isaak Schipper, was looking for a specific ‘add-in’ to his pre-existing FileMaker application, that could offer automated bar chart and scattergram creation using the criteria presented by Waring. Unfortunately, it was not possible to create charts using the basic FileMaker software.

One of the possible solutions was to buy a commercial software package for refractive outcome analysis. Our favourite was the “Outcome analysis software” from Perry Binder. This software was very expensive so, before investing hospital money, we decided to give a home-made development one more try. This new prototype was to be based either on a step-by-step extension of the FileMaker application (if possible) or on a new platform, using a combination of Microsoft Office components (Access, Excel and Visual Basic). At this stage we put together a list of needs and specifications for the prototype.

4.1. Needs assessment and task lists

The needs assessment had 2 main perspectives: firstly, the surgeon's perspective with the clinical needs of a data recording and analyzing system; and secondly, the software developer's perspective with the evaluation of technology specifications and requirements that could guarantee satisfying implementation of the clinical needs. The system should be different from clinical documentation in many EHRs, which are often dictated by billing and legal requirements.

Clinical task list

From the surgeon's perspective, the clinical task list consisted of the following points:

- Extension of the existing database (more fields/parameters)
- Automatic creation of Waring charts
- Easy to use interface
- Minimal costs (maximum £700)
- Compatible with Apple Macintosh and Windows PC

System task list

From the developer's perspective, the emphasis was set on usability and user-centred design rather than system design. Therefore, software documentation or printed manuals were replaced with 'wizards' and 'help & information' boxes in the software, linked to the tasks.

The developer's task list included:

- A Microsoft Windows-based software system (hospital requirement)
- A system that could use the existing data (300 cases)
- Extension of the existing database
- Implementation of 'macro functions' which were able to group and sort patient data
- Review and implementation of the xmCHART plug-in. The xmCHART 2.0 from the Austrian company X2Max was a macro code extension for FileMaker, which could create most charts offered by Excel.
- Acquiring the knowledge to program the xmCHART plug-in to produce graphs, as recommended by George Waring (Waring G, 2000).

- Implementation of macros that can create and label a chart from previously analysed data in combination with xmCHART
- Development in accordance with the low budget
- Easy installation (Runtime)
- English user interface

After a testing phase we realised that the chart creation with the FileMaker plug-in worked very well, and we decided to continue using FileMaker and to take this as the platform for the prototype development.

4.2. User interface and system design

We implemented all fields from the original FileMaker database into the new prototype, and re-designed the user-interface. We separated data collection and data analysis.

The data collection module was used to create, search and edit treatment records. It offered different pages: a patient list, a patient search site and a patient data entry/edit site with all the entry fields.

In the data analysis module the preoperative and postoperative refractive and visual acuity data of all records were grouped and analysed. The processed data then was used for the creation of the Waring charts. The analysis and calculation process was programmed using the macro function of FileMaker. The process was started by clicking a button. For the creation of the user interface the integrated design functions of FileMaker were used.

We were able to link our prototype application with a runtime extension that allowed running the application on any Windows or Macintosh based computer system without the need of pre-installed FileMaker software. This special version was offered by the "Developer Language Kit (DLK)" from FileMaker.

4.3. Implementation

The prototype was called "Proexcimer", a combination of the words "pro" (meaning "for") and "excimer" (the type of laser in laser vision correction). The final version of Proexcimer consisted of 3 modules: one for patient selection, one for data entry and one for the analysis.

Module 1: Patient list and patient selection

This module showed up after starting the application (Figure 4.3.1.). The patient list presented the surname and first name, the date of birth, the diagnosis (myopia, hyperopia, astigmatism), the treatment date, the treatment procedure (LASIK, LASEK or PRK), the surgeon's name, a selection of preoperative and postoperative distance visual acuity data, and a field with comments.

Name	Vorname	Ge..	Geburtstag	Diagnose	code1	FV prä od cc	FV prä od sph	FV prä od zyl	FV prä od sph aequi	FV prä os cc	FV prä os sph	FV prä os zyl	FV prä os sph aequi	Datum La..	Interve..	Operateur od	M
Giger	Claudia	f	10.11.1972	Hyperopie	x	1.00	-8.0	+2.5	-6.75	1.00	2.0	5.0	4.50	11.5.2001	erste	Dr. Schipper	
Herbert	Karl	m	22.11.1960			1.00	-4.5	0	-4.50	0.60	-5.0	3.25	-3.38				
Hoger	Ruedi	m	18.5.1969							1.25	-7.0		-7.00			PD Dr. Schipper	L
Honegger	Martin	m	18.5.1960	Myopie		0.60	-4.0	1.0	-3.50								
Krummenacher	Petra	f	10.11.1982	Myopie		0.80	-5.0	+2.0	-4.00					11.5.2001		PD Dr. Schipper	L
Meyer	Ruth	f	22.2.1944	Myopie		1.00	-5.5	1.25	-4.88								
Zuberbühler	Hanspeter	m	10.11.1970		x	0.50	-10.0	+2.5	-8.75	0.80	-3.25	+0.25	-3.13	11.5.2001	zweite	Dr. Schipper	

Figure 4.3.1. Screenshot of the Proexcimer prototype showing a list with patient data.

Module 2: Data entry

In the data entry module the data for the right (OD) and left eye (OS) were collected (Figure 4.3.2.). The fields included treatment data, preoperative and postoperative refractive, keratometric and visual acuity data, tonometry, haze and glare. The data was entered on 8 different sites.

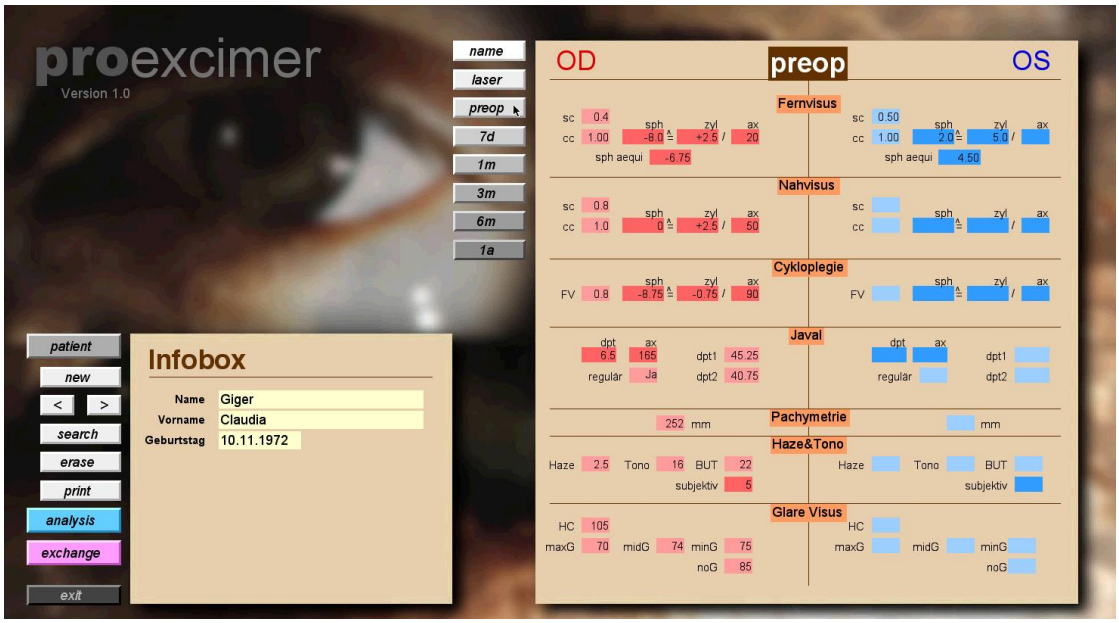


Figure 4.3.2. Screenshot of Proexcimer showing preoperative patient data for both eyes.

Module 3: Chart creation

The analysis method could be selected from the overview site showing the 6 integrated Waring graphs and an additional cylinder chart (Figure 4.3.3.). The data analysis, grouping, and chart creation was started with a "create chart" button. The final chart was shown in a media field in the FileMaker application and could be printed or saved as a JPG image (Figure 4.3.4.).

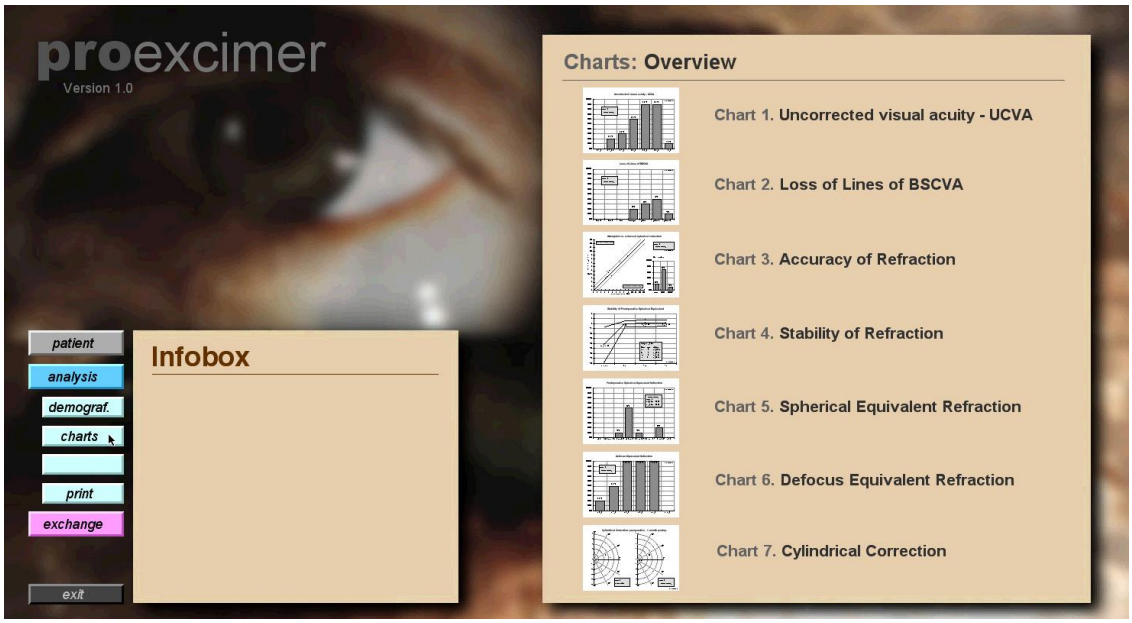


Figure 4.3.3. Screenshot of the Proexcimer prototype showing an overview of the analysis methods.

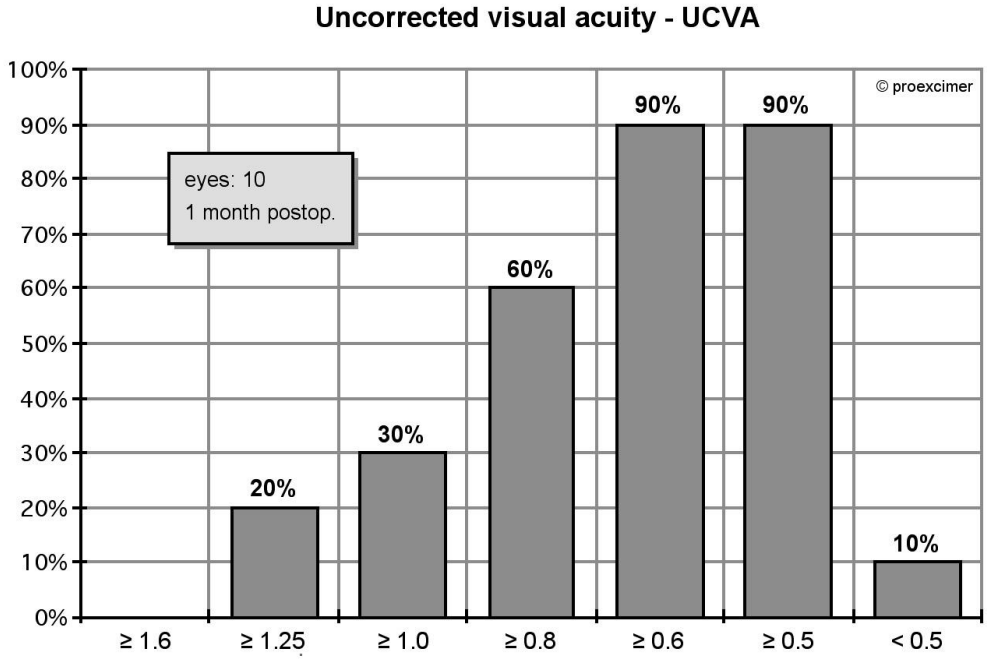


Figure 4.3.4. Uncorrected visual acuity chart created with the Proexcimer prototype software.

4.4. Evaluation of the prototype and conclusions

The prototype was used for 2 years. Although the general use of the software was easy and the application provided us with Waring graphs, there were many small, and some larger, difficulties with the system. In particular, the following serious problems occurred.

Problems with the FileMaker platform

- The software did not work and behaved similarly each time. Sometimes the charts showed up, sometimes not. Where was the error? Was there a 'bug' in the FileMaker Runtime software? Was it the Windows operating system?
- The FileMaker Runtime was only available for one operating system (either Mac or Win). Every software modification had to be done for each system separately each time. If one version was ready for use, the other had to be adjusted exactly the same for the other operating system. This caused delays and was a major source of inconsistency in the development process.
- The print configuration could not be saved in FileMaker as a preference. This was a common problem, and the FileMaker developer community complained

about it for many years. Unfortunately, the printers we used in the clinics and offices were all of different makes, further increasing the difficulty for standardised printouts.

- FileMaker Runtime offered the benefit of independence to the FileMaker installation, and offered good protection of the scripts of the application in 'runtime mode'. The disadvantage was that the Runtime version could not be used in a network environment. Therefore, each computer required an installation of our Proexcimer application. Similarly, software updates had to be done for each computer separately, which was very inconvenient as we modified the software quite regularly.
- FileMaker Server offered network functions, but also had to be installed on every computer. The disadvantage of this version was that the applications run in 'normal mode', allowing every user to see and modify scripts and to change layouts. In addition, the IT department of the hospital was happy to provide network support, but did not want to be involved in the application hosting or maintenance.

Problems with the development

- User activity could not be monitored with the FileMaker Runtime version.
- For standardised printouts we tried to convert the graphics into a PDF format. Unfortunately, PDF implementation was not possible with FileMaker Runtime.
- FileMaker offered only a basic set of mathematical operations. The consequence was that we could not program vector analysis calculations, and were not able to produce double angle vector diagrams.
- The *patient-related* system of saving the data (1 case = 1 patient) offered good overview of a single patient's outcome, but was unsatisfactory in analysing patient collectives. The *treatment-related* system (1 case = 1 treatment) was beneficial for the analysis of patient groups, and was the method of choice for the production of more demanding Waring graphs. The idea of implementing nomogram adjustment made it even more clear that, for the future development of Proexcimer, we would have to move from a patient-related system to a treatment-related one.

The development and maintenance of the prototype was stopped by the end of 2004. We gained the strong impression that platform and developer problems were too complex to

be solved with any FileMaker or Microsoft Office version. We needed a system that was more flexible; a system that could address the following needs and requirements:

- Network compatibility
- Platform independence
- Integration of common standards (pdf, Email)
- Good code and script protection (copyright issues)
- Easy maintenance
- Open source
- Familiar interface
- Wide range of mathematical and statistical functions

4.5. Summary

The main clinical needs that led to the development of a prototype system with the name "Proexcimer" were the extension of the existing database (more fields/parameters) and the integration of automatic Waring graph creation.

The basic modules of the FileMaker Runtime based application included a patient list, a patient search function and a patient data entry site.

The prototype was used over a period of 2 years and showed major flaws in the stability, functionality and maintainability. All these issues were linked to the FileMaker platform. Future development and improvement required significant changes to the system.

The main requirements of a successor software were network compatibility, platform independence, integration of common standards (pdf, Email), good code and script protection, and easy maintenance.

Chapter 5

DESIGN AND DEVELOPMENT OF THE IBRA SYSTEM

5. DESIGN AND DEVELOPMENT OF THE IBRA SYSTEM

In this Chapter we present the development and the implementation of the 'Internet Based Refractive Analysis' Software (IBRA), the successor of Proexcimer.

The FileMaker platform was abandoned in 2004 after it became clear that this would not allow further development or integration of new ideas and technologies.

This time we wanted to make sure that the new system was future-proof. We decided to undertake a serious review of alternative platforms and program languages. In addition, we designed a precise system methodology (Figure 5.1.1.) that followed a waterfall model (Royce 1970) with requirements, specifications, design, implementation and maintenance. This model was chosen for its linear and sequential development method with distinct goals for each phase. This approach was very close to our way of thinking, and allowed us easier scheduling and controlling of each development step. It was therefore preferred to other models, for example the spiral model.

On the level of implementation and maintenance the ‘classic’ waterfall model was extended with iterative steps. The iterative approaches allowed us to perform subtle changes in the structures that were deficient. To emphasise the iterative character, we have drawn bi-directional arrows in the figure to show that, at any time, the development could move one phase up or down. This also meets the fact that many of the development steps, e.g. verification and validation, were processes with recurrent episodes, depending on modifications on the needs, or resulting from a strategy that was set up to solve a specific problem.

A characteristic of our development was that the action plans evolved from user interface design in the first instance. From the beginning, we had a clear picture how the user interface had to appear, showing the data entry fields, the results and the Waring graphs. We followed this imaginary picture to its realization and modified it, along with technological specifications.

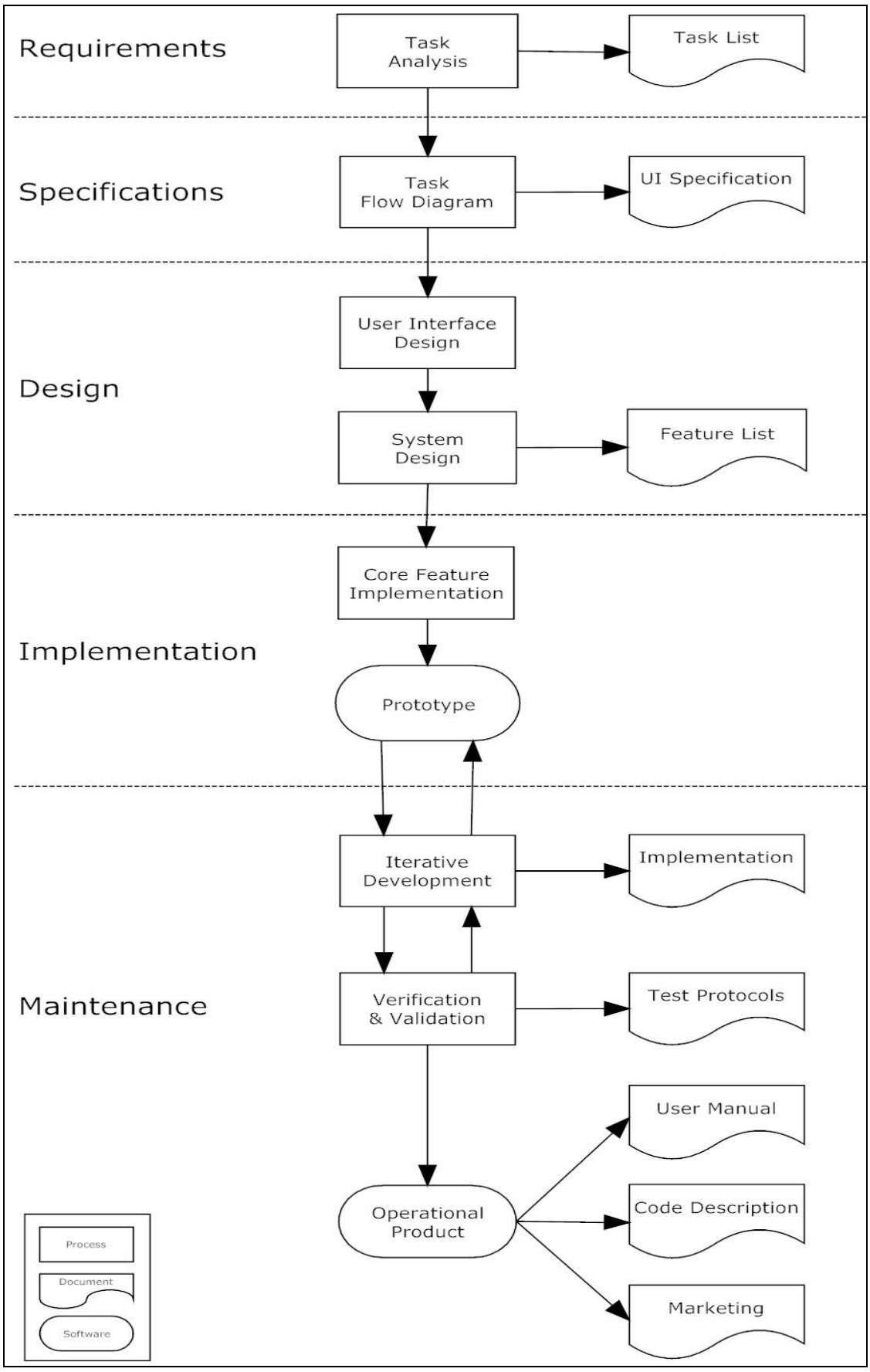


Figure 5.1.1. System methodology (modified waterfall model).

The individual steps in the methodology can be separated into 3 aspects: process, documentation and software. Each aspect is presented with a different shaped frame in Figure 5.1.1. The aspect ‘processes’ summarised cognitive steps, leading from one step to the next in the development. The aspect ‘documentation’ was for outputs in printed form, including the creation of lists and tables for the developer team, and the creation of guidelines for the software user. With ‘software’ we characterised steps related to coding and testing of program parts.

In the following sections each step is described with details, focusing on the 'why', 'what' and 'how' our system was developed or changed.

Many of the decisions regarding the different phases were made intuitively and thus difficult to put into words. Often retrospectively, the decision and its consequence could be recognized as a whole, and could be put into the grid of the waterfall or iterative model.

In addition, many decisions were made on a 'right time, right place' model. This means, for example, that at the phase of implementation the internet technology became more and more popular (right time). Living and working in an area with these ‘trendy’ changes (right place) was associated with the fact that more and more people were gaining experience of using an Internet platform. Being surrounded by such people made it possible to gain access to adequate knowledge and support regarding Internet programming (HTML and PHP). The decision to use one technology and to deny another was strongly influenced by similar trends and environmental premises.

The main reasons why Internet technology was used for the development of our software system are listed below:

- Network use without the need of network hosting
- Accessible at any location, even wireless (on the move, with the iPhone)
- Simple and common basic software to run applications (Internet Browser)
- Usable across different systems (Windows, Mac, UNIX, Palm, Symbian)
- Familiar user-interface (Google or Medline type)
- Fast with good Internet access
- Common use, 'a good friend' can help at the beginning
- Many tips and recommendations by users in web blogs and forum

- Many 'open source' tools available
- A general belief in 'the future of programming'
- Uncomplicated monitoring of user activities

5.1. Needs assessment (task analysis)

The limitation of the FileMaker Runtime platform was more evident with increasing clinical and operational needs. Some of the main problems of the platform included limited network compatibility, unreliable and insufficient core system (Runtime version and upgrades), reduced code protection, lack of common standards (PDF file creation) and difficulties in the way the operational software application could be maintained or monitored.

The IBRA system should address the following general needs and requirements:

- Network compatibility
- Open source
- Good code protection (copyright)
- Familiar interface
- Integration of common standards (pdf, Email)
- Easy to maintain
- Collection of ‘treatment data’ and not ‘patient data’

In addition, different and unexpected needs evolved within the first 2 years of the IBRA development. These needs came from surgeons' increasing demands, from educational interests and from commercial and promotional intentions.

5.1.1. Surgeon-oriented needs (The need for a professional version)

IBRA was used for an NHS outcome audit, analysing the refractive data of 400 treated eyes in 2005. The result of this audit showed that the outcome scattered widely. We assumed that this dispersion could be as a result of inaccurate calculation of the laser energy that was used to reshape the cornea, resulting in either too little or too much ablation of corneal tissue. Treatment calculations are modified by nomograms with the goal of improving laser treatment. Nomogram adjustments were usually calculated by the laser manufacturer but could be performed by the surgeon, too.

The integration of nomogram adjustments into IRBA would change the software's area of application; from being only user-related to check the surgeon's operating quality, IBRA would 'mature' to a program that could also change the patient's outcome and health. This could lead to a significant bonus for the user. But there were also doubts.

Nomogram calculations are complex and sometimes difficult to understand; they are reserved for more advanced and research orientated surgeons. The increased complexity of the IBRA functionality could potentially scare general refractive ophthalmic surgeons. We tried to solve this problem with a modification of the user-interface. We intended to provide only a certain amount of information and functionality on the screen that would fit the user's need. The software was split into 2 versions. The 'standard version' was for the general user and offered all the Waring graphs. The 'professional version' was for the refractive expert. It offered all the features of the standard version, and added the nomogram calculations (Table 5.1.1.).

5.1.2. Educational needs (The need for a database version)

Ophthalmologists in training have to collect precise data of all the interventions and operations they perform. This data collection (also called 'logbook') reflects the educational level of the trainee and is used by the training authority, The Royal College of Ophthalmologists (RCO), for assessments. To facilitate the collection, the RCO was offering an Excel spreadsheet 'logbook' that could be downloaded from their website. Most trainees downloaded this file, and installed it on the hospital computer for data collection.

The local deanery allocates trainees to hospitals. Often trainees have to travel between hospitals, and might perform surgery in 3 different theatres. Therefore, it became increasingly desirable to have the logbook 'always on board'. IBRA seemed to be a feasible alternative, and I was asked by the SHOs and SpRs at St James University Hospital in Leeds if IBRA could be used to collect cataract data.

After discussing the needs and options, we modified the IBRA professional version and added a site with fields for the collection of data relevant to cataract surgery. We called this separate version of IBRA, for the sole purpose of data collection, 'database version'.

5.1.3. Promotional needs (The need for a ReSTOR version)

Alcon Inc. is the world's leading American supplier for ophthalmic products with headquarters in Switzerland. The manager of the cataract division of Alcon was impressed by the features of IBRA, presented in 2004 at a congress in Lucerne. At this congress, Alcon was introducing a new multifocal intraocular lens for patients undergoing cataract surgery. This lens was called ReSTOR (AcrySof SA60D3).

Following several meetings with Alcon, we were funded for the development of a special IBRA version for surgeons that were using this new lens. This 'ReSTOR version' was similar to the database version, but was able to send the collected data directly and anonymously to the manufacturer's office. This was enabled by the implementation of e-mail and pdf functions.

This ReSTOR version was used over 3 years and, in accordance to the agreements of the co-operation, removed from IBRA in 2007. An overview of the IBRA versions is given in Table 5.1.1.

Version	**Features of IBRA**	**User group**	**Purpose / Needs**
Database	Database only	Trainee Ophthalmologists	Education related (logbook, requirements of The Royal Colleague of Ophthalmologist)
ReSTOR	Database Mailing tool	ReSTOR users only	Promotion related (quality control for Alcon)
Standard	Database Standard Graphs	General Ophthalmologists	User related (quality control for surgeon)
Professional	Database Standard Graphs Vector Analysis Nomogram	Refractive Specialist	Patient related (health outcome change)

Table 5.1.1. Overview of the different IBRA versions and the related user groups.

5.1.4. Commercial and marketing needs (The need for a website and a manual)

IBRA was presented at 2 international congresses in 2004. Many surgeons in the audience were keen to test and buy the IBRA system. However, at this time the software was only used at the Eye clinic in Lucerne. But there seemed no reason why the system couldn't be commercialised. The flexible platform and Internet technology created ideal conditions for easy access to the system from any location, even from abroad. On the other hand, placing the software on the market could move us much further up the ladder of responsibility; and accounting would become another requirement.

Should we go into business with IBRA? It took us several months to decide that licensing of IBRA was in our interests too. It could increase the level of awareness and acceptance, and would provide us with some financial cover of the taken investment.

The marketing and business issues were manifold: getting legal advice, founding a limited company, creating 'Terms and Conditions for the use of IBRA', developing structures for selling, renewing and updating existing licenses, programming a billing system with credit card payment, writing a manual and user instructions, providing user support, etc.

We could address most of the issues in 2006 by handing over the development and ownership of IBRA to Zubisoft GmbH, a company that was founded in 1998 by Bruno and Hans Zuberbuhler (Hans being the father of Bruno) for the distribution of office software for constructors and decorators.

A formal product website was created (www.zubisoft.com), providing information about the company, the software and its features, and the purchase options. Finally, a user-friendly documentation (Introduction) was created in German and implemented electronically into the IBRA system.

5.1.5. Maintenance and security needs (The need for a user administration system)

The start of the ReSTOR project and the commercial activities increased the number of surgeons that were using the IBRA system. This demanded improvements to our administrative site: easier user registration, emailing of username and password, changing of access codes, and other functions. For these reasons a web-based administration application was programmed that could manage registration, billing with invoice creation, username and password creation, validation management and communication with the users, e.g. sending e-mails with information about server maintenance times or software upgrades. In addition, this admin tool allowed the monitoring of users' access to the system, recording login dates and times, and allowing us to control the system use. This was an issue that evolved from an increased demand for system security.

5.2. Specifications (task flow diagram)

Access to IBRA was granted to persons having identified themselves by entering their username and password. For security reasons each database access was monitored. Following the login, the user reached the menu of IBRA. The user could choose from 3 main functions, grouped in different modules: 'Cases' for data recording and analysis of a single patient data; 'Analysis' for standard and advanced analysis of data from patient collectives; and 'Nomogram' for outcome and predictability calculations (Figure 5.2.1.). A download function was linked to the ‘Cases’ module, allowing storage of the patient data on the user's computer. Downloaded data was saved in .csv format. This facilitated further data processing in Microsoft EXCEL, SPSS or Minitab Software.

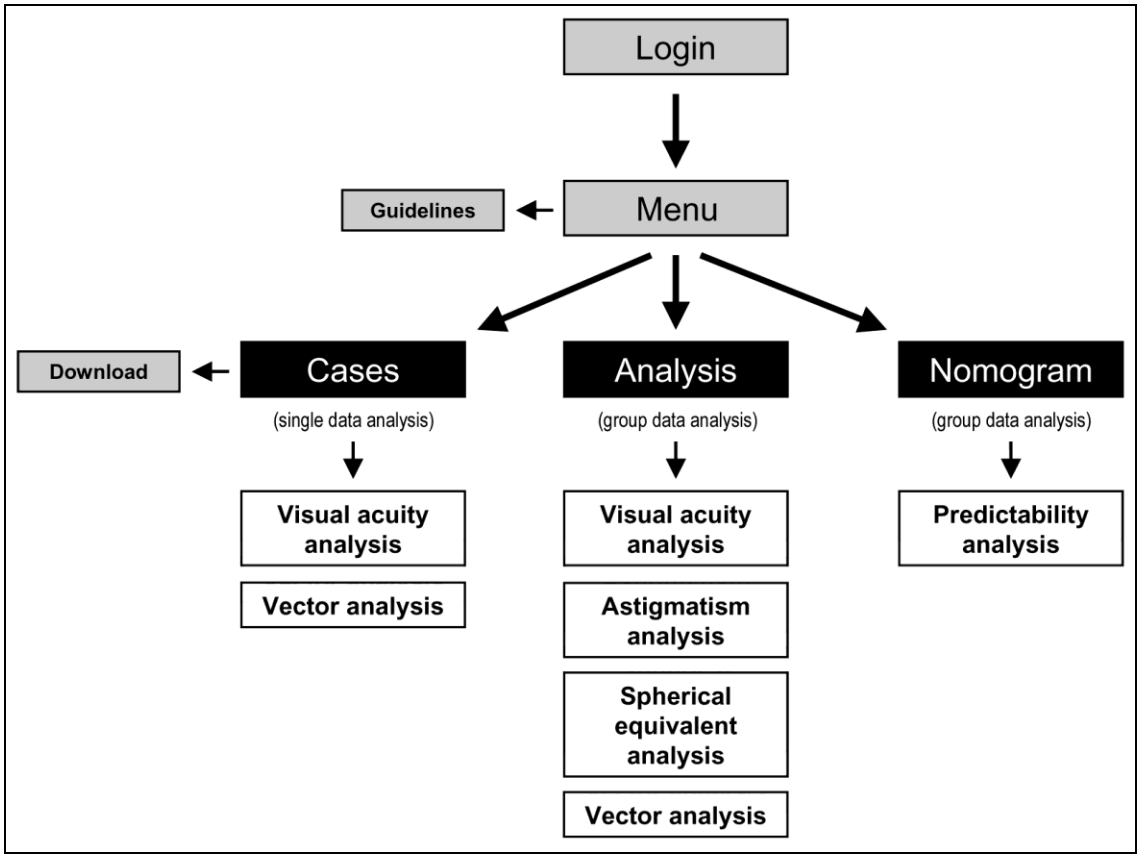


Figure 5.2.1. Summary of the functions of the software application with the three main modules "Cases", "Analysis" and "Nomogram".

5.3. User interface and system design

In a survey most Proexcimer users, and other surgeons, were asked about their user interface preferences relating to refractive analysis software. The results showed that

functionality was considered as more important than ‘fancy design’. The user-interface had to be easy to use, easy to understand, and standardized in relation to the data fields.

We decided to develop a user-interface that was ‘static’, and that did not allow user-specific interface modifications; a user-interface that was the same for every user and that could provide a high level of standardization, thus minimizing misunderstandings and data entry errors. We chose simplicity and cut back on flexibility.

A fundamental feature of the software was to use a well-known Internet browser (Microsoft Internet Explorer) as part of the user interface; assuming that all users were familiar with the use of the Internet and Microsoft operating systems. This could ease barriers many users have in starting to use new, ‘unfamiliar’ software. In addition, we implemented parameters that were well known by refractive surgeons.

The simplicity and familiarity of IBRA resulted in a brief learning curve. IBRA could be used immediately after introduction, both in the laser theatre and in the eye clinic.

Installation on local computers was not necessary and fast Internet access was the only condition. Software updates were performed on the web server only. The user did not have to change any software components, and could work with the latest version of the application following new login into IBRA.

IBRA was programmed using the computer languages PHP, HTML and JavaScript, and the MySQL database (Figure 5.3.1.).

- PHP stands for 'Hypertext Preprocessor' and is a reflective programming language used mainly in server-side application software. PHP requires the Zend engine (Zend Technologies, Israel) as a core scripting engine to parse and compile the program code.

- HTML stands for 'Hypertext Markup Language' and is the predominant language for the creation of web pages. It provides a means to describe the structure of text-base information in a document, and to supplement the text with interactive forms, embedded images, and other objects. HTML needs a web

browser to interpret the program code, to display and interact with the text and images and to communicate with the web server.

- JavaScript (Sun Microsystems, Inc., USA) is a client-side script language based on the concept of prototype-based programming. It enables scripting access to objects embedded in applications, such as HTML or PHP applications. JavaScript is loosely based on the language 'C' and relies on the JavaScript engine, which is embedded in the host environment, e.g. Microsoft Internet Explorer.

- MySQL (MySQL AB, Sweden) is a multi-threaded, multi-user SQL database management system. PHP has an application programming interface (API) that allows applications to access MySQL databases. The software tool 'MySQL Administrator' was used to structure and modify the database.

Figure 5.3.1. Structure of the hardware and software system with script languages (HTML, PHP and MySQL) and the databases management system (DBMS).

The patient data was recorded on the hard disk of the server. The storage system on the main server was a RAID level one configuration. This 'mirrored drive system' provided fault tolerance from disk errors and single disk failure. Array continued to operate so

long as at least one drive was functioning. For safety purposes, the data was saved 4 times a day on a second server at a different geographic location. The data transfer from the client computer to the server was protected with a 128-bit (or longer) key for encryption, using a SSL (Secure Sockets Layer) cryptographic protocol. This could provide IBRA users with similar technology used by online banking services.

In a later stage we implemented PDF printout functions, and programmed more complex outcome charts, e.g. for vector analysis. We choose software components that were easy to implement into IBRA, safe and available in the public domain with online tutorials and test files. For example, the 'FPDF' program is a ‘freeware’ software (www.fpdf.org) which we used as a PHP class extension for the creation of PDF files.

5.4. Overview of development

The prototype of refractive analysis software (Proexcimer) was used from 2002 until 2004 and then replaced by the IBRA system.

The IBRA system underwent different upgrading processes between 2004 and 2007, correcting code errors and extending the software with new database and analysis functions, resulting in the version of IBRA that was used for this research and the evaluations.

The main extension was the implementation of the nomogram calculation module. The main structural change was the splitting of the IBRA basic system into 4 different versions (database, standard, professional and ReSTOR). On the administrative side, a credit card payment system (MasterCard and VISA) was implemented in IBRA, and an admin tool was developed for easier registration and billing of users. After years of building-up we started to reduce the variety of data entry fields, as the problem of having too much information surpassed that of having too little (Schiff 2010). The forum function (for communication between IBRA users) was rarely used, and was therefore also removed from IBRA. The ReSTOR version was removed from IBRA following completion of the co-operative work with Alcon.

A summary of the development of the software system is shown in Table 5.4.1.

In 2007, the IBRA analysis system became the main refractive analysis software of the Refractive Laser unit at Moorfields Eye Hospital NHS Foundation Trust. A system 'start button' was implemented on the 'Clinical Services' website at Moorfields (Figure 5.4.1.).

Year	Name / Version	Technology used	Functions	Influenced by
2002	Proexcimer (Prototype)	FileMaker Runtime X2max Chart Plug-in	Database, 7 Graphs	Surgeon
2004	IBRA Prototype	HTML, PHP, JavaScript, Plug-ins (jpgraph)	Database, 8 Graphs + Forum	Surgeon
2005	IBRA v1	HTML, PHP, JavaScript, Plug-ins (jpgraph, fpdf)	Database, 10 Graphs + Vector Analysis + pdf printout - Forum	Surgeon Research
2007	IBRA v2	HTML, PHP, JavaScript, Plug-ins (jpgraph, fpdf) Link with Bank	Database, 10 Graphs, Vector Analysis + Nomogram analysis + Data export .csv format + Credit Card payments	Auditing Teaching Marketing

Table 5.4.1. IBRA development.

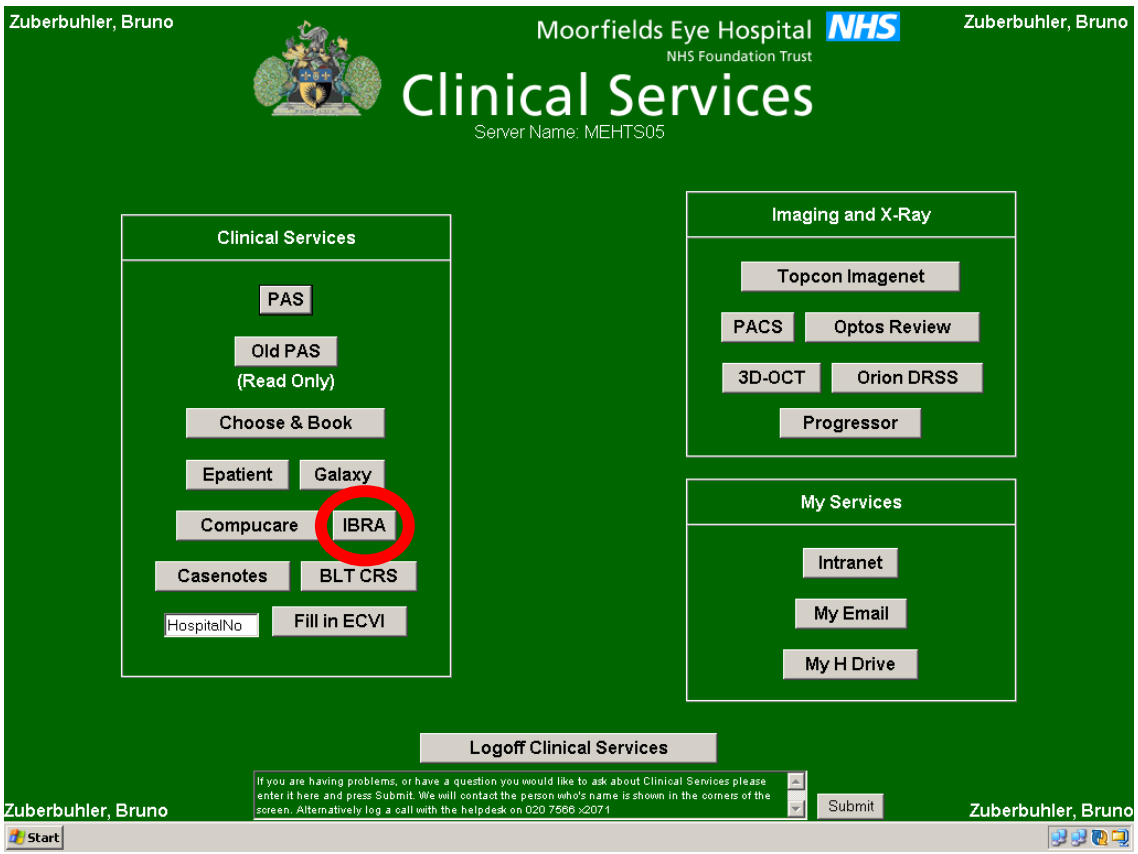


Figure 5.4.1 Implementation of the IBRA system into "Clinical Services" at Moorfields Eye Hospital NHS Foundation Trust in 2007.

5.5. Modules of implementation in the operational product

Following access to the Zubisoft website and login with the username and password, the user reached the main menu of IBRA (Figure 5.5.1.).

5.5.1. Main menu

The user could choose from 4 main functions (modules):

- Cases: to record and analyse single patient treatments (cases)
- Analysis: to analyse group data and to produce the Waring graphs
- Nomogram: to analyse group data and to calculate nomogram adjustments
- User: to change user data (e.g. password) and to set preferences (e.g. laser types)

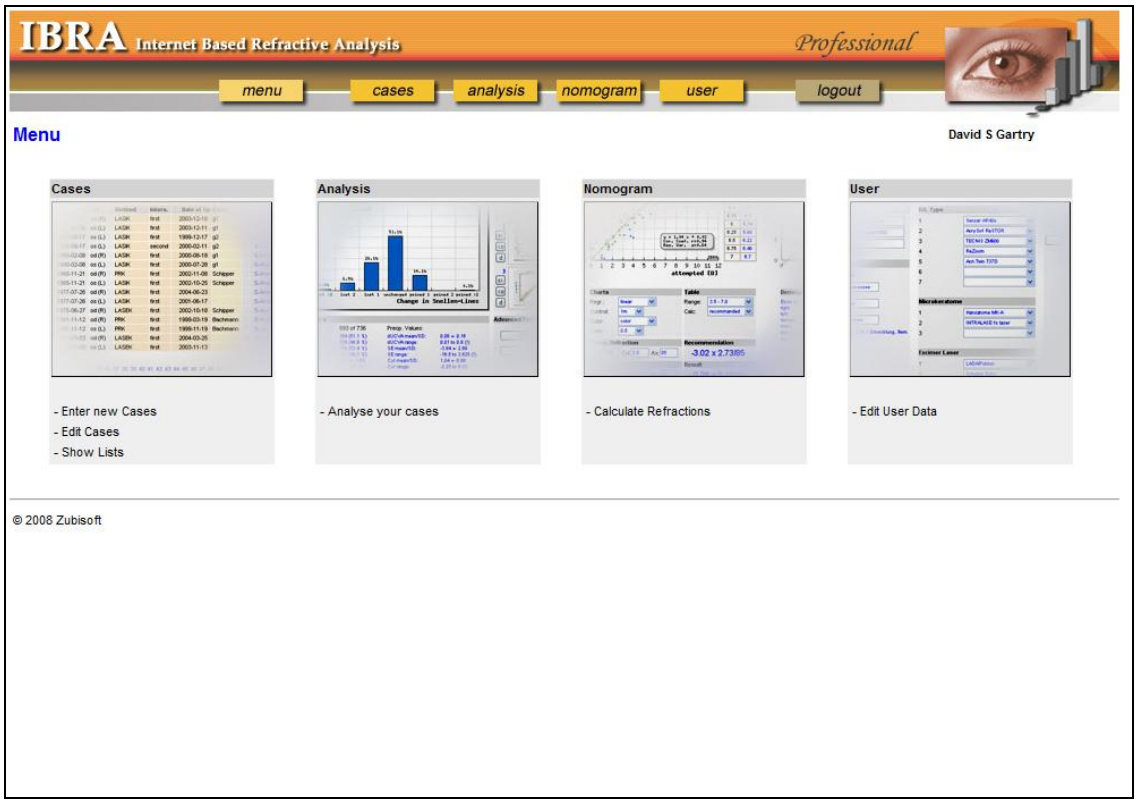


Figure 5.5.1. Screenshot of the "Menu" of the IBRA system.

5.5.2. The 'List of Cases'

A screenshot of this module is shown in Figure 5.5.2. At the 'List of Cases' site the user could add, duplicate or edit a case. By selecting the patient name, the user could modify an existing case record, for example by adding postoperative results to the database.

The top part of 'List of Cases' offered functions for viewing, sorting and searching cases. This part was an analogous design to the Medline website, to provide familiarity with case handling. The pull-down menu on the left showed a selection of lists with different sets of parameters, for example a list of preoperative and postoperative visual acuity data or a list of postoperative refractive data.

For security and privacy reasons, we entered initials in the fields of surname and first name, and used the hospital patient identification number (PID) instead of the National Health Service identification number (NID). The PID is a patient identification key that is generated randomly and used solely within one particular hospital; therefore, one patient can have many different PIDs. If anyone gained (unauthorised) access to the IBRA system, confidentiality would be maintained as they would not be able to identify an individual patient based on the recorded data.

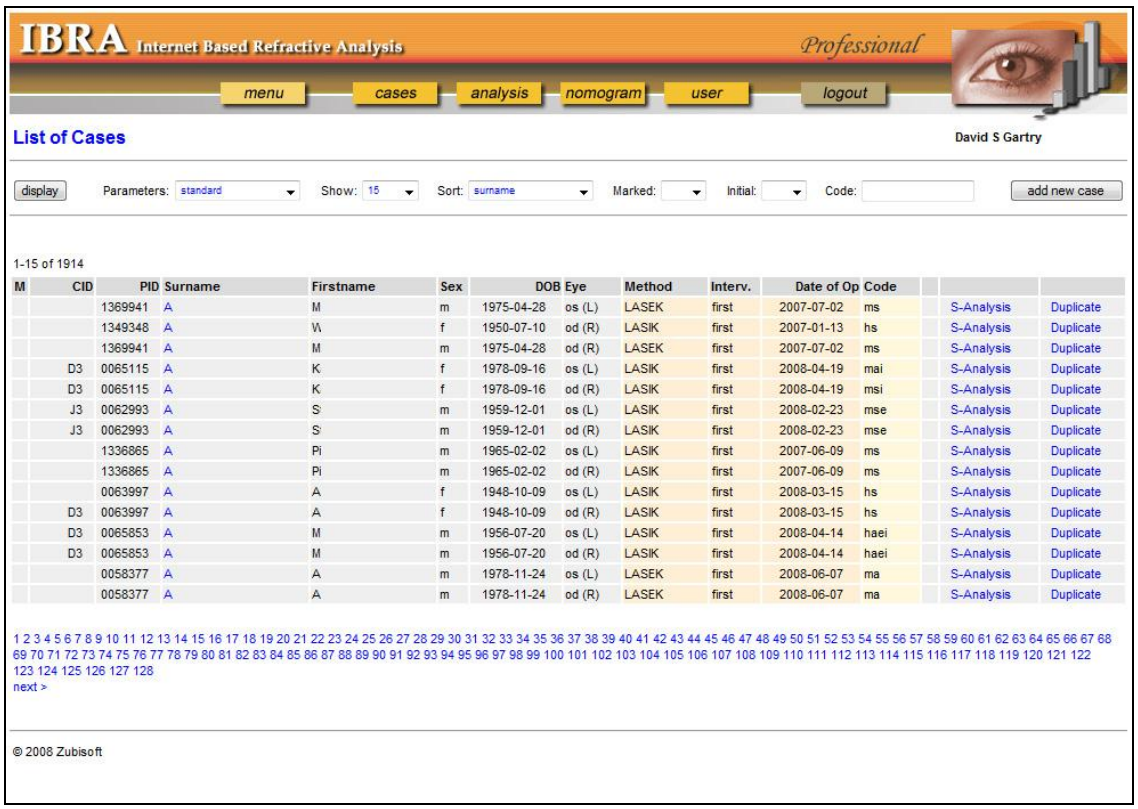


Figure 5.5.2. Screenshot of the "Cases" module with the site "List of Cases".

