

Visual Function in Patients with Macular Hole

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ABSTRACT

Visual Function in Patients with Macular Hole

Walter Wittich

Individuals with Macular Hole (MH) experience visual distortions and a drop in visual acuity. Surgical intervention can restore the retina structurally, but restoration of function remains to be investigated in more detail. The present study examined the rate of acuity recovery over time, using growth-curve analyses with Hierarchical Linear Modeling (HLM), as well as perceptual distortions before and after MH surgery. Pre-operative MH diameter, visual acuity (Snellen, ETDRS and Landolt-C) and perception of a vertical line were recorded in 25 eyes of 24 patients. Participants' perceptual reports of distortions were measured by classification of the line as solid, bent right/left, thinned at the center, or broken. Pre-operative MH diameter predicted pre-operative acuity but not rate of recovery; the latter depended on the patients' lens status instead. Participants with natural lenses and consequent cataract formation had slower recovery when compared to patients with already implanted intra-ocular lenses. The majority of patients (81%) reported symmetrical distortions of the line pre-operatively. After surgery, participants with larger MHs were more likely to retain residual distortions. The use of HLM provides insight into the functional recovery process after MH surgery. The perceptual reports indicate that the majority of MH patients fixate along the vertical axis, resulting in symmetrical perception of the line. Of particular interest is the group reporting thinning of the line preoperatively, as the center should be perceptually missing. Patients seem to fill in the information cortically, resulting in perception of a thinner line at the center.

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Visual Function in Patients with Macular Hole

Statement of the Problem

One of the most traditional components in the study of visual psychophysics is the assessment of visual acuity. The most common technique to obtain this measure entails reading an eye-chart, which also forms the gold-standard of acuity assessment in the clinical setting. The use of visual acuity in ophthalmology is based on the assumption that successful treatment by medical or surgical intervention is reflected in improvement of acuity and, therefore, visual functioning of the patient. In the area of age-related vision impairment, diseases such as Macular Degeneration and Diabetic Retinopathy, have received considerable attention, predominantly with the goal of using medical treatment to improve acuity. One case where surgical intervention is being evaluated with the use of eye-charts is Macular Hole (MH), which affects the central area of the retina (macula). In addition to acuity decline, this condition creates distortions (metamorphopsia) or blind spots (scotomas) in the central visual field that are often filled in perceptually.

The past decade has resulted in great advances of ophthalmic treatment techniques and has dramatically increased the success rate of surgical MH closure. This progress, however, has focused mostly on anatomical success while functional outcome remains secondary. Acuity is measured before and at some point after surgery and successful recovery is expressed in mean improvement or lines gained on a chart. Questions about the rate of functional recovery remain unanswered, even though it is generally accepted that optimal functional outcome is established at some point during

the initial 3 to 6 months after treatment. The investigation of recovery rate can only be accomplished with the use of growth curve analysis, which has, to date, not been attempted.

In addition to acuity decline, MH patients often experience distortions and scotomas in their visual world. Telephone poles seem bent and letters disappear while reading words. The detection and quantification of this type of metamorphopsia remains challenging. Clinical tests designed to measure distortions lack the proper parameters for optimal sensitivity. Furthermore, patients may be able to perceptually fill in the missing information and, with time, become unaware of their deficit. A simple and effective way of approaching the detection of distortions is by the presentation of a line. At present, however, optimal standardized parameters that allow for the reliable detection of distortions do not exist.

To what extent both acuity and the level of distortions depend on pre-operative patient characteristics remains unclear. The most likely factor influencing functional outcome is the level of anatomical damage, which is generally expressed as MH diameter, the largest distance between the inner edges of a MH. The recent development of Optical Coherence Tomography (OCT), a cross-sectional imaging technique for the retina, now enables the clinician as well as the researcher to measure MH characteristics at the micron-level *in vivo*. In addition to its clinical use, this tool holds great promise for the investigation of structure-function relationships in psychophysical research.

To date, visual acuity and metamorphopsia have predominantly been investigated separately; yet, it is logical to assume that acuity may, in part, be affected by the presence or absence of distortions. The present study investigated to what extent each of these

visual functions are measurable in patients with MH, before as well as after micro-surgical intervention to repair this retinal defect. By considering both functional aspects and structural characteristics in parallel, it was possible to examine the rate of functional recovery, the presence of distortions, whether distortions affect acuity, and if these functions depend on the pre-operative extent of anatomical damage.

Macular Hole

An Idiopathic Macular Hole (MH) is a localized circular defect of the central retina (see Figure 1) that occurs spontaneously and predominantly affects women above the age of 60 (la Cour & Friis, 2002). The etiology of this condition is still not completely understood (Altaweel & Ip, 2003; Smiddy & Flynn, 2004). Retinal tissue can either be torn laterally due to tension or separated from the underlying membrane because of shrinkage of the vitreous (S. W. Kang, Ahn, & Ham, 2003). The latter type of MH results in loss of tissue in the form of an operculum that is removed during surgery (Madreperla, McCuen, Hickingbotham, & Green, 1995); however, this only rarely results in a loss of photoreceptors. Symptoms of a MH include a sudden drop in visual acuity, which is usually the initial cause for contacting an ophthalmologist. Treatment includes a surgical procedure (vitrectomy) which facilitates closure of the retinal defect. Since Gass (1988; 1995) proposed a theoretical model about the evolution of MHs and established MH-stage criteria, treatment as well as vitreo-retinal microsurgery have advanced rapidly, resulting in high surgical success rate (Benson et al., 2001). The anatomical closure of a MH is the primary goal of the surgical procedure and has previously been defined as structural re-attachment of retinal tissue

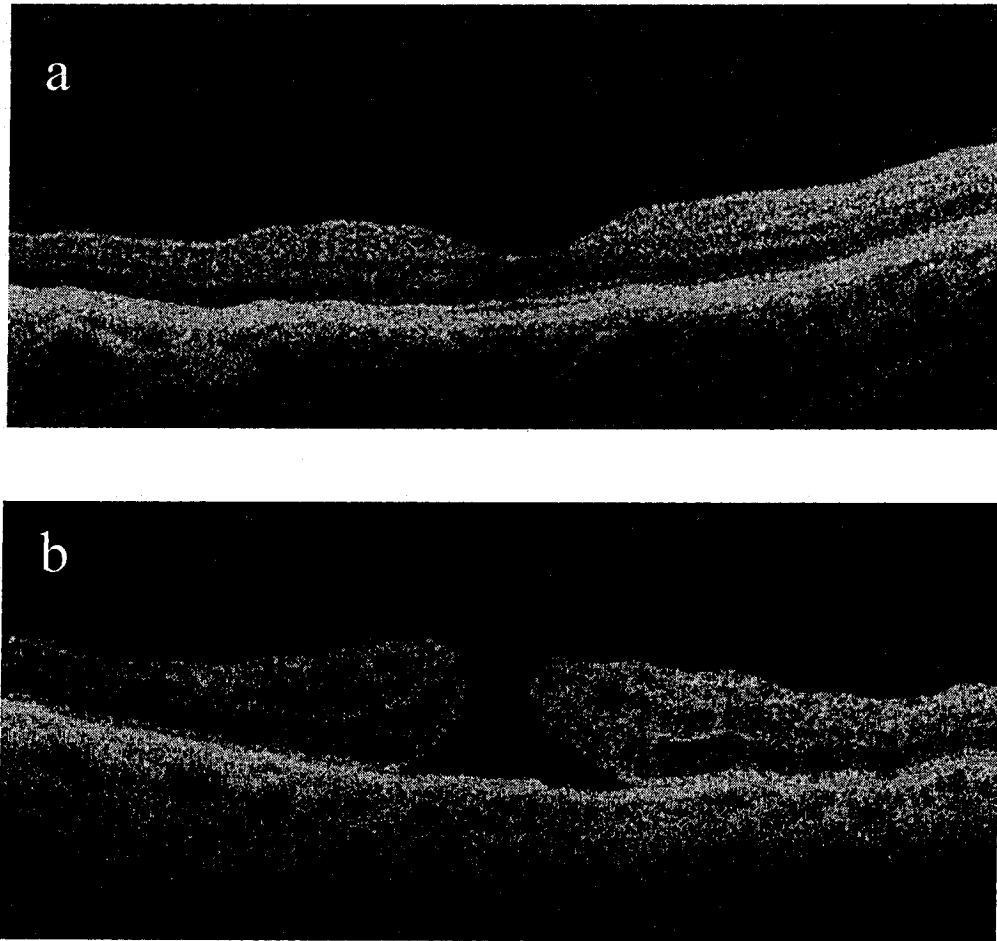


Figure 1. Optical Coherence Tomography (OCT): healthy central retina (a), and a scan showing a Macular Hole (b).