5.5.3. Data recording

For each case, a maximum of 242 parameters could be recorded. A case was defined as a single intervention or operation, usually a refractive laser eye treatment or a cataract operation.

The parameters were arranged on different pages. The pages included details of the patient and the operation (Figure 5.5.3.), data from preoperative and follow-up examinations (Figure 5.5.4.) and information regarding any complications and their management.

Postoperative data was recorded from visits at 7 days, 1 month, 3, 6, 12 and 24 months. The most important data for the creation of Waring graphs was the spherical value, the cylinder magnitude, the axis of the cylinder, the calculated spherical equivalent (SE), the uncorrected visual acuity (UCVA) and the best-corrected visual acuity (BCVA).

Other data that could be entered into the database was as follows: pachymetry, endothelial cell count (ECC), tear film break up time (BUT), intraocular pressure (IOP), contrast sensitivity (Pelli-Robson), root-mean-square (RMS, total and cumulative higher order), haze and overall satisfaction.

The parameters were all saved in the same MySQL table, allowing downloading of the data into one file. An Excel spreadsheet was created automatically when the data was downloaded from IBRA.

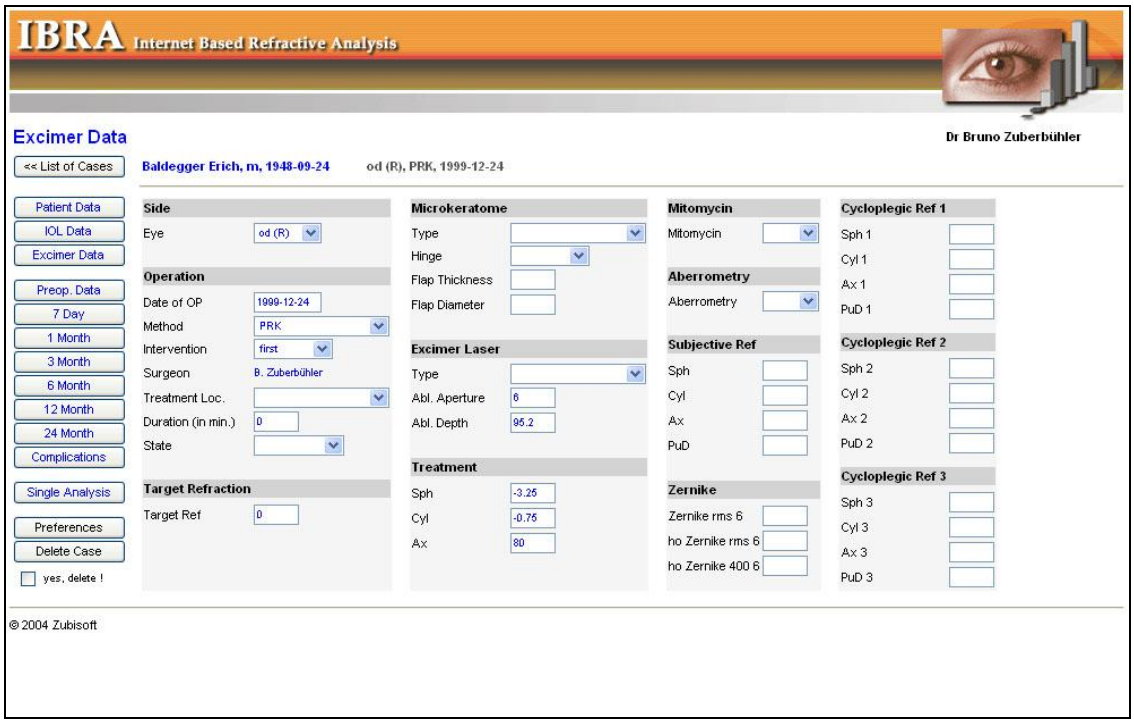


Figure 5.5.3. Screenshot of the 'Cases' module with the page 'Excimer Data' for data recording of treatment parameters, e.g. type of laser treatment, date of operation and target refraction.

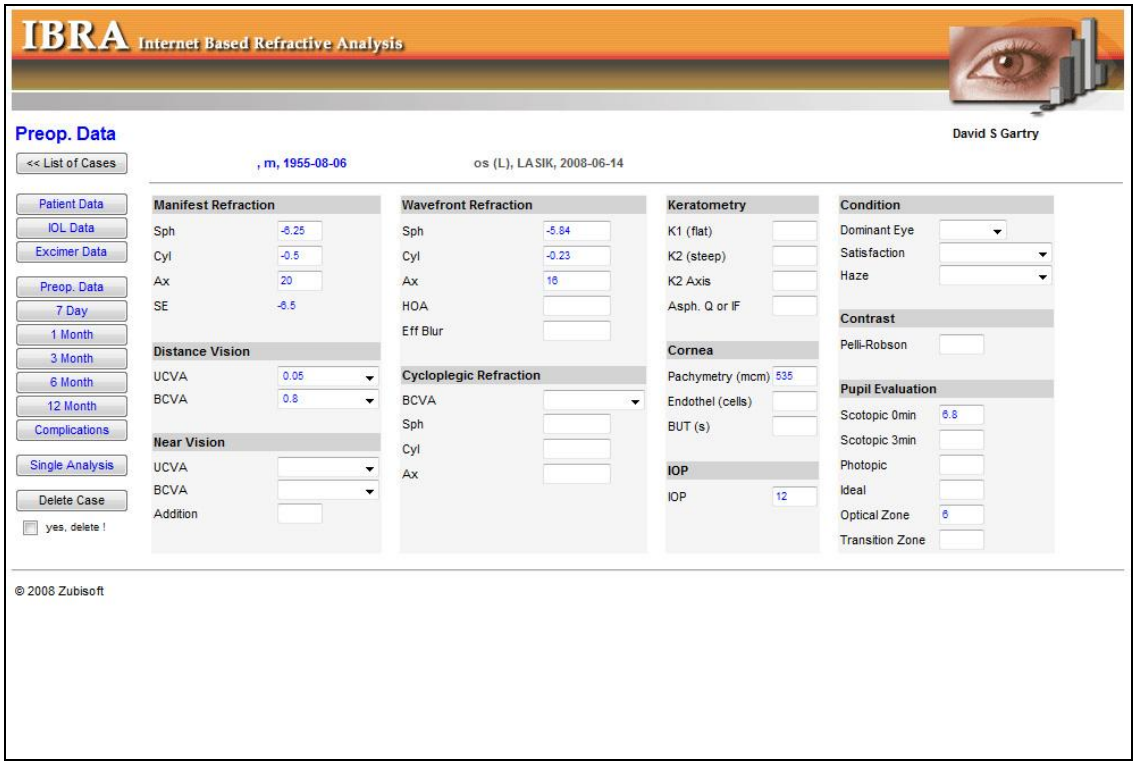


Figure 5.5.4. Screenshot of the 'Cases' module with the page 'Preop. Data' with data entry fields for preoperative parameters, such as distance and near visual acuity, refractive and keratometric data, contrast sensitivity and intraocular pressure.

5.5.4. Single visual and refractive analysis

An overview of one patient's main treatment data was provided by the 'Single Analysis' feature (Figure 5.5.5.), showing the postoperative course of visual acuity and spherical equivalent in graphical form, and also a table with key parameters. The figures were arranged with the table on one A4 page and converted to a downloadable pdf file. The purpose of this file creation was to provide the patient with a summary of treatment results that could be handed out or emailed at the end of treatment. The printed version could also serve as a 'hard copy'.

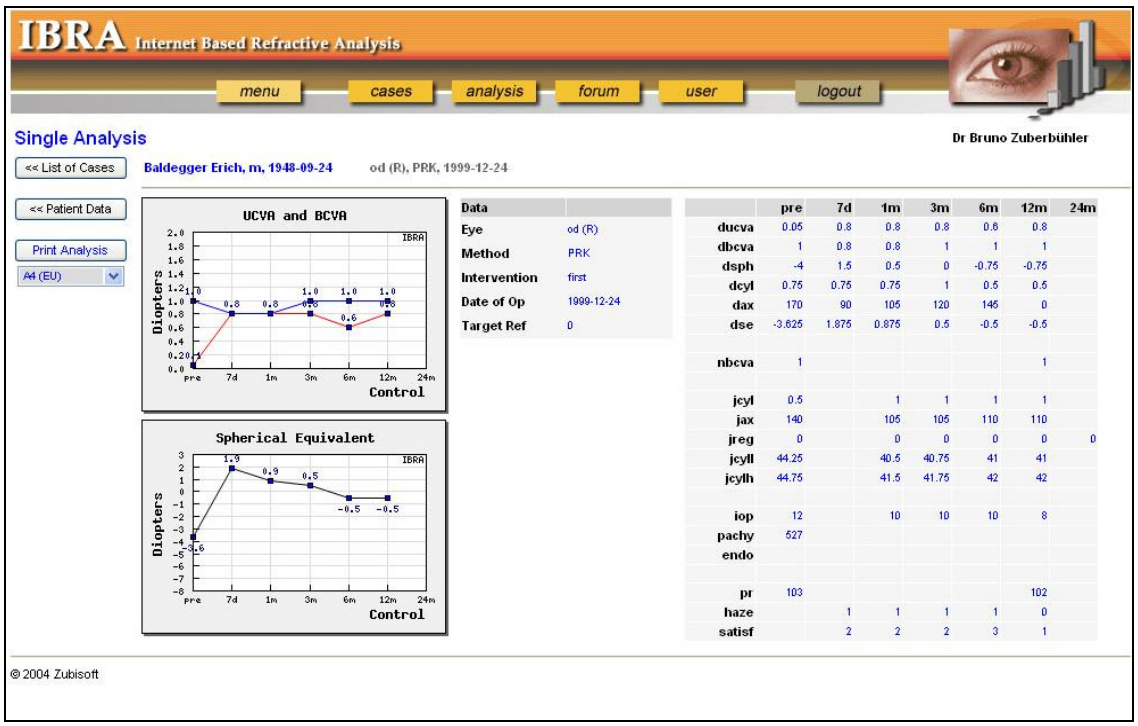


Figure 5.5.5 Screenshot of the "Cases" module with the page "Single Analysis" with a visual acuity chart (left top), a spherical equivalent chart (left bottom) and a table with all visual and refractive results over a period of 24 months (right).

5.5.5. Vector analysis

Refractive data (sphere, cylinder and axis of the manifest subjective refraction) was analysed using vector analysis as described by Noel Alpins (Alpins 2001). There were 2 different modules for vector analysis. The main module was used in conjunction with a single case treatment. The other module was for analyzing vector parameters of a series of cases and presented the results in a scattergram chart.

Using vector analysis, a patient's astigmatic changes could be analysed by consideration of the change in the astigmatic axis. The most important values were the target induced astigmatism vector (TIA), representing the astigmatic change the operation was intended to induce, the surgically induced astigmatism vector (SIA), representing the actual induced change in amount and axis of astigmatism following surgery, and the difference vector (DV), representing the required astigmatic change, the effect a second surgery would need to achieve the initial target. Using these values, the main indices for quality and precision of the treatment could be calculated, such as the correction index (CI= SIA/TIA), the index of success (IOS=DV/TIA) or the angle of error (AE = angle SIA minus TIA).

For better visualisation IBRA created 2 diagrams: the polar astigmatism diagram and the double angle vector diagram (Figure 5.5.6.). The calculated parameters were presented in a table for each postoperative review. The results (diagrams and table) could be printed or saved as a PDF file.

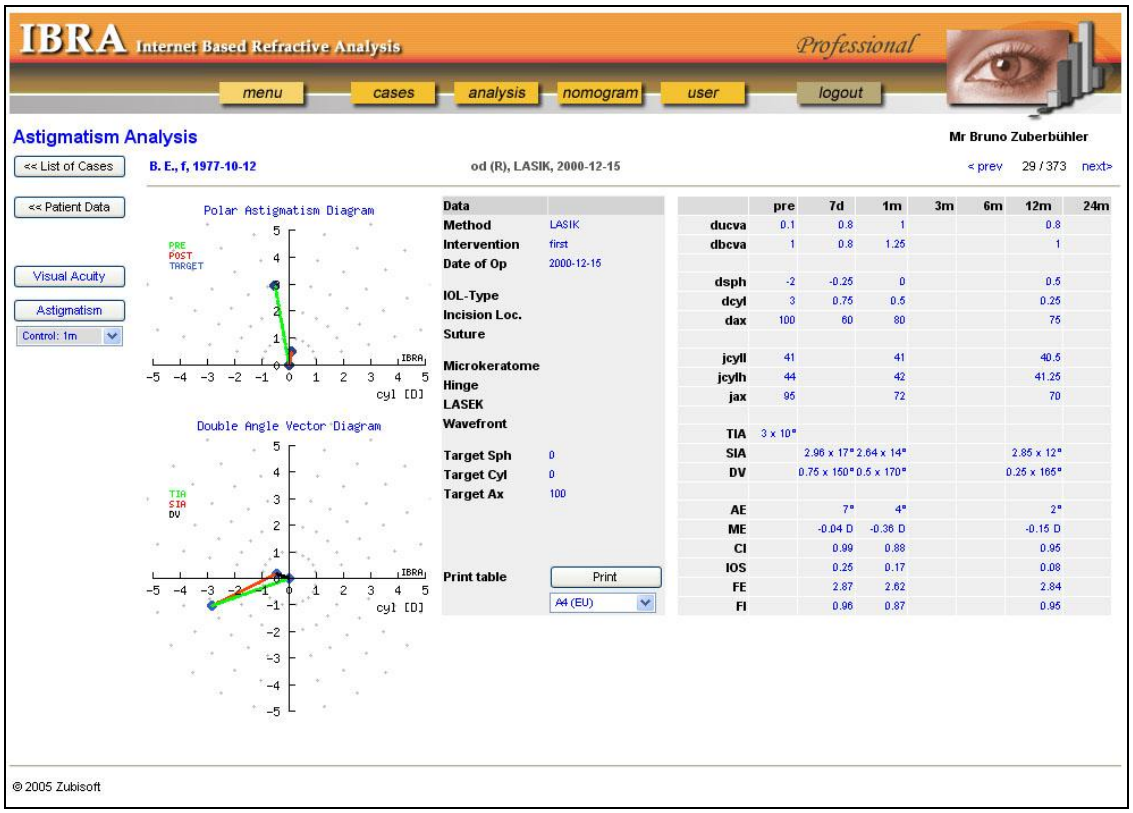


Figure 5.5.6. Screenshot of the 'Cases' module with vector analysis (Astigmatism Analysis) for one treated eye, showing a polar astigmatism diagram (left top), a double angle vector diagram (left bottom) and a table with main indices from the calculation (right).

Furthermore, IBRA was able to produce a 'vector chart' from patient groups. The software calculated TIA and SIA for each eye, and plotted the results on a scattergram with the TIA values on the x-axis and the SIA values on the y-axis (Figure 5.5.7., left). The scattergram offered valuable information about the overall astigmatic outcomes. Ideally, all results are aligned on the 45 degree line. The percentage of eyes with a deviation of less than 1.0 Diopter (D) from this ideal result is an important number that defines quality and predictability of the surgery.

Using only SIA values, IBRA calculated and displayed the mean SIA for a group of patients, called the 'centroid', in a double angle diagram. The centroid is a true

representative of the mean astigmatism, especially when the group is homogenous with localized clustering of the SIA points (Figure 5.5.7., right).

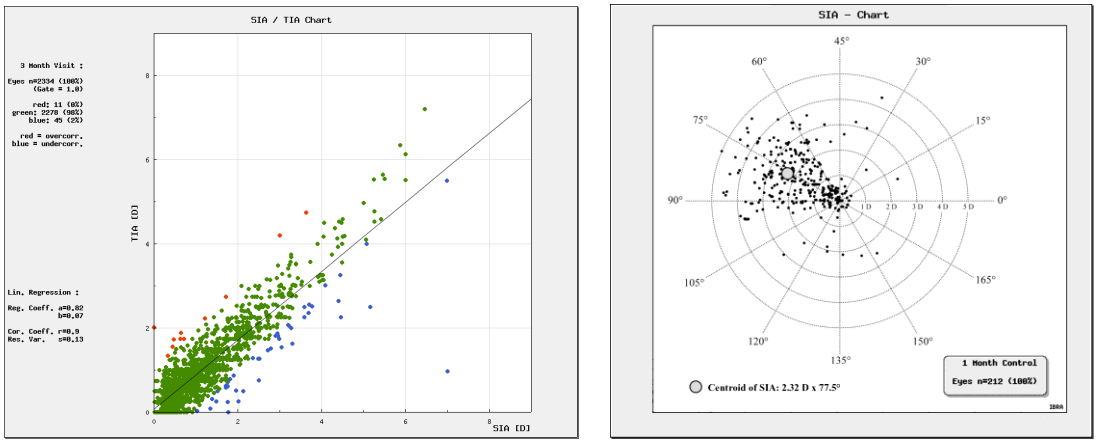


Figure 5.5.7. Left: Scattergram of 2334 treated eyes showing target induced astigmatism vector (TIA) versus surgically induced astigmatism vector (SIA) at 3 months follow-up, with linear regression line. 98% of eyes are within 1D of the TIA (green dots). Right: Scattergram of the mean surgically induced astigmatism vector (SIA) in a double angle diagram, called the 'centroid'.

5.5.6. Spherical equivalent outcome analysis

IBRA produced all internationally accepted Waring graphs. The 'Attempted versus achieved spherical equivalent (SE) chart' is a scattergram (Figure 5.5.8., left), having the advantage of presenting the outcome of every eye, so that no data is hidden in means or averages. The x-axis shows the attempted and the y-axis the achieved SE. If the attempted and the achieved SE are the same, the point falls on the 45 degree line in the scattergram, representing a perfect result.

The 'SE outcome chart' is a bar graph (Figure 5.5.8., right) that represents the postoperative spherical equivalent refraction grouped in SE categories, usually in 0.5 D steps. This allows the user to see how many eyes fall within a certain category. It further allows assessment of the range of refractive results.

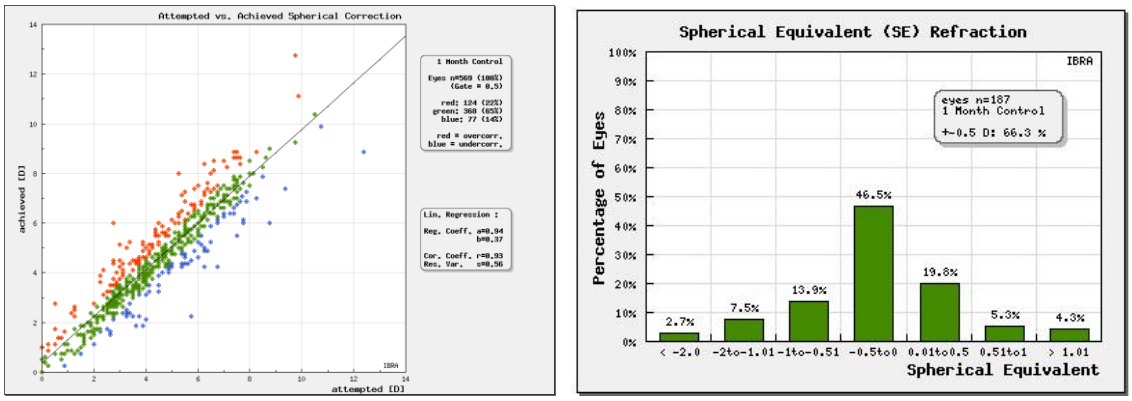


Figure 5.5.8. Left: Scattergram showing attempted spherical equivalent versus achieved spherical equivalent refraction one month following laser excimer treatment of 569 eyes. Right: Histogram of the postoperative spherical equivalent refraction of 187 eyes following laser vision correction. In this example, 66.3% of eyes were within 0.5D of emmetropia.

In the 'Stability of postoperative spherical equivalent (SE) chart' (Figure 5.5.9.) the mean SE refraction with standard deviation is presented over time. The standard deviation is important because an increase would demonstrate a considerable instability in the refraction, even though the mean value may show minimal change over time.

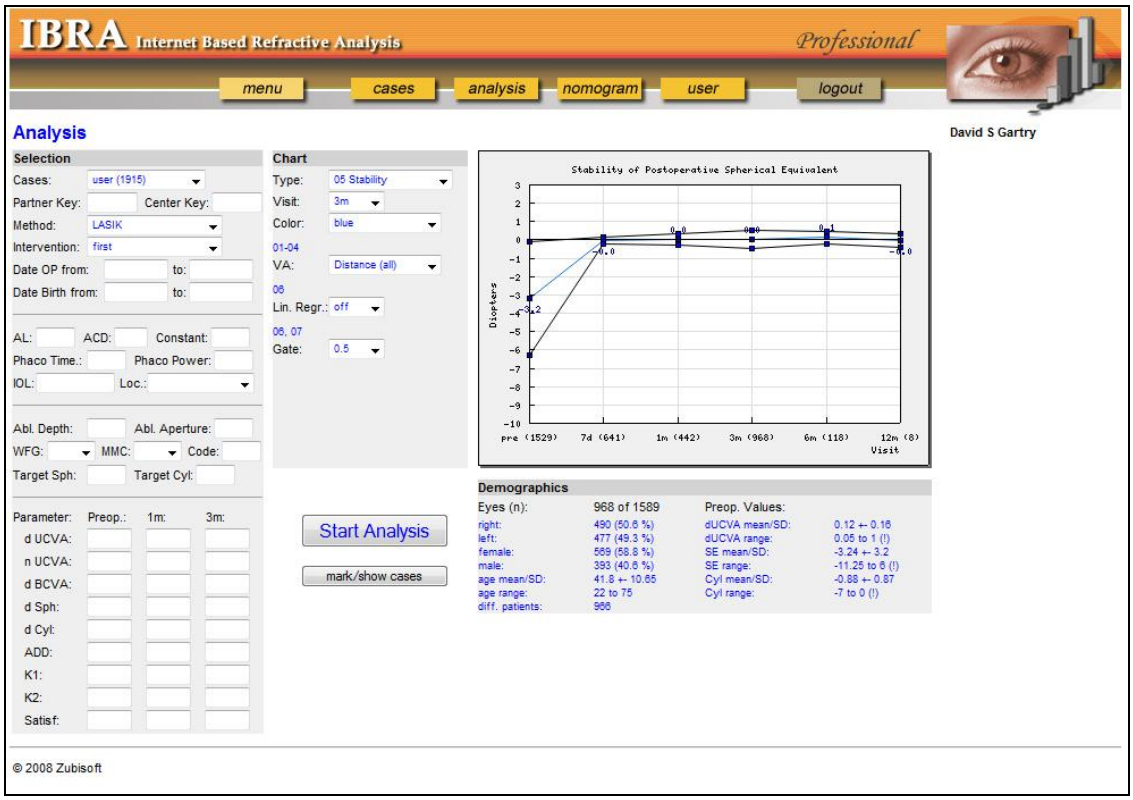


Figure 5.5.9. Screenshot of the "Analysis" module with a stability chart showing the mean spherical equivalent and standard deviation over time of a series of selected cases (968 eyes).

5.5.7. Defocus equivalent analysis

The 'Defocus Equivalent (DE) Refraction' chart (Figure 5.5.10.) is a cumulative bar graph that represents more accurately the reality of the refractive state of the eyes (Waring). To obtain the DE for an eye, the spherical equivalent was calculated by taking the sphere (respecting the sign) and adding half the cylinder (again respecting the sign). Then one-half of the cylinder value was added to the spherical equivalent, ignoring the sign.

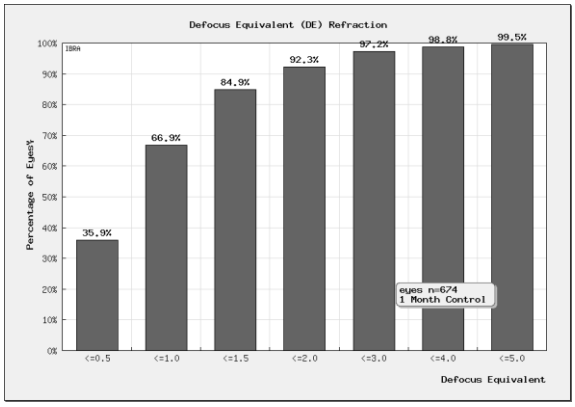


Figure 5.5.10. Defocus equivalent (DE) Refraction 1 month following laser vision correction.

5.5.8. Visual acuity outcome analysis

The 'Uncorrected Visual Acuity - UCVA' chart is a cumulative bar graph (Figure 5.5.11., left). Visualisation of UCVA results is relevant, as most patients aim for spectacle independence following laser vision correction. This chart allows accurate identification of the number of eyes that see 1.6 (±6/4), 1.25 (±6/5), 1.0 (6/6), and so on. Such a distinction can be used to differentiate among refractive surgery procedures, and to compare visual acuity results from different studies.

The 'Loss of Lines of BCVA' chart (Safety Chart) is a bar graph that shows the change in best-corrected visual acuity from preoperative to postoperative examination, in terms of the number of Snellen lines gained or lost (Figure 5.5.11., right). This measure answers the question: "If the refractive outcome is not totally acceptable, can patients put glasses on again and see as well as they did before surgery?" A loss of 2 or more Snellen lines has been generally adopted as the standard for safety. This is the reason why this chart is also called 'safety chart'.

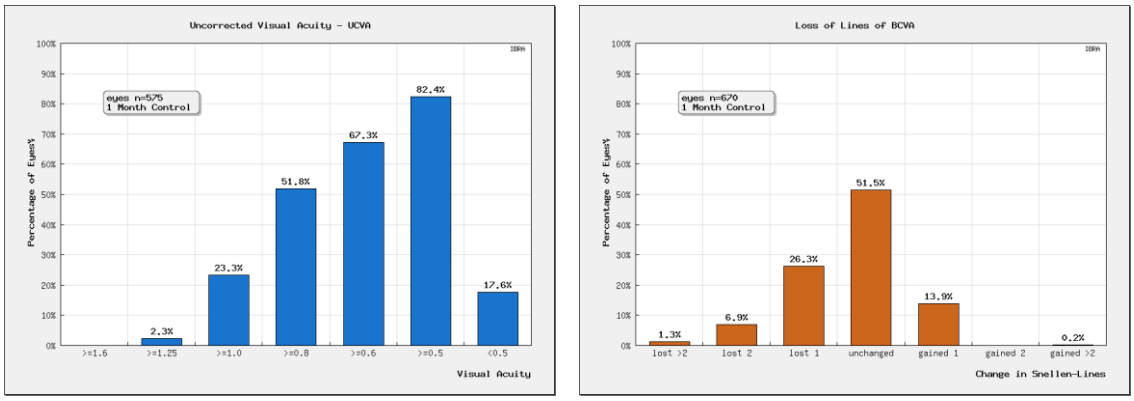


Figure 5.5.11. Left: Uncorrected visual acuity chart of 575 treated eyes 1 month following laser surgery. Right: Best-corrected visual acuity chart with change in Snellen lines (safety chart) for 670 treated eyes 1 month after refractive surgery. 8.2% of eyes lost 2 or more Snellen lines in this case series.

5.5.9. Nomogram calculation

The nomogram calculation derives from linear regression analysis of postoperative refractive data (Figure 5.5.12.). The analysis results in two formulas, one for spherical data and one for astigmatic data. The formulas are a mean of the effective result, and can be mathematically compared with a theoretical formula (the attempted outcome). The difference between the effective and the theoretical formula is the refractive error; the deviation from the attempted result. Again, this difference can be expressed by a calculation formula. This calculation formula was implemented into IBRA with the aim of optimising the effective outcome.

To explain this principle, the following calculations are provided as an example. A patient with a refraction of -3.0 D (sph) / +4.0 D (cyl) x 90° wishes to undergo laser eye surgery with a target of emmetropia. The nomogram calculation was used in the pre-assessment clinic to analyse previously treated patients with similar refractive errors. The calculation showed that most treated eyes resulted in an under-correction. Without changing the laser settings, the above patient would achieve (theoretically) a mild under-correction of -0.50 (sph) / +0.75 D (cyl) x 90°. The nomogram calculation in IBRA now recommends a boost of the refractive treatment to achieve a result closer to the target setting (emmetropia). In this example, the eye was treated with the recommended over-correction of 0.25D for the sphere, and 0.5D for the cylinder. The final total treatment was: -3.25 D (sph) / +4.50 D (cyl) x 90°. One month following laser vision correction the manifest refraction was 0 D (sph) / +0.25 D (cyl) x 90°, which is very close to emmetropia.

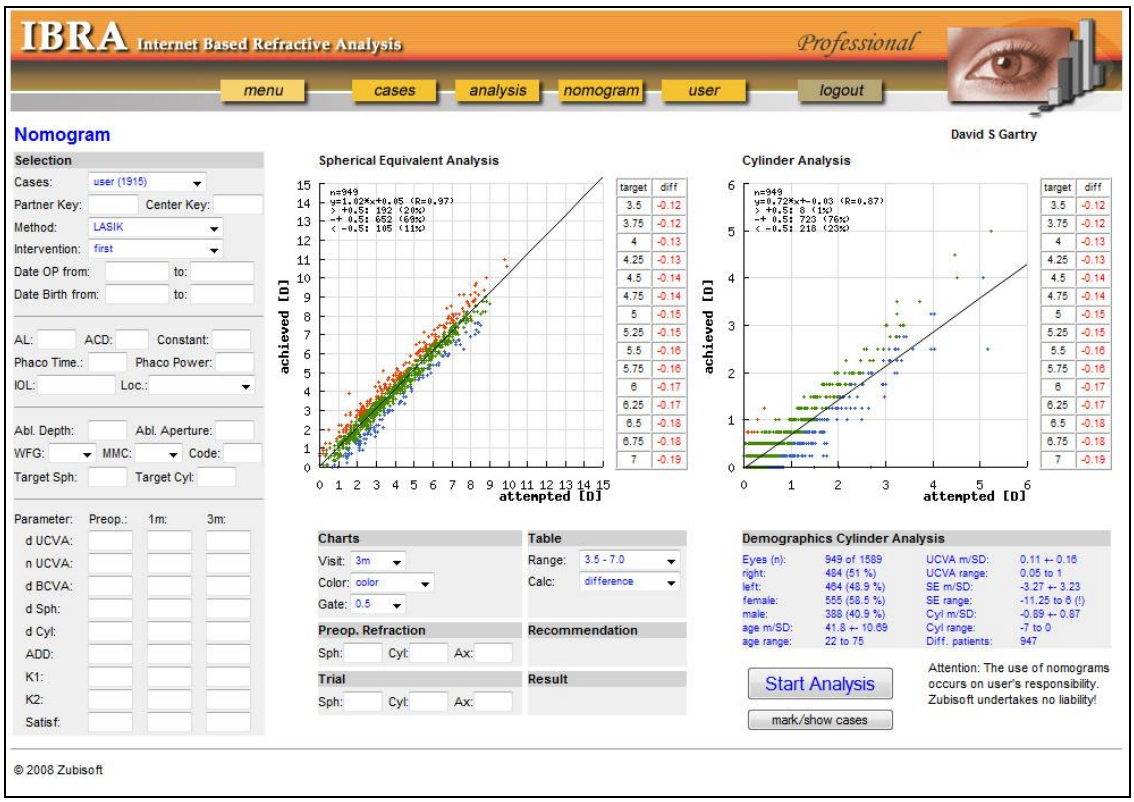


Figure 5.5.12. Screenshot of the 'Nomogram' module showing a predictability chart for the spherical equivalent (left) and the astigmatism (right) of 949 treated eyes 3 months after LASIK.

5.5.10. Satisfaction analysis

Preoperatively and postoperatively, every patient was asked to give their visual and overall satisfaction with the treatment. The patients' answers were graded from 1 (excellent) to 4 (very bad) and presented over time in the 'Satisfaction chart' (Figure 5.5.13.). We often observed an increase in satisfaction after the 6 month follow-ups, which might be linked to sensory adaptation processes.

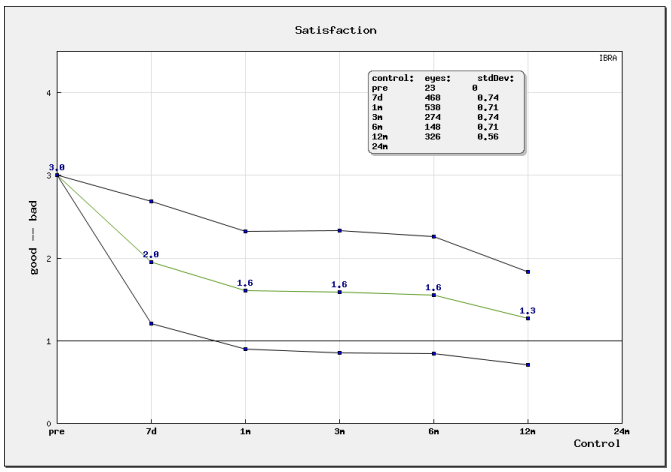


Figure 5.5.13. Patients' satisfaction over time.

5.5.11. Multicenter functions

Every case record contained the surgeon's name and the hospital site where the surgery was performed. The IBRA system allowed comparisons between different surgeons and locations. IBRA enabled users to create, change or cancel associations with other surgeons or hospitals, which they could then use for analyses. Every associated surgeon had to link their IBRA version to the group by entering a specific identification number. Only with this 'agreement to participation' was the software allowed to perform multi-user comparisons. Following the activation, all linked users gained the possibility of analyzing the data from their associate partners. However, incomplete data access was granted, and a limitation was integrated. The patient data from linked partners was only available for group analyses. At no time could a user select, identify, view or analyse one patient's data from an associate partner. This multicentre function could also be used for quality control issues between different countries or for data collection from multicentre clinical trials.

5.5.12. Download functions

A selection of data could be downloaded and stored from the IBRA system by the user at any time (Figure 5.5.14.). The system created a '.csv' format file, which then could be used in Microsoft Excel, SPSS or Minitab for descriptive or statistical analysis.

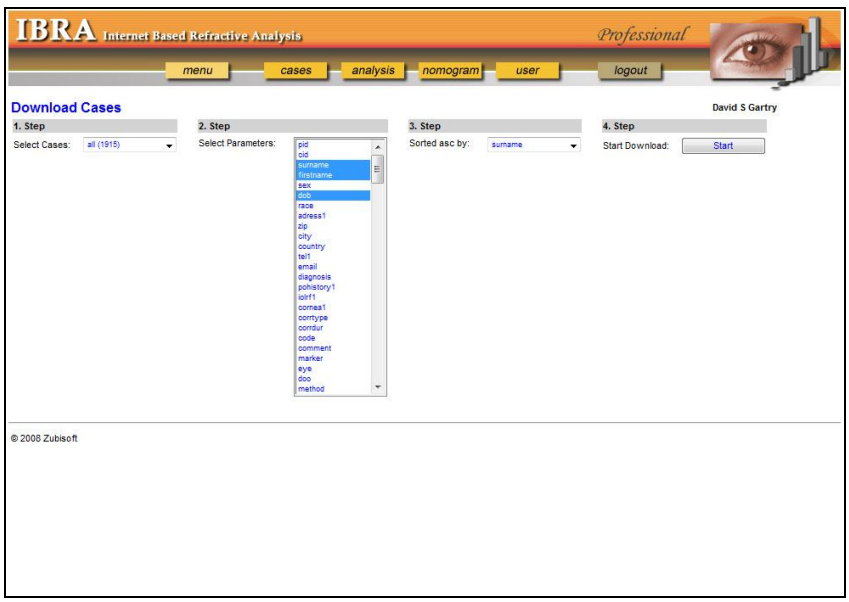


Figure 5.5.14 Screenshot of the "Download" module with case selection (left), parameter selection (middle) and sort function (right).

5.6. Summary

While most software systems evolved from co-operations between system developers and clinicians the development of IBRA was different. Development and clinical experience derived from a single person, providing a rational approach with a focus on clinical thinking and a system design that was practical and evidence-based.

This Chapter demonstrated the modified waterfall model as it was used for the development of the IBRA system. The needs of the system originated from clinical assessments, educational duties, commercial and promotional interests, and maintenance and security reasons. The chapter described how the different needs changed the direction of the system development and how web-based technology was used for implementing analysis tools and incorporating decision-supporting parts.

The operational IBRA system was presented with an extensive documentation of the main software modules (cases, analysis and nomogram) and the different analysis features.

Chapter 6

SYSTEM EVALUATION

6. SYSTEM EVALUATION

6.1. Introduction

Many examples have shown that electronic health care systems can increase the quality and efficiency of health care (Chaudhry 2006). However, there are also reports to show how such systems have failed to provide benefits, or have even caused negative effects (Han 2005). Systematic evaluation is thus an important requirement to assess the quality, value, effect and impact of information technology and applications in the health care environment. Evaluations can improve health information applications, safeguard high standards of care and enable the emergence of an evidence-based health informatics practice; it can even be seen as an ethical imperative for health informaticians (Ammenwerth 2004).

The reasons for the present evaluations were mainly pragmatic and ethical in nature (Friedman 2007). Following planning, design, implementation and successful testing of an operational version of the IBRA system, we were guided by many ‘needs to know’. We were keen to find out if our concept and the calculation algorithm of the system could deliver what they were developed for. Clinical and non-clinical questions were used as starting points to design the evaluation processes, in accordance with Professor Rigby’s recommendation: 'Start with aim and purpose, and select the appropriate methodology' that matches the question (Rigby 2003).

A synopsis of the aims, evaluation questions, used methods, the impact of the outcome and the actors is shown in Figure 6.1.1.

6.1.1. Clinical aims and evaluation methods

The main clinical aim was to analyse the impact of the treatment modifications on patients' health. The IBRA system allowed 2 different forms of treatment modifications: a general modification for refractive groups (e.g. simple myopia), and a patient-individual treatment modification.

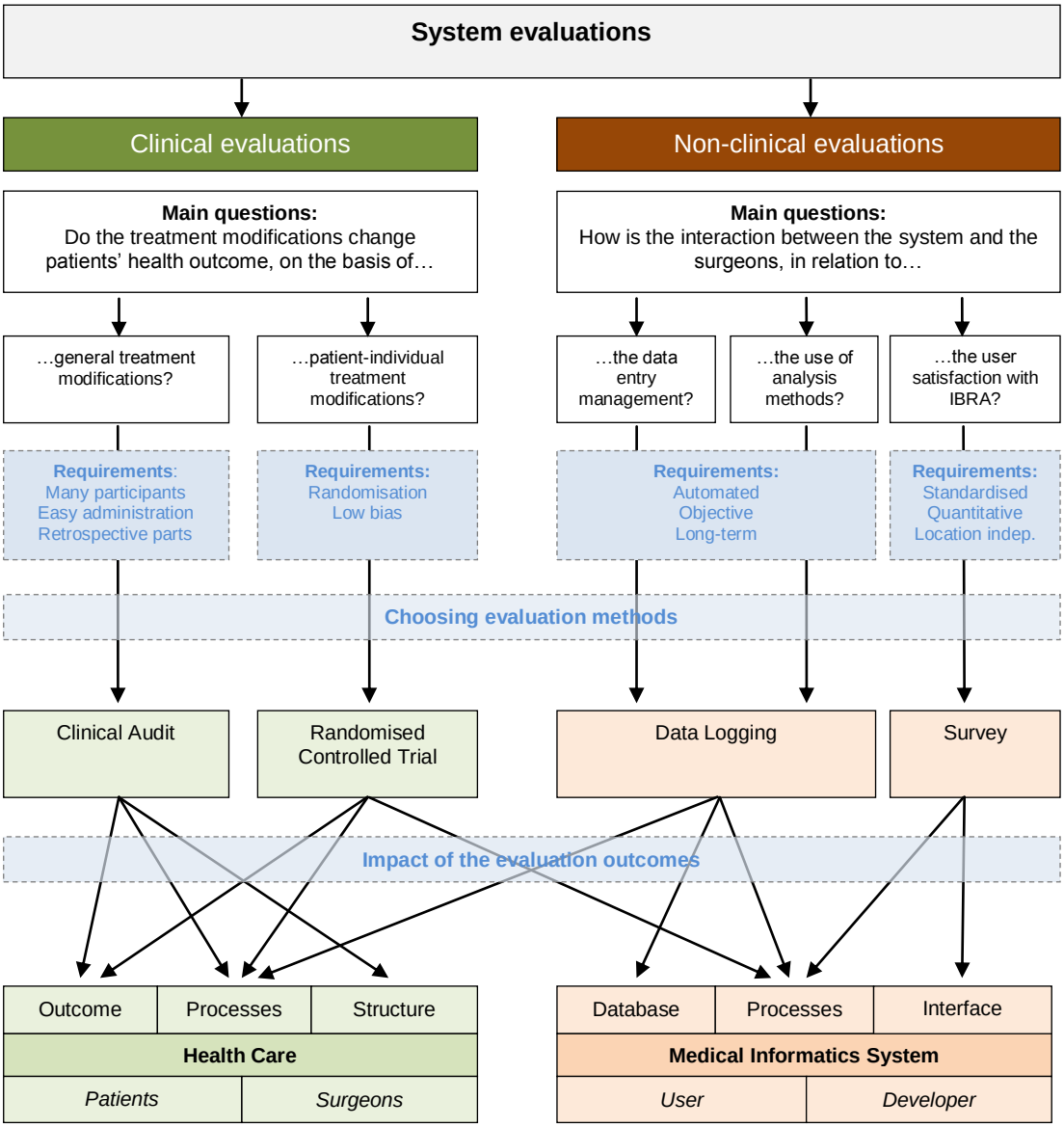


Figure 6.1.1. Overview of the system evaluations, the evaluation questions, the used methods, the impact of the outcome and the involved actors.

Meaningful analyses of treatment modifications with a *general adjustment* require a high number of participants. Appropriate methods of evaluation for this requirement can be non-randomised, as this allows easier recruitment with lower administrative complexity. Therefore, we decided to use a clinical audit for this evaluation. Clinical audit is a process that has been defined as: 'a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria (refractive outcome) and the implementation of change (treatment modification).

Where indicated, changes are implemented at an individual, team, or service level and further monitoring is used to confirm improvement in healthcare delivery' (Shaw 2002). Clinical audit is different from research in that it does not require formal review or approval from a Research Ethics Committee. This allowed us to use a retrospective analysis method for the first audit cycle to analyse the treatment errors, while the second audit cycle was prospectively designed and performed with the aim to analyse the outcome after treatment modification.

The concept of *patient-individual modifications* of the laser treatments is new. The best method to test the effectiveness of a new treatment is to undertake a randomised controlled trial (RCT), which is seen by many as the gold standard of evaluation (Meldrum 2000). The benefit of using an RCT for the evaluation was that it could eliminate bias in the treatment assignment and facilitate participant blinding. Another advantage of this method is that the randomisation generates an unpredictable sequence of allocations and provides comparable groups with valid statistics. For this research, the RCT should compare the standard treatment with the new, patient-individually adjusted, treatment in laser vision correction.

6.1.2. Non-clinical aims and evaluation methods

The non-clinical aim was to study the interaction between the IBRA system and the user. In particular, we focused the evaluation on 3 main questions. The first 2 questions addressed users' behaviour, while the 3rd question was linked to users' opinion.

1. How did users manage the data entry process?
2. Which outcome analysis methods were preferred by surgeons?
3. How was the user satisfaction with the system?

For the analysis of the *user behaviour* based questions of this research the method of data logging was very promising. Data logging is defined as: 'the collection of data from monitoring a process that passes through a particular point in a system, using integrated sensors, over a period of time' (Oxford Dictionary of Computing). The benefit of data logging for our evaluations was that it could take the readings automatically (in the background), over a long period of time (12 months), without human intervention, and with a high degree of accuracy. For the assessment of the data entry management we aimed to record 'time stamp' data generated at each step of the data entry process. For

the evaluation of the analysis methods we planned to monitor the IBRA analysis module and to record the type of analysis that was performed over time. The results of both evaluations could then be processed by specific software applications and presented as tables, scattergrams and bar graphs.

Finally, we decided to use a questionnaire for the remaining, *opinion based,* non-clinical evaluation to assess users' satisfaction. The advantage of a questionnaire for this research was that the responses could be gathered in a standardised way, so that the outcome could become more objective and could be analysed with quantitative methods. A well designed questionnaire could allow a relatively quick collection of the provided information; the small user group allowed individual management and could therefore guarantee a high return rate. For this evaluation process, a specific extra literature survey was performed in relation to the type and size of questionnaires, and with a view on commercially available questionnaire systems (QUIS, SUMI, and others). Detailed information on these systems and the created questionnaire are provided in the methods part of Section 6.6.

6.1.3. Organisation of the evaluation chapter

Each of the 5 evaluations is presented in the following in a separate section (6.2. to 6.6.). We followed the suggestion of Professor Wyatt to aim for publication of the results from the evaluation processes, even if negative (Wyatt 2003). Therefore, each evaluation is presented in a scientific format to facilitate conversion and conclusive reporting. Each section provides a discussion and conclusion of the main findings. Chapter 7 discusses the findings of the evaluations in relation to the overall research aims and objectives.

6.2. Refractive audits to evaluate general health changes

6.2.1. Introduction

Ophthalmic surgeons continuously try to improve the surgical processes with the aim to make the operation safer and the outcome more predictable. In refractive laser surgery 90% of the success comes from planning the surgery, including careful patient selection, extensive preoperative measurements of the eye and adequate determination of the treatment parameters. The key to the right patient selection bases on surgeons knowledge, skills and experience. It's a process that is learned and improved over many years of practice. Most preoperative measurements and tests are performed under standardized conditions by experienced and well trained optometrists reducing the biasing and errors in the testing phase to a minimum. Finally, the determination of the treatment parameters relies much on surgeon's experience, but is also linked to empirical data from previous treatments and manufacturer's recommendations. In a more iterative process the predictability improves over time, but will always depend on the laser equipment and the surgeon that performs the laser operation.

IBRA has an important supportive role in planning the laser treatment. It analyses the refractive and visual outcomes from patients treated with the same equipment and uses specific new algorithms to calculate factors that the surgeon can use to adjust the treatment parameters. The information IBRA provides is supporting the surgeon in making a decision on how much refractive correction the patient will receive, with the aim to achieve a higher amount of eyes that are closer to the target.

The aim of this evaluation was to study the IBRA analysis and decision making process and to evaluate the effectiveness of the adjustments. Therefore, two extensive, one-year audits were planned; the first to determine treatment adjustment factors, which than can be used for the second audit.

In particular, the aims and research questions of this evaluation were:

- To evaluate the system for the purpose of auditing (Can it be used for auditing?)
- To evaluate the refractive outcome of LASIK (How good is the treatment?)
- To evaluate strategies that can improve the results (How can the outcome be improved?
- To evaluate the calculation algorithm of IBRA (Do the algorithms work?)

- To analyse the refractive outcome of patients following the adjustment of the treatment algorithm (Does the use of IBRA change patient's health?)

The objectives were:

- To enter demographic, preoperative, operational and postoperative patient data from 2007 into the IBRA database.
- To use the tools of IBRA for the 2007 refractive outcome analysis.
- To present the results (Congress and Poster) and provide a platform for discussion between refractive experts.
- To identify patient groups which perform better or worse.
- To use the calculation algorithm of IBRA to define adjustment factors for outcome improvements.
- To treat the 2008 patients with a modified treatment profile.
- To enter the demographic, treatment and outcome data from 2008 into IBRA and to use the analysis tools of IBRA for the 2008 refractive outcome analysis.
- To use EXCEL and statistical software to identify changes between the 2007 and 2008 results.
- To discuss and interpret the results and the IBRA features.

6.2.2. Patients and methods

Methodology

Two audits were designed in February 2007, started in May 2007 and completed in August 2009 (Figure 6.2.1.). For both audits a total of 2011 patients were treated.

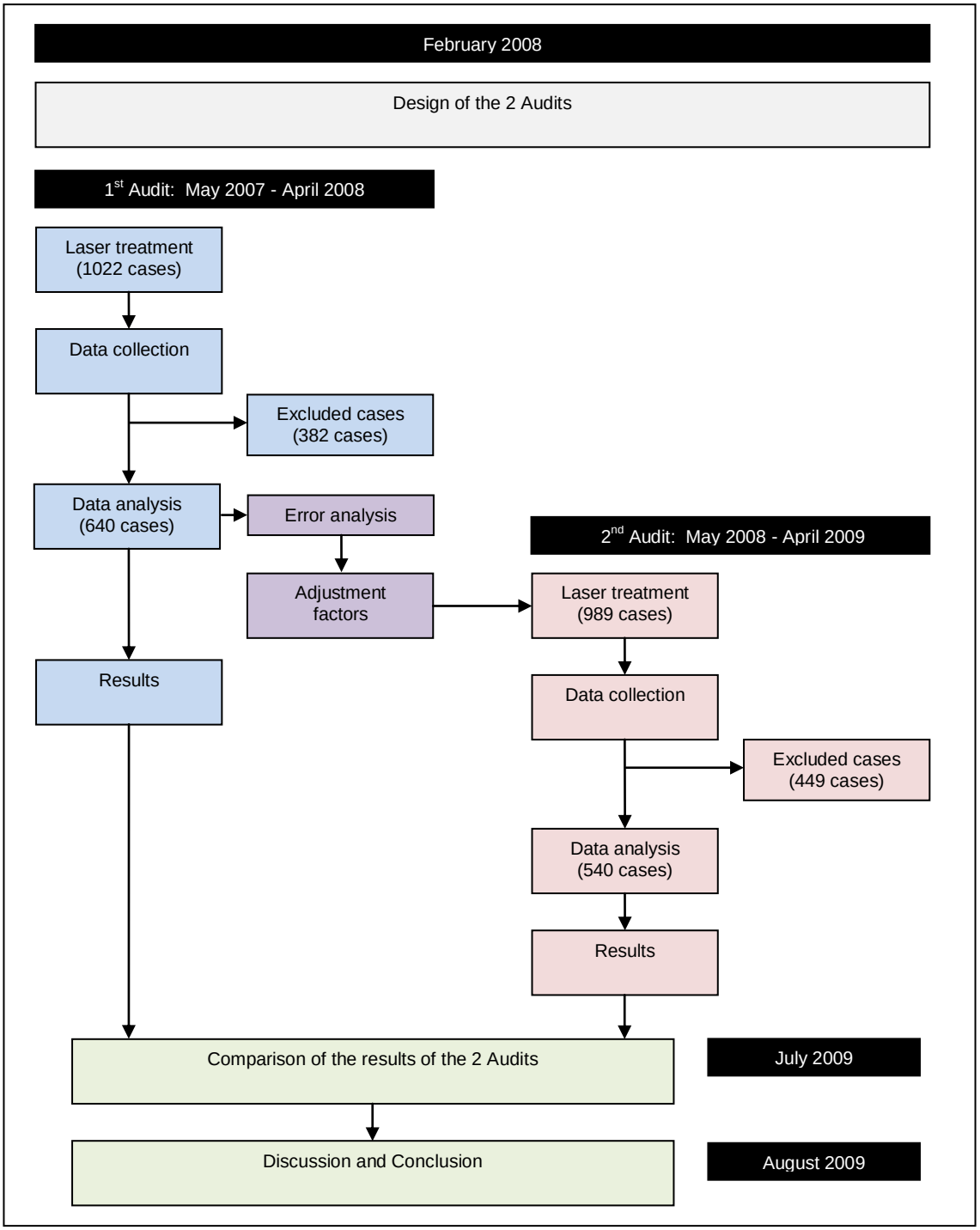


Figure 6.2.1. Methodology of the refractive Audits 2007 and 2008.

Patient demographics

From May 2007 until April 2008 (12 months, "Refractive Audit 2007") a total of 1022 eyes (cases) with refractive disorders were treated. A total of 382 cases were excluded (Table 6.2.1.). The remaining 640 cases, all treated with LASIK and a complete 3 months follow-up, were used for the Audit 2007.

From May 2008 until April 2009 (12 months, "Refractive Audit 2008") a total of 989 eyes (cases) with refractive disorders were treated, according to the modified treatment algorithm. A total of 449 cases were excluded (Table 6.2.1.). The remaining 540 LASIK cases with complete 3 months follow-up were used for the Audit 2008.

More details about the patient demographics are shown in Table 6.2.2. The only parameter that was statistically significant between the 2 groups was the postoperative spherical equivalent at 3 months ($p<0.001$).

	1st Audit (2007)	2nd Audit (2008)
Cases treated with LASEK	89	61
Cases that received a first enhancement	18	29
Cases that received a second enhancement	1	3
Cases with a one month follow-up only	34	6
Cases with a six months follow-up only	4	6
Cases with incomplete or missing data	142	271
Cases in which the refractive outcome was not aimed within 0.6 D of emmetropia	94	73
Total cases excluded	**382**	**449**

Table 6.2.1. Exclusion criteria for the 2 audits (Refractive Audits 2007 and 2008).

	1st Audit (2007)	2nd Audit (2008)	P
Eyes			
- Used for audit	640	540	
Age			
- Mean ± SD (years)	41.5 ± 10.5	41.6 ± 11.0	0.955
- Range (years)	21.7 ± 76.7	21.7 ± 72.2	
Sex			
- Female (percentage)	372 (58%)	307 (58%)	0.999
- Male (percentage)	271 (42%)	225 (42%)	
Diagnosis			
- Simple myopia	325 (50.8%)	317 (58.7%)	
- Compound myopic astigmatism	186 (29.1%)	141 (26.1%)	
- Simple hyperopia	77 (12.0%)	42 (7.8%)	
- Compound hyperopic astigmatism	35 (5.5%)	30 (5.6%)	
- Mixed astigmatism	17 (2.6%)	10 (1.8%)	
Spherical equivalent			
- Preoperative mean ± SD (D)	-3.02 ± 3.00	-3.36 ± 2.79	0.052
- Preoperative range (D)	-9.25 to 4.75	-8.875 to 6.00	
- At 3 months follow-up mean ± SD (D)	0.10 ± 0.43	-0.14 ± 0.43	**<0.001**
- At 3 months follow-up range (D)	-1.75 to 1.75	-1.625 to 1.625	
Subjective astigmatism			
- Preoperative mean ± SD (D)	-0.87 ± 0.83	-0.79 ± 0.78	0.127
- Preoperative range (D)	-5.5 to 0.00	-6.75 to 0.00	
- At 3 months follow-up mean ± SD (D)	-0.34 ± 0.31	-0.26 ± 0.30	0.876
- At 3 months follow-up range (D)	-2.75 to 0.00	-2.50 to 0.00	
Uncorrected visual acuity (LogMAR)			
- Preoperative mean ± SD	0.92 ± 0.33	0.80 ± 0.34	0.322
- At 3 months follow-up mean ± SD	0.00 ± 0.13	0.01 ± 0.14	0.668
Best-corrected visual acuity (LogMAR)			
- Preoperative mean ± SD	-0.04 ± 0.08	-0.04 ± 0.08	0.243
- At 3 months follow-up mean ± SD	-0.06 ± 0.08	-0.07 ± 0.07	0.657

Table 6.2.2. Patient demographics of the analysed groups (Refractive Audits 2007 and 2008).

Laser treatment (LASIK)

The corneal flap for LASIK was performed with a Hansatome microkeratome (Bausch & Lomb), a Moria M2 (Moria) microkeratome or with the Intralase Femto Laser. The size and depth of the flap was dependent to the spectacle refraction and the corneal curvature and was set between 120-180 µm thickness and 8.5-9.5 mm diameter. The corneal ablation was performed with a VISX S4 Excimer Laser (AMO) by a single surgeon (DSG). The target refraction was individualized for each patient. For patients that were aiming for independence to glasses for distance vision, the target was set slightly on the myopic side, with the purpose of undercorrection. The total treatment was limited to leave a residual corneal stromal bed of 250µ.

Postoperative measurements

The patients were refracted by in-house optometrists and uncorrected and best-corrected distance Snellen visual acuity was measured with the Snellen chart (UK version). Corneal astigmatism was assessed by Pentacam topography and wavefront measurements were performed with the WaveScan (AMO). All data was filled-in on special preoperative and postoperative assessment forms in the paper-based patient record.

Data entry into IBRA

The paper-based patient records were used for the data entry process. The preoperative, operative and postoperative parameters were entered into the Internet Based Refractive Analysis Software (IBRA). A minimum of 42 parameters for each treated eye (case) was collected. This was a time consuming process that was performed over more than 2 years and that required 4 hours of data entry every week.

Determination of the treatment parameters for the first Audit (2007)

The method of determine the settings for the laser treatments of the first audit was well established and represented the standard treatment at this time (Figure 6.2.2.).

The sphere value of the manifest refraction was used as treatment sphere when the difference between the manifest and the WaveScan sphere was less than 0.5 diopters (D). The cylinder value of the manifest refraction was used as treatment cylinder when the difference between the manifest and the WaveScan cylinder was less than 0.25D. The axis value of the manifest refraction was used as treatment axis when the difference between the manifest axis, the WaveScan axis and the axis of the Topography was less

than 10°. If the differences between the sphere, cylinder or axis parameters were bigger than the mentioned limits, the preoperative examination was repeated. Finally, the determined parameters were entered in the laser unit for the refractive treatment of the patients.

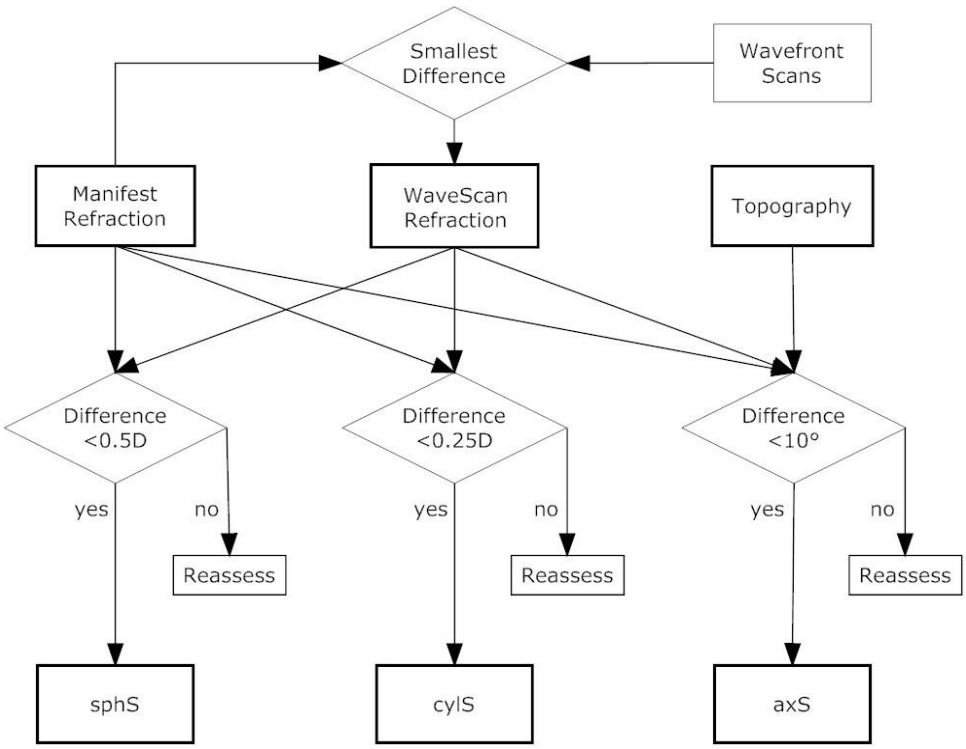


Figure 6.2.2 Determination of the standard treatment setting (Refractive Audit 2007).

Optimising the treatment for the second Audit (2008)

IBRA was used to analyse a total of 643 eyes from the first audit. The software compared the achieved versus the attempted spherical correction for all treated eyes and for subgroups of eyes with different preoperative refractive errors, based on focus of the principal meridians (Table 6.2.3.).

Groups	**Spherical equivalent (D)**	**Astigmatism (D)**
Simple myopia	<0	<1.0
Compound myopic astigmatism	<0	≥1.0
Simple hyperopia	>0	<1.0
Compound hyperopic astigmatism	>0	≥1.0
Mixed astigmatism	negative or positive	abs(0.5*cyl) ≥ abs(SE)

Table 6.2.3. Determination of the refractive disorder groups from preoperative spherical equivalent (SE) and astigmatism (cylinder).

Linear regression of the spherical correction was calculated for each of the 5 groups, which then was used to calculate the amount of spherical adjustment for each eye for the main groups (Table 6.2.5).

These factors were used to modify the treatment parameters for the second audit. Because the outcome should preferably be rather myopic (0 to -0.25D) then hyperopic we decided not to use the full amount of correction to prevent hyperopic outcomes.

Treatment parameters for the second Audit (2007)

The sphere value, cylinder value and axis were determined as for the treatment of the patients of the first audit. The sphere value then was modified based on the adjustment factors from the regression analysis of the results (Figure 6.2.3). The treatment parameters were used for all patients of one particular refractive disorder group.

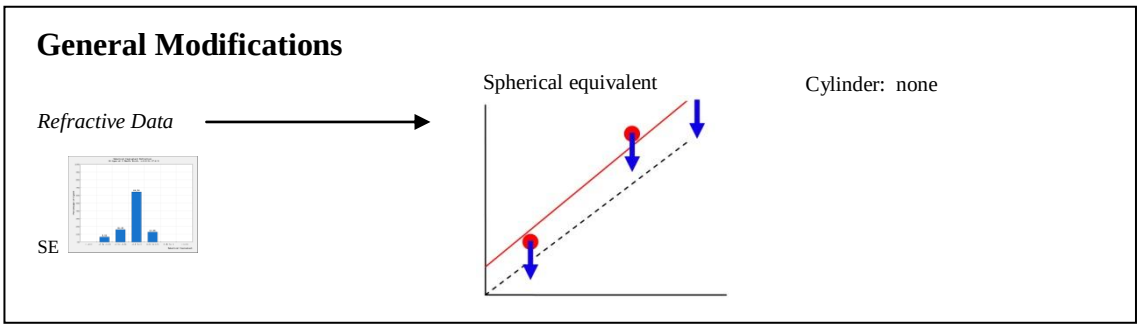


Figure 6.2.3. General modifications of laser treatments, based on linear regression analysis of the spherical equivalent and used as a fix amount (blue arrow) for all patients of one particular refractive disorder group.

Comparison of the Audit outcomes

The second audit used the same exclusion criteria. IBRA then analysed the outcome of 532 eyes. Additionally, the refractive results from both audits were compared and statistically analysed with the aim to determine the influence and precision of the treatment adjustment on the refractive outcome.

Main measure

The main measure was the refractive change, expressed by the change of spherical equivalent.

Data analysis and results

We focused on the analysis and presentation of the 3 main refractive disorders, counting for 92% of all diseases; including simple myopia, compound myopic astigmatism and simple hyperopia. IBRA was used for the refractive analysis and for the creation of the figures. For the postoperative analysis the results from the 3 months follow-up were used. This is the time interval in which the corneal changes have settled and the outcome has become stable.

Statistics

Microsoft EXCEL, Unistat and Minitab software packages were used for statistical analyses. For comparative statistics, the Wilcoxon matched pairs test was used. For independent samples, the Mann-Whitney U-test was used. P-values less than 0.05 were considered statistically significant.

Presentations

Preliminary results were presented under the title "Importance of outcome analysis in laser in-situ keratomileusis - Refining algorithms using IBRA" at the Annual Congress of the Royal College of Ophthalmology in Birmingham (19.05.2009). Some of the results were presented under the title "Refining algorithms in laser in-situ keratomileusis using IBRA" at the Centre for Health Informatics, City University London (05.05.2009). An article with the title "Nomogram adjustments for myopes and hyperopes in LASIK" was submitted for publication to the Journal "Ophthalmology" in June 2010.

6.2.3. Results

Refractive outcomes produced with IBRA

The refractive outcomes have been analysed with the 'spherical equivalent distribution' analysis (Figure 6.2.4.) and the 'spherical equivalent predictability' analysis.

In Figure 6.2.5. we present the refractive outcomes for the audit 2007; in Figure 6.2.6. the refractive outcomes for the audit 2008. A comparison of the postoperative spherical stability and the uncorrected visual acuity of the 2 audits is shown in Figure 6.2.7.

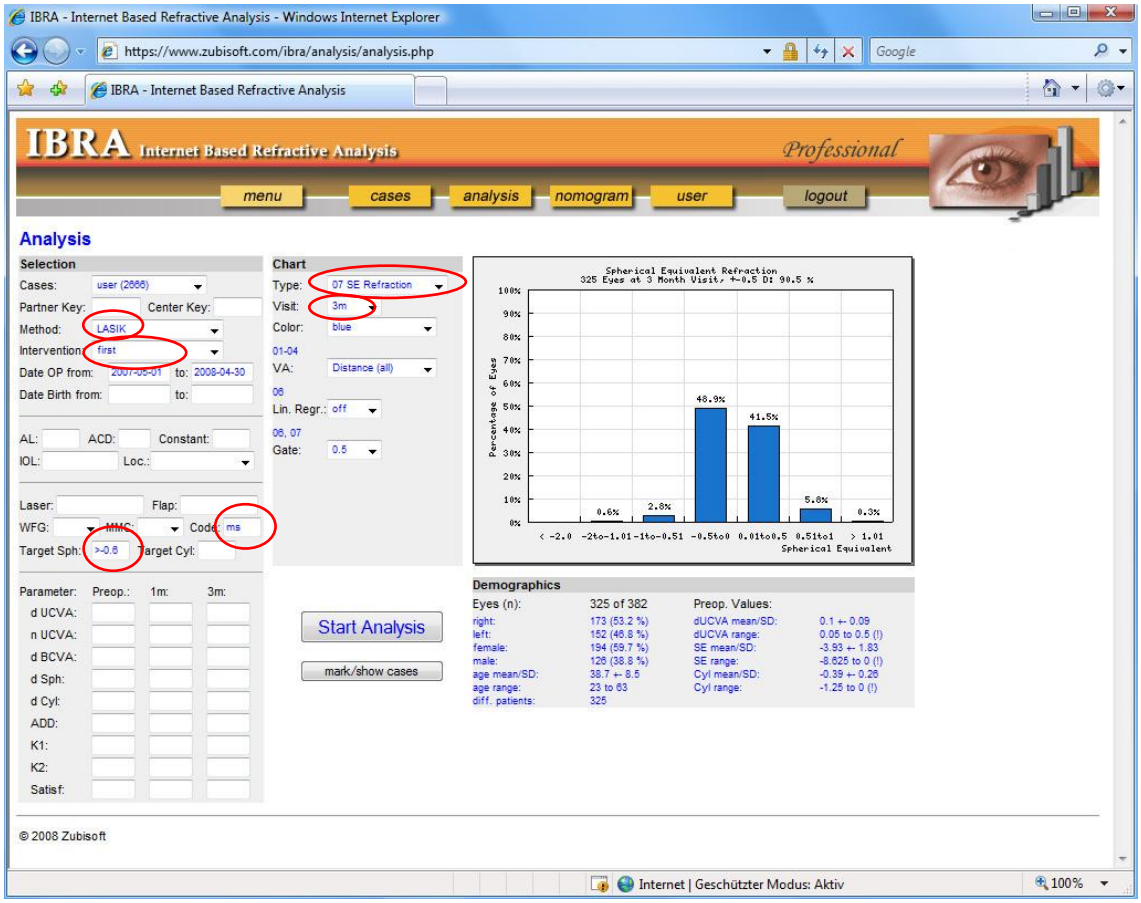


Figure 6.2.4. Screenshot from the analysis module in IBRA with selection criteria. The produced chart in the centre is shown as high resolution image B1 in Figure 6.2.5. Changing the selection criteria (see red circles) accordingly allowed producing all other charts.

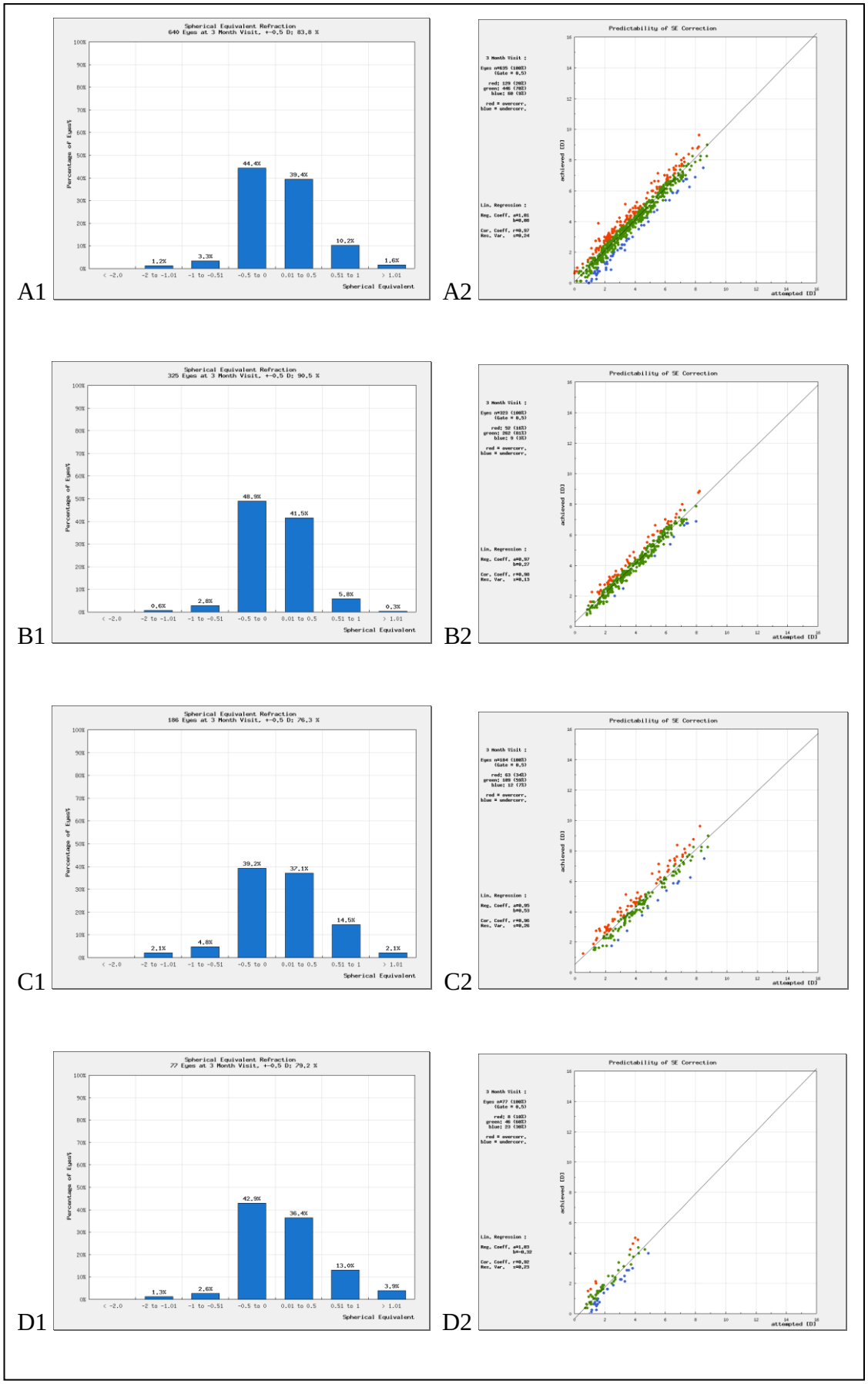


Figure 6.2.5. Refractive outcome 2007 produced with IBRA. A1 and A2: all cases; B1 and B2: simple myopia; C1 and C2: compound myopic astigmatism; D1 and D2: simple hyperopia.

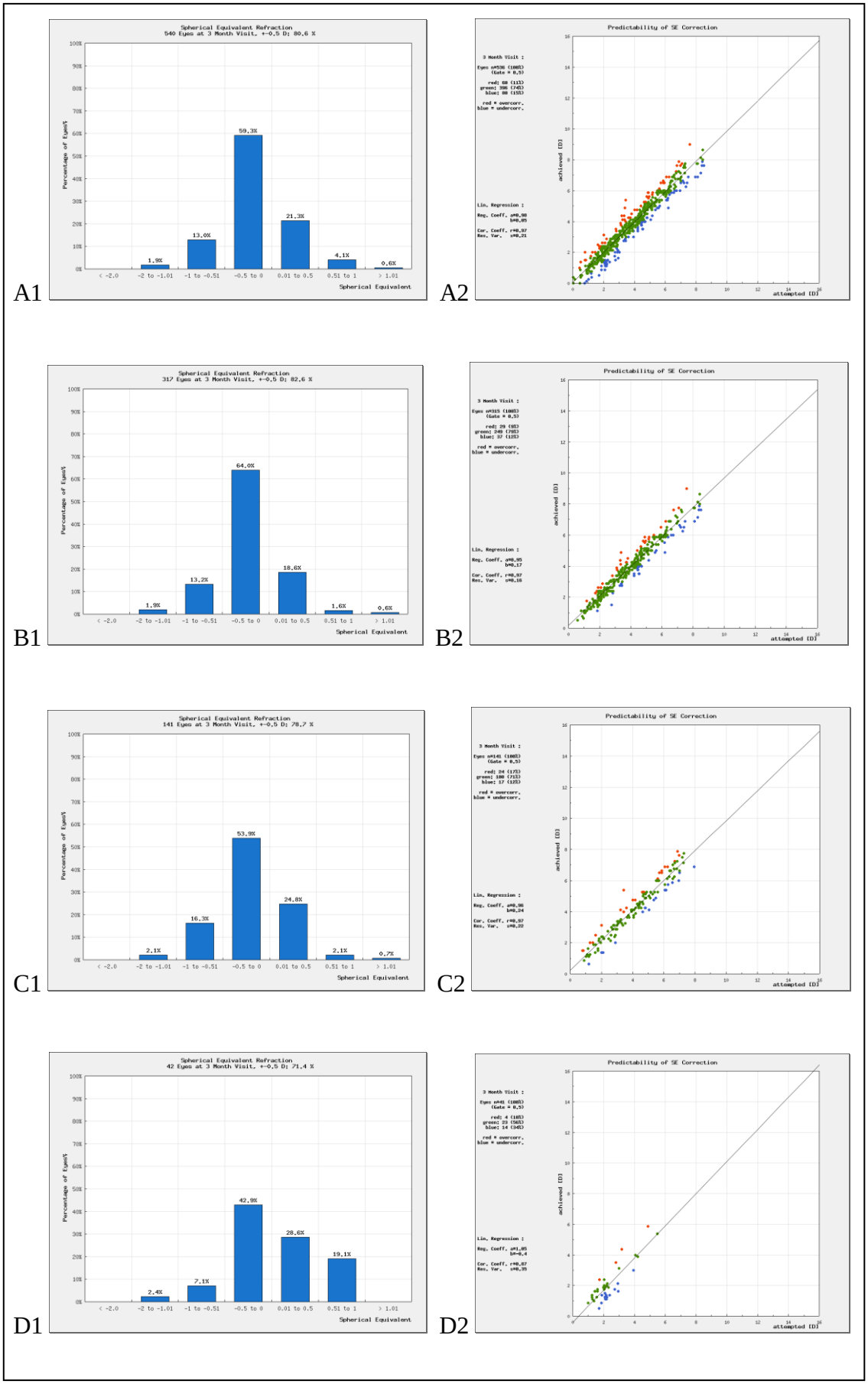


Figure 6.2.6. Refractive outcome 2008 produced with IBRA. A1 and A2: all cases; B1 and B2: simple myopia; C1 and C2: compound myopic astigmatism; D1 and D2: simple hyperopia.

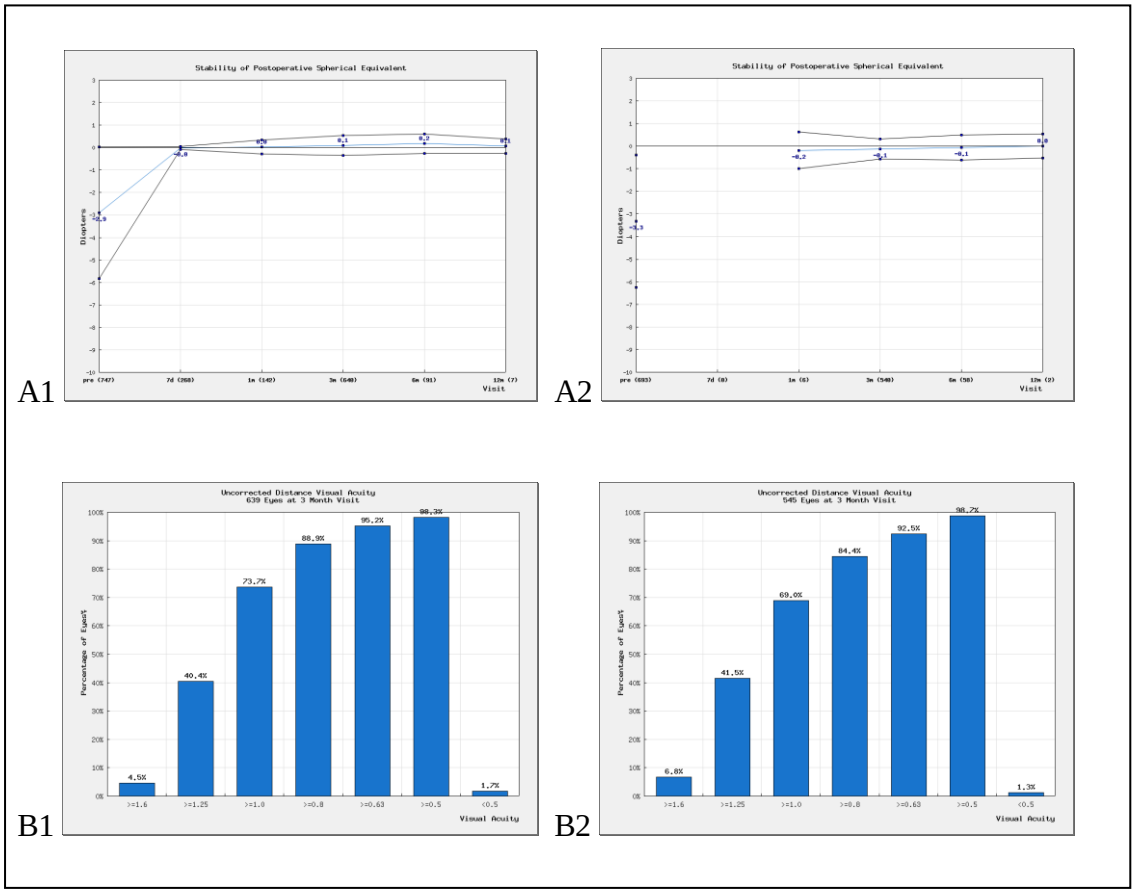


Figure 6.2.7. Refractive outcome 2007 and 2008 comparison of all treated cases regarding refractive stability (A1 and A2) and cumulative uncorrected visual acuity (B1 and B2). The charts are produced with IBRA 3 months results.

Refractive outcomes analysed with EXCEL

The calculated percentages and linear regression coefficients were taken from the charts and filled in a table separated by the refractive groups (Table 6.2.4.). Based on these refractive audit 2007 parameters the amount of spherical adjustment was determined for each group individually and summarised in table 6.2.5.

Group	N	Mean SE ± SD	± 0.5D of emmetropia	> 0.5D over-correction	Constant a	Constant b
Simple myopia	325	0.05 ± 0.39	91%	6%	0.97	0.27
Myopic astigmatism	186	0.13 ± 0.48	76%	17%	0.95	0.53
Simple Hyperopia	77	0.12 ± 0.44	79%	17%	1.03	-0.32

Table 6.2.4. Postoperative results from the first audit in 2007 for the 3 min refractive disorder groups.

Group	Spherical adjustment (D)
Simple myopia	-0.25
Compound myopic astigmatism	-0.40
Simple hyperopia	+0.20

Table 6.2.5. Patient groups and spherical adjustment

Statistical comparison between the outcomes

Data was exported with IBRA into a Microsoft EXCEL format. EXCEL then was used to calculate the mean and standard deviation of the postoperative spherical equivalent. In an additional step the data was exported from EXCEL into Unistat statistic software for the creation of box plots (Figures 6.2.8.-6.2.10) and for statistical comparison (Mann-Whitney U Test) of the spherical equivalent of the 2007 and 2008 groups.

Group	N	Mean SE ± SD	Diff to 2007	P Value	± 0.5D of emmetropia	Diff to 2007	> 0.5D over-correction	Diff to 2007
Simple myopia	317	-0.16 ± 0.40	-0.21	<0.0001	83%	-8%	2%	-4%
Myopic astigmatism	141	-0.17 ± 0.46	-0.30	<0.0001	79%	+3%	3%	-14%
Simple Hyperopia	42	0.03 ± 0.52	-0.09	0.3032	71%	-8%	19%	+2%

Table 6.2.6. Postoperative results from the second audit in 2008 with comparison to the 2007 results for the 3 main refractive disorder groups.

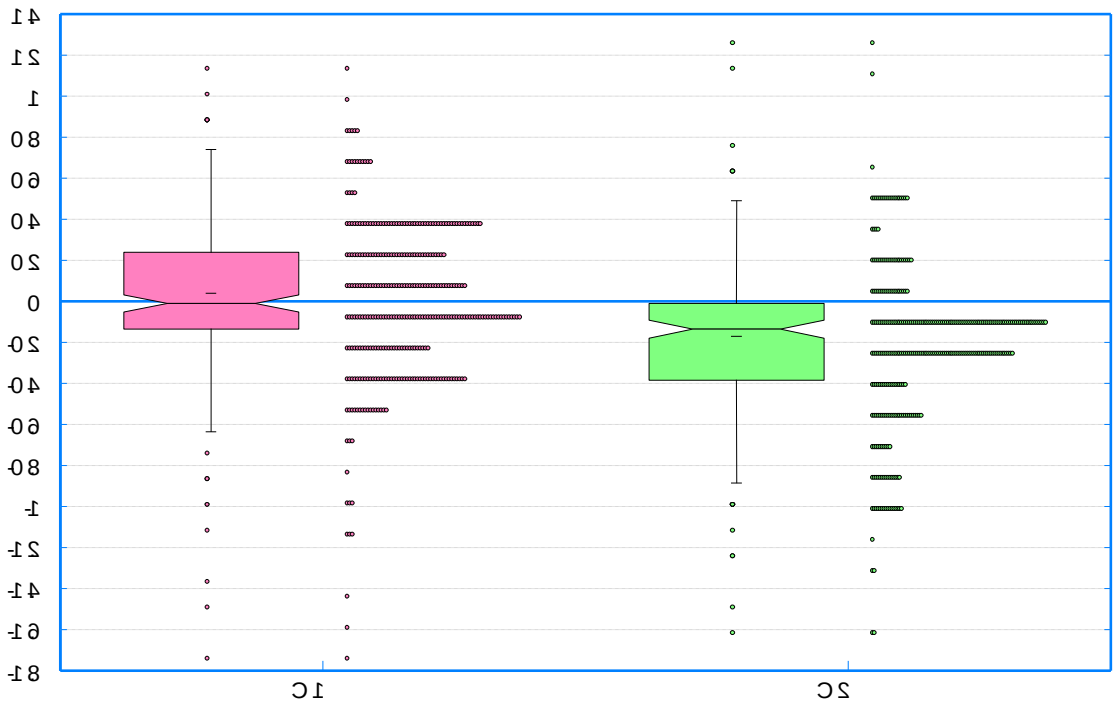


Figure 6.2.8. Comparison of the 3 months postoperative spherical equivalent (in D) of eyes with simple myopia between the first (C1) and second (C2) audit. The refractive aim was emmetropia or mild myopia (0 to -0.25 D) for the treated eyes of both groups. Statistically, the difference between the two groups was highly significant (Mann-Whitney U Test: p<0.0001).

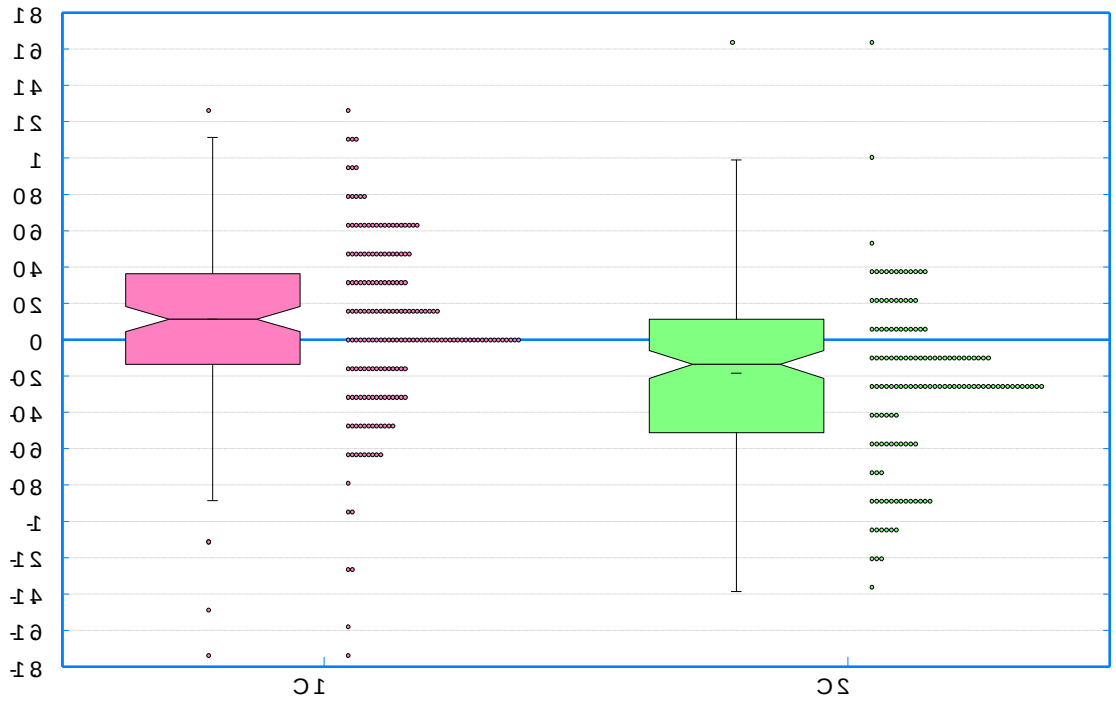


Figure 6.2.9. Comparison of the 3 months postoperative spherical equivalent (in D) of eyes with compound myopic astigmatism between the audits in 2007 (C1) and 2008 (C2). The refractive aim was emmetropia or mild myopia (0 to -0.25 D) for the treated eyes of both groups. Statistically, the difference between the two groups was highly significant (Mann-Whitney U Test: $p<0.0001$).

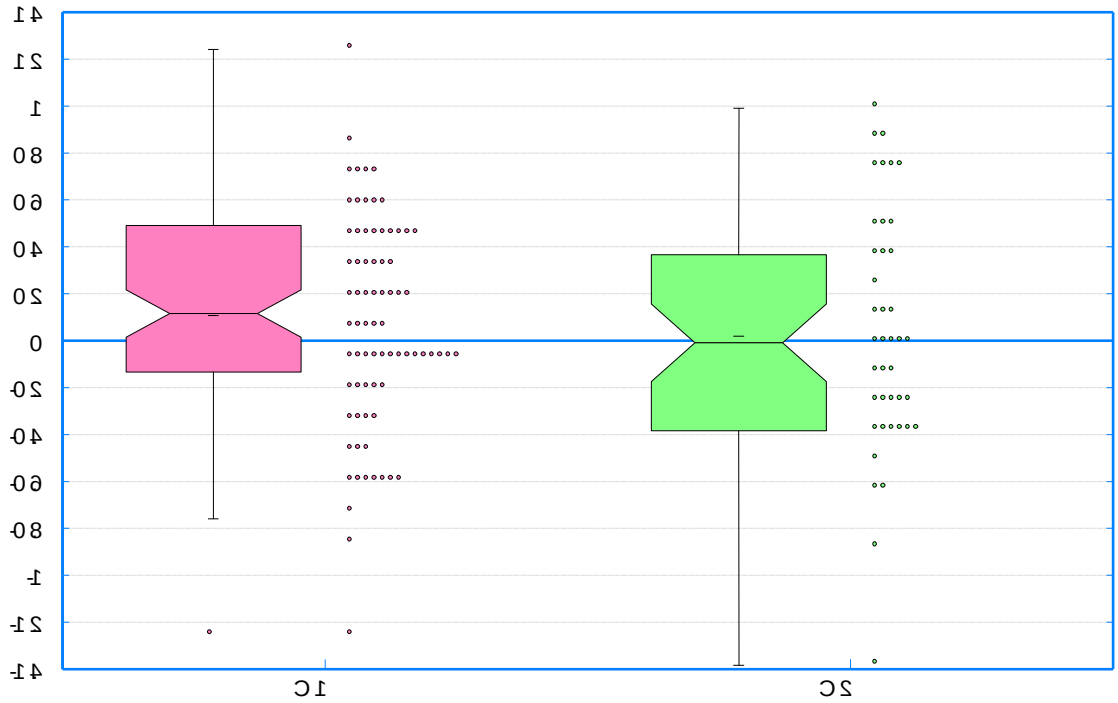


Figure 6.2.10. Comparison of the 3 months postoperative spherical equivalent (in D) of eyes with simple hyperopia between the audits in 2007 (C1) and 2008 (C2). The refractive aim was emmetropia or mild myopia (0 to -0.25 D) for the treated eyes of both groups. The difference between the two groups was statistically not significant (Mann-Whitney U Test: $p=0.3032$).

6.2.4. Discussion

The IBRA software allowed determining patient cohorts effectively with the use of group codes, e.g. ‘ma’ for myopic astigmatism. To reduce the bias for the nomogram calculation and to increase the homogeneity of the data we used multiple selection criteria. The final inclusion criteria determined eyes undergoing a first LASIK treatment with the aim to achieve a refractive result close to emmetropia and with a complete 3 months follow-up. This limitation reduced the number of cases available for the analysis by 47%. Because of the high amount of operations performed every year the remaining numbers were still good (640 cases for the first and 540 cases for the second audit).

Refractive groups

The refractive outcome analysis of the first audit was performed for each of the 5 groups with different refractive disorder: simple myopia and hyperopia, compound myopic and hyperopic astigmatism and mixed astigmatism. The prevalence of these refractive disorders is not equal. The 3 main disorders (simple myopia, simple hyperopia and compound myopic astigmatism) count for more than 92% of all cases. For this evaluation we focused on the main groups for the calculation of spherical adjustment factors and for comparison between the 2 audits.

Outcome for patients with simple myopia

The refractive analysis of the cases from the first audit has identified an overcorrection in the spherical treatment of patients with simple myopia. The mean spherical equivalent of eyes treated in 2007 was hyperopic. This did not meet the target refraction programmed at the beginning.

Hyperopic overcorrection in the treatment of myopic disorders can occur with different refractive lasers. Lopid-Gortzak et al (2008) addressed the problem of overcorrection with an (advanced) modification of the nomogram for the used Technolas 217 (Bausch and Lomb) laser. He could show that this reduced the rate of hyperopic overcorrection over that in earlier studies.

Regression analysis performed with IBRA showed a correlation between the attempted and the achieved spherical correction with an average overcorrection of +0.27 D. This overcorrection had a linear tendency over the full range of diopters. This means that eyes treated for -2.0D myopia showed the same mean overcorrection as eyes treated for -7.0D myopia (difference of only 0.1D).

Feder (2007) recommends for myopic patients the use of the Bansal-Kay myopia nomogram if treated with conventional LASIK; and to use no nomogram adjustment when treated with CustomVue wavefront guided LASIK. In the Bansal-Kay myopia nomogram for VISX S3 laser the amount of reduction increases with age and the amount of correction in the spherical equivalent (3^{rd} grad polynomial function). The myopic nomogram produced with IBRA for wavefront guided treatments showed little age dependency and did decrease with the amount of correction in the spherical equivalent (Figure 6.2.11.). We could prove that there is age and SE dependency for nomogram adjustments in myopic wavefront guided treatments, but less than previously reported; and that from an overall point of view the use of the IBRA nomogram can further improve the refractive outcome. Unfortunately, no reports are published on nomogram adjustments for wavefront guided treatments with the VISX S4 laser.

Once the exact amount of overcorrection was indentified we could use the IBRA algorithms to calculate the amount of adjustment for the treatment modification. For the second audit we decided to reduce the spherical treatment for simple myopes by 0.25D to achieve a more myopic outcome. The mean spherical equivalent of the second audit showed the desired change and a myopic shift of -0.21 D ($p<0.0001$) was measured (84% of the intended change). This was proving that the used nomogram adjustments worked effectively in achieving the desired refractive change.