(Tornambe, Poliner, & Cohen, 1998) . Functional improvement of vision, however, is not part of the definition of successful surgery, even though it is the ultimate goal of the surgeon as well as the patient. In an attempt to predict the degree to which vision will improve following surgical intervention, several preoperative factors have been identified. These include pre-operative Snellen acuity (Kokame & de Bustros, 1995; R. A. Scott, Ezra, West, & Gregor, 2000), size and duration of the MH (Benson et al., 2001; la Cour & Friis, 2002), as well as patient compliance to head-down positioning after the surgery (Krohn, 2005; Thompson, Smiddy, Glaser, Sjaarda, & Flynn, 1996). Furthermore, there have been reports of functional improvement up to five years following the surgical procedure (Leonard, Smiddy, Flynn, & Feuer, 1997; I. U. Scott, Moraczewski, Smiddy, Flynn, & Feuer, 2003), yet, few long-term follow-up studies have been published. A meta-analysis by Benson and his team (2001) indicated that approximately 80% of MH patients have improved function after surgery and 22-49% reach acuities of 20/40 (6/12) or better, even though these results do not always replicate easily (Tranos, Ghazi-Nouri, Rubin, Adams, & Charteris, 2004). Because estimating surgical outcome is important, the present study examined both the anatomical characteristics (MH diameter) and the functional consequences of MH (visual acuity loss and metamorphopsia).

Visual Acuity

The measurement of visual acuity has held a longstanding fascination for psychophysicists. In ancient Egypt, thresholds for acuity were established with the ability to resolve twin-stars (Kniestedt & Stamper, 2003). It was not until the 1800s that more standardized attempts were made to measure the ability to resolve and recognize

targets (optotypes) of different sizes. The most widely known product of this era is the Snellen eye-chart, originally developed in 1862, that is still commonly used today (Snellen, 1862). Even though the Snellen chart has become the gold-standard of acuity assessment in the applied setting, detailed evaluation of this measure has revealed several flaws in its design, resulting in the constant development of improved eye charts.

Letter difficulty was initially addressed by Sloan and her research team, resulting in ten standardized letters, matched for difficulty (Sloan, Rowland, & Altman, 1952). The Bailey-Lovie chart addressed issues of letter size, spacing, and test-retest variability (Bailey & Lovie, 1976; B. Brown & Lovie-Kitchin, 1993). In 1982, these improvements were incorporated in a chart used for the Early Treatment of Diabetic Retinopathy Study/ETDRS (Ferris, Kassoff, Bresnick, & Bailey, 1982). Within the current research literature, it is this ETDRS chart that has now replaced the Snellen chart as the standard scientific measure of choice.

Not all charts, however, are based on recognizing individual letters. Orientation tasks are commonly used when examining children, patients who are unfamiliar with the Latin alphabet or who are unable to communicate verbally. Here, the optotypes generally consist of one repeating symbol, where only the orientation of the target varies. The most commonly used orientation acuity charts are the Landolt-C and the Tumbling-E chart (Pointer, Gilmartin, & Larke, 1980). As these charts are commercially available in the same design as the ETDRS chart, several studies in India, Thailand, Japan, China, Nigeria and Russia have reported their findings in this format (Akogun, 1992; Atarashi et al., 2004; Bourne et al., 2003; Horiguchi, Suzuki, Kojima, & Shimada, 2001; Lee & Scudds, 2003; Limburg & Kumar, 1998; Proskurina, Rozenblum Iu, & Bershanskii, 1998).

Generally, recognition and orientation acuities are considered equivalent in their ability to express visual function in normal observers, because differences have been shown to be very small and deemed clinically insignificant (Raasch & Bailey, 1984; Raasch, Bailey, & Bullimore, 1998; Sloan et al., 1952). However, the extent to which these two types of acuities are indeed comparable in the presence of visual pathology remains to be evaluated in more detail.