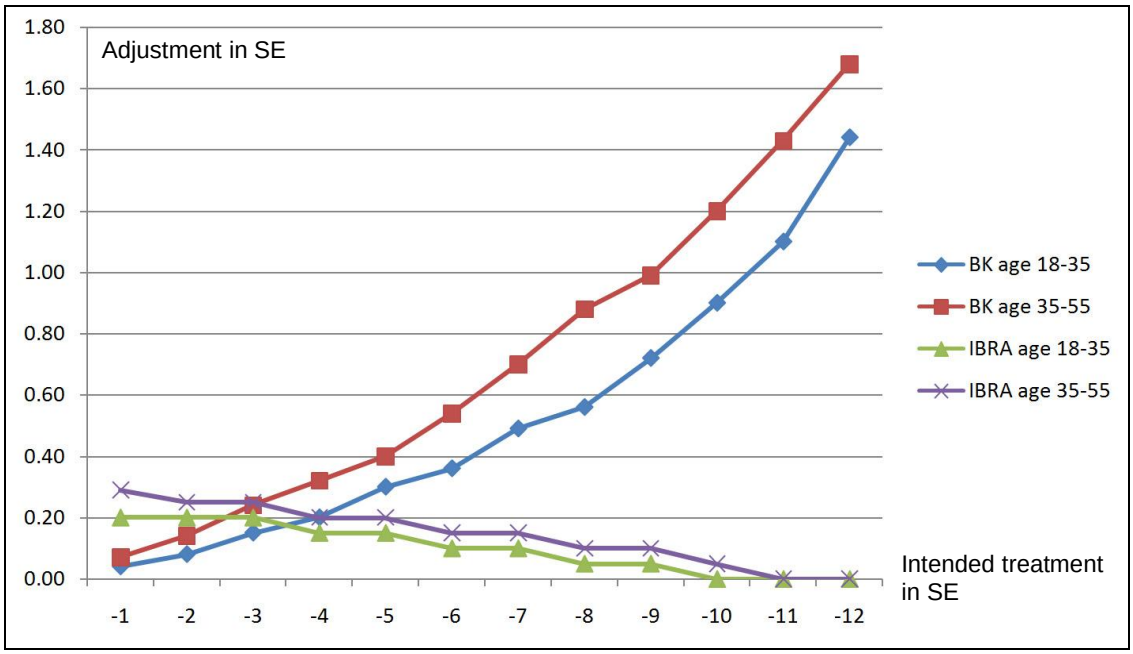


Figure 6.2.11. VISX simple myopia nomogram adjustment in the spherical equivalent (in D) based on Bansal-Kay (BK) and calculation from IBRA for 2 groups of age.

Outcome for patients with compound myopic astigmatism

We performed similar calculations for patients with compound myopic astigmatism. This is a patient group that usually performs worse than patients with simple myopia and that potentially could benefit more from nomogram adjustments.

The analysis of the refractive outcome from the first audit showed a mean spherical overcorrection of +0.53 D, comparing the achieved and the attempted spherical correction. We decided to reduce the spherical treatment for patient with myopic astigmatism for the second audit by 0.40 D, with the aim to shift the patients from the hyperopic into the myopic mean spherical equivalent. The final results showed a significant myopic shift of -0.30D ($p<0.0001$; 75% of the intended change).

Outcome for patients with simple hyperopia

For eyes with simple hyperopia the first audit showed a spherical undercorrection of -0.32 D. The mean postoperative spherical equivalent was still hyperopic at 3 months. For the nomogram adjustment we decided to increase the spherical treatment by +0.20 D with the aim to achieve a myopic mean postoperative spherical equivalent. Although we could measure a myopic change due to our adjustment, the SE difference between the first and the second audit was statistical not significant ($p=0.3032$).

We believe that the reason for this failure of the adjustment for the hyperopes could be linked to the ablation profile and to problems with accommodation surgeons are faced when treating patients with hyperopia. Zaldivar et al (2005) showed that the use of five surgical and technical modifications to the hyperopic LASIK procedure resulted in improved refractive outcomes and a lower rate of regression. These five changes were nomogram refinements accounting for accommodation, use of a 7.0-mm optical zone and a 9.5-mm transition zone, a targeted mean flap diameter of 10.5 mm, sequential interruption of the laser ablation, and cleaning of the interface.

Benefits and limitations of spherical nomogram adjustments

Computer simulation showed that individual nomograms significantly can improve the predictability of the refractive outcome. However, they are currently limited to approximately 90% within ±0.5 D (Mrochen 2005).

With this evaluation we gained similar experience. For the first audit we achieved 91% of eyes within ±0.5 D of emmetropia for the treatment of patients with simple myopia. With the nomogram adjustment we could optimise the spherical equivalent and could

move it to the myopic side. The same time the percentage of eyes within ±0.5D of emmetropia decreased to 83% with a higher amount of undercorrected eyes. Histogram analysis of the results showed for both audits similar distributions with nearly identical (level adjusted) distribution curves (Figure 6.2.12.). The very similar standard deviations for the spherical equivalent (±0.39 for 2007, ±0.40 for 2008) explain the similarity of the curves. Due to the treatment modifications the curve from the second audit shifted to the left, into the myopic range.

In summary, the performed nomogram adjustment changed the outcomes for all individual cases in the same way, as attempted. However, the modifications do not affect the standard deviation and therefore the shape of the distribution curve. As we aim for a mild myopic outcome any shift away from emmetropia (distribution curve aligned with the 0 D line) will consequently reduce the amount of eyes that will be within the ±0.5 D range of emmetropia. One of the future investigations should try to influence the distribution itself (the standard deviation) so that the results end-up closer together and showing a steeper curve.

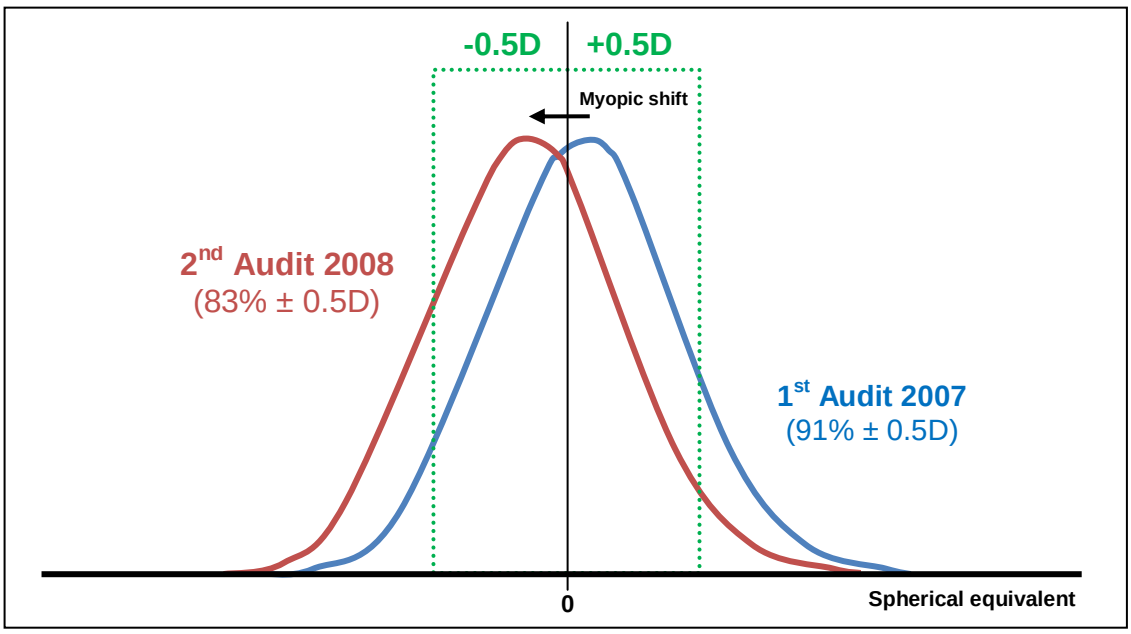


Figure 6.2.12. Distribution (level adjusted) of spherical equivalent 3 months after LASIK for patients with simple myopia. 91% of eyes of the first audit were within 0.5 D of emmetropia. Because of the myopic shift from the nomogram adjustment only 83% of eyes of the second audit were within 0.5 D of emmetropia. The distribution of the audits showed very similar curves which is a result from the quiet identical postoperative standard deviation of the spherical equivalent.

Benefits and limitations of IBRA

For this evaluation an extensive amount of data was entered into the web based software system. For each of the total 2011 treated eyes a standard set of 42 parameters was collected in a stepwise method. The data entry required approximately 8 min for each case, resulting in a total amount of 266 hours for this process. This is equivalent to 33 working days; or because the evaluation was carried out weekly over a period of 2 years, it is equivalent to half a day of data entry every week. This is a significant time commitment that, if performed by the surgeon, would require special planning and allocation in the agenda.

This evaluation showed that IBRA was able to record and process large amounts of refractive data effectively. IBRA was able to analyse refractive outcomes in multiple forms and the system platform presented to be highly reliable, safe and with similar performance during the full period of evaluation. It showed that the general performance was dependent on the speed of the broadband connection. However, the data could be accessed at any time and no data was lost or was not saved by the web-based system. IBRA could persuade with flexible use of the database from any location with Internet access and with easy handling. The produced refractive charts were clear and conform to the standards.

The unique point of IBRA is that it provides the surgeons with functions that help identifying patient groups that underperform and offers then algorithms that calculate adjustment factors for outcome optimisation. This transforms IBRA from a quality assessment to a quality controlling system.

Even if the tested version of IBRA requires significant manual input to gain the results from the different analysis and patient groups, future versions should be able to simplify and implement processes with more automatisation. The gain in precision in the planning process of patients' treatment should lead to a higher predictability and positive health change.

Future development of IBRA (conclusion)

IBRA has shown to be a precise instrument to improve the postoperative mean spherical equivalent refraction. It has shown that it does not influence the standard deviation of the result, and therefore the scatter and steepness of the distribution curve. Other reasons are responsible in influencing the scatter of the results. We believe that these reasons include age, healing processes and astigmatic changes. Age and cylinder refraction can be addressed with IBRA. An evaluation should be made as to whether

age-related nomogram adjustment of sphere combined with cylinder correction bears the potential for reducing the standard deviation of the outcome. This could potentially increase the amount of eyes within 0.5 D of emmetropia.

The present evaluation has not shown a change in cylinder, as expected. Generally, cylinder modifications have to be performed patient-individual. This is a more risky undertaking, because changes in cylinder are much less tolerated by patients when they go wrong. And one of these changes is the problem of cylinder overcorrection, which leads to an uncomfortable change of the cylinder axis of 90 degrees. A randomised controlled trial on patient-individual treatment modifications will further evaluate cylinder adjustments in laser vision correction (see Section 6.3).

The current results have not shown an influence on the mean visual acuities. The improvements from nomogram adjustment might be too small, and corrections from hyperopia to emmetropia usually do not change the uncorrected visual acuity as young patients have the ability to accommodate for good sight.

6.2.5. Conclusions

We have shown that IBRA can identify patient groups with over- and undercorrection effectively; that it can calculate accurate nomograms for adjustments of future treatment, and that these modified treatments can lead to the desired health outcome change.

The integrated algorithms work effective for simple myopia and myopic astigmatism, but do not work well for hyperopia. Further, we have proven that the concept of nomogram adjustment can bring benefit to wavefront guided treatments. This stays in contrast to a widely recommended practice (Feder 2007).

A third audit cycle is not required as we achieved the refractive goal with the second audit.

6.3. Patient-individual modification of laser settings in the treatment of astigmatic myopia with laser in-situ keratomileusis

6.3.1. Introduction

Background and rationale

Refractive eye laser treatment is a specialised field of eye surgery that focuses on improving the optical state of the eye, using an excimer laser beam to reshape the surface of the cornea. In successful treatments, the induced refractive change equals the preoperative refractive error.

This research (2007 Audit) has shown us that some refractive disorder groups performed better than others. For example, 79-81% of eyes with simple myopia were within 0.5D of the target refraction, while only 56-59% of eyes with myopic astigmatism achieved this result.

The implementation of nomogram calculations into the IBRA system increased the functionality, and allowed surgeons to calculate adjustment factors for nomogram optimisations. Theoretically, this should improve the outcome of patient groups, and also individuals such as patients with compound myopic astigmatism.

The 2008 Audit with spherical modification showed improvement of the predictability, but the myopic astigmatism group still achieved a lower performance than the other studied patient groups. We believed that the higher level of over-correction and distribution in eyes with astigmatic myopia was a result of inaccurate determination of treatment settings. We assumed that, without taking individual modifications of the cylinder treatment into account, the predictability could not be further improved for this group. An additional positive treatment effect we attributed to individualization of treatment settings.

At that time, commercially available software was not able to analyse refractive data patient-individually. To meet these needs, we developed a new calculation formula which we implemented into a separate module for the IBRA system. Based on the

patient's preoperative refraction, the formula individually calculated the amount of change in the treatment setting necessary to reach the target refraction more precisely.

The use of the new system had the potential to further improve the refractive outcome (patient health change). This was clinically needed to increase postoperative uncorrected visual acuity, to increase patient satisfaction, to decrease the number of follow-up visits and to decrease the rate of re-treatments. Such a treatment could also improve cost-effectiveness in refractive laser eye surgery.

A literature review showed that this was the first research worldwide that clinically evaluated the benefit of patient-individual modifications of laser treatment settings.

Aims

The aim of this research was to improve the health outcome of patients with astigmatic myopia.

Objectives

The objectives of the research were to plan and undertake a randomised controlled trial to evaluate patient individual treatment modifications with cylinder adjustments, as provided by the IBRA system.

Study design

The design of the RCT was developed in co-operation with the Research and Development (R&D) Department at Moorfields Eye Hospital NHS Foundation Trust ('Moorfields') and Professor David Gartry, Head of the Refractive Department at Moorfields. The research protocol was approved by Professor Roger Hitchings, Director of the Research Department at Moorfields, and sent to The Royal Marsden Research Ethics Committee.

The following documents were submitted to the Ethics Committee on 14 July 2008:

- Application Form (IRAS online system)
- Investigators' CV
- Study Protocol
- Covering Letter
- Letter from Sponsor (Moorfields for R&D support)

- GP / Consultant Information Sheets
- Participant Information Sheet
- Participant Consent Form
- Laser Treatment Information Sheet
- Laser Treatment Consent Form

Following a presentation of the project at the Ethics Committee meeting, and a revision and clarification of the trial protocol, we received a letter confirming favourable opinion (Appendix 6). Our trial was given the REC reference number 08/H0801/99. The trial started on 2 October 2008. Additionally, we submitted the protocol and confirmation letter to the Ethics Committee of the City University London where it was also approved.

Professor Gartry took over the part of study introduction and asking patients to participate, while I was responsible for preoperative assessments, postoperative follow-ups and data collection. For the randomisation, the R&D Department provided us with closed envelopes containing labelled paper to show either 'Standard' or 'IBRA' treatment. To simplify the process of calculating adjustment parameters, we used the developed formula and created a table with adjustment factors that could be used at any time and location without the use of the formula or a computer (Appendix 7). We treated the first participant in November 2008.

Research Funding

Parallel to the planning of the research, we applied for funding for the PhD research and for the clinical trial. We sent applications to Moorfields Special Trustees, where the research was qualified as important and necessary, but where funding was not permitted because of its ‘private practice nature’, ‘not showing an impact on current NHS treatment regimes’. We also sent an application for funding to the Swiss National Science Foundation (SNF), who responded with a negative decision for personal funding because the research was not performed in co-operation with a Swiss University, and also a negative decision for project funding because the project did 'not have an impact on the health change of Swiss Nationals.' Finally, Moorfields granted us free R&D support and statistical advice. Professor David Gartry allowed us to use his private practice set-up and his private patients for the controlled trial at no extra cost.

6.3.2. Methods

Summary of the original treatment protocol

The study design was a single-blinded, randomised controlled trial comparing standard treatment and modified treatment in laser vision correction (Figure 6.3.1.).

The aim was to establish the clinical effectiveness of patient-individual nomogram adjustments in a high-volume refractive laser practice (Figure 6.3.2. and Figure 6.3.3.).

Patients were recruited in private practice surgery at Moorfields Eye Hospital NHS Foundation Trust. Randomisation was carried out independently by the R&D Department at Moorfields. Ethic approval was awarded by The Royal Marsden Research Ethics Committee. Research Management and Governance approval was obtained from Moorfields.

The main inclusion criterion was astigmatic myopia, as defined as astigmatism of ≥1.0 D with a negative spherical equivalent (also 'compound myopic astigmatism'). Patients with corneal or retinal disorders were excluded from the trial. All participants received an information sheet (Appendix 2) to take home. If the participant agreed to take part in the study, the Chief Investigator (DSG) or Principal Investigator (BZ) obtained informed consent (Appendix 3 and Appendix 4) and arranged the appointments and, in accordance with the participant, defined the refractive target of each eye.

Depending on the treatment group, the participants either received standard wavefront LASIK treatment or modified (IBRA) wavefront LASIK treatment, both performed in a similar way with the VISX S4 laser, performed by the Chief Investigator. Slit-lamp examination was performed within 24-48 hours to confirm the LASIK flap position and 3 months later, together with subjective refraction and uncorrected and best-corrected visual acuity assessment. The data of the 3 month review was collected with the data collection sheet (Appendix 5) and entered into Excel and Minitab for descriptive and statistical analysis.

Main outcome measure was the percentage of eyes achieving a postoperative spherical equivalent (SE) within 0.5D of the target SE.

The original research protocol with detailed descriptions of the treatment settings and calculations for both groups is shown in Appendix 1.

Changes to the method and protocol

The research methods and the protocol were not changed during the study period.

Settings and data collection

- Refractive Surgery Unit, Moorfields Eye Hospital (MEH), London
- Department of Research and Development (R&D), MEH
- Centre for Health Informatics (CHI), City University London
- Health and Safety Executives' (HSE's) Research Ethics Committee (REC)

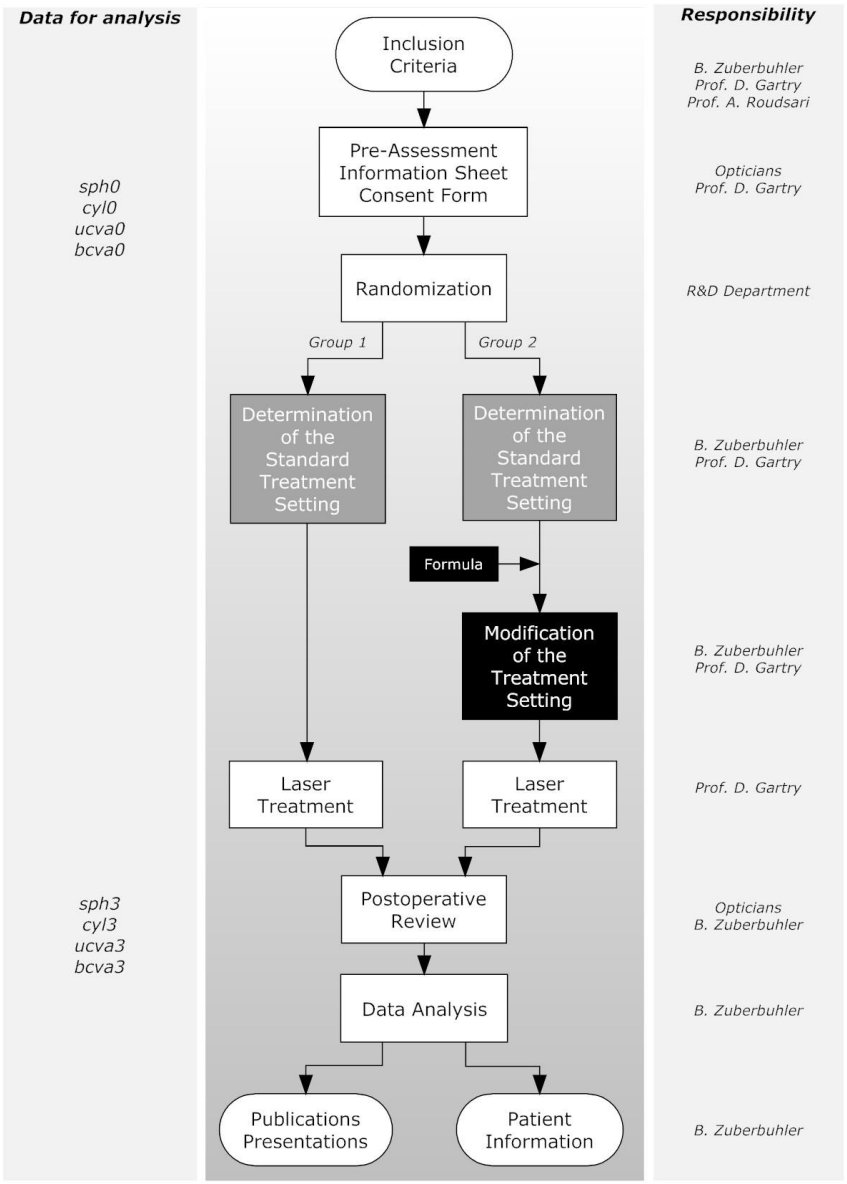


Figure 6.3.1. Research design.

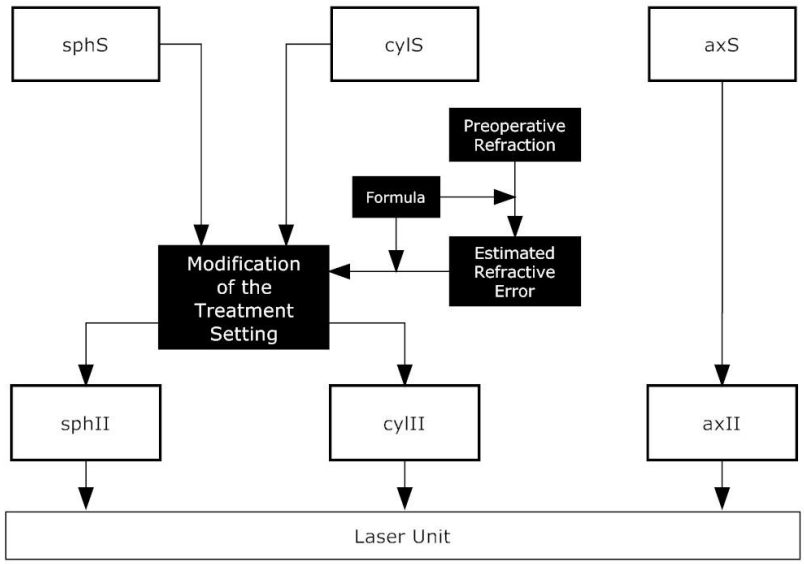


Figure 6.3.2. Modification of the treatment settings, based on the standard treatment refraction (sphS, cylS and axS).

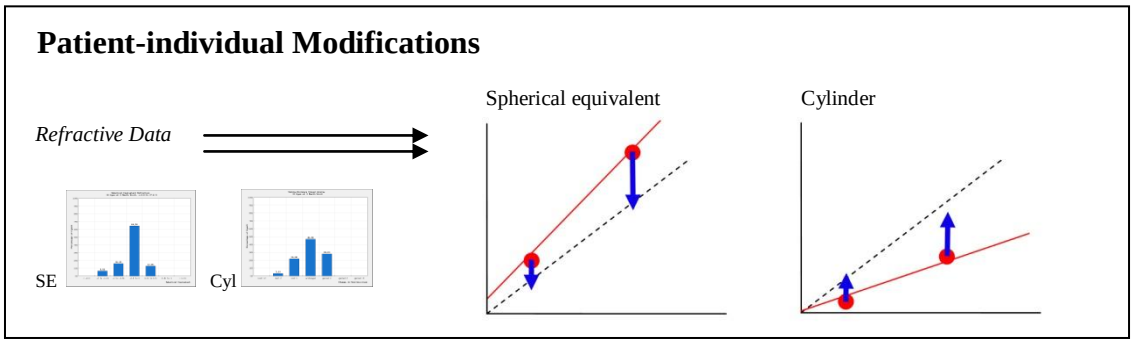


Figure 6.3.3. Patient-individual modifications of the laser treatments, based on analysis of spherical and astigmatic outcome data. Each patient received individual adjustments (blue arrows) for the sphere and cylinder correction.

Refractive error:

SEerror [%] = $18 * SE^{-0.72} + 0.5 * Cyl$

Cylerror [%] = $32 * Cyl^{-0.31}$

Modification of the treatment setting:

SE change [D] = SE/100*SEerror + 0.25*Cyl/100*Cylerror

Cyl change [D] = 0.5*Cyl/100*Cylerror

Example:

Use of above formulas for an astigmatic myopic eye.

Preoperative SE= -5.25 and Cyl=-2.25.

SEerror = 6.58 %

Cylerror = 24.89 %

SE change = 0.49 D

Cyl change = 0.28 D

Comments:

SE = preop. spherical equivalent

Cyl = preop.e cylinder

*SE **over**-correction*

*Cylinder **under**-correction*

taken off the standard treatment SE

added to the standard treatment cyl

Figure 6.3.4. Formulas for the calculation of the refractive error and the modification of the treatment setting, with comments (right side) and example.

6.3.3. Recruitment

Recruitment of participants

During the recruitment phase of the study, between November 2008 and December 2009 (13 months), 79 eyes of 45 participants were randomised into the 2 study groups.

Termination of recruitment and study

Unfortunately, the slowdown in recruiting participants forced us to terminate the recruitment process prematurely. The 'Declaration of the end of a study' form was submitted to the R&D Department in February 2010, containing an action plan, including the review of all participants and the collection of the 3 month postoperative results of all treated eyes (Appendix 8). We were aware that the numbers were too low for complex statistical analysis (underpowered), and we aimed for descriptive analysis of the results.

Follow-up assessments

At the end a total of 73 operated eyes (92%) were reviewed at the 3 month visit (Figure 6.3.5.; CONSORT style, Schulz KF 2010). We sent a reminder letter to the remaining participants, but did not receive any feedback and ultimately could not state the reasons for their 'not attending'.

Demographics

No significant difference was seen between the 2 groups regarding gender and age profile (Table 6.3.1.).

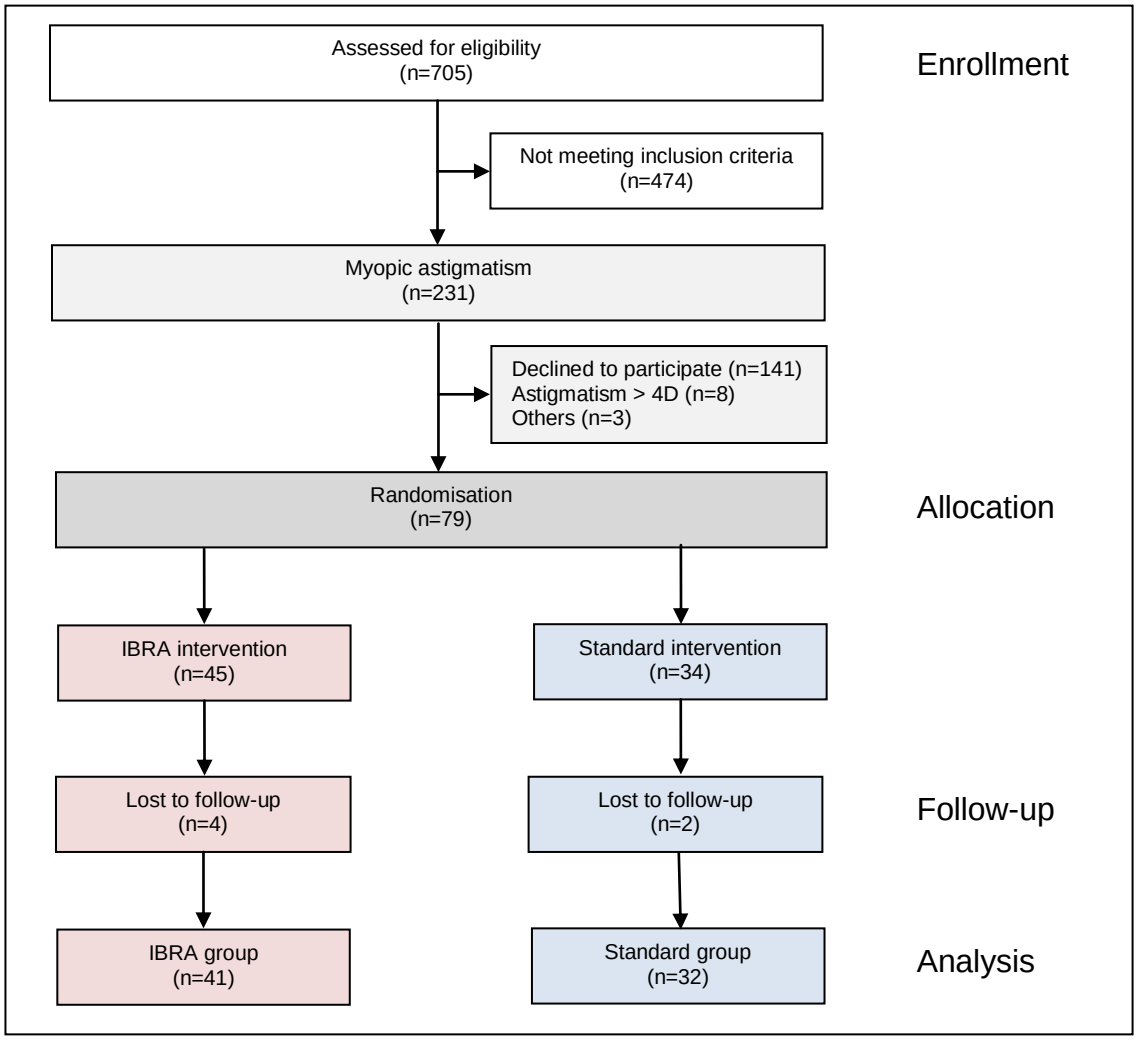


Figure 6.3.5. Flow diagram of the progress through the phases (CONSORT) with number of eyes (n) of the two randomised groups meeting the main inclusion criteria (myopic astigmatism and no ocular comorbidity).

	IBRA	Standard	P (Chi2)
Eyes	41	32	
Mean Age ± SD (y)	39.5 ± 9.6	38.3 ± 10.3	
Age <40	49%	53%	0.713
Female	68%	75%	0.530
Male	32%	25%	0.530

Table 6.3.1. Participants demographics.

6.3.4. Results

Descriptive data

A total of 73 eyes were analysed (Raw data: Appendix 9). Of these, 32 eyes were treated with the standard regime and 41 eyes with the new treatment algorithm. Statistically, no difference could be seen between the 2 study groups regarding preoperative spherical equivalent, astigmatism and best-corrected visual acuity (Table 6.3.2.).

	IBRA	Standard	P (U-Test)
Preoperative spherical equivalent (D)			
• Mean	-5.27	-5.03	0.352
• SD ±	2.49	2.32	
• Range	-10.0 to -0.6	-12.0 to -1.8	
Preoperative astigmatism (D)			
• Mean	-1.54	-1.51	0.548
• SD ±	0.64	0.65	
• Range	-4.0 to -1.0	-3.5 to -1.0	
Preoperative BCVA (LogMAR)			
• Mean	-0.03	-0.06	0.082
• SD ±	0.06	0.07	
• Range	-0.1 to 0.2	-0.2 to 0.1	

Table 6.3.2. Preoperative refractive and visual data.

Primary outcome

Primary outcome measure was the percentage of eyes achieving a postoperative spherical equivalent (SE) within 0.5D of the target SE. 51% of eyes of the IBRA group achieved a postoperative SE within 0.5D of the target. Statistically a significantly better outcome was shown by eyes from the standard group, achieving a rate of 78% (Table 6.3.3. and Figure 6.3.7. left; p=0.027). No difference between the 2 groups was seen when comparing eyes achieving their target within 1D, or when comparing eyes achieving emmetropia within 0.5D.

	IBRA	Standard	P (Fisher's)
Postoperative SE (D)			
• Mean	-0.56	-0.32	**0.049**
• SD ±	0.61	0.40	
• Range	-2.1 to 0.63	-1.3 to 0.25	
Predictability			
• Eyes within 0.5D of target SE	51%	78%	**0.027**
• Eyes within 1.0D of target SE	83%	97%	0.072
• Eyes within 0.5D of emmetropia	59%	78%	0.087
• Eyes within 1.0D of emmetropia	78%	94%	0.099

Table 6.3.3. Postoperative spherical equivalent (SE) and predictability

The mean postoperative SE of the IBRA group was -0.56D, which was significantly lower than the mean postoperative SE of the standard group at -0.32D (Table 6.3.3. and box plot Figure 6.3.6.; p=0.049).

This myopic shift of the IBRA group was also seen in the SE histogram (Figure 6.3.7., middle). Generally for both groups the higher the preoperative SE was, the higher the postoperative SE resulted (Figure 6.3.7. right).

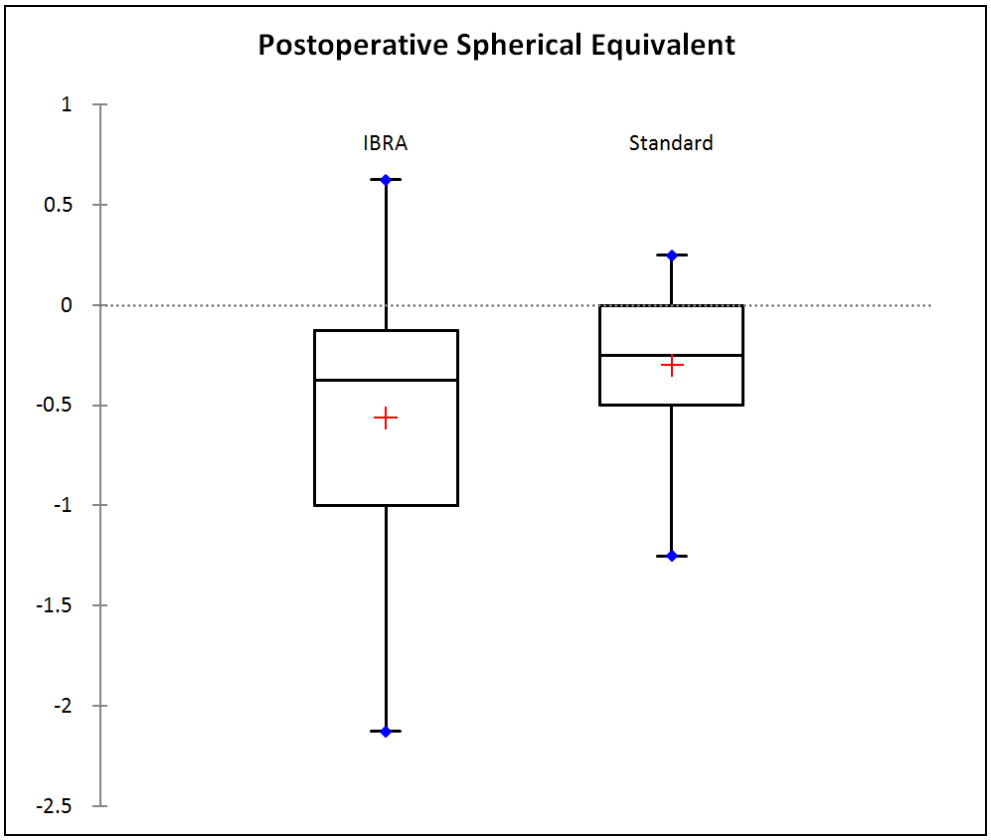


Figure 6.3.6. Postoperative spherical equivalent of the IBRA and Standard groups (p=0.049).

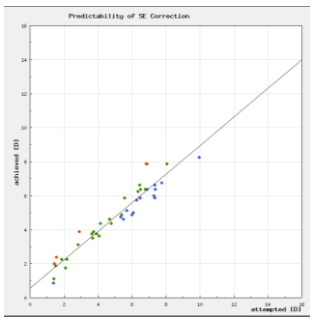
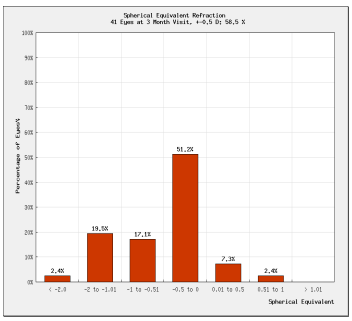
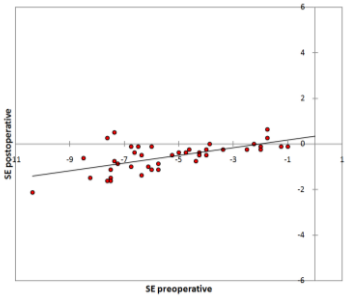
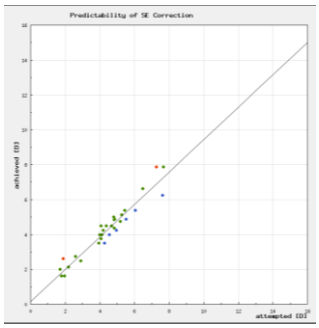
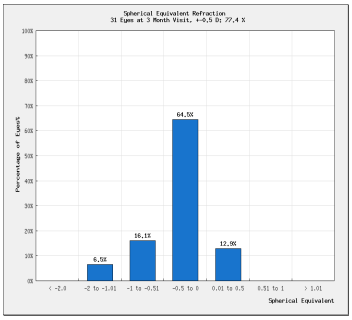
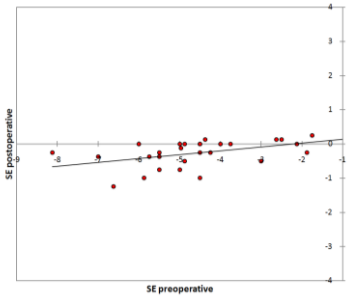
SE Predictability	SE Distribution	SE Change
 IBRA	 IBRA	 IBRA
 Standard	 Standard	 Standard

Figure 6.3.7. Spherical equivalent predictability, distribution (histogram) and scattergram.

Secondary outcomes

There was no difference between the 2 groups related to the mean postoperative cylinder or the predictability of astigmatic changes (Table 6.3.4. and Figure 6.3.8. left).

	IBRA	Standard	P (Fisher's exact test)
Postoperative subjective cylinder (D)			
• Mean	-0.35	-0.37	0.836
• SD ±	0.32	0.34	
• Range	-1.0 to 0	-1.0 to 0	
Postoperative cylinder distribution			
• Within 0.25D	63%	50%	0.340
• Within 0.50D	76%	78%	1.000
• Within 0.75D	93%	90%	1.000
• Within 1.00D	100%	100%	

Table 6.3.4. Cylinder changes (astigmatism).

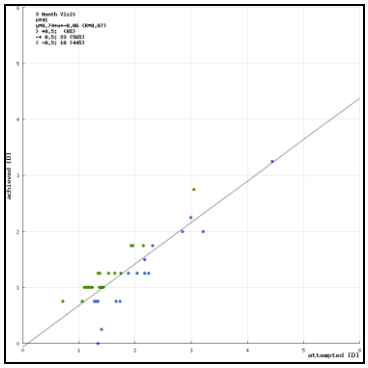
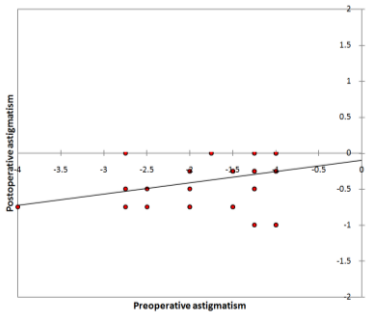
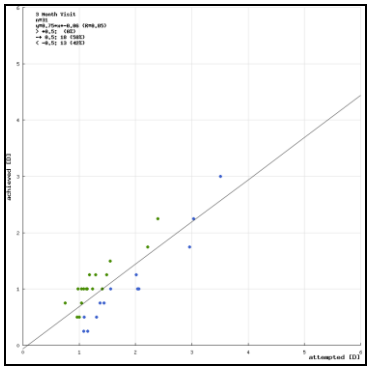
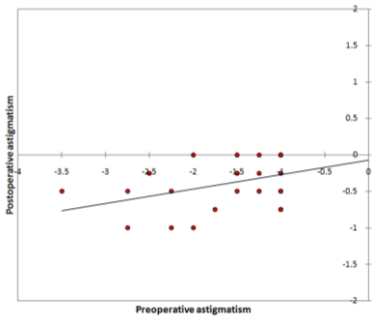
Cylinder Predictability	Cylinder Change
 IBRA	 IBRA
 Standard	 Standard

Figure 6.3.8. Astigmatic predictability and changes.

The mean uncorrected visual acuity of the standard group was better, but the difference was statistically not significant (Table 6.3.5 and Figure 6.3.9 and Figure 6.3.10 left; p=0.489). There was no difference in the mean postoperative best-corrected visual acuity. The IBRA group performed significantly better in the 'safety distribution', with numbers of eyes losing or gaining Snellen lines of best-corrected visual acuity (Table 6.3.5 and Figure 6.3.10 right).

	IBRA	Standard	P (Fisher's exact test)
Postoperative UCVA (LogMAR) • Mean • SD ± • Range	 0.12 0.25 -0.2 to 0.7	 0.01 0.14 -0.2 to 0.3	0.102
Postoperative BCVA (LogMAR) • Mean • SD ± • Range	 -0.07 0.07 -0.2 to 0.2	 -0.08 0.08 -0.2 to 0.2	0.489
Postoperative BCVA • Lost 1 Snellen line or more • Unchanged • Gained 1 Snellen line or more	 0% 58.5% 41.5%	 25% 46.9% 28.1%	**0.003**

Table 6.3.5. Uncorrected and best-corrected visual acuity

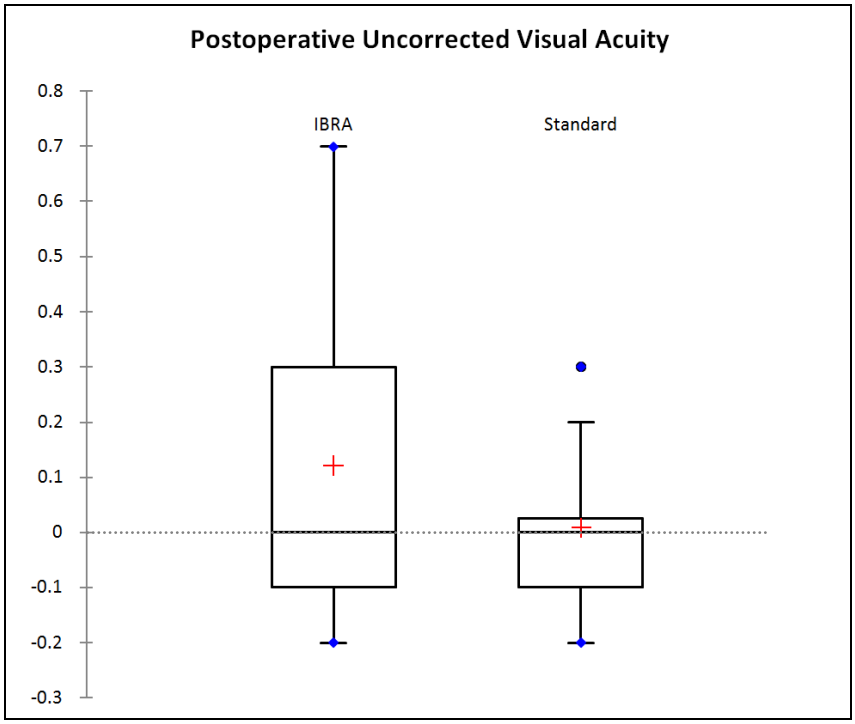


Figure 6.3.9. Postoperative uncorrected visual acuity (LogMAR; p=0.102).

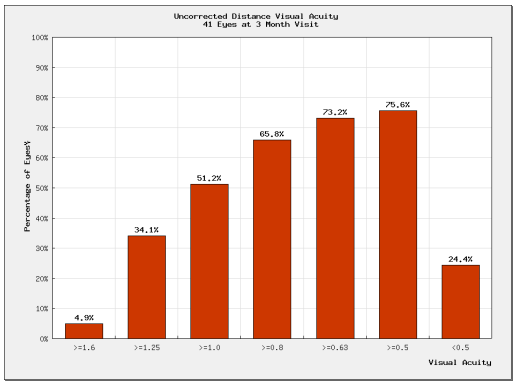
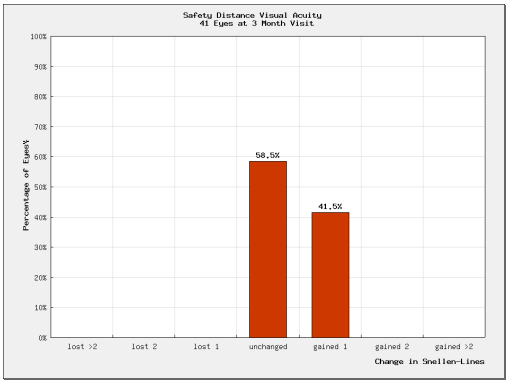
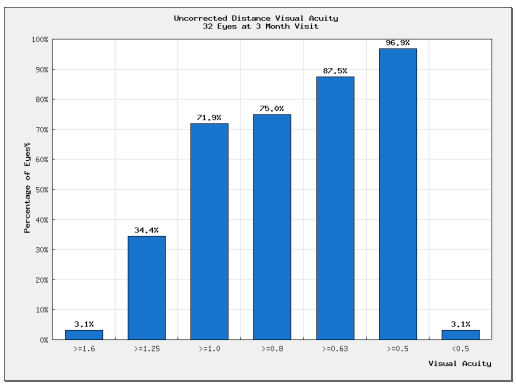
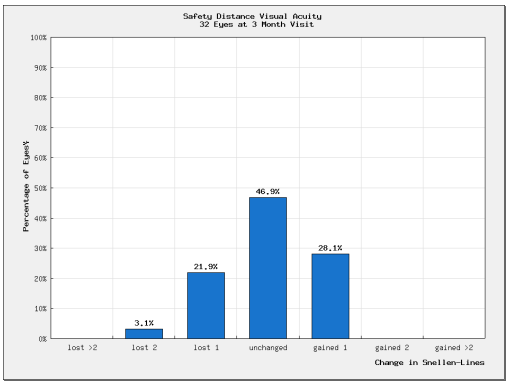
Uncorrected visual acuity	**Best-corrected visual acuity (safety)**
 IBRA	 IBRA
 Standard	 Standard

Figure 6.3.10. Visual acuity outcomes. The safety chart of the IBRA group is significantly better.

Complications

None of the treated eyes incurred any serious complication. In 7 eyes (17%) of the IBRA group and 2 eyes (6%) of the standard group, a re-treatment (enhancement) was requested by participants who were unhappy with the postoperative uncorrected visual acuity and myopic spherical equivalent (Table 6.3.6). Statistically, there was no difference between the 2 groups related to enhancements.

	IBRA	Standard	P (Fisher's exact test)
Enhancements • For myopic postoperative SE	7 (17%)	2 (6%)	0.163

Table 6.3.6. Enhancement rate

6.3.5. Discussion

Recruitment and selection

During the first 6 months recruitment was satisfying and we could meet the recruitment goals. The following 6 months showed a slowdown in the recruitment. We attributed the problems to economic and patient-related factors.

As a consequence of the financial crisis in 2009, we saw fewer patients in the private practice. In addition, these patients were more careful with spending money and requested 'confirmation' that their 'investment' in their eye treatment guaranteed best outcomes. Generally, patients expected perfect laser vision correction. However, the nature of randomised controlled trials is such that this cannot necessarily be guaranteed, and many patients were confused and sometimes frustrated having been informed about the trial and its aim 'to find the best possible treatment'. They could not understand that 'the best surgeon' was not sure about the 'best treatment'. At this stage many patients decided to postpone their operation until the question of the best treatment could be answered. Some very sceptical patients even criticised the surgeon's competency and wanted to look for another surgeon 'who would provide them with the best treatment'.

To improve recruitment, we tried to change current practice. We modified the scheduling and the information part of the assessment. We took more time to explain all the details, and we discussed the background of the trial in greater depth. However, we

still wanted to remain neutral and we did not want to influence patients in their decision making process.

Unfortunately, despite the extra effort and changes, no significant improvement in the recruitment rate ensued, and we discussed the situation with the R&D department with a view either to further changes or termination. We agreed to set an interim recruitment target over a period of 2 months but, ultimately, we were unable to meet this target.

Overall we recruited 73 participants with pre- and postoperative data for analysis. Clearly, we recruited fewer patients than the original sample size estimate of 128 participants with 90% power (or 98 participants with 80% power). We therefore performed mainly descriptive analysis. We calculated p-values for presentation purposes only, with the idea that it might help in the determination of outcome tendencies.

Clinical outcomes

With the individual nomogram adjustments, we aimed to improve the predictability of the treatment. Each patient received an individualized treatment adjustment aiming for a postoperative spherical equivalent (SE) more myopic and closer to emmetropia. A second aim was to reduce the scatter, and to bring the outcomes closer together (smaller standard deviation), by adjusting the cylinder component.

The analysis of the data showed that participants receiving the IBRA treatment showed a significant myopic change in SE. The postoperative SE of the IBRA group was 0.24D more myopic then the SE of the standard group. Based on the formula that was used for the calculation of the adjustments, this myopic shift was intended to be between 0.22D and 0.47D, in linear correlation to the preoperative sphere (0.22D for sphere with -8.5D; and 0.47D for sphere with 0 to -0.5D; average of 0.37D). As we aimed more for mild under-correction, the achieved myopic shift of 0.24D was satisfying (65% of intended change) and in accordance with our first aim of achieving myopic correction.

The distribution of the postoperative SE of the IBRA group, as compared to that of the Standard group, showed a higher standard deviation and a wider range (0.61D compared to 0.4D). In combination with the myopic shift, this resulted in a significantly lower percentage of eyes ending up within 0.5D of the target SE (51% for the IBRA group and

78% for the standard group). This was in opposition to our second aim, and we could not find an explanation for the increase in scatter. Generally, the IBRA treatment (as used for the 2007 Audit) showed an over-correction for participants with a low preoperative SE, and an under-correction for those with a high preoperative SE. No such tendency could be seen for the standard treatment in the controlled trial.

Apart from spherical modifications, the IBRA treatment included adjustments for the cylinder, based on our assumptions. This should have contributed to a decrease of the distribution. However, the analysis of the postoperative mean cylinder of the 2 groups did not show a benefit from the performed cylinder adjustment. In fact, there was no difference between the 2 groups from a statistical point of view. The intended cylinder changes of up to 0.36 D (average of 0.14D), depending on the preoperative cylinder, seemed to disappear in the overall treatment (mean induced cylinder change was 0.02D, only 14% of the intended change).

In 2007, the average postoperative SE for patients with myopic astigmatism was 0.13 D (± 0.48 D), and 59% of eyes were within 0.5D of the target SE. Participants of the standard group of this RCT were treated with the same 2007 Audit parameters, but their results were much more myopic and generally better; the mean postoperative SE was -0.32 D (± 0.40 D) and 78% of eyes achieved their target SE within 0.5D. How can we explain this difference? Although we are not aware of any software or hardware change of the laser unit we assume that, with the move from the older location on the 2nd floor at Moorfields Eye Hospital to the new treatment suite on the 5th floor in February 2009, the machine started performing slightly differently, resulting in a myopic shift (we consider this also as a source of bias). This, of course, had an implication on our IBRA treatment too, showing significant under-correction with a postoperative SE of -0.56 D (±0.61 D) and only 51% of eyes achieving the target SE within 0.5 D. Linked to the higher myopia, the participants' UCVA was lower.

Taking into account all changes, including the attempted myopic change from the IBRA algorithm, the wider scatter of the IBRA outcomes, and the unintended myopic shift from the laser machine, we have to conclude that the better treatment in this trial was the standard treatment. Compared to the literature our results meet the standards, which are between 50-75% for eyes achieving the SE target within 0.5D.

Safety and enhancements

None of the eyes of either group had signs of infection or inflammation. None of the eyes of the IBRA group lost one or more Snellen lines of best-corrected visual acuity (safety analysis). In fact, the IBRA group showed a significantly better best-corrected visual result with a higher percentage of eyes remaining unchanged or gaining one or more Snellen lines (p=0.003). The reason for this remained unclear.

Although the IBRA modifications worked as planned, the unintended additional myopic correction from the laser machine made the ultimate outcome short-sighted. The higher amount of eyes with significant postoperative myopia in the IBRA group reduced the potential for good uncorrected visual acuity, and increased the rate of re-treatments (enhancements). For this trial, we consider this myopic over-correction as adverse event, although the difference between the numbers of enhancements between the 2 groups was statistically not significant.

Strengths of the study

This study has shown that the used formulas work in a safe way and that the nomogram adjustments were effective in changing the spherical equivalent as attempted.

Weaknesses of the study

The individualisation of the nomogram adjustment did not influence the scatter positively, or reduce the postoperative astigmatism. The other main weakness was the reduced sample size. Although the number of participants was quite high for a randomised trial in private practice, the study ultimately remained underpowered and the statistical results have to be viewed with this understanding.

Limitations of the study and generalisability

The formulas we developed in this research were based on preoperative and postoperative data from our laser centre with a particular equipment and treatment regime. As equipment and treatments differ from surgeon to surgeon, the presented formula cannot be used in another set-up without modifications. However, we believe that other laser equipment would not behave differently and that the change we intended to achieve would not be better or worse with different set-ups. Therefore, we do not recommend repeating this trial in the same form.

The patient individual approach for cylinder adjustments did not show a significant improvement in patient outcomes (scatter) and the individual spherical changes were not superior to general modifications, as presented in the audit cycles in Section 6.2.

6.3.6. Conclusions

Patients judge the success of refractive laser treatments by post-operative visual acuity and the end of spectacle dependence, both of which are ultimately determined by the refractive outcome. This in turn depends on the spherical equivalent distribution around emmetropia and the postoperative amount of astigmatism, both important measures of the effectiveness and precision of laser vision correction.

This research has proven that individual nomogram adjustments are effective and safe in changing the refractive outcome. The adjustments worked much better for spherical changes, and seemed to be nearly ineffective for small cylinder changes. Overall, the individualisation did not show a benefit over general nomogram modifications, as performed for the refractive Audit in 2008. They did not show an improvement regarding the scatter of the results either. Patients with myopic undercorrection were more likely to request further treatments (enhancements).

Recommendations for health-care provision

The best way to change the refractive outcome of patients with combined myopic astigmatism is to analyse a series of results (approx. 50 treated eyes) and to perform simple linear regression analysis from attempted versus achieved spherical equivalent refraction. The surgeon can then use the y-intercept (‘b’) from the calculated equation of the straight line ($y = m*x + b$) for general nomogram modifications. If the slope (‘m’) is far from the ideal 45 degree line (value of 1.0), an additional fix amount of adjustment can be added to the nomogram adjustment for patients requiring a higher amount of correction. The best threshold for adding extra nomogram adjustments has been shown to be around 6D of correction.

The introduction of Revalidation by The Royal College of Ophthalmologists brings with it a need for large amounts of comparative data which can be referred to by practising clinicians. Selecting and setting standards as a basis for revalidation can be challenging, especially with the large number of variables involved. It is known, for example, that

refractive outcomes of LASIK are influenced by the surgeon's experience and familiarity with the technique (Teus 2007).

Implications and recommendations for future research

Improving the scatter of treated eyes remains an unsolved task. New approaches and research are required to investigate the possible impact of other factors, including healing conditions, ophthalmic treatment (antibiotic and anti-inflammatory eye drops), ablation profiles, and more detailed patient characteristics (ethnic origin, living and working situation, etc).

Implications for IBRA and its development

This research has shown that it is possible to implement a calculation algorithm into IBRA which provides the surgeon with automated nomogram adjustments. However, the implementation of individual adjustment factors into patient treatment is more complex, and has shown little benefit to the refractive outcome. We therefore recommend not to develop individual nomogram adjustments further, but to focus on general treatment modifications based on refractive disorder groups. This concept should be implemented into the next IBRA version and may include the creation of adjustment tables for the different refractive groups.

6.3.7. Acknowledgements

We would like to give special thanks to Professor David Gartry for his generosity in undertaking this difficult trial within his private laser practice, a highly competitive field of ophthalmology.

6.3.8. Other information

Registration number: 08/H0801/99
Original protocol: Appendix 1
Funding: Professor David Gartry (Chief investigator and surgeon)
Research Department, Moorfields Eye Hospital

6.4. Management of refractive data entry processes

6.4.1. Introduction

The introduction of electronic medical records has changed the format used to document individual patient care and medical history. Traditionally, medical records have been written on paper and kept in folders. With electronic records, the database of the system is updated either by manual or automated data entry. In Ophthalmology, data is entered manually. In other fields, for example in multicentre research, optical character recognition (OCR) has become a viable technique for automated data entry (Hardin 2005).

Generally, data entry systems face 2 major challenges:

- Minimising data entry errors (validation)

  The introduction of computer based data entry forms and data collection tools have led to improvements in accuracy of the entered data. In 1999 Hunter et al. compared paper-based and electronic acquisition of data in an audit analysing laparoscopic surgical procedures. An independent chart review of 22% of all records showed that the electronic data acquisition had superior data and coding accuracy ($p<0.01$). Another method to improve the data entry process is to validate the entered data at the stage of data entry. Kruse (2008) showed that built-in functions of validation can effectively detect entry errors, and can provide rapid feedback to the collector. Additional positive influence on the data accuracy can be achieved by training the data collectors. This can include written instructions (e.g. a handbook for standardised data collection), a review of a standard data set and its definitions, a system walk-through and specific practice (Jansen 2005; Arts 2003).

- Optimising time requirements for the data entry process (efficiency).

  The challenge of data entry efficiency is complex and determined by the user-interface, the system response (e.g. speed), the data set, and user-individual factors such as cognitive skills with data handling, technical abilities, and time pressure. Different approaches are used to assess the resource utilisation. One method is to compare the efficiency of performing a specific task on 2 different systems by the same users. Another approach is to observe and compare different users performing the same data entry processes with only one system. Efficiency

can then be determined by evaluating the time requirements or number of steps required to manage the data entry. Information gained from such assessment can enable improvement of human computer interaction (user interface). Typical optimisation processes include a reduction of the total number of steps or the percentage of mental effort, required for the tasks (Saitwal 2010).

Recently the cost of data entry processes, and cost-effectiveness in providing the same data recording accuracy, has become an important criterion (Murphy 2009). In 2009, Pavlović et al. could prove that electronic data collection processes were able to decrease data collection costs by up to 55%; whereas in less developed countries organisational, managerial and social challenges must be addressed beyond technical and financial aspects (Ndira 2008).

For this research we were looking at the collection of refractive data, formed by a distinctive set of parameters, such as the sphere, cylinder, cylinder axis, and others (Kaye 2002). The recording of refractive data is a specific process, comprising completion of a certain number of data entry fields, usually with results from preoperative and postoperative subjective refraction. We have chosen to assess time requirements at different steps of this data collection process from multi-user single-system assessment.

Data can be collected in different ways. Some surgeons prefer to enter the data stepwise alongside patient visits, while other surgeons prefer to collect a staple of patient records, after the patient has been discharged, to enter the data in one go. From personal experience, the time needed for data collection is usually overestimated by the collector (surgeon); and underestimated by the developer of the system. In fact, there is a general perception amongst refractive surgeons that data collection and entry into software systems is time consuming, and therefore detracts from the delivery of good clinical care.

Not long ago, the collection and analysis of refractive outcome data, as provided by IBRA, became an increasingly important requirement of refractive surgery practice. This data can be used to demonstrate the high quality results of an individual to the patient, and also to external commissioners. The Quality and Revalidation Initiatives of

The Royal College of Ophthalmologists underpin this importance in the provision of auditable outcomes of surgery.

The aim of this evaluation was to analyse the time taken to input data into the IBRA system, and also to analyse different methods of data entry and their relative efficiency.

The objectives were:

- To compare the different methods of data collection (stepwise, one-step).
- To analyse the time effort for different steps of the data collection.
- To identify the most efficient way of collecting data.
- To analyse time and learning curve effects.
- To identify flaws in the process of data collection, which may then help to improve future versions of IBRA.
- To record a minimum of 1,000 data entries for this evaluation process.

6.4.2. Methods

This was a user-related, behaviour-based system evaluation. Three specific software modules were designed and implemented into the basic IBRA code for logging (Module A) and analysis (Module B and C) of data entry processes of each user. Because a high amount of data was expected to be recorded, all logging processes were developed as automated routines.

Data logging

Module A was used to measure the time each individual user required to enter data into the database at 3 different parts (sections) of the data collection pathway (Figure 6.4.1). The first part of data collection was related to the demographic patient data (T1). During the second part the user entered the preoperative and surgical data (T2); and the third part was for the collection of postoperative (follow-up) data. The total time required to enter a full set of data for one case (= one treatment of one eye) was calculated by adding the times of all 3 parts (T Total = T1+T2+T3).

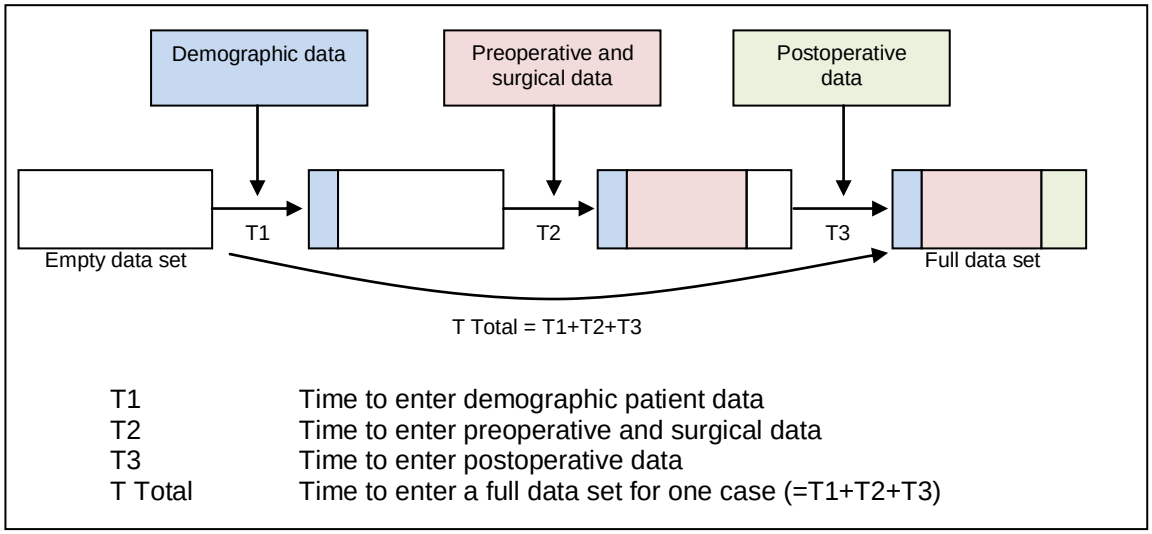


Figure 6.4.1. Data logging at different steps of the data entry process.

The data recording started in December 2008. All recorded data was stored in a MySQL database (Table 6.4.1.). In particular, the following set of data was collected each time a user was entering data into IBRA (= 1 data entry process):

- id: individual file id
- date: date of the data entry
- userid: the user's id
- caseid: the patient's case id (treatment id)
- part: step of the data collection (T1, T2 or T3, see above)
- time: the time in seconds taken for data entry for this part

	Feld	Typ	Kollation	Attribute	Null
	id	int(10)			Nein
	date	date			Nein
	userid	int(10)			Nein
	caseid	int(10)			Nein
	part	int(10)			Nein
	time	int(10)			Nein

id	date	userid	caseid	part	time
188	2009-01-05	110	6514	1	240
189	2009-01-05	110	6513	1	607
190	2009-01-05	100	6518	1	68
191	2009-01-05	110	6519	3	39
192	2009-01-05	110	6522	1	264
193	2009-01-05	110	6523	3	30
194	2009-01-05	110	6524	3	18
195	2009-01-05	110	6526	3	42
196	2009-01-05	110	6528	3	29
197	2009-01-05	110	6530	3	21
198	2009-01-05	110	6529	3	38

Table 6.4.1. Structure and data example of the MySQL database from the logging process.

Data analysis and presentation

For the analysis and presentation of the logged data, Module B was developed based on PHP programming. Module B was able to calculate mean, standard deviation and range of the time taken in seconds for each part of the data entry process (T1, T2 or T3). These results were presented in table form on a web site accessible only by the investigators.

With the implementation of Module C, the logged data could be presented in scattergram form, with the x-axis showing the date of the data entry and the y-axis showing the length of time needed. The programming of this module required the open-source, graph-creating, PHP library 'JpGraph' that could be used by the PHP scripts. The graphs were presented in a HTML media container on the web site.

Patient data / parameters

Up to 55 different parameters were entered for each patient treatment (Table 6.4.2.).

	Minimal set (22 parameters)	**Standard set (42 parameters)**	**Extensive set (55 parameters)**
Patient data	Patient ID Surname	Patient ID Surname First name Sex Date of birth Code Diagnosis	Patient ID Surname First name Sex Date of birth Code Diagnosis Past ocular history Past corneal history
Preoperative data	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA Wavefront refraction sph Wavefront refraction sph Wavefront refraction sph Pachymetry IOP Scotopic pupil Optical zone	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA Wavefront refraction sph Wavefront refraction sph Wavefront refraction sph Pachymetry IOP Scotopic pupil Optical zone Transition zone Keratometry K1 Keratometry K2 Keratometry K2 Ax
Excimer data	Eye Date of operation Method Intervention Target refraction sph Target refraction cyl Target refraction ax Refractive treatment sph Refractive treatment cyl Refractive treatment ax	Eye Date of operation Method Intervention Target refraction sph Target refraction cyl Target refraction ax Refractive treatment sph Refractive treatment cyl Refractive treatment ax Physician adjustments sph Physician adjustments cyl Physician adjustments nomo Flap technique Excimer laser type	Eye Date of operation Method Intervention Target refraction sph Target refraction cyl Target refraction ax Refractive treatment sph Refractive treatment cyl Refractive treatment ax Physician adjustments sph Physician adjustments cyl Physician adjustments nomo Flap technique Excimer laser type Laser program Hinge position Ablation aperture Ablation depth
Postoperative data (3 month)	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA IOP Satisfaction Haze	Manifest refraction sph Manifest refraction cyl Manifest refraction ax Distance UCVA Distance BCVA IOP Satisfaction Haze Keratometry K1 Keratometry K2 Keratometry K2 Ax

Table 6.4.2. Data collection sets: minimal set, standard set and extensive set.

6.4.3. Results

A total of 1,898 data entry processes were recorded from 11 different IBRA users over a period of 12 months.

A first gross analysis of user data entry method allowed us to divide the users into two main groups regarding their entry technique.

- One group of 5 users performed a *stepwise* data collection with separate data entry for demographic data, preoperative/surgical data and postoperative data. The data based on a standard data set (Table 6.4.2) and was entered along with the patient review. This could be seen in a data entry pattern with recurrent entry processes, often in weekly intervals (e.g. Figures 6.4.2.).
- The 6 users of a second group preferred to enter data in *one-go*. The preoperative, surgical and postoperative data of up to 100 treated eyes was entered into IBRA after the final clinical visit. Two users entered a standard set, 1 user an extensive set, and 3 users entered a minimal data set.

Stepwise data collection

We analysed 444 processes of demographic data collection. A mean of 62 s was required to enter the 7 demographic parameters of a standard data set (Table 6.4.3. and Figure 6.4.2.). The analysis of 213 processes of preoperative and surgical data collection showed that users required a mean of 257 s to collect the 27 parameters of this part (Figure 6.4.3.). Finally, we analysed 705 processes of postoperative data collection. A mean of 51 s was required to enter the 8 postoperative parameters of the standard data set (Figures 6.4.4.). Summarising all 3 parts resulted in a mean of 370 s (6 min 10 s), which was required to enter a full standard data set for one patient (42 parameters).

Parameter	N	Mean	± 1 SD	Range	Figure
T1	444	62 s	± 19 s	30 s - 100 s	6.4.2
T2	213	257 s	± 204 s	74 s - 934 s	6.4.3
T3	705	51 s	± 31 s	10 s - 178 s	6.4.4
Total		**370 s**			

Table 6.4.3. Time requirements (mean and SD) to enter demographic data (T1), preoperative and surgical data (T2) and postoperative data (T3) for a standard data set with 42 parameters. N = number of analysed data entry processes.

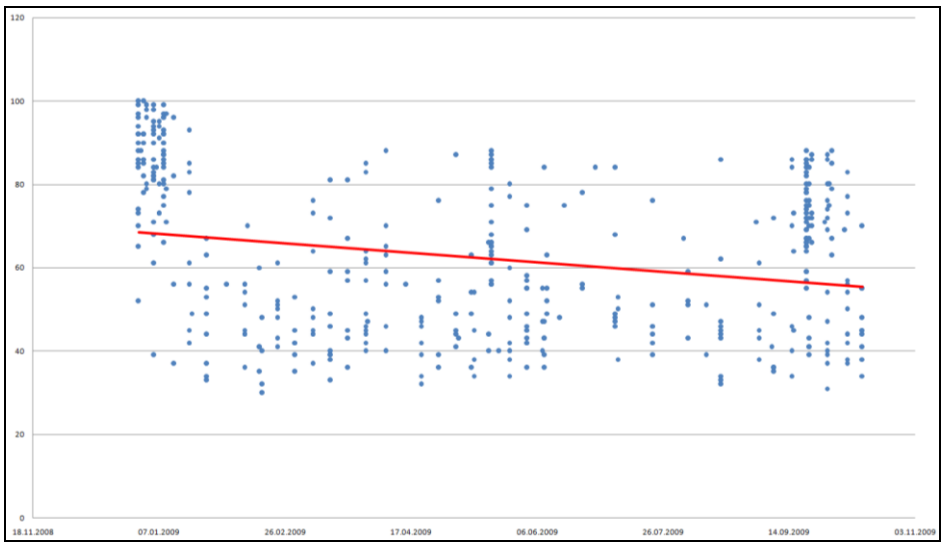


Figure 6.4.2. Data entry of demographic data of all users (step 1, T1).

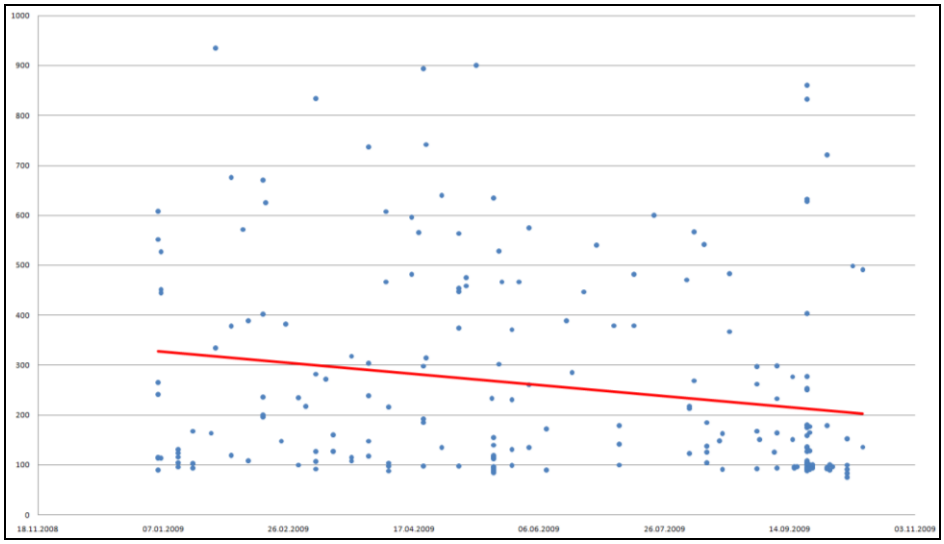


Figure 6.4.3. Data entry of preoperative and surgical data of all users (step 2, T2).

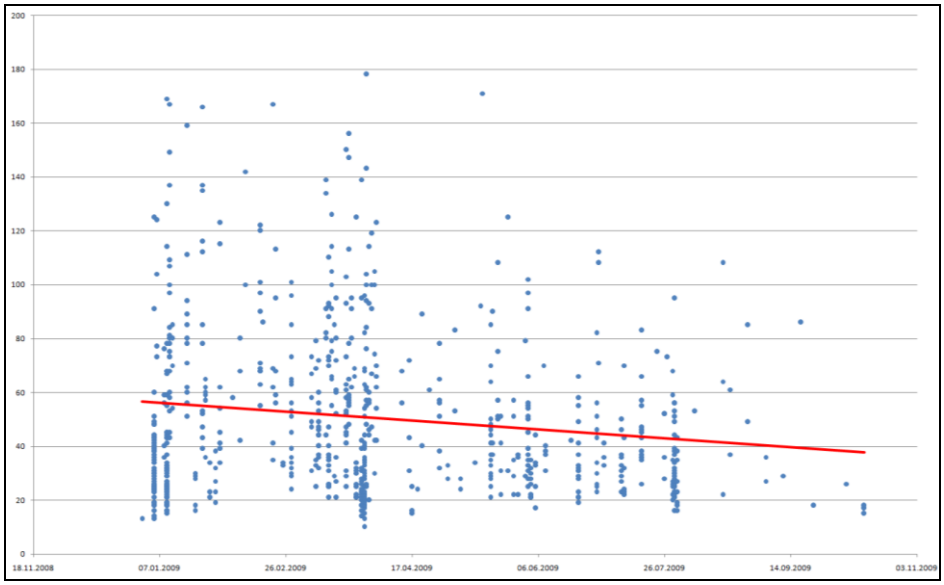


Figure 6.4.4. Data entry of postoperative data of all users (step 3, T3).

Learning effects

The analysis of 180 processes of postoperative data collection for one particular user, a beginner, revealed a reduction of time taken over time (Figure 6.4.5). The statistical comparison of the time requirements at the beginning and 2 months later showed a significant improvement in efficiency (Mann-Whitney U-Test, $p<0.0003$, Figure 6.4.6). Learning effects reduced the time requirement by approximately 26%.

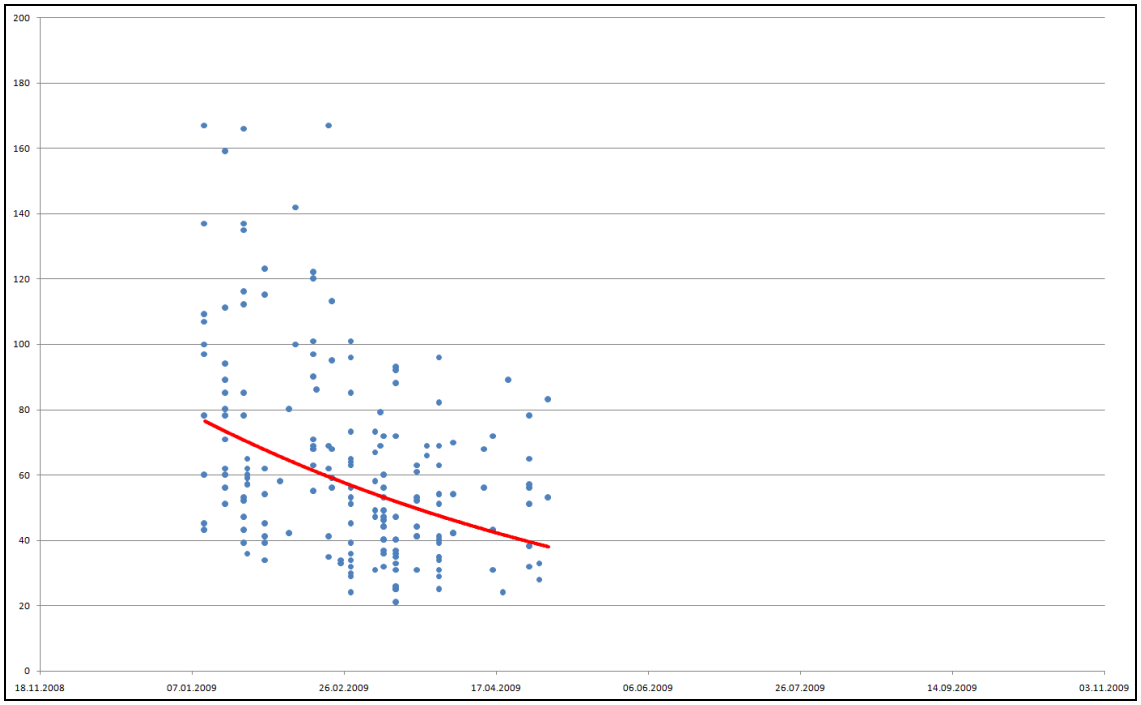


Figure 6.4.5. Stepwise data entry. Each blue dot in this figure represents a data entry process. This example shows the same user entering postoperative data (T3) into IBRA. The vertical position of the dot (y-axis) provides information on the time in seconds required for data collection. The x-axis shows the date the entry was performed. The data entry pattern reveals a weekly data entry process (mostly Saturdays). Curve fitting analysis (red line) demonstrated a significant reduction of time requirements over time ($p<0.0003$).

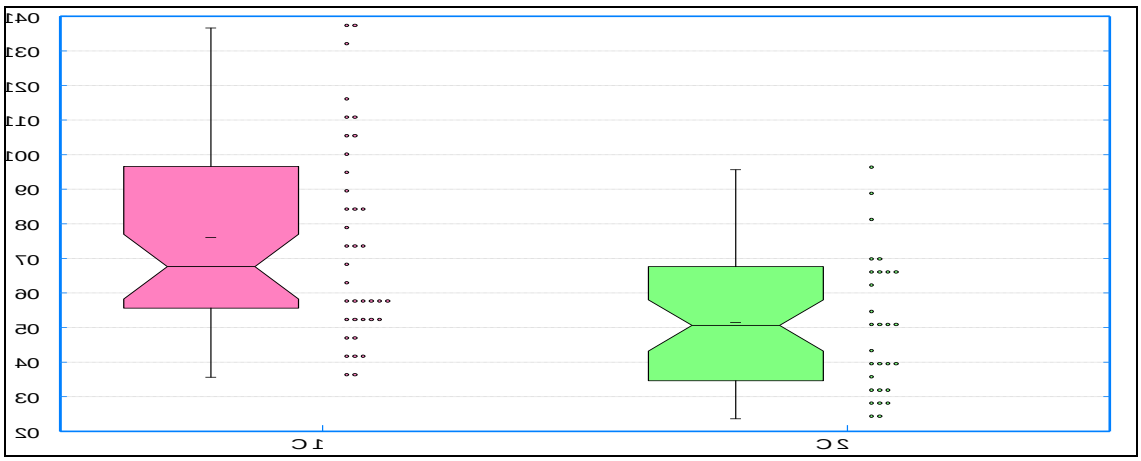


Figure 6.4.6. Stepwise data entry. The left box plot (C1) shows the time in seconds required to enter postoperative data (T3) in the first months of IBRA use. The right box plot (C2) shows the time requirements two months later. The reduction was statistically significant ($p<0.0003$).

Data entry in one-go

The analyses of the data entry processes from users performing the 'one-go' method showed users entering 3 different sets of data, each with a different number of parameters: minimal, standard and extensive.

Three users entered the minimal data set. This consisted of 22 parameters, allowing the calculation of 7 of 10 refractive outcome analyses. Two users entered the (recommended) standard set of data consisting of 42 parameters and allowing production of all 10 refractive outcome analyses. Finally, one user entered 55 parameters for each treatment into the IBRA database (extensive set). Although more data was entered, this did not increase the numbers of possible outcome analyses. The benefit of the additional data was the possibility it offered for future data analysis using a combination of IBRA, Microsoft EXCEL and statistic software.

The analysis of 441 one-go data entry processes showed that it required a mean of 131 s (2 min 10 s) to enter all 22 parameters of a minimal data set (Figure 6.4.7. and Table 6.4.4.). The mean time that was required to enter a standard data set with 42 parameters was 275 s (4 min 35 s), with a range between 140 s to 519 s. The mean time to enter the extensive data set with 55 parameters was 620 s (10 min 20s, Figure 6.4.8.).

Parameter	N	Mean	± 1 SD	Range	Figure
Minimal set (22 parameters)	441	131 s	± 61 s	55 s - 492 s	6.4.7
Standard set (42 parameters)	71	275 s	± 103 s	140 s - 519 s	-
Extensive set (55 parameters)	85	620 s	± 205 s	139 s - 1258 s	6.4.8

Table 6.4.4. Time amount required to enter a minimal set, a standard set and an extensive set of data with the one-go method. N = number of analysed data entry processes.

Data entry intervals

Independent from the entering method (stepwise or on-go), we could identify 2 main patterns of data entry regarding the date and frequency the data was entered (intervals): some users entered the data on a regular, often weekly basis (see Figure 6.4.5.), and others entered the data block wise, e.g. once every 6-9 months (Figure 6.4.7.)

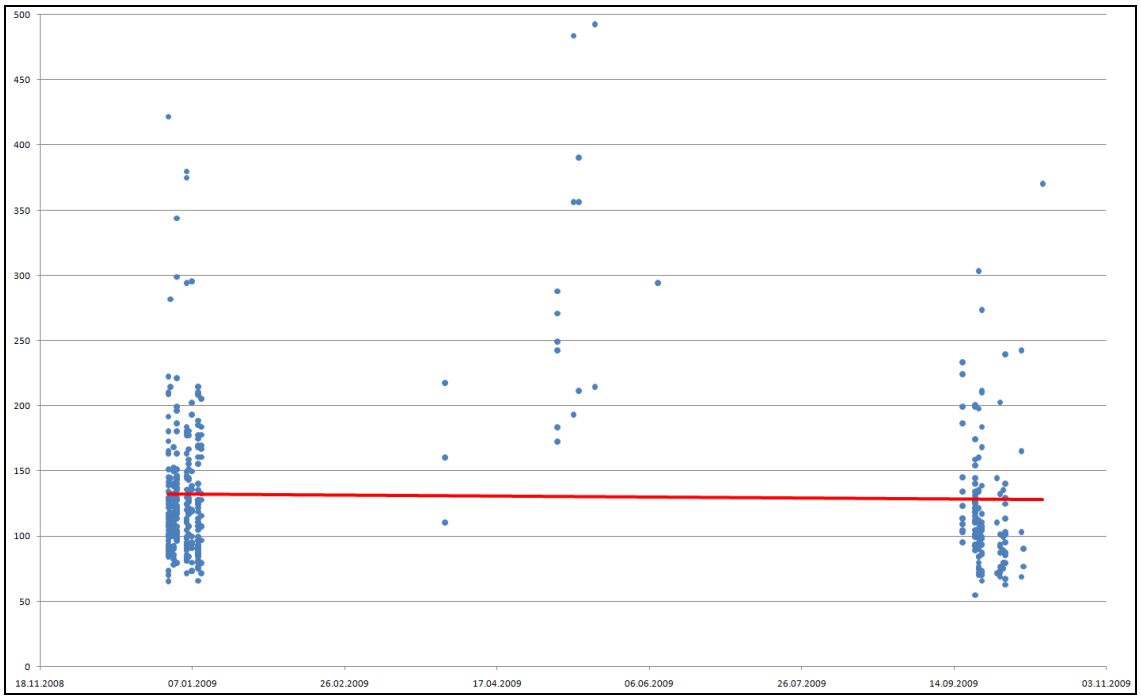


Figure 6.4.7. Data entry in one-go (minimal set). Each blue dot in this figure reflects a data entry process by the same user. In this example, 221 cases are shown and an average of 139 seconds was required to enter a minimal data set with 22 parameters.

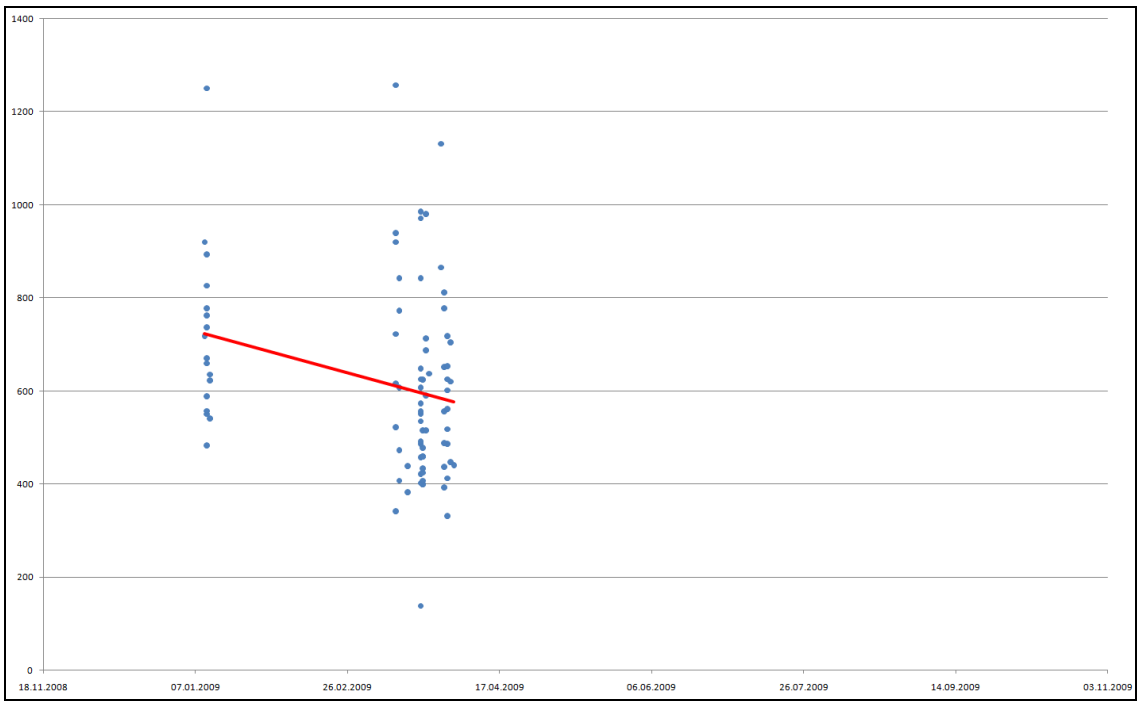


Figure 6.4.8. Data entry in one-go (extensive set). A total of 112 cases were entered by single users. An average of 610 seconds was required to enter an extensive data set with 55 parameters. The data entry process was repeated 2 months later. The standard deviation was large, maybe due to a complex search process to find the results of all 55 parameters. In particular, the collection of past ocular and medical history can take some time; and some patient files consist of more than 1,000 pages.

6.4.4. Discussion

Electronic health record systems face barriers to their implementation by healthcare service providers. One of the main barriers to implementation is the perceived additional time required to input data into the system. This study evaluates the data entry management and the time requirements for a large series of data entry processes by different users.

Primary outcomes

We have shown that it requires a mean of 6 min 10 s to perform a standard data collection with 42 parameters using a stepwise data entry method. The most time demanding step was the entering of preoperative and surgical data, requiring three quarters (70%) of the total time. This step required completion of 27 of the 42 standard set fields (64% of fields) placed at 2 different sites.

This evaluation showed that the process of data entry could be sped up for the same amount of data by an average of 95s per process when using the one-go data entry method instead of the stepwise procedure. With an average of only 275 s for a standard data set, this method would allow entry of 13 complete cases into IBRA in 1 hour.

The data entry process can further be accelerated by minimizing the amount of data entered. Although this will reduce the amount of outcome analyses that can be performed, some surgeons might prefer this compromise. Another disadvantage of minimal data sets is that they do not allow complex data separation on the basis of patient data or excimer data (see table 6.4.2.).

Learning curve effects

The results from this evaluation showed that the data entry process was subject to learning curve effects, with a reduction in the time requirements by 26%. Although cognitive psychology has explained the variability in performance and has shown that speed-up is ubiquitous (RITTER), no such evidence has been published for the collection of complex refractive data. This study showed that the improvement was slow and limited after a period of approximately 8 weeks (flat learning curve, HERMANN 1885 and BILLS 1934). Based on these results, and the knowledge that the completion of most tasks get faster with practice, we expect a general increase in efficiency following an introduction period.

Limitations of the evaluation

The study uses the responses of a variety of individuals who were unaware of the time recording at each step. Clearly this process is subject to ability variation among the users. This variation is perhaps unimportant, though, as a variety of skill levels probably better represents the reality of clinical practice where some users may be adept at using IT systems whilst others may be novices. Secondly, the method of time collection relied upon the input of certain pieces of data to be recorded as a complete event.

In a review of the literature regarding this subject, it is clear that there is a concept of time efficiency which has been explored in a variety of papers, with differing approaches. Most papers adopt either a qualitative or quantitative approach to the benefit of health informatics. Our particular study adopts a quantitative approach to the time required to complete certain fields of data as a measure of the usability of the

system. Of course, this does not examine the quality of the data outputs or the quality of the data input process. Indeed, examining one system in isolation will not provide objective data about this data system in comparison with others available commercially for this particular application. However, this study is not concerned specifically with the application, rather the time required and the process of using it, in terms of impact on time for a busy surgeon. Thus comparative data is not essential. In future, however, it may be instructive to compare this software with other packages to provide comparative data.

The methodology of this study did not investigate the role external factors contribute to the time efficiency of clinicians. This perhaps needs to be better understood in order to evaluate how clinicians are most likely to use such software in their daily practice. Also the technical ability of clinicians was not assessed; therefore the group of 11 may have had widely differing experience with IT systems. This will certainly have an impact on their organizational abilities in terms of when data was entered, and also the speed at which they navigate the system. This issue was mitigated to some extent in this study, by the demonstration of the learning effect of using the system over time.

The true time impact of EHR systems must consider the data entry process by users, as in this study, but also the utilisation of that data after the event, for example the time to retrieve that data when required for analysis. This aspect of the system has not been measured in this study. Comparison with current manual methods of data extraction from written records needs to be performed in order to demonstrate the true time gain by the use of these systems. Data input will always take time, partly due to the interface but also due to the fact that, in general, EHR systems require a more complete data set to be entered than for paper records. The importance of accurate data retrieval has been discussed, with regard to the advent of quality care initiatives and the requirement of surgeons to demonstrate their clinical competence in terms of the process of revalidation.

Implications for future research and the IBRA development

Further work is needed to establish the minimum data set needed to provide meaningful outcomes. This was not the scope of this particular study. In addition, data comparing performance of EHRs with other methodologies needs to be produced in order to demonstrate the full benefit of this system. The obvious comparison is with the paper

record systems, currently in existence. However, it is not possible to measure the benefits of accurately recorded data, which requires less storage and is arguably more secure than paper records, or the ease of producing outcome measures with data from paper records compared with electronic software systems.

The data entry process could be improved with removal of irrelevant entry fields and rearrangement of relevant fields on one single entry site. This would allow shorter navigation through the system and would reduce search processes. For example, the fields for preoperative and surgical data could be placed on the same site.

Currently there is a paucity of research regarding EHR implementation. This is in part due to a lack of rigorous methods available to measure meaningful outcomes. Studies such as ours use a continuous observation of work processes as captured by time and activity monitoring. However this does not assess all aspects of the use of a software system. In a highly specialised environment, such as refractive surgery, it is more likely that uniform care delivery patterns are established. Therefore, there will be less variability in the use of such systems. This factor mitigates, in some way, the need to examine other aspects of usage.

Recommendations for new IBRA users

For beginners, we recommend starting with a minimal data set and entering the data with the one-step method. This will require only a mean of 2 min 11s per case, allowing entering of up to 27 cases per hour into the system. Once the handling of the system has become easier, the amount of recorded data can be increased for more sophisticated analyses.

If a user is able to spend more time at the beginning of the process, then we recommend entering a standard set of data with the stepwise method. Performing the data entry parallel to the clinical appointments will require minimal extra time. With this approach the time consuming process of data collection may look and feel easier, promoting continuation of the data entry process. Finally, each user has to balance the factors of time efficiency and outcome possibilities individually.

6.4.5. Conclusions

The study analysed a large number of data entry processes. The developed software for the data logging worked smoothly and was efficient in the logging process and in the analysis of the data. The results have shown a considerable amount of time is required to enter a standard set of data (a minimum of 370s with the stepwise approach). This process improves and reaches its optimum after approximately 8 weeks (26% less time requirement). The data entry completed in one-go was identified as the fastest way to enter the data into IBRA. Up to 27 cases could be entered with this approach per hour, and is therefore recommended for new IBRA users.

The ability to produce accurate data which demonstrates good quality results within standards of professional acceptability will form an integral part of the revalidation of all specialists. Software systems, such as IBRA, can enable this accurate data to be collected and processed with minimal effort by the individual clinician. This outcome data may then be used to certify the competence of the practitioner. In addition, the system can be used to facilitate clinical research, as a by-product of good clinical care.

Moreover, patients seeking refractive surgery are often well-researched, due to freely available information, which is easy to access on the internet. Consequently, expectations amongst patients are high and it is therefore important to have evidence of excellence in practice. Providing refractive outcome data may enable a patient to be more confident in the choice of surgeon performing their surgery.

This evaluation process revealed potential for optimisation of the IBRA system mainly in the reorganisation, consolidation and reduction of the data entry fields. Adjusting these points in the next IBRA upgrade should not be complicated, and may bear the potential to accelerate the process of data entry. This could then be confirmed by performing a new, second cycle of evaluation, using the same data logging tools from this evaluation process.

6.5. System functionality

6.5.1. Introduction

Most current professional software offers far more functions than the standard user needs. Often, an increase in software function and diversity means decreased simplicity. The need for navigation through menus and tabs, the higher demand of computing power and a reduction in efficiency are some of the possible consequences. In our opinion, software should sharply match user interest and need and omit unused functions.

The users of refractive analysis software, such as IBRA, are mainly refractive surgeons. Sometimes nurses and secretaries provide support with data collection. Analysis standards have been set up by surgical and medical associations, e.g. The Royal College of Ophthalmologists, and have been reported in books and international publications. One standard, which is used by many refractive surgeons for the presentation of refractive outcomes after laser eye surgery, was published by George Waring (see Waring Graphs in Chapter 3). Mr Waring suggested calculating a set of 6 graphs to reflect the visual and refractive outcomes of a series of refractive laser treatments, and allow easy comparison between different presentations. All 6 analysis methods were implemented into IBRA, and 4 extra charts showing visual outcomes and vectorial astigmatic changes were added.

As surgeons are often obstinate in taking on good ideas from colleagues or professional bodies, a standard recommendation might still not circulate generally. In addition, standard recommendations are made for the general use of a wide international clientele and might not, therefore, be sufficient or relevant for surgeons from different countries with different conditions or legislations.

The aim of this evaluation was to analyse user analysis preferences by monitoring the use of IBRA. We gave IBRA users the choice of 10 different analysis methods, and then evaluated the following questions:

- Which methods are the preferred ones?
- Which analysis method was used most?
- Which postoperative review is most relevant?

The objectives were:

- To evaluate the analysis behaviour of IBRA users.
- To compare user preferences with international recommendations.
- To evaluate the attractiveness of the 4 extra charts that were implemented into IBRA.
- To evaluate differences between the use of refractive analysis functions in England, Ireland and Switzerland.
- To record the data of a minimum of 1,000 analysis processes, logged by a software add-in developed for this evaluation process.

6.5.2. Methods

This was a user-related, behaviour based system evaluation. Specific software modules were developed and implemented, and IBRA adjustments were performed for the process of data logging and analysis. All processes were created as automated routines, requiring minimal maintenance.