Of particular interest for the present study is a set of eye charts which were developed specifically for MH patients (Horiguchi et al., 2001). These charts each display multiple identical Landolt-C targets with a different size of target on each chart. The concept underlying these charts is that, by looking anywhere on the chart, at least one of the targets will fall on the most sensitive area of the retina and the patient will be able to identify it. The authors did question if this measure reflects practical visual ability or assesses optimal visual acuity. Practical acuity would be the conscious ability of the patient to use the most sensitive part of the retina, whereas optimal acuity is the best possible resolution when a target is passively presented to the same location, without conscious effort by the patient. Patients may not necessarily be consciously able to use the part of their retina that is capable of optimal resolution. Horiguchi and his team were able to obtain acuities with their new chart that were significantly better when compared to data collected with the standardized Landolt-C chart. This raised the question as to which type of acuity chart would be a better indicator of the resolving power of the retina in patients with MH, as the level of visual impairment pre-operatively is often used as a predictor for functional and structural outcome after treatment (Kokame & de Bustros, 1995; R. A. Scott et al., 2000). The importance of choosing the proper acuity chart

becomes particularly clear when one considers that acuity is the dominant dependent variable in ophthalmologic research used to evaluate the success of a procedure statistically.

From the researcher's perspective, acuity measurement creates an interesting additional challenge when attempting to run statistical analyses. Acuity is traditionally expressed as a Snellen fraction; for example, 20/20 (6/6) generally indicates "normal vision" while 20/200 (6/60) in the better eye, with best standard corrective lenses, expresses the North American limit for "legal blindness". The direct interpretation of the fraction indicates that a person with 20/200 (6/60) acuity can see from a distance of 20 ft (6 m) what a normal observer is able to see from 200 ft (60 m) away. However, this type of interpretation does not directly allow for statistical comparison of acuity. This fraction must, therefore, be transformed in order to adhere to the basic requirement of linearity in the data for statistical techniques (Holladay, 1997). For this purpose, the logMAR scale (logarithm of the Minimum Angle of Resolution) was developed. This conversion takes the logarithm to the base 10 of the inverse value of the fraction, which transforms 20/20 to a value of 0 while 20/200 becomes a value of 1. This conversion represents a useful simplification for research in vision impairment because increasing logMAR values represent increasing vision impairment while the value zero represents normal acuity and negative values indicate better than normal vision.

The analysis of research data in the area of vision impairment has predominantly relied on analysis of variance (ANOVA). Specifically, the research literature evaluating medical/surgical treatment outcome and change in visual function is dominated by *t*-tests and one-way ANOVAs. This approach to the study of change, however, inherently

reduces the amount of information that can be utilized within the analysis. The evaluation of visual acuity before and after treatment interventions generally requires the collapse of data across time-spans in order to create discrete measurement levels for the sake of mean comparison. Especially when conducting research with patients affected by age-related eye diseases, it becomes difficult to assure that measurements are taken with each individual at similar intervals throughout the study. Often, data collection opportunities are dictated by the clinical schedule of the eye-care professional or the personal schedule of the patient, neither of which may be easily coordinated with the timing requirements of a research study. It is for this reason that the recent advent of Hierarchical Linear Modeling (HLM) offers a more flexible and sensitive approach (Raudenbush & Bryk, 2002).

HLM offers a unique way of approaching the study of change over time by examining and comparing individual growth curves, using their slopes and intercepts. The hierarchical component of HLM divides data obtained from the individual over time (σ^2 represents within-person variance, Level 1) and data that differ among individuals (τ represents between-persons variance, Level 2). In the case of visual acuity in MH patients, for example, improvement of acuity after surgery can be considered Level 1 variability while differences in MH size among patients form Level 2 data. As regression equations represent each individual's acuity over time, the analysis becomes flexible with regard to testing dates. Even a missing time point will not exclude the participant's data from the analysis, as long as at least three data points have been collected in order to calculate a regression equation. In addition to its flexibility, HLM is able to address questions about the rate of change (expressed in the slope), a type of information that

ANOVA is unable to investigate. To date, HLM has not been used in the evaluation of MH surgery and its functional outcome.

HLM also allows for the examination of the effect of a common surgical complication on visual acuity: the development of cataract. MH surgery is a highly invasive procedure and results in secondary cataract in more than 75% of patients within one year after the procedure (Benson et al., 2001). The evaluation of surgical outcome via acuity is, therefore, at times obscured by the impairment created in the presence of scatter induced by the lens opacity. By comparing patients who develop MH before cataract with patients who undergo lens extraction prior to MH surgery, one can shed light on the observed functional recovery process after MH surgery, specifically from the patient's point of view.