Every time a user performed an outcome analysis with IBRA, the system recorded the following data:

- id: individual record id
- date: date when the analysis was performed
- userid: the user's id
- type: the type of analysis that was performed (W1-6 = Waring analysis type 1-6):
    - c_pred_se = Predictability of spherical equivalent comparison (W1)
    - c_se = Distribution analysis of spherical equivalent refraction (W2)
    - c_de = Analysis of the defocus equivalent refraction (W3)
    - c_ucva = Cumulative analysis on uncorrected visual acuity (W4)
    - c_safe = Analysis of best corrected visual acuity change (Safety, W5)
    - c_stab = Analysis of spherical equivalent over time (Stability, W6)
    - c_bcva = Cumulative analysis on best corrected visual acuity
    - c_effic = Comparison of the best corrected versus the uncorrected visual acuity (efficiency)
    - c_tiasia = Comparison of target induced astigmatism (TIA) and surgically induced vector astigmatism (SIA)

    - c_vector = Astigmatism analysis (vector analysis)
- visit: interval between operation and postoperative review:
    - 0 = preoperative review
    - 7 = postoperative review at 7 days
    - 1 = postoperative review at 1 month
    - 3 = postoperative review at 3 months
    - 6 = postoperative review at 6 months
    - 12 = postoperative review at 12 months

A MySQL database was configured on the IBRA server for data collection (Table 6.5.1.). The data was then analysed with IBRA and exported as a table (Table 6.5.2.) into Microsoft EXCEL for further analysis.

	Feld	Typ	Kollation	Attribute	Null	Standard	Extra	Aktion
	id	int(10)			Nein		auto_increment	
	date	date			Nein	0000-00-00		
	userid	int(10)			Nein	0		
	type	varchar(30)	utf8_general_ci		Nein	0		
	visit	int(10)			Nein	0		

Table 6.5.1. MySQL database structure as used for the evaluation process.

id	date	userid	type	visit
2432	2009-08-02	100	c_ucva	1
2433	2009-08-02	100	c_ucva	1
2434	2009-08-02	100	c_ucva	1
2435	2009-08-02	118	c_ucva	1
2436	2009-08-02	118	c_ucva	3
2437	2009-08-02	118	c_bcva	3
2438	2009-08-02	118	c_safe	3
2439	2009-08-02	118	c_effic	3
2440	2009-08-02	118	c_stab	3
2441	2009-08-02	118	c_pred_se	3
2442	2009-08-02	118	c_se	3
2443	2009-08-02	118	c_de	3
2444	2009-08-02	100	c_ucva	6
2445	2009-08-02	100	c_bcva	3

Table 6.5.2. MySQL data export in form of a table.

6.5.3. Results

A total of 2,480 files of analysis processes by15 different users were recorded between December 2008 and September 2009.

The usage of the analysis function over time is shown in Figure 6.5.1. Each blue dot in this figure represents one analysis process (one file). The files are separate for each individual user (vertical axis showing the user id). Some of the users stopped using the software before or during the evaluation process. This explains why some of the horizontal lines do not show usage of the analysis function (e.g. no blue dots for user 104).

The red circle encloses a group of processes performed by IBRA users, who were intensively using the analysis function to prepare outcome figures for the presentation of their refractive portfolio at an exam led by The Royal College of Ophthalmologists. This exam took place in March 2009 (green vertical line). Following that event, some of the users then stopped using IBRA for the remainder of the evaluation period.

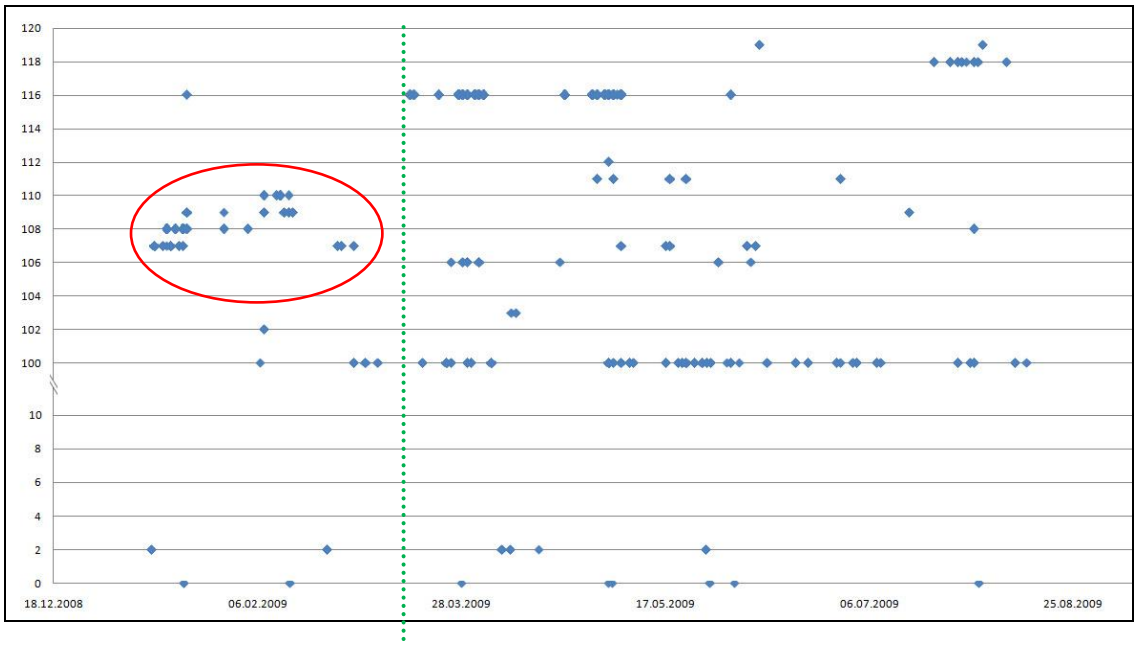


Figure 6.5.1. Usage of the refractive outcome analysis function of IBRA for the evaluation period of 9 months (horizontal axis) for each individual user (user id on the vertical axis). The red circle shows a group of user activity that was linked to an outcome presentation at the Royal College of Ophthalmologists in March 2009 (green vertical line).

The recorded data was separated by the type of analysis performed, and the preoperative and postoperative visit (Table 6.5.3.). The results show that some of the analysis methods were used much more often than others (Figure 6.5.2.). The 4 most commonly used methods made up 85.9% of all analysis performed. In descending frequency these were: UCVA analysis (30.3%), spherical equivalent predictability (27.8%), spherical equivalent distribution (14.4%) and analysis of changes in the best-corrected visual acuity (13.4%). All Waring analyses and graphs together made up 91% of the performed analysis methods. The additional 4 analysis methods implemented into IBRA from various sources were used very rarely and, notably, the 2 vector methods were used together in only 0.4% (11 times in 2480 analysis processes).

The 3 month results were used in 69%, the 1 month results in 16.8% and the 6 month results in 6.5% of the analysis processes. Only 3% of the analysis processes were performed on preoperative data (Figure 6.5.3.).

Analysis method	**Follow-up period**							
	0	**7**	**1**	**3**	**6**	**12**	**Total**	
Predictability (W1)	5	6	25	614	24	16	**690**	27.8%
SE (W2)	24	4	24	287	11	6	**356**	14.4%
DE (W3)	1	0	6	24	8	3	**42**	1.7%
UCVA (W4)	22	9	289	385	24	22	**751**	30.3%
Safety (W5)	4	4	24	225	61	15	**333**	13.4%
Stability (W6)	2	0	13	48	13	8	**84**	3.4%
Efficiency	0	1	13	54	4	9	**81**	3.3%
BCVA	16	2	16	69	16	13	**132**	5.3%
TIA/SIA	0	0	2	3	0	0	**5**	0.2%
Vector	0	0	4	2	0	0	**6**	0.2%
Total	**74**	**26**	**416**	**1711**	**161**	**92**	**2480**	100%
	3.0%	1.0%	16.8%	69.0%	6.5%	3.7%	100%	

Table 6.5.3. Amount of analysis methods performed.

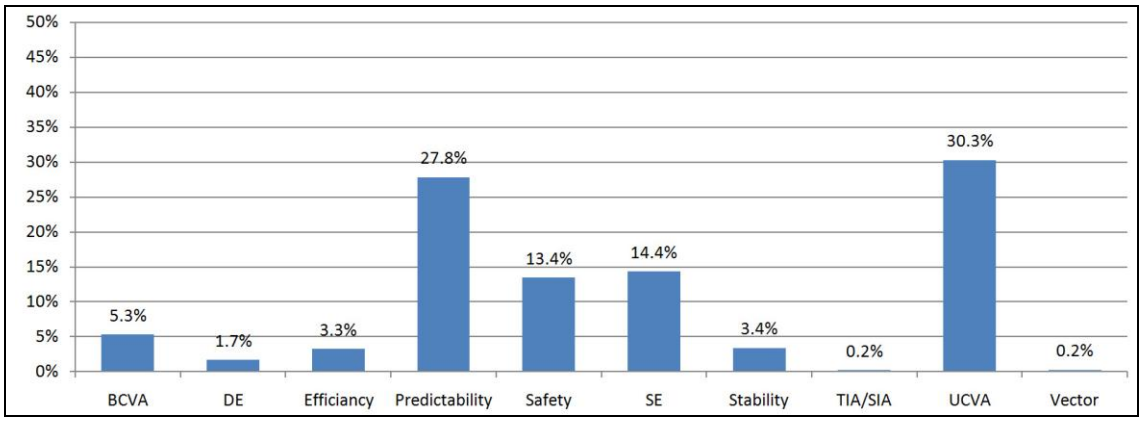


Figure 6.5.2. Usage of the analysis methods (in percentage).

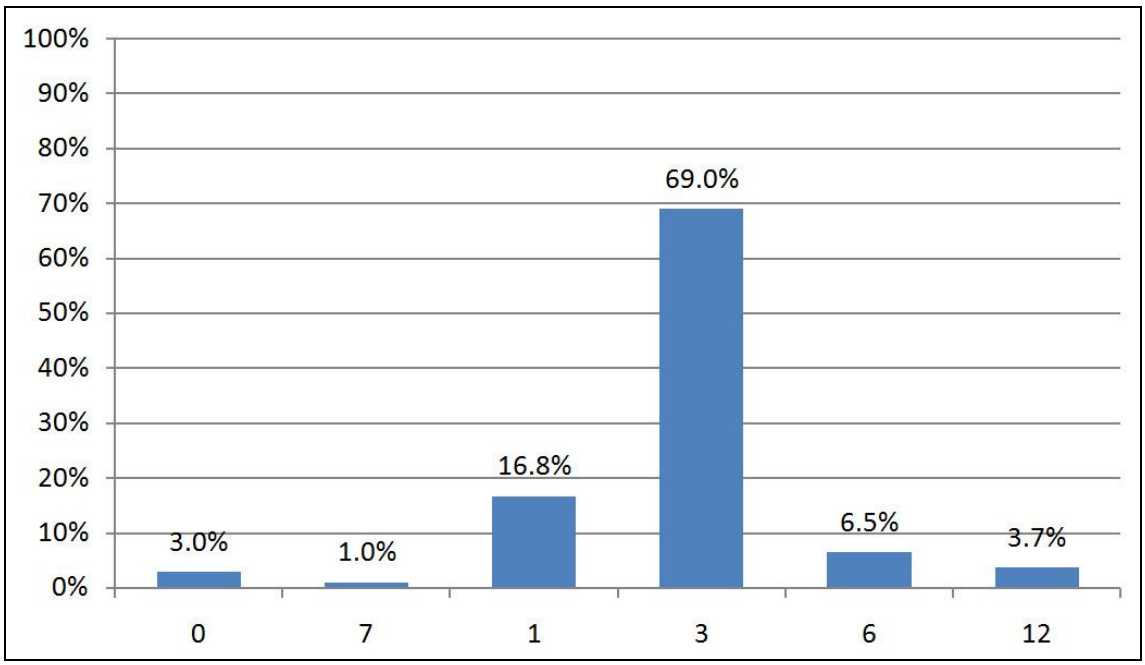


Figure 6.5.3. Follow-up period chosen for the outcome analysis process (in percentage).

The preferences for certain analysis methods were analysed for each user. As some of the methods were used much more often than others, we decided to focus on the 6 most commonly used types. The remaining 4 types were summarised in the "Rest" position at the end of Table 6.5.4.

The location of the laser practice of each user was added in the table (see "Nat" for nation in Table 6.5.4.). In summary, the IBRA users had their origin in 4 different countries:

- Switzerland (CH): 3 users were operating on patients and using the IBRA system in Switzerland. These users together used the analysis process 51 times.
- England (E): this was the main group, consisting of 7 users that had their laser practice in England and used the analysis processes of IBRA 1740 times.
- Ireland (I): 4 users were operating on their patients in Ireland, and used the analysis functions of IBRA 662 times.
- Australia (A): One (new) user in Australia used the IBRA system for analysis only 7 times.

User	Nat	BCVA	Predictability	Safety	SE	UCVA	Stability	Rest	Total
0	CH	2	4	1	0	1	0	1	**9**
2	CH	1	1	0	0	36	1	0	**39**
65	CH	0	0	0	0	2	1	0	**3**
100	E	18	423	53	113	136	8	4	**755**
102	E	1	2	0	0	1	0	0	**4**
103	E	0	0	0	0	3	0	0	**3**
106	E	6	0	0	24	6	0	8	**44**
107	E	5	66	20	31	55	19	4	**200**
111	E	2	8	14	13	22	1	11	**71**
116	E	33	122	141	134	212	1	20	**663**
108	I	26	30	26	17	69	13	33	**214**
109	I	6	10	59	5	54	14	9	**157**
110	I	2	5	3	1	6	2	3	**22**
118	I	30	19	16	18	143	24	40	**290**
119	A	0	0	0	0	6	0	1	**7**
Total		**132**	**690**	**333**	**356**	**751**	**84**	**134**	**2480**
		5.3%	27.8%	13.4%	14.4%	30.3%	3.4%	5.4%	100%

Table 6.5.4. The frequency of the 6 most commonly used analyses methods for each user. Nations: CH = Switzerland (3 users), E = England (7 users), I = Ireland (4 users), and A = Australia (1 user).

Users from the same country were grouped, and the single user from Australian was excluded. Figure 6.5.4. shows the frequency of the most commonly used analysis methods in the remaining 3 countries, in percentage of all used methods.

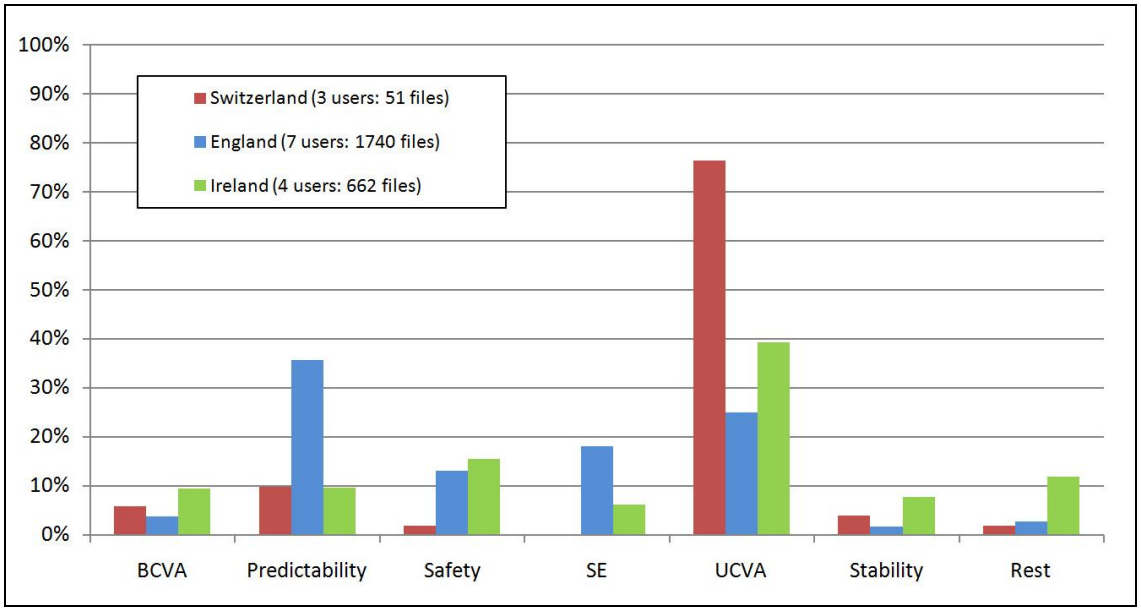


Figure 6.5.4. The frequency of the 6 most commonly used analyses methods for each user group.

6.5.4. Discussion

For this evaluation, additional software modules were developed and implemented into IBRA for the data logging process. This process was shown to be effective in collecting important user data relating to the use of analysis functions. The data was saved in an SQL database on the IBRA server, and then exported into Microsoft Excel for further processing. A total of 2480 analysis processes were recorded.

This evaluation showed that most users performed refractive outcome analysis on a regular basis approximately once a month. We were surprised by this result, because we expected most users to allocate one or two episodes a year for this quality controlling process. Obviously, and maybe because the analysis processes were automated and did not require any further effort, most users showed a high interest in the outcome analysis and used this function more regularly.

One group of users showed a different user pattern. These users performed analysis intensively for a short period in January and February 2009, but rarely thereafter. An interview with each user identified the reason for this behaviour. A certification process for refractive laser surgeons conducted by the Royal College of Ophthalmologist (RCO) led these users to operate the IBRA analysis tools intensively to produce the required charts. The figures and outcome results had to be sent to the RCO Committee for acceptance before March 2009. Once the results had been submitted, the users no longer required the analysis functions of IBRA. This was the explanation for the decrease in activity after March 2009.

This evaluation revealed that users prefer to perform one of the 6 recommended Waring analysis types (91% of all performed analysis). The 2 most commonly used analysis functions were the analysis and comparison of attempt versus achieved spherical equivalent refraction (SE Predictability; 30.3%) and the analysis of changes in the uncorrected visual acuity (UCVA; 27.8%). The 4 additional, non-Waring type, analysis methods implemented in IBRA were almost completely ignored. The vectorial analyses seemed to be especially unpopular, and were used in only 0.4% of all analyses. Vector analysis is complex, and astigmatic outcome results are difficult to interpret. This could be the reason why users were looking for more straightforward analysis methods for both calculation and interpretation of the results. This theory was supported by the fact that the defocus equivalent refraction, which is the most complex analysis method from

the group of Waring analyses, was also used much less frequently (in only 1.7% of all analyses).

Nearly 70% of the analysis was performed on the 3 month postoperative results. This could be linked to published data (Reinstein 2009, Liu 2008) that showed that refractive results do not change after 3 months, and remain stable up to 7 years postoperatively. This might also explain why stability analysis was used so rarely (in only 3.4% of all analyses), for reviewing refractive changes over a period of one year following the operation. The low number of analyses performed from the 6 and 12 month data has another reason. The treatment effect is considered to be stable 3 months after surgery. Therefore, most patients are discharged at this time, making it impossible to record data after 3 months. This is the reason why there is much less data to analyse from these follow-ups.

A surprisingly small percentage (3%) of analysis was performed on preoperative data. Although outcome analysis mainly means analysis of the postoperative results, it is a widely accepted practice to compare such postoperative results (e.g. BCVA chart) with the preoperative situation (e.g. loss of BCVA?).

This evaluation showed that users from different European countries share similar preferences regarding analysis functions, and perform the analysis predominantly from the 3 month postoperative data. The most commonly used methods, independent from the geographical location, were the uncorrected visual acuity analysis (UCVA), the spherical equivalent predictability analysis, the safety analysis and the spherical equivalent histogram analysis. These, again, are methods which all form part of the Waring recommendation.

Users from Switzerland very rarely used the 2 analysis functions safety and spherical equivalent histogram analysis. The reason for this is not clear, and the low user number (3) and number of analysed cases provide space for bias. In contrast, users in Ireland showed a higher interest for diversification and used nearly all of the available analysis functions of IBRA.

6.5.5. Conclusions

We have shown that IBRA was used frequently for outcome analysis. Most users preferred to use the 4 main Waring analysis methods, and to perform the analysis from the 3 months postoperative data.

Generally, users liked to perform analyses with methods that were simple to use and to understand, and that were recommended by others (Waring analysis). The user pattern was not significantly different between users in different European countries.

Future evaluations could add the type of surgery (LASIK or LASEK), and the type of preoperative refractive disorder group (myopia or hyperopia) to the recorded data. This would allow us to study whether different analysis methods are used for different patient collectives. This information could be used for IBRA modifications.

6.6. Survey on user satisfaction

6.6.1. Introduction

The use of a web-based software system is not yet common in ophthalmology and can cause scepticism regarding a variety of issues including accessibility, speed and security. With the use of descriptive evaluation techniques, our aim for the IBRA system was to analyse user satisfaction. For this evaluation we decided to use a questionnaire, which would offer a wide range of standardization and would not influence the user during the evaluation process (less bias).

A literature review demonstrated more than 10 different questionnaires designed for software and interface usability evaluation. Five of these surveys are described in more detail in table 6.6.1.

The 'Questionnaire for User Interface Satisfaction' (QUIS) and the 'Software Usability Measurement Inventory' (SUMI) were shown to be more common. These two commercially available survey systems use a standardized questionnaire. They each provide a software tool that analyses the collected data from the questionnaires and compares the outcome with a reference database. Unfortunately a report for a single analysis costs approximately £1,000, exceeding our budget.

Another survey system was ISO 9126. It uses 6 quality characteristics, similar to the criteria we wanted to investigate. We choose ISO 9126 as a basis to create a 'home-made' questionnaire, implementing main component questions from QUIS Version 5.0 (1998), adding overall questions and modifying the answering structure (QUIS 7.0).

The aims of the survey were:

- To analyse different aspects of user satisfaction.
- To assess the handling of the user interface.
- To determine the reliability (and safety) of the system.
- To identify the effect of the system on the decision making process for treatments.
- To evaluate value for money.

The objectives were:

- To design a questionnaire, based on structured interview techniques.
- To administer the questionnaire to system users.
- To use qualitative research methods to gain and analyse the results.
- To interpret the results.
- To formulate recommendations for system modification.

Questionnaire	Description
a) Questionnaire for User Interface Satisfaction (QUIS)	The "Questionnaire for User Interface Satisfaction" (QUIS) aims to provide a measure of overall satisfaction. Additionally, it evaluates some aspects of the user interface based on user opinions. It consists of the following 9 scales: screen, terminology and system information, learning, technical manuals and online help, system capabilities, online tutorials, multimedia, teleconferencing and software installations. A short (47 Items) and a long version (126 Items) of QUIS are available. The short version should be used, if there are limited time resources, or if motivational problems of the user can be anticipated. The use of QUIS is charged.
b) Software Usability Measurement Inventory (SUMI)	The "Software Usability Measurement Inventory" (SUMI) is a widely tested method of measuring software quality from the end user's point of view. SUMI consists of 50 statements to which the user has to reply that they agree, don't know, or disagree. The evaluation system is backed by a reference database embedded in an analysis and report generation tool. The use of SUMI is charged per report (basic fee: 1200 Euro per report).
c) Website Analysis and Measurement Inventory (WAMMI)	The "Website Analysis and Measurement Inventory" (WAMMI) questionnaire chooses questions to capture user's personal views on the usability of an Internet site. The questions of WAMMI are tested and standardized and should not be changed therefore. The use of WAMMI is charged.
d) ISO 12119	According to ISO 12119[3] each software product consists of the following components: product description, user documentation, interface (program), software (data) and package. Main focus of ISO 12119 is the product description and package.
e) ISO 9126	According to ISO 9126[5] six quality characteristics are established for a software product, which are functionality, reliability, usability, efficiency, maintainability and portability. Each of the product components (ISO 12119) are evaluated as per these characteristics. The main focus of ISO 9126 is the user interface and software workflow.

Table 6.6.1. Overview of questionnaires for usability and user satisfaction evaluation.

6.6.2. Methods

For the design and administration we followed a 5 step model presented by Professor John Stasko (The College of Computing at Georgia Tech, Atlanta). The 5 steps include the aims and objectives of the survey (see introduction), the determination of the sampling group, the writing of the questionnaire, the administration of the questionnaire and the interpretation of the questionnaire (see discussion).

Determining the sample group

The sample group of the survey was formed by the surgeons, optometrists and secretaries who were using the IBRA system. We aimed for a minimum of 10 participants to be recruited for the survey.

Writing the questionnaire

A prototype was designed, and handed to 2 IBRA users for a pilot. The prototype consisted of a structured question part with predefined answers (forced choice format). The questions were short, precise and neutral (as recommended by Boynton 2004), taking no longer than 10 minutes to answer (as recommended by Dorman 1997). The feedback from the pilot was implemented into the final design.

The distributed, final questionnaire is shown in Appendix 10. It comprises a cover letter, followed by a section with personal questions and then the main section with 6 questions on general use, 18 questions on different aspects of interface use and satisfaction, and 3 overall questions (costs, significance and uniqueness). The questions were scored on a 9 point scale. If the question was not applicable, the participants could state this with ticking the box 'NA'.

Administering the questionnaire

The questionnaire was emailed to 7 participants, and handed over personally to 6 participants. They were each given 2 weeks to complete the survey and return it via email. A reminder was sent to those participants who had not returned their surveys within 4 weeks. The scored answers were entered into a database (Excel) for further analysis.

6.6.3. Results

Raw data

The raw data is shown in Table 6.6.2.

User	Sex	Age Gr	Exp S	Exp I	Usage	Similar	G1	G2	G3	G4	G5	G6	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	C1	C2	C3
User 1	f	2	4	4	3	0				8			7	7	7	8	8	8	7	x	8	7	7	7	x	8	7	7	8	7	x	x	x
User 2	m	3	1	3	1	0	8	7	4	8	8	7	9	8	8	8	8	9	9	x	9	6	9	x	x	6	9	9	8	9	5	9	8
User 3	f	4	1	4	3	0	7	7	7	7	5	x	8	8	8						8	8	8	8	x	6	8	9	8	x	5	7	7
User 4	m	2	1	1	2	0	7	7	7	7	7	7	7	7	8	7	7	7	8	7	7	6	7	7	7	8	8	8	7	7	4	7	7
User 5	m	4	1	4	4	0	8	8	8	7	9	8	8	8	8	8	9	8	8	x	9	7	8	x	x	9	9	9	8	7	6	9	8
User 6	m	2	2	4	1	1	6	6	5	7	4	3	8	8	8	8	8	8	3	8	8	5	4	8	x	8	8	8	6	6	6	x	3
User 7	m	3	1	4	1	0	5	4	4	8	3	1	4	3	2	7	6	2	2	x	8	4	3	5	4	2	8	8	2	4	4	2	1
User 8	f	2	1	3	2	0	7	7	7	8	8	7	6	5	5	6	7	6	6	7	8	8	7	8	x	5	7	8	8	7	x	x	8
User 9	m	4	1	4	1	0	8	2	8	1	1	7	7	8	8	8	8	8	8	x	1	1	1	7	7	8	8	8	8	8	5	9	9
User 10	f	2	4	2	2	1	6	7	4	6	7	8	7	8	8	8	8	8	6	8	8	7	9	x	x	9	9	x	3	5	x	x	x
User 11	m	3	1	4	3	0	7	8	7	8	8	8	5	6	6	7	8	8	8	7	9	8	8	7	7	8	9	9	8	7	6	9	8
User 12	m	2	2	4	3	0	6	8	7	8	5	3	7	5	x	8	8	x	3	3	6	8	9	x	5	6	9	8	x	7	5	8	4
User 13	m	2	2	2	2	1	6	8	8	8	8	2	7	8	6	6	7	7	4	x	8	3	6	5	x	8	8	7	4	5	4	8	6

Table 6.6.2. Replies from all 13 users (raw data).

Participants reply

The collection of all replies was delayed by 3 months, despite the emailing of multiple reminders to participants. When we eventually received all 13 completed questionnaires, we used them for the analysis.

54% of the participants were under age 40 (Figure 6.6.1. A). Eleven of the participants were refractive surgeons, one participant was a secretary and one an optometrist. Eight of the surgeons had more than 3 years' experience in refractive surgery (Figure 6.6.1. B). Most participants had been using the system for more than one year (Figure 6.6.2. A). Three participants had experience with other refractive software.

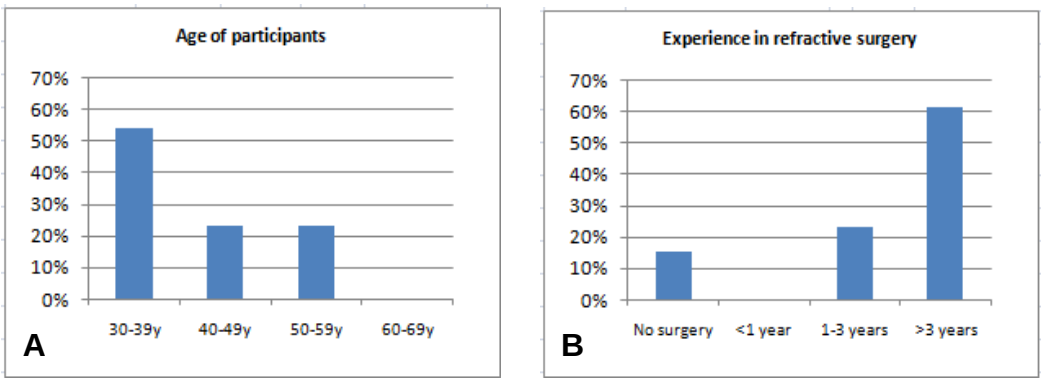


Figure 6.6.1. Participants demographics: A: age; B: surgical experience.

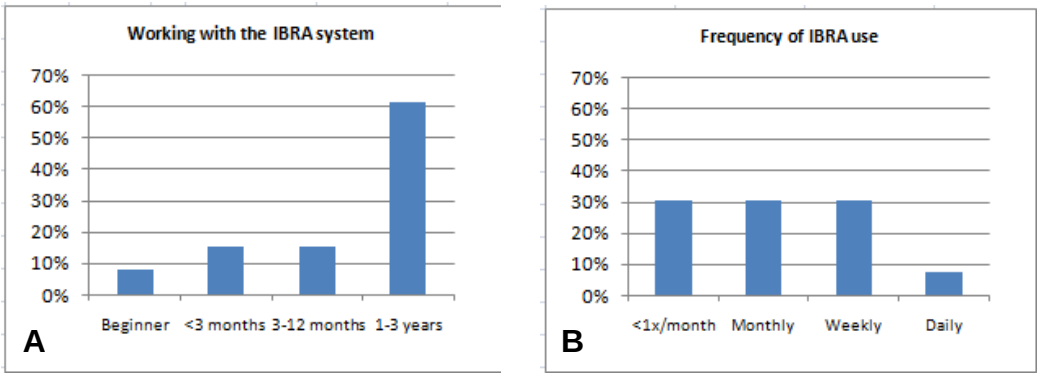


Figure 6.6.2. Participants demographics: A: Experience with the IBRA system; B: Frequency of IBRA use.

Outcomes

We grouped the different questions in relation to their characteristic (e.g. Terminology), and performed group analysis with mean and standard deviation (Table 6.6.3. and Figure 6.6.3.). The scoring for each question is shown in Table 6.4.4. The meaning of the lowest (1pt) and highest scoring (9pt) is also expressed in the table. Generally, high scoring was linked to a positive result.

	Characteristics	Mean	SD
	General use	6.4	1.9
	Screen (presentation)	6.9	1.6
	Terminology	7.0	1.5
	Learning	6.6	1.9
	Capabilities	7.8	1.1
	Interface (interaction)	6.5	1.8
	Overall	6.3	1.9

Table 6.6.3. Mean scoring with standard deviation (SD) for each characteristic.

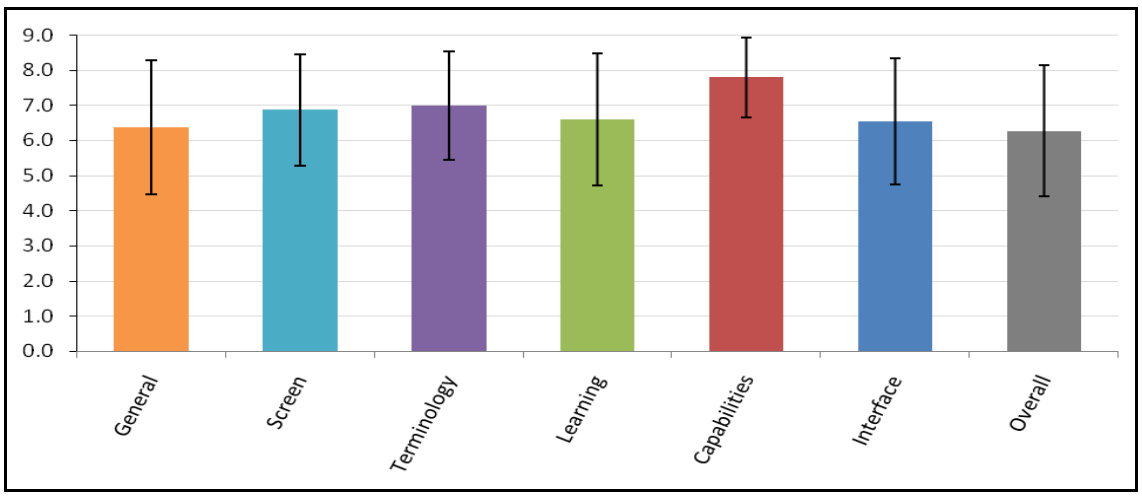


Figure 6.6.3. Questionnaire scores for each characteristic (with SD).

No	Question	Selection from (1pt)	Selection to (9pt)	Replies	Sum (pt)	Mean	SD	Range	Ind
G1	The general use of the system is...	terrible	wonderful	12	81	6.8	1.0	5-8	*1*
G2	The general use of the system is...	frustrating	satisfying	12	79	6.6	1.8	2-8	
G3	The general use of the system is...	dull	stimulating	12	76	6.3	1.6	4-8	
G4	The general use of the system is...	difficult	easy	13	91	7.0	1.9	1-8	
G5	The general use of the system is...	inadequate	adequate	12	73	6.1	2.5	1-9	
G6	The general use of the system is...	rigid	flexible	11	61	5.5	2.7	1-8	*2*
1	Characters on the computer screen	hard to read	easy to read	13	90	6.9	1.3	4-9	*3*
2	Organization of information on the screen	confusing	very clear	13	89	6.8	1.6	3-8	
3	Sequence of screens	confusing	very clear	12	82	6.8	1.9	2-8	
4	Use of terms throughout system	inconsistent	consistent	12	89	7.4	0.8	6-8	*4*
5	Computer terminology is related to the task you are doing	never	always	12	92	7.7	0.8	6-9	
6	Position of messages on the screen	inconsistent	consistent	11	79	7.2	1.9	2-9	
7	Computer keeps you informed about what it is doing	never	always	12	72	6	2.4	2-9	*5*
8	Error messages	unhelpful	helpful	6	40	6.7	1.9	3-8	*6*
9	Learning to operate the system is	difficult	easy	13	97	7.5	2.1	1-9	*7*
10	Exploring new features by trial and error	difficult	easy	13	78	6	2.2	1-8	
11	Tasks can be performed in a straight-forward manner	never	always	13	86	6.6	2.5	1-9	
12	Help messages on the screen are	unhelpful	helpful	9	62	6.9	1.2	5-8	
13	Supplemental reference materials	confusing	very clear	5	30	6	1.4	4-7	*8*
14	System speed	too slow	fast	13	91	7	2	2-9	*9*
15	System reliability	unreliable	reliable	13	107	8.2	0.7	7-9	
16	System security	unsafe	safe	12	98	8.2	0.7	7-9	
17	Correcting your mistakes	difficult	easy	12	78	6.5	2.2	2-8	*10*
18	Experienced and inexperienced users' needs are taken into consideration	never	always	12	79	6.6	1.4	4-9	
C1	How do you assess the costs of the system?	too expensive	to cheap	10	50	5	0.8	4-6	*11*
C2	How do you assess the significance of the system on your practice?	low	high	9	68	7.6	2.2	2-9	*12*
C3	How do you assess the uniqueness of the system in your field of expertise?	low	high	11	69	6.3	2.5	1-9	*13*

Table 6.6.4. Questions and questionnaire scores (Mean, SD, and Range). The index numbers (Ind) relate to the numbers used in the discussion part.

6.6.4. Discussion

From a general point of view the IBRA system scored well and there was not much difference between the characteristics. With an emphasis on highest and lowest scorers, and also standard deviation, we will discuss the results from the different characteristics in the following parts. The index numbers at the beginning of each paragraph, for example (1), refer to the index numbers in the last column of Table 6.6.4.

General use of the system

(1) The general use of the system was scored as satisfying, stimulating and easy.

(2) About 50% of the users considered the system to be rigid. This question received the second lowest scoring of all questions and showed the highest standard deviation of the scoring. In particular, one user experienced difficulties learning to operate the system (performing tasks, exploring new features) and submitted a very low score.

Screen

(3) Good scoring was received relating to the displayed information and the style in which the software displayed the characters on the screen, allowing the information to be read easily. Information was arranged and organised on the screen clearly, and the sequence of screens was assessed as clear.

Terminology

(4) The users were happy with the formulation of messages, the position in which the messages were placed on the screen and the consistency of messages displayed throughout the system. They stated that the terminology was related to the task. This positive feedback might be based on the fact that the system used a lot of ophthalmic terminology. Generally, medical language is complex but precise. This supports understanding, and can lead to a reduction in critical incidents.

(5) Many users were not pleased with the information the system provided regarding 'what the system is doing'. This might be linked to the fact that the system is very quick in performing tasks and therefore rarely creates long enough waiting times to ask the question 'What is the system doing right now?'.

(6) Most users realised that the system did not report error messages, and answered the question with 'not applicable'. The software was designed in such a way that every task produced a result. Some users had problems with the data analysis and found that the description of the 'selection fields' was not clear enough. We believe that IBRA could

be improved with a validation system to check field entries, including the ones from the selection part, before performing the analysis; and if they are completed incorrectly, the system could show an error message with guidance for correction.

Learnability

(7) There was a wide range of scoring for the questions regarding learnability. Although most users stated that IBRA was easy to use, there were 2 users in particular who had difficulties in learning and understanding the system, and also in understanding functions relating to system performance.

(8) As the system did not provide a detailed user manual, the response to question 13 was often ‘not applicable’. Similarly, a help message only occurred on one site where the task was more complex.

Speed, reliability and security

(9) Good scorings were seen regarding speed, reliability and security. The system was assessed as reliable and safe. These questions scored highest, with the lowest standard deviation. As the system is web-based, the speed of the Internet connection, the power of the personal computer and the used Internet browser were relevant too. In addition, time of day of use of the system was significant, as the Internet generally slows down in a hospital network during the normal working hours with more users causing higher data traffic. Despite any possible restriction, most users rated the system speed as 'sufficient' or 'fast'.

User Interface

(10) The questions 17 and 18 on user-interface and error messages were answered too heterogeneously, reflecting the fact that the questions were difficult to answer in the provided context (mainly question 18), and that generally the system did not show error messages.

Overall questions

(11) The questions on costs (question C1) could only be answered by participants who would buy such a system, i.e. surgeons, who considered the price of the system too high (£490 for 1 year's usage). The related question received the lowest scoring in the entire questionnaire.

(12) As for the costs issue, the question on clinical significance could only be answered by refractive surgeons, as only they would use the results from the IBRA outcome analysis to modify the treatment parameters (nomograms). The high scoring for this question showed a general satisfaction with the system and the provided support in decision making.

(13) Although the significance of the system was generally assessed as high, the uniqueness of the system was assessed as moderate. The lower scoring was caused by 1-2 very low scorings from 1 user who had previously assessed the system as rigid.

6.6.5. Conclusion

Summary of strengths

This survey showed high user satisfaction, with a mean scoring of 6.7 from 9 points. The user interface, the screens and sequences of sites related to tasks were stated to be clear. The system was acknowledged to have a significant importance in the decision making process (Table 6.6.5.). Users were pleased with the reliability of the system and satisfied with the speed of the web-based application. Overall, users provided an impressive positive statement on 'tender points', such as safety and security issues, which is important for the wider acceptance of this technology and the future success of the IBRA system.

Strengths	Weaknesses
✓ Significance (supports decision making) ✓ Security ✓ Reliability ✓ User-interface and speed	- Rigidity - Documentation - Learnability - Price

Table 6.6.5. Summary of user satisfaction.

Summary of weaknesses

The main criterion was system rigidity. Although rigidity increased the reliability of the system (homogenisation of the entered data provided better analysis), the decreased flexibility was not appreciated and did not reflect the newest developments of web-based software applications. Such newer systems, as seen for example on the current

BBC website (Glow, a JavaScript library), present information in content boxes that can be edited by the user and freely positioned on the screen (drag and drop widget). A similar structure could be implemented into IBRA too, but this would require a complete re-design of the current user-interface and a change of large parts of the program code.

The price of the system was assessed to be too high; and many users requested a user manual and criticized the spare documentation provided with IBRA, as well as the limited guidance through the system.

Recommendations for future development

With future upgrades, some of the criticized points can be improved and, primarily, effort should be put into the production of a user manual (or of video tutorials), including a section on ‘Introduction to IBRA’. A review of the price should follow.

Chapter 7

DISCUSSION

7. DISCUSSION

7.1. Achievements related to the research objectives

In this section we will discuss the achievements of the research in view of the main clinical objectives as formulated at the beginning. Generally, we tried to follow the objectives as close as possible.

Objective 1

To develop a system that can combine data collection and analysis and offer tools for standardised outcome presentation.

The starting point of this research was a simple FileMaker application for data collection. The permanent re-development and continuation of improvement, combined with a determination for completeness, made this system grow to a multi-functional, user-friendly data analysis system. The range of implemented refractive analysis techniques, including outcome analysis with Waring graph creation, nomogram analysis and vector analysis, made this system unique to the market.

While the analysis of data is much appreciated by the surgeons, data collection is time consuming and perceived as a troublesome undertaking. For the first time, the required amount of work could be determined in seconds. This research also contributed information on data collection techniques and we could indicate the most time effective approach. This is important, as a lengthy process could compromise continuation of data collection and could lead to early termination of outcome analysis. The results from this research identified the data entry process with the one-go technique as the fastest way to enter the data into IBRA. Up to 27 cases could be entered with this approach per hour, enabling the surgeon to perform 5 of 6 Waring graphs finally. We have submitted an article to Eye, a peer-reviewed Journal, to publish our results.

The final version of IBRA offered 10 analysis methods, including the 6 standard Waring graphs. With the use of data logging processes we investigated which analysis methods are liked by refractive surgeons, and which are not. The results from our study showed that the majority of surgeons only use 4 different analysis methods, which are all from the set of Waring analyses. The remaining 6 methods were ignored almost

completely. The popular analysis methods are among the less complex ones, and we believe that it is this that made the difference. These graphs are used because they are easy to create and easy to understand; and it appears that surgeons prefer methods that do without the fancy stuff and go for the simple and straightforward.

Monitoring user activity and analyzing the outcome analysis procedures allowed us to identify key aspects of activity. This research showed that users performed the outcome analyses separated for each of the 5 refractive disorder groups, although this was not facilitated by the IBRA system automatically. The separation seems to make sense. Surprisingly, this concept has never been published and we know that some surgeons are clearly not aware of it or would know how to do it. We therefore aim to report on this aspect, and we will publish our results and experience in an ophthalmic journal within the next 12 months. In addition, we recommend modifying IBRA allowing separation and analysis of patient data based on the different refractive disorder groups, e.g. all patients with compound myopic astigmatism.

Objective 2

To make the system easily accessible, secure, safe, flexible and capable of future developments.

Many surgeons provide services to different hospitals at different locations. The pre-assessment for laser vision correction is usually performed in the private practice unit. The laser treatment is then undertaken in a centre specialised for laser treatments, providing the expensive laser equipment to many surgeons. Finally, the follow-up might be held in the private unit, in the clinic of a general hospital or at an optician's practice. As the data is created at different locations, so the software system for the data collection needs to be accessible from these locations. For many years the hospital's Intranet was regarded as the only solution for access of software programs at different locations in the same hospital. This research showed the inefficiency of Intranet-based systems for refractive eye surgeons.

Web-based software systems are easy to access from any computer with Internet access. When this research was started, such systems were rarely seen in hospital environments and we were faced with the critical view of the surgeons. Questions about security and

reliability challenged the system development of IBRA initially, and we believed that these aspects could get out of control and endanger the further system development. The increasing popularity of the Internet and the introduction of e-banking systems caused a reduction of adverse attitudes over the years. Phenomenally, also, the acceptance of web-based system in ophthalmology increased so much that questions on speed (question 14), reliability (15) and security (16) scored the highest of all questions in our survey; and showed the smallest difference between the replies.

This research lead to the development of the world-wide first refractive analysis software that was completely web-based. The results from the user satisfaction survey have proven that the perception of Internet technology has changed, and that web-based systems can be well accepted even by critical surgeons. We believe that the continuous attention to details, the high system reliability, the permanent accessibility, the right level of security measures with password protection and encrypted connections, and the privacy protection were important precursors for this acceptance.

The web-based programming platform was also received positively from the developer's point of view. HTML, PHP and JavaScript offered all the tools to develop complex software systems and to extend them with ready-made add-ins, e.g. for the creation of charts or pdf files. Many of the tools were freely available and 'home-made' tutorials explained how to integrate the extra features into the software system.

The positive user feedbacks and our own convincing experience made us believe that all system developers should include the range of Internet technologies into the evaluation when planning software projects for medical professionals.

Objective 3

To develop and integrate means that can provide information on how refractive laser treatments could be improved.

Without doubt, the Waring graphs are helpful in analysing the quality of laser vision correction. For example, they report exactly how many eyes had 6/6 uncorrected visual acuity after surgery, or how many eyes were within 0.5 D of emmetropia. The Waring graphs may also indicate errors in treatments. For example, if a high percentage of

myopic eyes end-up significantly hyperopic, an overcorrection is diagnosed. However, the Waring graphs do not provide accurate information on how the treatment could be optimised. This is the domain of nomogram calculation.

We performed linear regression analysis and best fit analysis on spherical and cylindrical outcome data to determine outcome formulas. These formulas were integrated into a calculation algorithm that could determine treatment adjustment factors. The surgeon could use these factors at the stage of treatment programming to optimise the nomograms of the laser controller software. Although other software offer nomogram functions (e.g. Datagraph-med), none of these systems integrated the calculation algorithms in a form that could provide adjustment factors for groups or individuals; this is unique to IBRA. With the creation and implementation of the nomogram formulas, IBRA changed its character from a quality reporting to a quality controlling system, supporting the surgeon in decision-making.

Objective 4
To test the system in a clinical environment
with real patient treatments.

In this research we performed extensive testing of the IBRA system at Moorfields Eye Hospital NHS Foundation Trust, and at 4 laser centres in the north of England and Ireland. At the end, the IBRA system was used by a total of 11 surgeons. These users were all specialists in refractive laser eye surgery and some of them already had experience with refractive analysis software. It was therefore interesting to see how they would perceive and accept the web-based IBRA system in their daily practice. A survey on user satisfaction showed generally high scoring in most fields. In particular, the users seemed to like the easy use of the system and attributed a high clinical significance of the system. Another point that was much appreciated was the accessibility of the system from different locations, and in fact, monitoring of users' IP address showed that IBRA was used from many different locations (office and home).

As the data is gained at the preoperative, intraoperative and postoperative visits, we aimed to find out how the data finally was entered into IBRA by each surgeon. Many questions about it persist. For example, how much time does it take to enter the data for

one treatment? Is it fast to enter the data in one-go or stepwise with the visits? Will we see learning curve effects? Therefore, during a period of 1 year, we monitored the data collection processes with data logging technologies, running in the background of IBRA. Although we emphasised the importance of collecting a standard set of 44 parameters for each patient in a step-wise method, the analysis of the monitored processes showed that most surgeons did not follow this recommendation and entered either a smaller or larger amount of data (22 or 52 parameters), or used a different approach (one-go method). This allowed us to compare the different methods and data sets and to identify the quickest data entry method, which was the one-go method. Further, we could show that there was an experience curve effect reducing the time requirements by up to 26%.

This research was the first research in London (maybe the UK) that prospectively evaluated the influence of nomogram adjustment on the outcome of patients treated in a private setting. To find refractive surgeons willing to undertake research on their private patients proved complicated. The refractive surgeons feared that the extra risk of the clinical trial could reduce the confidence of their private patients in the offered treatment. As a consequence, this could reduce the word of mouth advertising and could finally damage the surgeon's reputation. In consideration of the facts, we were delighted to find, with Professor Gartry, a partner in undertaking a series of prospective outcome analyses on his private patients.

This research showed that the IBRA system was an excellent instrument in collecting refractive data and undertaking clinical audits on a large series of patients. Our two audits included 2011 treated eyes and ran over a period of 24 months. During this time, no problems were encountered in using IBRA for the data collection, and notably, there was permanent access to the system.

We have shown that IBRA can identify patient groups with over- and undercorrection effectively; that it can calculate accurate nomograms for adjustments of future treatment, and that these modified treatments can lead to the desired health outcome change. The integrated algorithms worked effectively for simple myopia and myopic astigmatism, but did not work sufficient for hyperopia.

Further, we have proven that the concept of nomogram adjustment can bring benefit to wavefront guided treatments. This stays in contrast to a widely accepted opinion and practice.

Objective 5

To evaluate the system impact on patient's health.

The formulas we developed based on theoretical models we created. This has not been done before and therefore there was no evidence that it would lead to the attempted change. In contrast, if the treatment adjustment would show a malfunction it could even damage the eye and worsen the outcome. We had to be very careful with the determination of the adjustment factors to minimise the risk as much as possible.

To evaluate our formulas, the nomogram adjustment and their effect on health changes, we performed two large studies: a study on 2 consecutive audits evaluating general nomogram adjustments for common refractive disorders and a randomised controlled trial evaluating patient-individual nomogram adjustments for patients with myopic astigmatism.

The results from the studies showed that the new formulas were effective in general nomogram modifications, achieving between 75-84% of the intended change. These adjustments were limited to the change of the treatment spherical equivalent and applied to all patients from a refractive disorder group in the same way. For example, patients with simple myopia showed a mean over-correction of 0.27D in the first audit. As a consequence, the treatment sphere, as programmed in the laser, was lowered by 0.25D. The results of the second audit showed an average effective change of the spherical equivalent of 0.21D for the simple myopes. Similar changes were made for 2 other refractive disorder groups.

This research showed that all myopic eyes (simple and astigmatic myopia) performed well with the treatment modifications, while the hyperopic eyes did not show the desired change in spherical equivalent. The reason for this could be the very different ablation profile that is applied during the surgery (Figure 7.1.1). Briefly, myopic treatments remove tissue from the centre of the cornea in the shape of a discus, finally

flattening the cornea. Hyperopic ablation profiles have a ring shaped structure that looks like a doughnut; finally steepening the central corneal curvature. Further research is required to investigate nomogram adjustment effects in relation to the ablation profile.

Figure 7.1.1. Ablation profile for myopic treatments (left) and hyperopic treatments (right).

To analyse patient-individual health changes, we undertook a randomised controlled trial on 79 eyes with myopic astigmatism. Every patient received a different modification, based on spherical equivalent and cylinder value, as assessed preoperatively. This clinical trial showed that the 2 groups performed significantly differently, and that the difference was caused by the nomogram adjustments. The results of this trial confirmed the effectiveness of nomogram modifications on spherical changes, but revealed a lack of effectiveness of astigmatic changes. Statistically, we could not identify a difference in postoperative astigmatism between the 2 groups, though this is what we aimed for. Further research is required to evaluate cylinder modifications in nomogram adjustments, and the effect of other parameters that could influence the postoperative outcome (e.g. age or healing processes).

Statistically, there was no difference between the randomised groups relating to loss of Snellen lines, the number of patients with over-corrections, under-corrections or outliers, and the number of patients requiring additional treatments (enhancements). The results of this research showed that carefully planned nomogram modifications are safe, and can therefore be performed by any surgeon with minimal risk.

Objective 6

To improve the understanding of nomogram adjustments.

From a general point of view, nomogram adjustments require careful data collection. We have demonstrated that there are different ways to manage the data collection, and have outlined the pros and cons of each of these.

This is the first research that has clinically proven the effectiveness of nomogram adjustment in large private practice series. We demonstrated that changes of spherical equivalents can be achieved with high precision. On the other hand, patient-individual modifications were not superior to general treatment modifications. In part, this is linked to the refractive cylinders, which seem to be more resistant to adjustments. Further, we learned that hyperopic nomogram adjustments perform differently to myopic adjustments and require more investigations.

7.2. Publications and Presentations (July 2010)

This research has been subject to many publications and presentations (Table 7.2.1., Table 7.2.4 and Table 7.2.5.). The process of publishing the results and experiences from this research is still ongoing. Some articles have been submitted to peer-reviewed Journals (Table 7.2.2.), others are in preparation (Table 7.2.3.).

No	Authors, Title, Journal
1	Zuberbuhler B, Schipper I. Proexcimer - Refractive database and analysis for laser excimer surgery. Ophta 2003,6,25-27.
2	Zuberbuhler B, Galloway P, Reddy A, Saldana M, Gale R. A web-based information system for management and analysis of patient data after refractive eye surgery. Comput Methods Programs Biomed. 2007 Dec;88(3):210-6.
3	Joung M. Comparing surgery results. Eye World 2008, online article ID 4386.
4	Finnegan G. Online audit system helps surgeons improve results by tweaking algorithms. Etimes Jan 2009
5	Bucher C, Zuberbuhler B, Goggin M, Esterman A, Schipper I. Corneal limbal marking in the treatment of myopic astigmatism with the excimer laser. J Refract Surg. 2009 Sep 2:1-7.

Table 7.2.1. Published articles on IBRA

No	Title	Submission
1	Management of data entry processes in refractive laser eye surgery	Eye, 22.6.2010
2	Patient satisfaction after laser vision correction	Eye, 19.6.2010
3	Multi-centre study on refractive outcomes of LASIK and LASEK for different refractive disorder groups	BJO, 29.7.2010
4	Nomogram adjustments for myopes and hyperopes in LASIK	Ophthalmology, 2.8.2010

Table 7.2.2. Articles submitted to the Journal

No	Title	Journal
1	Difficulties in undertake private practice research in the UK	BMJ
2	Visual outcomes in a large multicentre study	Eye
3	Comparison of refractive analysis systems	CMPB
4	How to analyse refractive data - Update on the Waring graphs	JCRS
5	Patient-individual nomogram adjustment in refractive laser surgery - a randomised controlled trial.	Klimo

Table 7.2.3 Articles in preparation

No	Date	Format	Title	Venue
1	07.06.2003	Guest Speaker	Management of patient data after refractive surgery	6th Swiss Refractive Congress, Lucerne
2	09.09.2003	Free Paper	Analysis of patient data following LASIK (Laser in-situ keratomileusis)	XXI Congress of the ESCRS, Munich
3	07.06.2004	Guest Speaker	Refractive outcome analysis with IBRA	7. Swiss Refractive, Lucerne
4	24.06.2004	Free Paper	Internet Based Refractive Analysis	17. Congress of the DOC, Nürnberg
5	May 2008	Guest Speaker	Introduction to IBRA	Annual Refractive Meeting, Moorfields Eye Hospital
6	02.12.2008	Guest Speaker	Refractive Outcome analysis	Basic LASIK course, Moorfields Eye Hospital, London
7	March 2009	Transfer Seminar	Internet Based Refractive Analysis	Centre for Health Informatics, City University
8	06.11.2009	Guest Speaker	Refractive data collection and analysis using outcome analysis software.	Optimax Annual Meeting, London

Table 7.2.4. Presentations held at international congresses

No	Date	Format	Title	Venue
1	18.09.2004	Poster	Internet Based Refractive Analysis	97th Congress of the Swiss Ophthalmological Society, Lugano
2	05.05.2009	Poster	Refining algorithms in laser in-situ keratomileusis using IBRA.	Centre for Health Informatics, City University
3	19.05.2009	Poster	Importance of outcome analysis in laser in-situ keratomileusis	Annual Congress of the RCO, Birmingham
4	25.05.2010	Poster	Refractive outcomes of LASIK – A United Kingdom multicentre study	The Royal College of Ophthalmologists Annual Congress, Liverpool
5	25.05.2010	Poster	United Kingdom multicentre study comparing visual outcomes of LASIK and LASEK for myopes and hyperopes	The Royal College of Ophthalmologists Annual Congress, Liverpool
6	25.05.2010	Poster	Patient Satisfaction Outcomes following LASIK and LASEK in a large United Kingdom multicentre study	The Royal College of Ophthalmologists Annual Congress, Liverpool
7	25.05.2010	Poster	An Analysis of the time requirement for the data entry process for refractive outcome analysis	The Royal College of Ophthalmologists Annual Congress, Liverpool

Table 7.2.5. Poster presentations

7.3. Limitations and recommendations

7.3.1 System related limitations and recommendations

Although there are many positive aspects about the IBRA system with generally high user satisfaction, we were able to identify some points that need to be addressed for future development. We have split these corrections into 'must have' and 'nice to have' features, and we will discuss the individual topics below.

One new insight we gained from this research is the fact that refractive outcome analysis has to be performed for each refractive disorder group independently, as these groups perform differently clinically. This concept cannot be addressed by IBRA accurately. Although the system allows multiple ways of case selection, the separation of the different groups has to be done manually by coding the groups. This is inconvenient, and the next IBRA update will need to address this problem with a new analysis module. This module could implement another finding of this research: the fact that most surgeons use only 4 Waring analyses for the outcome presentation, and that they read out key results from each analysis, e.g. how many patients (in %) were within 0.5D of emmetropia. For the IBRA update, we recommend presenting the outcomes in a table where the rows mark the 5 refractive groups and the columns are formed by the key results from the 4 analysis methods. We believe that IBRA should offer this or a similar table soon, as it will make a major contribution to the provision of refractive outcome analyses.

This research underpins the fact that refractive analysis is only as good as the data that was entered before. The analysis of the data of the 2 audit cycles with more than 2000 treatments showed that the data was not distributed homogenously, mainly for 2 reasons. Firstly, the wrong data was entered. This data error can be overlooked, especially if the entered false data still looks potentially reasonable, e.g. with punctuation errors such as the spherical equivalent of -12.5D instead of -1.25D. Secondly, every treatment has a natural distribution of results, and the existence of outliers is normal in any distribution. Many of the outliers in ophthalmology are linked to medical conditions. One common condition in high myopic eyes is called amblyopia, a disorder of the visual system that is characterized by poor or indistinct vision in an eye that is otherwise physically normal. This could lead to the situation of a patient having 6/12 uncorrected visual acuity with the right eye and 6/6 with the left eye, although both

eyes are emmetropic. How can we identify outliers and how can they be separated between data entry errors or disease? We strongly believe that IBRA should have a tool that allows, in a first action, to identify outliers and marginal data. The identified data then can be checked manually for entry errors or ocular history. In a second step the software should be able to mark the outlier data so it can be excluded from the general analysis. This would certainly provide a better representation of the average population, and could increase the precision of the general nomogram calculation. Such an outlier module should be implemented into IBRA as soon as possible.

Other points that could improve the system in the future are listed below.

- One user made an interesting request. He was asking for a way to gain an overview of one particular patient's treatment; summarising the multiple treatments this patient underwent in one table or figure on a single page. Currently, IBRA does not offer such a patient related presentation of the data. All presentations are treatment related and are presented in lists of cases (1 case = 1 treatment). While patients normally only have 2 treatments (one for the right eye, one for the left), reflected by 2 cases, the existing summary in the case list might provide a satisfying overview. On the other hand, up to 10% of patients undergo 2nd or 3rd treatments and might have up to 6 treatments in total. We believe that the request from the user is significant, and we plan to develop a module for IBRA that will show a summary of the treatments (cases) of a specific patient in a simple form. This would allow the surgeon to review a patient's treatments as a whole and might provide valuable insight, especially in situations where the treatment was less than optimal.
- This research showed that the collection of a minimal data set (22 parameters) in a one-go technique was the quickest way to enter the treatment data. Currently, these 22 parameters are spread over 4 different pages. We believe that we can accelerate the data entry process with a re-arrangement of the 22 parameters on a single 'summary page'. This would minimise navigation through the pages, and would simplify the search for specific fields out of the offered selection.
- Some surgeons use an electronic patient record (EPR) system in their private practice. These systems allow the extraction of data from connected, 'freestanding' diagnostic equipment, such as perimeters and auto-refractors. The measured data then can be presented with the EPR tools for analysis. This is particularly helpful in the management of glaucoma patients (pressure curve) or

cataract patients (visual acuity curve), which make the ‘bread and butter’ of a private practice. Besides the clinical application, the EPR system is used to arrange the next appointment, to code the diagnosis and treatment, and to invoice the patient. Generally, the EPR system has become irreplaceable in many private practices, and a link between the EPR and IBRA is desirable. This would minimise the chance of double data entry processes and increase the acceptance of IBRA among users who already have an EPR. The data transfer could be performed either via SFTP (SSH File Transfer Protocol) or FTPS (FTP over SSL), which adds SSL encryption to FTP (as specified in RFC 4217).

- Potentially, IBRA could also be linked to laser controller software, allowing adjustment of laser settings directly from the IBRA user-interface. This option bears high potential but could be risky in the case of malfunction of the application. We contacted 2 manufacturers (WaveLight and Bausch&Lomb) with the idea. The concept was regarded as interesting, but no manufacturer was happy to invest in such an implementation at this time.
- Another interesting field of development could be the involvement of patients in the process of data recording. A software module could be implemented into IBRA that would allow patients to access their treatment cases and to provide a feedback related to the course of healing, comfort (pain) or visual change. With this additional information the system could become more content-rich yet remain succinct and efficient for the surgeon.

7.3.2 User related limitations and recommendations

The user satisfaction survey showed generally high scores. One field that was identified with potential for improvement related to ‘supplemental reference materials’. We have to admit that the documentation is an issue we neglected for a long time. At the beginning of the development we believed that, in keeping the user-interface as simple as possible, the software would also be easy to use. With the implementation of vector analysis and nomogram calculations, the software became much more complex and the IBRA screen was now filled with selection fields, data entry fields and action buttons. Although we re-arranged the user-interface, the application might remain confusing for the more amateur computer user. We acknowledge that documentation is required. We believe that good documentation could be a great help in understanding all the features of IBRA, and that it could include recommendations related to the management of data

collection and analysis, as gained from this research. As IBRA is based on Internet technology, we think that the documentation should either take the form of a brochure in pdf file format or, in line with time and technology, a video tutorial from screen-recording. As this is important, it is one of the tasks we will address with the next upgrade of IBRA.

A second important issue is linked to user support. The lack of documentation, as reported above, had a significant consequence to our support system. We received many emails, mainly from new users of the software, requesting information regarding the data entry process and analysis methods. To facilitate an easier start-up, we tried to visit the user and to demonstrate the software on their computer. This was possible at Moorfields in London, but how could we do this with users in Dublin, Leeds or Germany? Another concept was required. A feasible alternative method, which we tried a few times, was to use IBRA simultaneously from different locations (while we used IBRA at the University, the user accessed IBRA in the clinic). To allow synchronicity of use we were also linked via phone line, allowing us to explore and discuss the functions of IBRA step by step. A full demonstration of the features of IBRA took about 30 minutes. Those surgeons introduced to IBRA in this way very much appreciated this method and send less emails with support requests. The negative side of this system was that it required planning of appointments for the demonstration and that we could not see what the user was doing on the screen. Sometimes, when there was a problem with the use on the surgeon's side, we simply couldn't find out why it happened. This made us look into other technologies and, in particular, one system caught our attention; it was the use of the TeamViewer software. This system required the installation of the main program on our computer, and an installation of a smaller application on the user's computer (download from the IBRA website). The main program was then connected to the user's computer via the Internet, allowing desktop sharing and remote control, as if we were sitting right in front of the user's computer. System tests in our office were very successful. However, this system has not been tested with real users, as it is uncertain how surgeons would react to such an 'intrusive' support system, although the increasing complexity of IBRA and number of users will require further refinement of the support system. This has to be developed parallel to the development of the software features, and it is likely to make a similarly important contribution to the success of the whole system.

7.3.3 Patient related limitations and recommendations

The most difficult task in this research was the recruitment for the randomised controlled trial. This process was tough, slow and complicated from the beginning. Further aggravation came with the finance crisis in 2009, which hit all social levels and even made people with higher incomes more cost-aware. Finally, after 18 months of recruitment we were very disappointed and moved when we had to terminate the trial prematurely due to lack of recruitment.

We believe that, besides 'reputation factors' the high demands of private patients might be the reason why generally no controlled trials are performed in private settings. In fact, this was the first trial performed at the refractive unit at Moorfields Eye Hospital, one of the largest eye hospitals in the world. We now intend to publish the results of our experience and its impression on private practice research in the British Medical Journal, in order to provide other surgeons with an insight into the potential risks and obstacles of private practice research beforehand.

This research provided us with excellent outcome data, and new knowledge related to nomogram adjustment. We could prove that general adjustments (Figure 7.3.1.) work well for some patient groups. We could further show that individual nomogram adjustments (Figure 7.3.2.) work well for spherical adjustments, but did not sufficiently adjust the cylindrical component. Further investigations are required to analyse new concepts and strategies of nomogram adjustments, and to evaluate other factors (e.g. age and healing factors) that could be implemented into formulas, promising a positive effect on the outcome, e.g. in the reduction of the scatter of the results (Figure 7.3.3. and Figure 7.3.4). This research provides an essential platform for any future research.

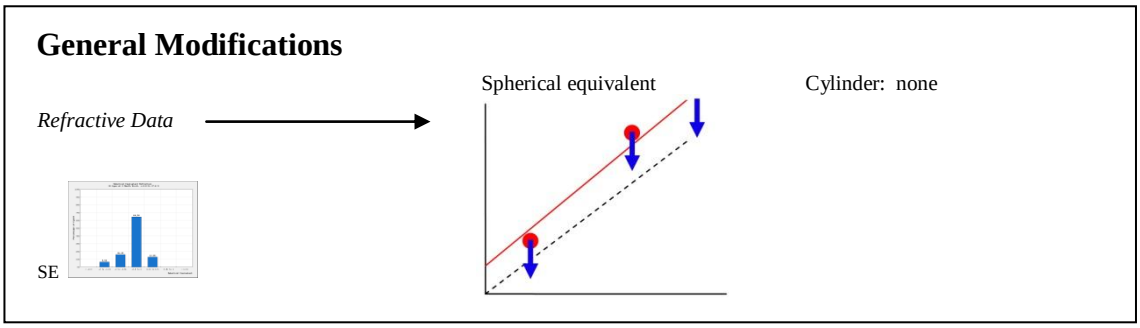


Figure 7.3.1. General modifications of laser treatments, based on linear regression analysis of the spherical equivalent with a fix amount of adjustment (blue arrow) for all patients.

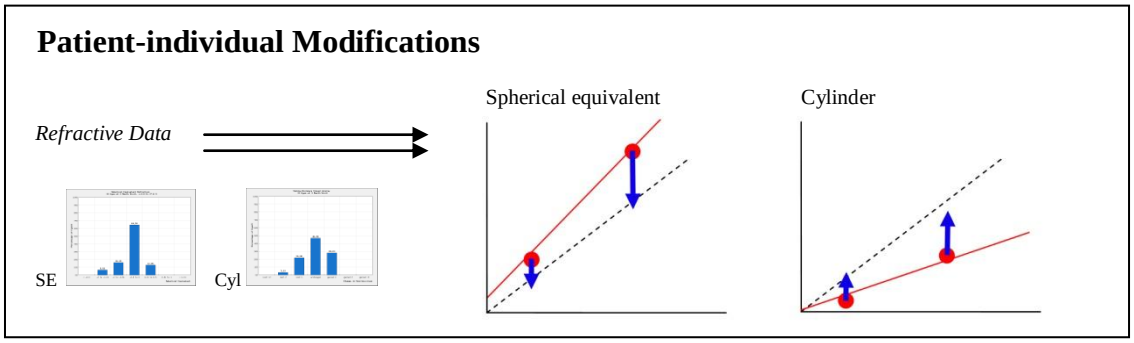


Figure 7.3.2. Patient-individual modifications of the laser treatments, based on analysis of spherical and astigmatic outcome data. Each patient received individual adjustments (blue arrows) for the sphere and cylinder correction.

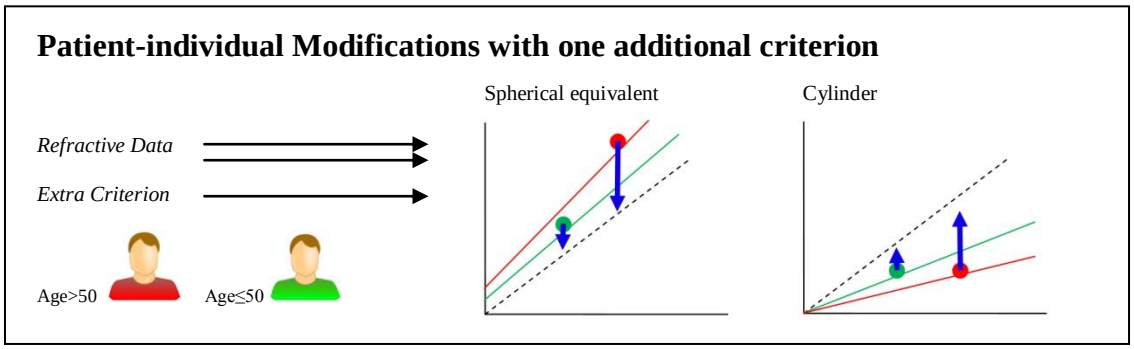


Figure 7.3.3. Next step in patient-individual modifications of laser treatments with one additional criterion, e.g. age, pachymetry, ablation, or residual stromal bed. Beside of individualisation of the treatment sphere and cylinder an additional adjustment process is programmed dependent on the extra criterion, e.g. younger patients receive lower adjustments.

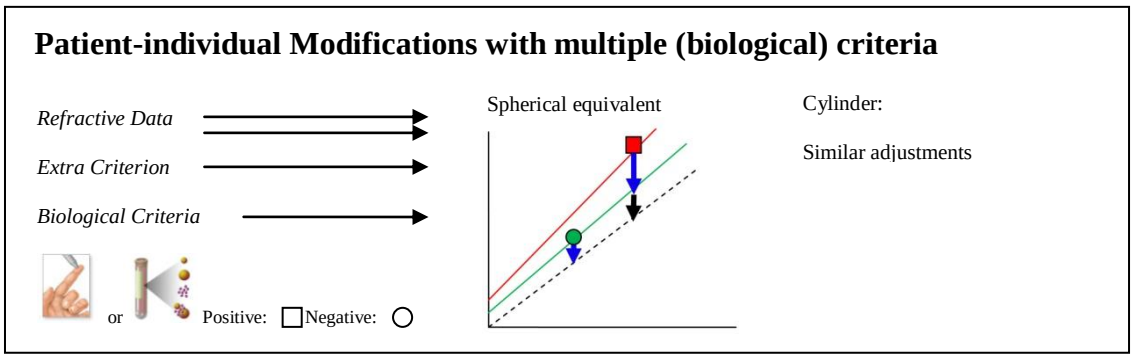


Figure 7.3.4. Future concept of patient-individual modifications of laser treatments with additional criterion from non-invasive investigation and with biological criteria from invasive tests, such as blood test, prick test or cell analysis from mucosal swab. Patients with positive test results (rectangle) will receive extra adjustments (black arrow).

The findings on spherical and cylindrical nomogram adjustment from this research are to be implemented into the next generation of the IBRA system. We recommend a modification of the existing nomogram tool with the aim of providing adjustment factors that implement general and patient-individual aspects of nomogram modification. Potentially, the best way of presenting the new adjustment factors is to create a table that contains some separation by individual factors, for example age at surgery or amount of preoperative astigmatism.

The use of the IBRA system since 2004 has led to a large collection of refractive data from the participating surgeons in the UK and Ireland. In total, we were able to collect the data of 22,000 treated eyes. Generally, the collection and analysis of refractive outcome data has become an increasingly important requirement of refractive surgery practice. The Quality Standard and Revalidation initiatives of The Royal College of Ophthalmologists underpin this importance in the provision of auditable outcomes of surgery. We will try to use and publish our data to demonstrate outcomes to patients and to external commissioners. We hope that our contributions may be included in the creation of future standards to describe outcomes in refractive laser surgery.

Chapter 8

CONCLUSIONS

8. CONCLUSIONS

This research has provided us with a unique web-based software system for the management of outcomes in laser vision correction, and with a framework within which the method of nomogram adjustment could be evaluated. The system was used manifold in real private practice settings, and showed effective modification of patient health outcome. This research has made a major impact on surgeon management of laser eye surgery. Overall, we have met the promises and aims of this research 'to record, analyse and improve the health outcome in patients undergoing laser vision correction' in all points.

A summary of unique features of this research includes:

- The research system is the only system on the market that offers standard, vector and nomogram analysis in one integrated solution.
- We have developed unique calculation algorithms for the calculation of patient-individual nomogram adjustments.
- This is the only refractive analysis system that has been systematically evaluated, including a randomised control trial.
- This is the first time that a refractive analysis system has scientifically proven effectiveness in producing a positive health change in a large number of treated eyes.
- This research showed that carefully applied nomogram adjustments are safe and can be performed by any refractive surgeon using refractive analysis software.
- This is the first fully web-based refractive analysis system.
- We have performed the first ever randomised control trial in the high-volume private practice refractive laser unit at Moorfields Eye Hospital.
- We have performed an up-to-date review on available refractive outcome software.

The results of this research have contributed to the process of defining an optimal treatment regime for patients with complex refractive disorders undergoing laser vision correction. The formulas and calculation algorithms we developed and used are adaptive, and can be implemented into future research with minimal changes. Further research is required to analyse new concepts and strategies of nomogram adjustments

and to evaluate factors other than refractive ones (e.g. healing factors) influencing the outcome of laser vision correction.

We have demonstrated that surgeons from different countries have similar requirements regarding refractive analysis, and we have provided information on the effectiveness of data entry methods related to refractive data.

In total, we collected results from more than 22,000 laser treatments. The analysis of this multi-centre data may provide a useful contribution to the upcoming ‘Revalidation Standards’ of The Royal College of Ophthalmologists.

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Appendix 1

CLINICAL TRIAL PROTOCOL

Clinical Trial Protocol

1. GENERAL INFORMATION

Title
Patient-individual modification of laser settings in the treatment of astigmatic myopia with laser in-situ keratomileusis

Protocol Version
07/07/2008

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Participating Institutions

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- Department of Corneal and External Eye Disease, Moorfields Eye Hospital, London
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- Statistical Advice Unit, Moorfields Eye Hospital, London
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2. PROJECT SUMMARY

The treatment of myopia (short-sightedness) with refractive eye laser surgery has become widely available. The Refractive Audit 2007 analyzed 2310 eyes after laser in-situ keratomileusis (LASIK) and showed that the treatment of eyes with myopia (simple myopia) was superior to the treatment of eyes with combined myopia and astigmatism (abnormality in the shape of the cornea). Whereas 79% of eyes with simple myopia achieved the treatment target within 0.5 diopters (D), only 56% of eyes with astigmatic myopia were within 0.5D of the target refraction. It was suggested that a patient-individual modification of the treatment parameters could improve the outcome in such eyes. Based on this idea a software system with a calculation formula was developed that enables patient-individual optimization of the treatment settings. The aim of the research is to evaluate this new system for LASIK in eyes with astigmatic myopia. The methodology includes a randomized clinical trial with two groups. Participants of group 1 will receive the standard treatment regime; participants of group 2 will be treated using the new formula. This research will be conducted at Moorfields Eye Hospital within 2 years. It will make a major contribution to a new and affordable technique that can improve patient's health and the cost-effectiveness in refractive eye laser surgery.

3. BACKGROUND AND RATIONAL

Background

Refractive eyes laser surgery is a specialized field of eye surgery that focuses on improving the optical state of the eye using an excimer laser beam to reshape the surface of the cornea. In successful treatments the induced refractive change equals the preoperative refractive error. Therefore, in many cases, it can eliminate the need for glasses. Otherwise, overcorrection or undercorrection may worsen the preoperative situation, may increase the need for visual aids and laser re-treatments.

A total of 2310 eyes were analyzed for the Refractive Audit 2007 that were treated at Moorfields Eye Hospital for myopia (short-sightedness), hyperopia (long-sightedness) and astigmatism (irregular or toric curvature of the cornea). Especially the outcome of eyes with combined myopia and astigmatism was disappointing. Only 56% of these eyes were within 0.5 diopters (D) of the attempted spherical equivalent refraction (simple myopia: 79% of eyes, Figure 1).

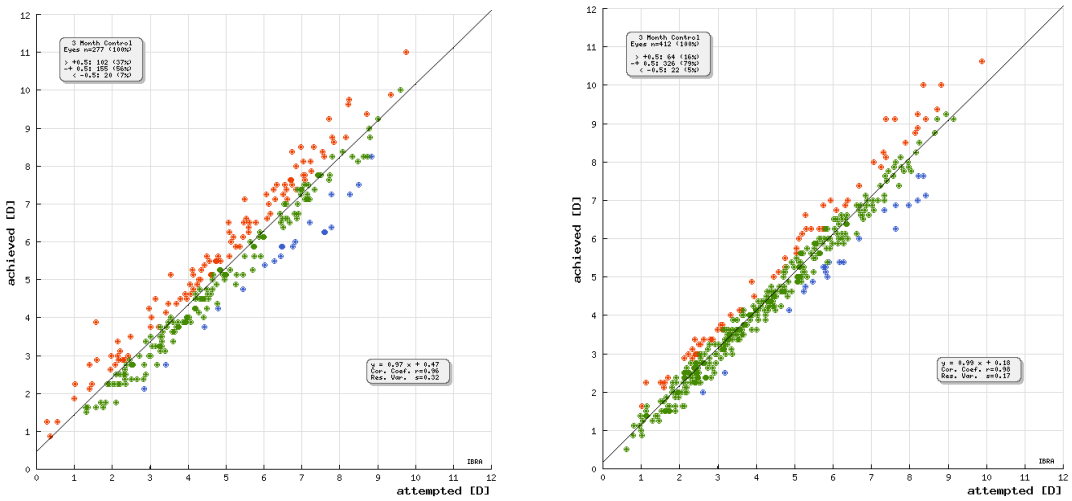

Figure 1 *Predictability of the spherical equivalent (SE) 3 months after laser in-situ keratomileusis for 277 eyes with combined myopia and astigmatism (left scattergram), compared to 412 eyes with simple myopia (right scattergram). Results from the Refractive Audit 2007 at Moorfields Eye Hospital.*

Rational

We believe that the higher amount of overcorrection and distribution in eyes with astigmatic myopia is a result of the inaccurate determination of the treatment setting. We assume that the outcome can be improved in these eyes by a patient-individual modification of the treatment setting. Up-to-date, the available software systems are not able to analyze refractive data patient-individually, and they are not able to provide the surgeon with modified treatment parameters. To meet these needs, we developed such a system with a calculation formula at Moorfields Eye Hospital. Based on patient's preoperative refraction, the formula individually calculates the amount of change in the treatment setting that is necessary to reach the target refraction more precisely.

The use of the new system has the potential to improve the refractive outcome (patient health change). This is clinically needed to increase the postoperative uncorrected visual acuity, to increase patient's satisfaction, to decrease the number of follow-up visits and to decrease the rate of re-treatments. Such a treatment can improve the cost-effectiveness in refractive eye laser surgery.

This is the first research that clinically evaluates the benefit of a system that modifies the laser treatment settings patient-individually. This is mandatory for clinical trials of current and future treatment regimes.

4. AIM AND OBJECTIVES

The aim of this research is

- To improve the health outcome in patients with astigmatic myopia.

The objectives of the research are

- To plan and undertake a randomized clinical trial.
- To use the new calculation system and formula to modify the treatment settings.
- To compare the results of the new treatment regime with the standard.

5. METHODOLOGY

Inclusion criteria

The study population for this randomized clinical trial (RCT) will consist of healthy female and male participants. The main inclusion criterion is astigmatic myopia, as defined as astigmatism of ≥1.0 D with a negative spherical equivalent (also "compound myopic astigmatism"). The research design is shown in Figure 2.

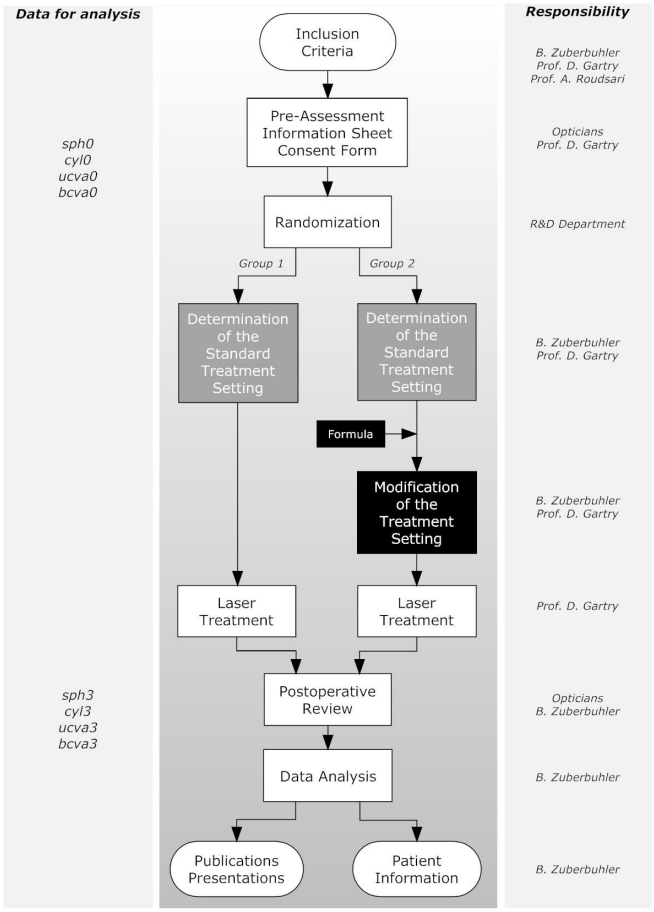

Figure 2 *Research design.*

Sample size
To detect as significant at 5% level a difference of this size with 80% power, we would need to recruit 49 subjects per treatment group. With a potential loss to follow-up of 20-30% (coming back rate of 70-80% in the Refractive Audit 2007), the sample size is adjusted to a total number of 128 participants.

Information and informed consent
The appointments will take place at Moorfields Eye Hospital, Arthur Steele Unit, 205 City Road, London, EC1V 1JN. The Chief will approach all participants or Principal Investigator and the study will be explained to them. Participants will be given an information sheet (Attachment 1) to take away and discuss with anyone they wish. They will also be given the opportunity to ask any questions before they decide whether or not to participate. If the participant agrees to take part in the study, the Chief or Principal Investigator will obtain informed consent (Attachment 2 and Attachment 3) and arrange an appointment for the study procedures to be performed. If participants are unable to understand what is involved and are unable to give their informed consent, they will not be included in the study.

Pre-Treatment assessment
The initial consultation can take approx. 50 min and will normally include an assessment of the accuracy of the patient's subjective refraction, auto-refraction, wavefront measurement, computerized corneal topography (corneal shape) and pachymetry (corneal thickness), determined by opticians. Further, the consultation includes a detailed examination of the eye, performed by the Chief or Principal Investigator. The data of the subjective refraction (sph0, cyl0 and ax0), the uncorrected and best-corrected visual acuity (ucva0 and bcva0), the wavefront refraction and the topography data will be collected for the research.

Randomization
The Research & Development (R&D) Department at Moorfields Eye Hospital will perform randomization of the participants. The R&D Department will allocate each participant either to group 1 or group 2. Further, each participant will be given an identification number.

Treatment setting determination
Chief or Principal Investigator, in accordance with the participant, will define the refractive target of each eye. The amount of refractive change necessary to achieve this target is prescribed by the laser treatment setting. The laser treatment setting consists of the parameters treatment sphere (sphS), treatment cylinder (cylS) and treatment axis (axS). These parameters will be determined for each participant individually, based on the current standard regime for participants allocated to group 1, and based on the new treatment regime for participants allocated to group 2.

Standard treatment setting (Group 1)
The process to determine the treatment setting for group 1 is shown in Figure 3. This process is well established and currently in use as standard regime. It was also used for the treatment of all patients in 2007 (Refractive Audit 2007). The sphere value of the manifest refraction will be used as treatment sphere (sphS) when the difference between the manifest and the WaveScan sphere is less than 0.5 diopters (D). The cylinder value of the manifest refraction will be used as treatment cylinder (cylS) when the difference between the manifest and the WaveScan cylinder is less than 0.25D. And the axis value of the manifest refraction will be used as treatment axis (axS) when the difference

between the manifest axis, the WaveScan axis and the axis of the Topography is less than 10°. If the differences between the sphere, cylinder or axis parameters are bigger than the mentioned limits, the preoperative examination will be repeated. Finally, the determined parameters will be entered in the laser unit for the treatment of the participants.

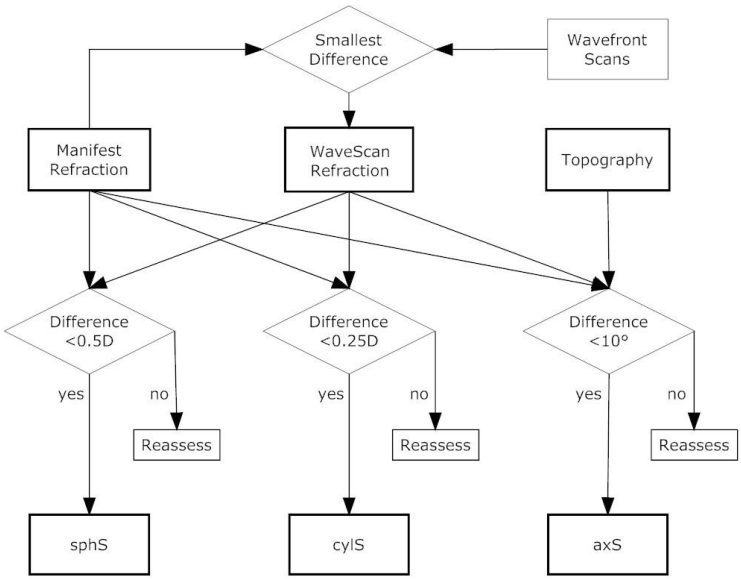

Figure 3 *Determination of the standard treatment setting (sphS, cylS and axS) as used for the laser treatment of patients with astigmatic myopia in 2007 (Refractive Audit 2007).*

Modified treatment setting (Group 2)

Participants allocated to group 2 will receive a modified treatment setting. In a first step, the treatment sphere (sphS), treatment cylinder (cylS) and treatment axis (axS) are determined identically as described above "as standard" for group 1. This standard setting is the default for the modification (Figure 4). Based on the preoperative refraction (SE and cylinder) the first part of the new formula (Figure 5) calculates the estimated refractive error: the amount of SE overcorrection (SEerror, in %) and cylinder undercorrection (Cylerror, in %). Subsequently, these values are used by the second part of the formula to calculate the amount the standard setting has to be changed (SE change and Cyl change, in D). The "SE change" will be subtracted from the treatment SE and the "Cyl change" will be added to treatment cylinder; finally resulting in the new treatment sphere (sphII) and treatment cylinder (cylII). The setting for the treatment axis (axS) will not be changed (axS =axII). The modified treatment sphere (sphII) and treatment cylinder (cylII) will be entered in the laser unit for the treatment of participants of group 2.

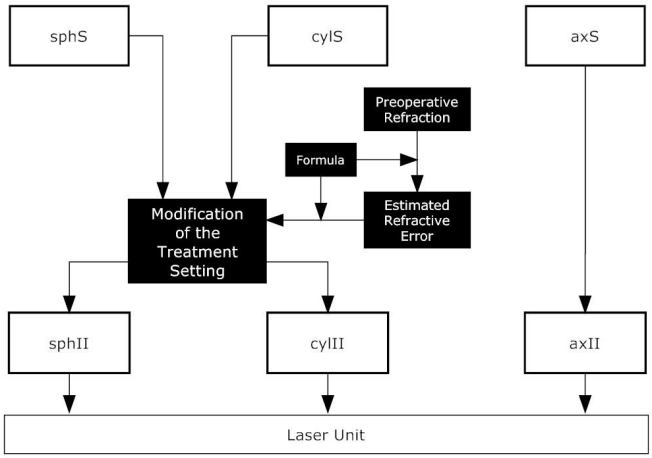

Figure 4 *Modification of the treatment setting, based on the standard treatment refraction (sphS, cylS and axS).*

Refractive error: SEerror [%] = $18 * SE^{-0.72} + 0.5 * Cyl$ Cylerror [%] = $32 * Cyl^{-0.31}$ **Modification of the treatment setting:** SE change [D] = SE/100*SEerror + 0.25*Cyl/100*Cylerror Cyl change [D] = 0.5*Cyl/100*Cylerror **Example:** *Use of above formulas for an astigmatic myopic eye.* *Preoperative SE= -5.25 and Cyl=-2.25.* *SEerror = 6.58 %* *Cylerror = 24.89 %* *SE change = 0.49 D* *Cyl change = 0.28 D*	**Comments:** *SE = preoperative spherical equivalent* *Cyl = preoperative cylinder* *SE overcorrection* *Cylinder undercorrection* *to be taken off the standard treatment SE* *to be added to the standard treatment cyl*

Figure 5 *Formulas for the calculation of the refractive error and the modification of the treatment setting, with comments (right side) and example.*

Laser treatment

Following the determination of the treatment setting the participants of both groups will undergo identical wavefront-guided or refraction based laser in-situ keratomileusis (LASIK) at Moorfields Eye Hospital, Refractive Laser Suite (4th floor main hospital), performed by the Chief Investigator. A superiorly hinged corneal flap of 160µ thickness and 8.5 to 9.0mm diameter will be cut with the Hansatome microkeratome (Bausch & Lomb, Germany). Alternatively, the FS60 Femtosecond Laser (Intralase, UK) may be used for the creation of the corneal flap. In combination with LASIK this procedure is called "IntraLASIK". The flap will be folded upwards and the ablation will be performed using the laser treatment setting. Following replacement of the flap the interface will be rinsed and antibiotic and anti-inflammatory eye drops will be given. The laser procedure will take approx. 40 min for each participant, including the preparation of the laser and instruments. After the treatment the participants are allowed to go home. Standard eye drops (anti-inflammatory, antibiotic and lubricant drops) are used every 2 hours for the first week.

Postoperative review
Careful slit-lamp examination is performed within 24-48 hours to confirm that the LASIK flap is properly positioned. Rarely, participants will be reviewed at 4 weeks time. The main follow-up appointment is at 3 months time and includes slit-lamp examination, subjective refraction (sph3, cyl3 and ax3) and uncorrected and best-corrected visual acuity assessment (ucva3 and bcva3), determined by opticians. The data of the 3 months review will be used for the research. The postoperative review will take approx. 30 min and will take place at Moorfields Eye Hospital, Arthur Steele Unit, 205 City Road, London, EC1V 1JN. Because we anticipate a high loss to follow-up, patients who fail to attend will be contacted to obtain qualitative comments, to establish whether treatment outcome influences non-attendance.

6. DATA MANAGEMENT AND ANALYSIS

Main outcome measure
Main outcome measure is the percentage of eyes achieving a postoperative spherical equivalent (SE) within 0.5D of the target SE. Generally, the SE is the sum of the sphere (sph) and half of the cylinder (cyl) value (SE=Sph+0.5*Cyl). With conventional treatment settings this has been shown to be 56% (Based on the Refractive Audit 2007 at Moorfields Eye Hospital). With the new treatment settings we would expect to increase this to 79%. Sphere and cylinder value will be assessed by subjective refraction.

Data management
The data will be collected by the Principal Investigator on data collection sheets (Attachment 4) and entered into the SQL database designed by the R&D Department.. Personal information will be kept in locked, secure-access filing cabinets or on password-protected institute computers. Only research personnel will have access to the data. Data will be stored for 2 years, in accordance with the Data Protection Act 1998. Data that leaves the hospital will be anonymized.

Data analysis
Baseline characteristics of the two groups will be compared to assess the adequacy of randomisation. A Chi-square test will be used to compare the proportion of patients with successful outcomes in each group. Logistic regression will be employed should there be any marked difference in any prognostic factor between treatment groups. We will conduct an available case analysis but will also contact patients who are lost to follow-up to ensure that their reasons for DNA are not associated with the likelihood of a good outcome.

Timetable
The study will be completed within 2 years.

7. ETHICAL CONSIDERATIONS

Full ethical commission approval will be obtained. Potential participants will be assured that their involvement is entirely voluntary, that they can withdraw from the study at any time and that their normal clinical management will not be affected in any way should they decide not to take part in the study.

8. ATTACHMENTS

- Attachment 1 : Participant information sheet
- Attachment 2: Participant consent form
- Attachment 3: Consent form IntraLASIK 2008
- Attachment 4: Data collection sheet

9. REFERENCES

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Appendix 2

PARTICIPANT INFORMATION SHEET

Moorfields Eye Hospital NHS
NHS Foundation Trust

City Road
London
EC1V 2PD

Tel: 020 7253 3411

Participant information sheet

You are being invited to take part in a research study conducted by Moorfields Eye Hospital NHS Foundation Trust. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

This study is approved by and follows the guidelines of the National Research Ethics Service (NRES) with the idea to protect the rights, safety, dignity and well being of research participants, whilst facilitating and promoting ethical research within the NHS. In addition, this study is approved by the Moorfields Eye Hospital Institutional Review Board.

What is the title of the research?
The title of the research is: "Individual optimization of the laser settings in eyes with astigmatic myopia undergoing laser in-situ keratomileusis (LASIK)."

Why have I been chosen?
You are being asked to participate because you are a healthy person with combined shortsightedness (myopia) and astigmatism.

Why is this study being done?
The refractive laser unit at Moorfields Eye Hospital is a leading laser center in Europe. Regular audits of the patient outcome and optimizing of the treatment regime is part of the quality controlling system. Whereas the laser treatment of myopia reached the highest possible level of precision, the treatment of combined myopia and astigmatism is more difficult because of the nature of the disease. During the last 2 years, surgeons at Moorfields Eye Hospital developed a new calculation method with the aim to optimise the treatment parameters. This should result in a more accurate outcome in patients with myopia and astigmatism. This study is part of the evaluation process of this new method.

Do I have to take part?
We assure that your involvement is entirely voluntary, that you can withdraw from the study at any time and that your normal clinical management will not be affected in any way should you decide not to take part in the study. If you decide not to participate you can still undergo laser eye surgery.

Will I be paid for participating in the research?
Participants will not receive money for taking part in the research study. The laser surgery fees apply to participants and non-participants alike.

What are the potential benefits of taking part?
The potential benefit is a better refractive outcome, an improved uncorrected distance visual acuity and a lower rate of re-treatments.

What will happen to me if I take part?
In this study participants will be randomized to one of 2 groups. Participants in group 1 will be treated with the standard, well established treatment regime. Participants in group 2 will be treated with the new method. The only difference between the two groups is the amount of correction for the myopia and for the astigmatism that will be entered in the controller software of the laser unit. No difference exists between the 2 groups regarding the preoperative assessment, the operational technique, the postoperative treatment and the reviews. All participants will be treated by the same surgeon (Prof. Gartry).

What are the risks of the study?
There are no physical risks associated with this study. There is, however, the potential risk of overcorrection or undercorrection in the refractive outcome.

What if something goes wrong?
Complaints can be addressed to the Chief Investigator or to Moorfields Eye Hospital, Complaints Manager, 162 City Road, London, EC1V 2PD. We assure that everything possible will be done to manage your concern effectively and efficiently.

Will my taking part in this study be kept confidential?
Your information will be kept in a secure electronic database at Moorfields Eye Hospital and may be used for future studies within the next 2 years.

What will happen to the results of the research study?
The results of the research will be published in ophthalmological journals (in 2009/2010). It will not be possible to identify individual participants in any of the reports or publications. Each participant will receive a summary of the results after publication. A copy of the whole article can be obtained from the Chief Investigator.

Thank you very much for taking the time to read this information. Should you agree to take part in this research, your generosity ensures that future generations will benefit. If you have any questions regarding the research study or the information sheet, please contact your GP or one of the following investigators.

Chief Investigator: Prof. David Gartry
Head of Refractive Surgery Unit
Moorfields Eye Hospital NHS Foundation Trust, London
Department of Optometry and Visual Science, City University London

Associate Investigator: Prof. Abdul Roudsari
Head of Centre for Health Informatics
City University London, City University London

Principal Investigator: Dr. Bruno Zuberbuhler
Moorfields Eye Hospital NHS Foundation Trust, London
Centre for Health Informatics, City University London

Appendix 3

PARTICIPANT CONSENT FORM

Moorfields Eye Hospital NHS
NHS Foundation Trust

City Road
London
EC1V 2PD

Tel: 020 7253 3411

Participant consent form

Name of participant:
……..

Patient ID:
……

Title of the project:
……...

Members of the research team:
…….....

- I agree to take part in the above research. I have read the Participant Information Sheet, which is attached to this form. I understand what my role will be in this research, and all my questions have been answered to my satisfaction.
- I understand that I am free to withdraw from the research at any time, for any reason and
  without prejudice.
- I have been informed that the confidentiality of the information I provide will be safeguarded.
- I am free to ask any questions at any time before and during the study.
- I have been provided with a copy of this form and the Participant Information Sheet.
- Inform GP or other health professional

Data Protection: I agree to the processing of personal data that I have supplied for any purposes connected with the Research Project as outlined to me.

Name of participant
(print)……..…….Signed……..….Date……

Name of surgeon
(print)……..…..Signed……..….Date……

Name of witness
(print)……..…..Signed……..….Date……

Three copies should be made, for (1) participant, (2) researcher, (3) hospital notes.

Appendix 4

CONSENT FORM INTRA-LASIK 2008

Moorfields Eye Hospital NHS
NHS Foundation Trust

City Road
London
EC1V 2PD

Tel: 020 7253 3411

Consent form IntraLASIK 2008

Statement of Informed Consent to Undergo Wavefront-Guided or Refraction (Sight-Test) based IntraLASIK or Microkeratome LASIK

Carefully read each paragraph/statement and having read and understood each statement please initial each on the dotted lines that follow each section. In signing this form, you are stating that you have read and understand this consent form. Although it contains medical terms that you may not completely understand on first reading, you have had the opportunity to ask questions and had them answered to your satisfaction such that you understand the information on this form.

In giving my permission for undergoing LASIK treatment, I declare that I have read and understood the following information:

1) I confirm that I have read and understand this information sheet regarding LASIK contained in this document and have had the opportunity to ask questions.

Initial .....

2) I understand that the femto-LASIK procedure involves surgical elevation of a LASIK corneal flap and excimer laser surgery involves the removal of a thin layer of tissue from my cornea.

Initial .....

3) I have discussed the operation with my Ophthalmic Surgeon and the risks and benefits of such a procedure have been detailed in as far as current information regarding this procedure allows. Although it would be impossible to have every conceivable outcome and complication explained I have had all my questions answered to my satisfaction.

Initial .....

4) I understand that wavefront-guided femto-LASIK treatment is a relatively new procedure and therefore this technique remains the subject of clinical investigation. The long-term effects of this treatment are not yet definitely known. Treatment is elective and it must be considered investigational.

Initial .....

5) I understand that the final outcome of this procedure is dependent on the individual surgeon, the wavefront laser scan, the excimer laser system, the surgical technique and the healing process of each patient. This may result in under or over-correcting of my refraction and may alter the quality of my vision. The final amount of correction of my myopia or hyperopia and/or astigmatism and higher order aberrations cannot be guaranteed. If the healing process is irregular it may affect the quality of my vision or cause a reduction in the sharpness of this vision.

Initial .....

6) I understand that there may be short-term and long-term side effects of this procedure. The following immediate complications of the procedure include, tearing of the LASIK flap, irregularity in the flap due to stretching of the tissue, reticulations, wrinkles and folds in the flap, complete loss of the flap or tearing to become a free cap, infection, inflammation, late displacement, melting of the flap, melting of the cornea, chronic prickling or sharp pains. There may be damage to the corneal endothelium. Glaucoma due to the use of steroid drops, drooping of the eyelid due to inflammation and steroid drops. Other long-term problems include potential bulging of the cornea (ectasia) and refractive instability with fluctuation in vision. Some scarring irregularity or haziness of the cornea, glare, haloes or 'star burst effects' around bright lights, though the Wavefront Guided treatment aims to correct this. There may be permanent long sight or persistent myopia (near sight) requiring spectacle or contact lens wear. There may be a persisting prickling sensation. Recurrent problems with the epithelium of the cornea where it may grow under the flap of the cornea. Although it is anticipated that this complication will be very rare, a reactivation of *Herpes simplex* virus may occur if the virus is present in the nerves of the eye. Some of these effects may produce a permanent reduction in best-corrected vision (with contact lenses or glasses). There may be dry eye symptoms after treatment and this may be severe for a period of up to 9 months. There may be an imbalance between the eyes, double vision, ghosting of vision, reduced contrast of vision, blood vessels may grow into the cornea, recurrent discomfort and pain due to recurrent erosion where the surface epithelial cells repeatedly are loose and are dislodged. Increased light sensitivity may occur.

Initial .....

7) It is possible that my desired result from this procedure may not be obtained and I may still need to wear glasses, contact lenses or undergo further corneal surgery in order to obtain the best vision possible. It may be that the LASIK treatment under- or over-corrects and the flap may need to be lifted to apply further laser treatment. The corneal surface epithelium may grow under the protective flap and it may require treatment to remove this unwanted ingrowth of cells. It may be that further re-treatment of the lasered eye may not be beneficial and treatment to the other eye may not be advisable.

Initial .....

8) I understand that after the age of 40-45 most normally sighted individuals require reading glasses, therefore if I have my myopia corrected by excimer laser I will still require reading glasses when I enter the 40-45 year old age group.

Initial .....

9) For completeness the following symptoms have been reported or are anticipated. Difference in spectacle requirement between both eyes if only one eye is treated, making comfortable spectacle correction for both eyes difficult (anisometropia). Difference in image size between the two eyes (aniseikonia). Double vision (diplopia). Fluctuating vision and decreased visual acuity. Possible inability to wear contact lenses. However, I understand that it is impossible to state every possible complication that may occur following surgery and therefore those complications stated in this consent form do not form a complete or exhaustive list.

Initial .....

10) I understand that by consenting to undergo this LASIK procedure, to obtain the best result I must comply with the use of topical medication prescribed by David Gartry and that attendance for follow-up will be recommended after laser treatment.

Initial .....

11) I understand that my identity will be kept confidential in any reports or journal articles. I give permission for medical data concerning my operation and any subsequent treatment to be submitted for publication and to regulatory agencies and for my records to be entered onto the Moorfields electronic patient administration system and David Gartry's electronic records.

Initial .....

12) In signing this Informed Consent Form for performing the LASIK procedure, I am stating that I have read this Informed Consent and I fully understand it and the possible risks, complications and benefits that can result from the surgery. My decision to undergo LASIK is my own and has been made without duress of any kind. The nature of this treatment has been fully explained and understood by me.

Initial .....

I also consent to such further or alternative measures as may be found to be necessary during the course of the treatment and to the administration of a local anaesthetic for any of these purposes. I agree to undergo LASIK treatment. The nature of this treatment has been fully explained to and understood by me. I agree that my GP be informed of my involvement in this treatment.

PROCEDURE IntraLASIK Wavefront-Guided excimer laser treatment (iLASIK)
IntraLASIK Refraction-Based excimer laser treatment
Microkeratome LASIK Wavefront-Guided excimer laser treatment
Microkeratome Refraction-Based excimer laser treatment

EYE(S) FOR TREATMENT Right Left Both Eyes

PATIENT **Print Name** .....

Signature ..... Date .....

SURGEON **Signature** ..... Date .....
David S Gartry, Consultant Ophthalmic Surgeon

WITNESS **Print Name** .....

Signature ..... Date .....

Appendix 5

DATA COLLECTION SHEET

Data collection sheet

Research Title:
Patient-individual modification of laser settings in the treatment of astigmatic myopia with laser in-situ keratomileusis

Chief Investigator: Prof. David Gartry, Moorfields Eye Hospital
Principal Investigator: Dr. Bruno Zuberbuhler, Moorfields Eye Hospital

Patient ID

Age of participant

Eye

Preoperative assessment

Uncorrected visual acuity:

Manifest refraction: sph cyl ax

Best-corrected visual acuity:

WaveScan refraction: sph cyl ax

Operational details

Refractive treatment: sph cyl ax

Target refraction: sph cyl ax

Comments:

3 months follow-up

Uncorrected visual acuity:

Subjective refraction: sph cyl ax

Best-corrected visual acuity:

.

Appendix 6

DECISION LETTER ETHICS COMMITTEE

NHS

National Research Ethics Service

The Royal Marsden Research Ethics Committee

St Georges University of London
South London REC Office (1)
Room 1.13
1st Floor - Jenner Wing
Blackshaw Road
Tooting, London
SW17 0RE

[redacted]

02 October 2008

Professor David Gartry
Consultant Ophthalmic Surgeon
[redacted]

Dear Professor Gartry,

Full title of study: **Patient-individual modification of laser settings in the treatment of compound myopic astigmatism with laser in-situ keratomileusis: a randomized controlled trial**

REC reference number: **08/H0801/99**

Thank you for your letter of 12 September 2008, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered at the meeting of the Sub-Committee of the REC held on 19 September 2008. A list of the members who were present at the meeting is attached.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The Committee has designated this study as exempt from site-specific assessment (SSA). The favourable opinion for the study applies to all sites involved in the research. There is no requirement for other Local Research Ethics Committees to be informed or SSA to be carried out at each site.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Application	1.0	14 July 2008
Investigator CV		14 July 2008
Protocol	02	
Covering Letter		16 July 2008
Covering Letter		10 September 2008
Letter from Sponsor		16 July 2008
GP/Consultant Information Sheets	01	14 July 2008
Participant Information Sheet: with track changes	02	09 September 2008
Participant Consent Form: with track changes	02	09 September 2008
Response to Request for Further Information	01	12 September 2008

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

08/H0801/99 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

[redacted]

Ms Shelley Dolan
Chair

Email: royalmarsden.rec@stgeorges.nhs.uk

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers"

Copy to: *Mrs Sue Lydeard, Moorfields Eye Hospital NHS Foundation Trust*
Ms Jane Lawrence, R&D Manager, RMH

The Royal Marsden Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 19 September 2008

Ms Shelley Dolan	Chief Nurse	Chair
Dr Paul Farquhar-Smith	Consultant Anaesthetics, Pain & ITU	Vice Chair

Appendix 7

IBRA TREATMENT ADJUSTMENT TABLE

IBRA treatment adjustment table

PATIENT STICKER

Upper value: to be added to the treatment **sphere**
Lower value: to be added to the treatment **cylinder**

Treatment cylinder →

	0	**-0.25**	**-0.5**	**-0.75**	**-1**	**-1.25**	**-1.5**	**-1.75**	**-2**	**-2.25**	**-2.5**	**-2.75**	**-3**	**-3.25**	**-3.5**	**-3.75**	**-4**
0.0	0.47	0.48	0.49	0.50	0.52	0.53	0.54	0.55	0.56	0.57	0.58	0.59	0.61	0.62	0.63	0.64	0.65
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-0.5	0.46	0.47	0.48	0.49	0.50	0.51	0.52	0.53	0.55	0.56	0.57	0.58	0.59	0.60	0.61	0.62	0.64
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-1.0	0.44	0.45	0.46	0.47	0.49	0.50	0.51	0.52	0.53	0.54	0.55	0.56	0.58	0.59	0.60	0.61	0.62
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-1.5	0.43	0.44	0.45	0.46	0.47	0.48	0.49	0.50	0.52	0.53	0.54	0.55	0.56	0.57	0.58	0.59	0.61
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-2.0	0.41	0.42	0.43	0.44	0.46	0.47	0.48	0.49	0.50	0.51	0.52	0.53	0.55	0.56	0.57	0.58	0.59
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-2.5	0.40	0.41	0.42	0.43	0.44	0.45	0.46	0.47	0.49	0.50	0.51	0.52	0.53	0.54	0.55	0.56	0.58
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-3.0	0.38	0.39	0.40	0.41	0.43	0.44	0.45	0.46	0.47	0.48	0.49	0.50	0.52	0.53	0.54	0.55	0.56
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-3.5	0.37	0.38	0.39	0.40	0.41	0.42	0.43	0.44	0.46	0.47	0.48	0.49	0.50	0.51	0.52	0.53	0.55
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-4.0	0.35	0.36	0.37	0.38	0.40	0.41	0.42	0.43	0.44	0.45	0.46	0.47	0.49	0.50	0.51	0.52	0.53
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-4.5	0.34	0.35	0.36	0.37	0.38	0.39	0.40	0.41	0.43	0.44	0.45	0.46	0.47	0.48	0.49	0.50	0.52
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-5.0	0.32	0.33	0.34	0.35	0.36	0.38	0.39	0.40	0.41	0.42	0.43	0.44	0.45	0.47	0.48	0.49	0.50
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-5.5	0.31	0.32	0.33	0.34	0.35	0.36	0.37	0.38	0.40	0.41	0.42	0.43	0.44	0.45	0.46	0.47	0.49
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-6.0	0.29	0.30	0.31	0.32	0.34	0.35	0.36	0.37	0.38	0.39	0.40	0.41	0.43	0.44	0.45	0.46	0.47
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-6.5	0.27	0.29	0.30	0.31	0.32	0.33	0.34	0.35	0.36	0.38	0.39	0.40	0.41	0.42	0.43	0.44	0.45
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-7.0	0.26	0.27	0.28	0.29	0.31	0.32	0.33	0.34	0.35	0.36	0.37	0.38	0.40	0.41	0.42	0.43	0.44
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-7.5	0.24	0.26	0.27	0.28	0.29	0.30	0.31	0.32	0.33	0.35	0.36	0.37	0.38	0.39	0.40	0.41	0.42
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-8.0	0.23	0.24	0.25	0.26	0.28	0.29	0.30	0.31	0.32	0.33	0.34	0.35	0.37	0.38	0.39	0.40	0.41
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36
-8.5	0.22	0.23	0.24	0.25	0.26	0.27	0.28	0.29	0.31	0.32	0.33	0.34	0.35	0.36	0.37	0.38	0.40
	0.00	-0.02	-0.05	-0.07	-0.09	-0.11	-0.14	-0.16	-0.18	-0.20	-0.23	-0.25	-0.27	-0.29	-0.32	-0.34	-0.36

↓ *Treatment sphere*

	Sph	Cyl	Ax
Standard treatment			
Adjustment			
IBRA treatment			

Appendix 8

DECLARATION OF THE END OF A STUDY

National Patient Safety Agency

National Research Ethics Service

DECLARATION OF THE END OF A STUDY

(For all studies except clinical trials of investigational medicinal products)

To be completed in typescript by the Chief Investigator and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC") within 90 days of the conclusion of the study or within 15 days of early termination. For questions with Yes/No options please indicate answer in bold type.

1. Details of Chief Investigator

Name:	Professor David Gartry
Address:	[redacted]
[redacted]	[redacted]
Email:	[redacted]
[redacted]	[redacted]

2. Details of study

Full title of study:	Patient-individual modification of laser settings in the treatment of compound myopic astigmatism with laser in-situ keratomileusis: a randomized controlled trial.
Research sponsor:	Private (Prof Gartry)
Name of main REC:	The Royal Marsden Research Ethics Committee
Main REC reference number:	08/H0801/99

3. Study duration

Date study commenced:	20 October 2008
Date study ended:	19 February 2010
Did this study terminate prematurely?	***Yes*** ~~*/ No*~~ *If yes please complete sections 4, 5 & 6, if no please go direct to section 7.*

4. Circumstances of early termination

What is the justification for this early termination?
The reason for the termination is the slow and finally stagnating recruitment process. **Background** The problems in recruiting can be attributed to increasing expectations of highly demanding private patients. In the current financial crisis there are fewer private patients and they only intend to undergo laser vision correction when they are sure that they will receive the best possible treatment, resulting in the best possible outcome. With this idea patients are searching for 'the best surgeon' that can fulfil their demands. Over the last 6 months it has become more and more difficult to convince patients to participate on a randomized trial that evaluates 2 different treatment regimes to find out which one's the better. Most patients get confused and frustrated after they have been informed about the trial and its aim. They can hardly understand that 'the best surgeon' is not sure about the optimal treatment. At this stage many patients decide to postpone their operation until the question of the best treatment has been answered. In addition, some very sceptical patients criticize the surgeon's competency and search for another surgeon 'who knows the best treatment'. **Action taken in the past** We have tried to change our way of recruiting multiple times. We have changed the scheduling of asking, the way of providing information and its content, and we have extended the time spent for explanation. In December 2009 we discussed the situation with the R&D department and have agreed to set interim recruitment targets. Unfortunately, the recruitment could not be improved (target not met) and by the end of January we finally decided to terminate the trial. **Action plan / data** We intend to trace and review all 45 participants and to collect the 3 months postoperative results of all 79 treated eyes. We are aware that the numbers are too low for complex statistical analysis (underpowered), but we aim to perform descriptive analysis of the results. We will present our results in the final report within the next 12 months. If the results are conclusive we will aim for publication.

5. Temporary halt

Is this a temporary halt to the study?	~~*Yes*~~ / ***No***
If yes, what is the justification for temporarily halting the study? When do you expect the study to re-start?	*e.g. Safety, difficulties recruiting participants, trial has not commenced, other reasons.*

6. Potential implications for research participants

Are there any potential implications for research participants as a result of terminating/halting the study prematurely? Please describe the steps taken to address them.	No implications expected.

7. Final report on the research

Is a summary of the final report on the research enclosed with this form?	~~*Yes*~~ / ***No, we will provide a report < 12 months.*** *If no, please forward within 12 months of the end of the study.*

8. Declaration

Signature of Chief Investigator:	[redacted]
Print name:	David Gartry
Date of submission:	19/02/2010

Appendix 9

RAW DATA FROM THE CLINICAL TRIAL

Raw data Randomised Controlled Trial - Standard group

No	pid	dob	eye	doo	targetref	targetcyl	targetax	shapingsph	shapingcyl	shapingax	ducva0	ducva3	dbcva0	dbcva3	dsph0	dsph3	dcyl0	dcyl3	dax0	dax3	pachy0	pupil	satisf3
1	74272	19.06.1965	os (L)	12.01.2009	-0.02	0.14	115	-3.98	-0.89	115	0.16	1	1	1.25	-4	-0.5	-1	0	115	0	545	6	1
2	75378	30.11.1947	os (L)	24.11.2008	-0.46	0.31	164	-3.29	-0.81	164	0.25	0.5	0.8	0.63	-3.75	-0.5	-1	-0.5	165	160	583	5.2	1.5
2	75378	30.11.1947	od (R)	24.11.2008	-0.16	0.09	175	-2.34	-1.09	175	0.32	0.63	1	0.8	-2.5	-0.25	-1	-0.5	175	170	599	5.3	1.5
5	76734	31.10.1979	od (R)	20.12.2008	0.18	-0.02	35	-4.18	-0.98	35		1.25	1.25	1.25	-4	0	-1	0	65		537	6.9	1
6	74614	29.07.1971	os (L)	20.12.2008	-0.48	-0.04	170	-4.52	-1.96	170		1.6	1.25	1.6	-5	0	-2	0	170		548	5.7	1
6	74614	29.07.1971	od (R)	20.12.2008	-0.38	0.09	21	-4.62	-1.09	21		1.25	1.25	1.25	-5	-0.25	-1	0	20		562	5.9	1
10	74272	19.06.1965	od (R)	12.01.2009	-0.11	-0.04	64	-3.89	-0.79	64	0.16	1.25	1	1.25	-4	0.25	-1	-0.5	65	70	543	6.2	1
11	77258	11.05.1965	od (R)	14.02.2009	0.28	0.05	97	-3.28	-1.55	97		1.25	1.25	1.25	-3	0	-1.5	0	105	0	526	4.4	1
13	75412	30.04.1980	os (L)	28.02.2009	-0.17	0.23	5	-8.08	-1.23	5	0.1	0.5	1	1	-8.25	-0.75	-1	-0.75	5	0	556	6.6	2
16	79107	07.07.1987	od (R)	07.03.2009	0	0.04	89	-1.25	-1.04	89		1.25	1	1.25	-1.25	0	-1	-0.25	85	170	551	5.7	1
17	78897	28.02.1984	os (L)	14.03.2009	-0.38	0.16	150	-3.37	-1.41	150	0.08	1	1.25	1	-3.75	0.25	-1.25	-0.25	150	70	559	7.3	1
21	79787	19.05.1961	od (R)	21.03.2009	-0.31	0.01	112	-2.44	-3.51	112	0.08	1	1	1.25	-2.75	0	-3.5	-0.5	115	105	512	5.6	1
22	78775	02.10.1981	os (L)	21.03.2009	-0.03	-0.21	161	-4.22	-1.29	161	0.1	1.25	1.25	1.25	-4.22	0	-1.5	-0.25	160	5	520	6.9	1
23	78775	02.10.1981	od (R)	21.03.2009	-0.23	-0.01	22	-4.52	-1.49	22	0.1	1.25	1.25	1.25	-4.75	-0.25	-1.5	-0.25	25	0	531	7.1	1
27	80140	24.10.1975	od (R)	28.03.2009	0.02	-0.07	123	-4.27	-1.18	123		1.25	1.25	1.25	-4.25	0	-1.25	0	123	0	633	5.5	1
28	77870	06.08.1967	os (L)	18.04.2009	-0.15	0.19	159	-4.1	-1.44	159		1	1.25	1.25	-4.25	-0.25	-1.25	-0.5	160	175	573	5.2	1
29	77870	06.08.1967	od (R)	18.04.2009	-0.21	0.04	7	-4.29	-1.04	7		1.25	1.25	1.25	-4.5	0	-1	0	8	0	567	5.3	1
32	79668	17.09.1967	os (L)	20.04.2009	-0.39	0.15	180	-4.86	-1.15	0		1	1.25	1.25	-5.25	0	-1	-0.75	175	170	499		1
33	79668	17.09.1967	od (R)	20.04.2009	-0.56	0.08	176	-5.94	-1.08	176		1	1	1.25	-6.5	0	-1	-0.75	170	150	511		1
34	80826	31.10.1976	os (L)	20.04.2009	-0.69	0.21	159	-4.56	-2.96	159		0.5	1	1.25	-5.25	-0.75	-2.75	-1	162	170	607	4.7	1
38	81148	25.09.1972	os (L)	25.04.2009	-0.24	-0.24	158	-4.51	-1.96	158		0.63	1.25	1	-4.75	-0.5	-2.25	-1	160	165	590	7.1	1
39	81148	25.09.1972	od (R)	25.04.2009	-0.34	0.06	21	-4.41	-1.56	21		0.8	1.25	1.25	-4.75	-0.5	-1.5	-0.5	20	5	580	7.2	1
41	80694	12.02.1959	os (L)	02.05.2009	-0.09	0.08	50	-4.41	-0.83	50	0.05	0.63	1.25	1.25	-4.5	-0.75	-1	0	50	0	537	4.6	1
44	79818	03.09.1969	os (L)	11.05.2009	-0.19	0.13	13	-3.56	-1.13	13	0.1	1	1	1.25	-3.75	-0.25	-1	0	10		553	6.7	1
46	80965	16.10.1963	os (L)	16.05.2009	-0.26	0.06	2	-3.24	-2.06	2	0.08	0.63	1	1.25	-3.5	-0.5	-2	-1	178	167	581	6.7	1.5
48	77882	08.03.1969	os (L)	23.05.2009	-0.18	0.29	55	-1.57	-2.04	55	0.1	1	1.25	1.25	-1.75	0.5	-1.75	-0.75	58	45	564	6.5	1
49	82289	17.06.1984	os (L)	23.05.2009	-0.09	0.13	180	-3.41	-1.13	180	0.08	1.25	1.6	1.25	-3.5	0	-1	0	180	0	583	7.1	1
50	81674	09.07.1979	od (R)	30.05.2009	-0.18	0.24	92	-1.07	-1.24	92	0.25	1.6	1.25	1.6	-1.25	0.25	-1	0	95		560	6.7	1
51	82133	30.01.1982	os (L)	30.05.2009	-0.58	-0.1	78	-0.72	-2.4	78	0.16	1.25	1.25	1.25	-1.25	0.25	-2.5	-0.25	82	80	554	7.1	1
51	82133	30.01.1982	od (R)	30.05.2009	-0.09	0.28	103	-0.66	-3.03	103	0.2	1	1	1	-0.75	0.25	-2.75	-0.5	110	125	546	7.8	1
55	56942	31.05.1981	os (L)	24.10.2009	-1.2	0.3	5	-8.8	-2.3	5	0.001		1		-10		-2		175		566	3.5	
55	56942	31.05.1981	od (R)	24.10.2009	-2	0.08	13	-9	-1.83	13	0.001		0.8		-11		-1.75		4		551	3.24	
58	81553	04.03.1970	od (R)	06.06.2009	0.03	0.12	13	-1.28	-1.33	13	0.25	1	1.25	1.25	-1.25	0	-1.25	-0.5	12	20	517	6.3	1
59	82466	12.08.1981	od (R)	01.08.2009	-0.43	-0.03	169	-6.57	-2.22	169	0.01	1	1.25	1.25	-7	0	-2.25	-0.5	168	20	541	6.9	1

Raw data Randomised Controlled Trial - IBRA group

No	pid	dob	eye	doo	targetref	targetcyl	targetax	shapingsph	shapingcyl	shapingax	ducva0	ducva3	dbcva0	dbcva3	dsph0	dsph3	dcyl0	dcyl3	dax0	dax3	pachy0	pupil	satisf3
3	75641	27.08.1968	os (L)	29.11.2008	-0.03	0.11	176	0.28	-1.36	176	0.63		1.25		-0.25		-1.25		175		542	7.1	
3	75641	27.08.1968	od (R)	29.11.2008	-0.53	0.15	5	0.53	-1.4	5	0.63		1		0		-1.25		0		542	7.1	
4	75437	16.10.1955	os (L)	20.12.2008	-0.56	0.14	167	-0.69	-1.64	167		1.25	1.25	1.25	-1.25	0	-1.5	-0.25	168	135	615	5.2	1
4	75438	16.10.1955	od (R)	20.12.2008	-0.52	0.34	15	-1.48	-1.34	12		1.25	1	1.25	-2	0.25	-1	-1	15	17.5	613	5.1	1
7	13690	28.12.1978	os (L)	09.02.2009	-0.01	0.03	170	-5.74	-1.53	170	0.05	1.25	1	1.25	-5.75	0	-1.5	-0.25	175	0	589	6.4	1
7	13690	28.12.1978	od (R)	09.02.2009	0.08	0.04	16	-5.83	-1.29	16	0.05	1	1.25	1.25	-5.75	-0.25	-1.25	-0.5	15	0	587	6.3	1
8	37185	17.02.1972	os (L)	31.01.2009	-0.59	0.18	176	-5.91	-1.93	176	0.05	1.25	1.25	1.25	-6.5	0.5	-1.75	0	175	0	550	4.4	1
8	37185	17.02.1972	od (R)	31.01.2009	-0.95	0.3	9	-5.3	-3.05	9	0.05	1.25	1	1.25	-6.25	0.25	-2.75	0	10	0	555	4.7	1
9	78309	30.05.1962	od (R)	07.02.2009	-0.55	0.12	174	-7.7	-1.38	174	0.08		1		-8.25		-1.25		175		569	5.4	
9	78309	30.05.1962	os (L)	07.02.2009	-0.5	0.04	23	-7.75	-0.79	23	0.08		1		-8.25		-1		15		559	4.8	
12	74611	20.03.1972	od (R)	23.02.2009	-0.7	-0.54	176	-2.55	-0.71	163		1.25	1.25	1.25	-3.25	0.25	-1.25	-0.5	180	5	552	5.4	1
14	75412	30.04.1980	od (R)	28.02.2009	-0.27	0.28	15	-6.73	-1.28	15	0.1	0.32	1	1	-7	-1	-1	-1	10	0	562	6.6	2
15	79107	07.07.1987	os (L)	07.03.2009	-0.45	0.1	80	-1.3	-1.1	80		1.25	1	1.25	-1.75	0	-1	0	85	0	551	6.2	1
18	77203	29.09.1985	os (L)	21.03.2009	-0.36	0.18	179	-5.64	-1.43	179	0.01	1.25	1	1.25	-6	-0.25	-1.25	-0.25	10	180	555	8.2	1
19	77203	29.09.1985	od (R)	21.03.2009	-0.36	0.14	176	-5.64	-1.64	176	0.08	1.25	1	1.25	-6	0	-1.5	-0.25	180	180	531	7.8	1
20	79787	19.05.1961	os (L)	21.03.2009	-0.61	0.24	55	-2.64	-2.99	55	0.08	1	1	1.25	-3.25	0	-2.75	-0.5	55	105	519	6.1	1
24	79672	14.12.1958	os (L)	21.03.2009	-0.61	0.12	175	-2.14	-1.37	175		1.25	1.25	1.25	-2.75	-0.25	-1.25	0	177	0	568	6.2	1
25	79672	14.12.1958	od (R)	21.03.2009	-0.38	0.15	3	-3.37	-1.4	3		0.8	1.25	1.25	-3.75	-0.25	-1.25	-1	58	5	577	6.2	1
26	80140	24.10.1975	os (L)	28.03.2009	-0.61	0.34	45	-4.89	-1.34	45		1.25	1.25	1.25	-5.5	0	-1	-0.25	44	98	621	6	1
30	80345	19.12.1960	os (L)	18.04.2009	-0.24	0.16	20	-6.51	-1.66	20		0.4	0.63	0.63	-6.75	-1.25	-1.5	-0.75	20	180	541	4.7	1
31	80345	19.12.1960	od (R)	18.04.2009	-0.13	0.21	116	-6.33	-1.96	116		0.63	0.8	1	-6.5	-0.75	-1.75	0	104	0	548	5.1	1
35	80826	31.10.1976	od (R)	20.04.2009	-0.29	-0.35	26	-5.71	-2.15	26		0.8	1	1.25	-6	-0.5	-2.5	-0.75	28	15	610	4.3	1
36	79155	09.08.1962	os (L)	25.04.2009	-0.59	0.17	175	-6.66	-2.17	175		0.2	1	1.25	-7.25	-1.25	-2	-0.5	172	160	508	6.9	1.5
37	79155	09.08.1962	od (R)	25.04.2009	-0.88	0.54	180	-5.87	-2.04	180		0.32	1	1	-6.75	-1	-1.5	-0.25	4	0	501	7.5	1.5
40	80694	12.02.1959	od (R)	02.05.2009	-0.5	0.25	94	-4.5	-1.75	94	0.01	0.8	1.25	1.25	-5	-0.75	-1.5	-0.25	93	110	534	4.4	1
42	81238	01.10.1977	od (R)	16.05.2009	-0.65	0.46	179	-8.35	-3.21	179	0.001	0.25	1	1	-9	-1.75	-2.75	-0.75	180	170	563	4.8	1
43	81238	01.10.1977	os (L)	16.05.2009	-0.68	0.44	2	-5.82	-4.44	2	0.05	0.63	1	1	-6.5	-0.25	-4	-0.75	3	5	550	5.3	1
45	80965	16.10.1963	od (R)	16.05.2009	-0.44	0.24	10	-3.56	-2.24	10	0.08	0.63	1	1.25	-4	0	-2	-0.75	10	5	591	6.7	1
47	77882	08.03.1969	od (R)	23.05.2009	-0.55	0.34	161	-2.2	-2.84	161	0.08	0.8	1	1	-2.75	0	-2.5	-0.5	160	170	572	6.3	1
52	81970	04.01.1976	os (L)	01.06.2009	-0.47	0.09	179	-5.03	-1.34	179	0.05	0.32	1.25	1.25	-5.5	-1	-1.25	0	3	0	514	5.7	1.5
52	81970	04.01.1976	od (R)	01.06.2009	-0.54	0.11	7	-5.71	-1.11	7	0.05	0.32	1.25	1.25	-6.25	-1	-1	0	7	0	511	5.6	1.5
53	80177	13.04.1963	os (L)	06.06.2009	-0.6	0.17	11	-2.65	-2.17	11	0.08	1	1.25	1.25	-3.25	0	-2	-0.75	12	5	541	5.5	1
53	80177	13.04.1963	od (R)	06.06.2009	-0.42	0.15	4	-3.33	-1.15	4	0.08	1	1.25	1.25	-3.75	-0.5	-1	0	170	0	538	5.2	1
54	82942	13.08.1959	os (L)	13.06.2009	-0.41	0.14	179	-6.59	-1.39	179	0.01	0.32	1	1.25	-7	-1.5	-1.25	-0.25	180	110	547	6.4	1
54	82942	13.08.1959	od (R)	13.06.2009	-0.39	0.15	173	-5.36	-1.4	173	0.05	0.4	1	1.25	-5.75	-1.25	-1.25	-0.25	168	55	559	6.2	1
56	82355	05.05.1965	os (L)	15.06.2009	-0.42	0.21	23	-3.08	-1.21	23	0.08	0.8	1	1.25	-3.5	-0.5	-1	0	50	0	563	7.1	1
56	82355	05.05.1965	od (R)	15.06.2009	-0.42	0.31	180	-4.33	-2.31	180	0.05	0.32	1	1	-4.75	-1	-2	-0.25	180	100	562	6.4	1
57	80457	27.10.1978	os (L)	10.08.2009	-0.13	0.23	173	-5.12	-1.75	173	0.05	0.5	1.25	1.25	-5.25	-0.75	-1.5	-0.75	170	170	553	6.8	1.5
57	80457	27.10.1978	od (R)	10.08.2009	-0.04	0.24	12	-4.71	-0.49	12	0.08	1	1	1.25	-4.75	-0.5	-1	0	180		549	6.7	1
60	85443	15.09.1984	os (L)	03.08.2009	-0.52	0.36	37	-0.73	-1.36	37	0.25	1.6	1.25	1.6	-1.25	0.25	-1	0	28		517	6.8	1
60	85443	15.09.1984	od (R)	03.08.2009	-0.36	0.32	105	-0.89	-1.32	105	0.25	1.6	1.25	1.6	-1.25	0.75	-1	-0.25	103	135	524	7.7	1
61	83933	06.11.1959	os (L)	28.09.2009	0.06	0.15	78	0.31	-2.15	78	0.5	1	1	1	-0.25	0	-2	-0.25	85	100	530	6.2	1
61	83933	06.11.1959	od (R)	28.09.2009	0.19	0.38	93	0.44	-1.88	93	0.5	1	1	1	-0.25	0	-1.5	-0.25	95	0	523	6.1	1
101	64143	05.03.1978	od (R)	19.09.2009	0.01	0.17	93	-1.51	-1.17	93	0.2	1.25	1.25	1.25	-1.5	-0.25	-1	0	95	0	526	7.6	1
102	83192	18.04.1964	od (R)	10.10.2009	-0.01	0.06	82	-4.24	-1.06	82	0.08	0.8	1	1	-4.25	-0.25	-1	-0.25	82	43	558	6.6	1

Appendix 10

USER SATISFACTION QUESTIONNAIRE

User satisfaction questionnaire for IBRA

London, 11/11/2009

Dear IBRA user

The IBRA software has been developed by ophthalmologists, taking their needs into account for the functionality of the system. Your opinion is important and can help improving future software versions.

With this questionnaire we would like to ask you about your overall impression on IBRA and about your satisfaction with the user interface and system capabilities. This questionnaire is part of my PhD research at the Centre for Health Informatics at the City University London under the supervision of Professor Abdul Roudsari. I would highly appreciate your participation and support with this user satisfaction evaluation.

It takes only 5-10 minutes to fill in your answers directly into the word file. Save the file after your completion and email it back to me [redacted] if possible within the next 2 weeks. Many thanks in advance! Certainly, your data will be kept confidentially.

If you can't email the file, please send a printed and answered version of the questionnaire to:

[redacted]

Please feel free to contact me on [redacted] in regards to any queries you may have.

Yours sincerely

Bruno Zuberbuhler

A. Questions related to the user

Instructions for part A: Please fill-in an 'x' in the box next to your answer.
Example: [x] Your answer.

Gender: [ ] Female [ ] Male

Age: [ ] 20-29y [ ] 50-59y
[ ] 30-39y [ ] 60-69y
[ ] 40-49y

How would you consider your experience in refractive surgery?
[ ] >3 years
[ ] 1-3 years
[ ] < 1 year
[ ] I don't do refractive surgery (Fellows and secretaries)

Since how long do you work with the IBRA system?
[ ] Just started
[ ] Less than 3 months
[ ] 3-12 months
[ ] 1-3 years

How often do you use the IBRA system?
[ ] Less than 1x / month
[ ] 1-4x / month
[ ] 1-4x / week
[ ] Daily

Do you have experience in using similar software? [ ] Yes [ ] No

B. Overall reactions to the IBRA system

Instructions for part B to D: Please fill-in a number (1-9) or an 'x' in the box next to your answer.
NA = Not Applicable
Examples:

Your No	NA
[7]	[ ]
Your No	NA
[ ]	[x]

The general use of the system is...	terrible wonderful 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
	frustrating satisfying 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
	dull stimulating 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
	difficult easy 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
	inadequate adequate 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
	rigid flexible 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

C. Main component questions

Screen

1. Characters on the computer screen	hard to read easy to read 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
2. Organization of information on the screen	confusing very clear 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
3. Sequence of screens	confusing very clear 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

Terminology and system information

4. Use of terms throughout system	inconsistent consistent 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
5. Computer terminology is related to the task you are doing	never always 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
6. Position of messages on the screen	inconsistent consistent 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
7. Computer keeps you informed about what it is doing	never always 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
8. Error messages	unhelpful helpful 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

Learning

9. Learning to operate the system is	difficult easy 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
10. Exploring new features by trial and error	difficult easy 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
11. Tasks can be performed in a straight-forward manner	never always 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
12. Help messages on the screen are	unhelpful helpful 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
13. Supplemental reference materials	confusing very clear 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

System capabilities

14. System speed	too slow fast 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
15. System reliability	unreliable reliable 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
16. System security	unsafe safe 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

User satisfaction of the human-computer interface

17. Correcting your mistakes	difficult easy 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
18. Experienced and inexperienced users' needs are taken into consideration	never always 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

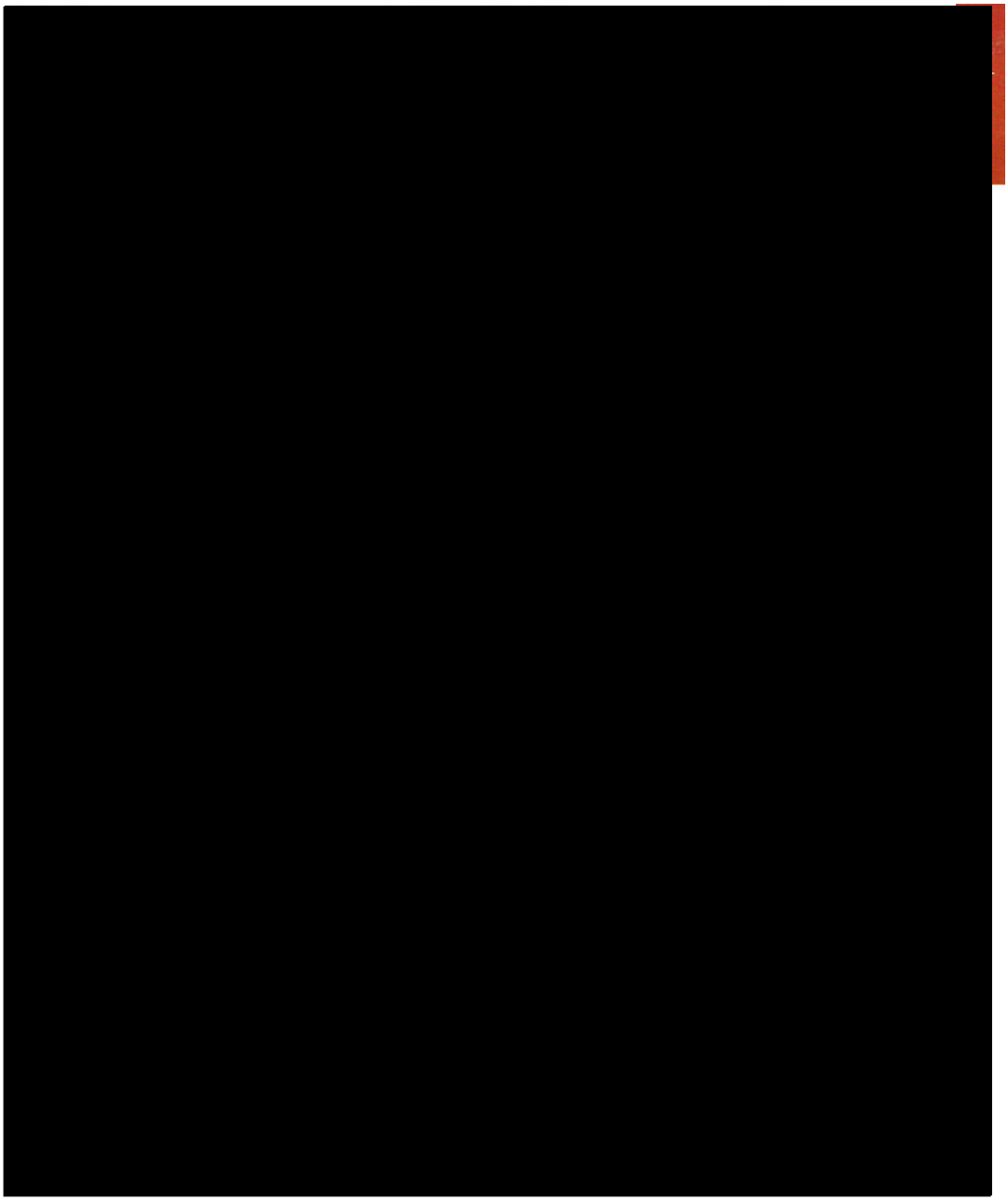
D. Conclusions

1. How do you assess the costs of the system?	too expensive to cheap 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
2. How do you assess the significance of the system on your practice?	low high 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]
3. How do you assess the uniqueness of the system in your field of expertise?	low high 1 2 3 4 5 6 7 8 9	Your No [ ]	NA [ ]

Many thanks for taking your time!

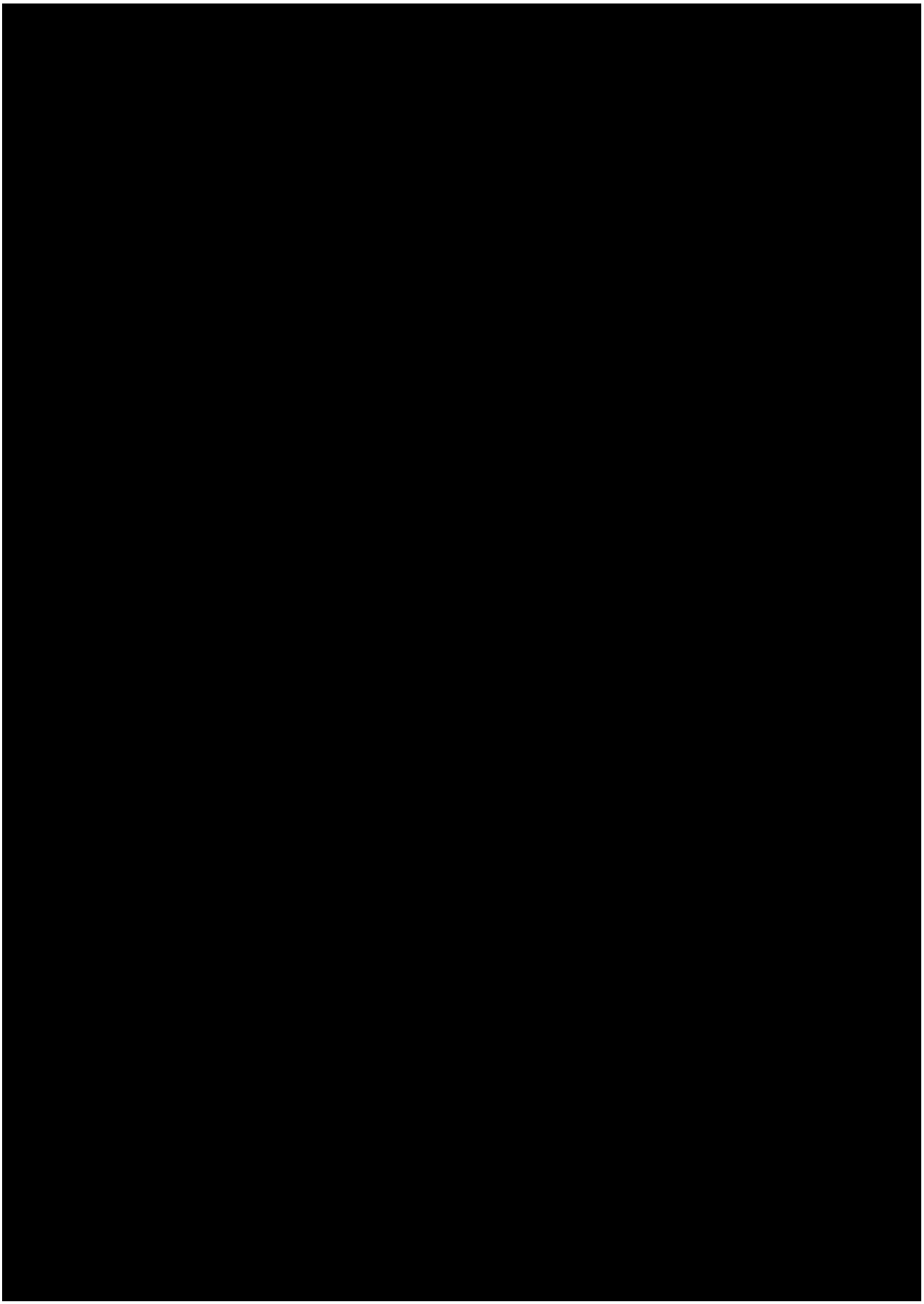
Appendix 11

ARTICLE ON IBRA IN EUROTIMES MARCH 2009



Appendix 12

ARTICLE ON IBRA IN EYEWORLD 2009



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