Perceptual filling-in

Even though acuity is the dominant psychophysical test in the clinical setting, it has its limitations. The most relevant mechanism influencing acuity in MH patients is a phenomenon called perceptual filling-in. Though commonly investigated in basic psychophysics, only a small group of neuro-ophthalmologists has fully considered the impact of perceptual filling-in on clinical patient evaluation (Achard, Safran, Duret, & Ragama, 1995; Dosso, Ustun-Yenice, & Safran, 2000; Safran, 1997).

Perceptual filling-in refers to the illusion of filling in at the cortical level of information that is absent due to an incomplete stimulus or damage to the sensory system. This phenomenon is most apparent in vision at the location of the optic nerve head and has been extensively studied in this context since its original description in the early 19th

century (Troxler, 1803). In addition, research on this topic has relied on the use of artificially created scotomas as well as lesions in the retina and the cortex (Pessoa & De Weerd, 2003; Pessoa, Thompson, & Noe, 1998).

The psychophysical investigation of perceptual filling-in is divided into three main research approaches: perceptual completion at the optic nervehead, completion of artificial scotomas (where the stimulus is partially absent) and completion across pathological scotomas (either in the retina or the visual cortex). Among these three approaches, the research literature focusing on the optic nerve head is most extensive. This includes work with macaque monkeys (Fiorani, Rosa, Gattass, & Rocha-Miranda, 1992; Komatsu, Kinoshita, & Murakami, 2000, 2002; Komatsu, Murakami, & Kinoshita, 1996) as well as humans (R. J. Brown & Thurmond, 1993; Durgin, Tripathy, & Levi, 1995; Kawabata, 1983). The goal of these studies is mapping specific areas of the visual cortex and examining their receptive field properties.

The discovery that artificially created scotomas can also be filled in perceptually has opened up new possibilities of investigation. Generally, a display is presented in which an area off the fixation point differs. For example, a full-field grey screen is presented with a fixation target. At a specific point in the peripheral visual field, a black square with .5 degree diameter is continuously shown. With time (generally within seconds) such a stabilized region (artificial scotoma) is filled in with information from the surrounding areas, creating a perceptually continuous grey display. The theoretical explanation for this phenomenon is based on the fact that the human visual system is designed to detect change. With stable fixation, the missing stimulus is ignored and completed at the cortical level. Interestingly, the majority of human studies using this

approach have investigated filling-in in the periphery at more than eight degrees of visual angle away from the optical axis (De Weerd, Desimone, & Ungerleider, 1998; De Weerd, Gattass, Desimone, & Ungerleider, 1995; Dosso et al., 2000; Liu, Slotnick, & Yantis, 2004; Ramachandran & Gregory, 1991; Ramachandran, Gregory, & Aiken, 1993; Reich, Levi, & Frishman, 2000; Sakaguchi, 2001, 2003; Welchman & Harris, 2000).

Research on actual scotomas induced by retinal lesions is dominated by work with animals, specifically cats (Calford et al., 2000; Calford, Wright, Metha, & Taglianetti, 2003; Matsuura et al., 2002; Young, Waleszczyk, Burke, Calford, & Dreher, 2002) and monkeys (Gilbert & Wiesel, 1992; Kaas, Collins, & Chino, 2003). These studies also investigated scotomas that are minimally six degrees away from the optical axis. In the animal model, it is possible to create specific lesions in the retina and directly examine the effects at the cortical level. The focus of this type of research is plasticity in the visual system and changes in the visual cortex that are induced by the introduction of a lesion in the peripheral retina.

While lesions in the retina have been examined in the context of cortical reorganization, damage to the primary visual cortex (V1), specifically near or in the occipital pole, has been correlated with scotomas within the central visual field (Larkin, 1980; Mirza, Biller, & Jay, 2004; Rizzo & Robin, 1996). Unfortunately, these case descriptions are inherently difficult to interpret because naturally occurring lesions caused by stroke or accidental injury do not follow similar patterns. In addition, because changes of receptive field-size can be detected within minutes after the injury, the examination of visual defects should be not only size- but time-dependent (Gilbert & Wiesel, 1992).

Very little work has focused on perceptual filling-in at the fovea, mostly because artificial scotomas are very difficult to create in this location. At the same time, it is ethically unthinkable to deliberately create central scotomas in humans, as retinal damage is irreversible, even though one case description is available where the researcher stared at the sun in order to study the effect (Craik, 1966). In order to expand understanding of perceptual filling-in in the central visual field, a few studies have turned to ocular pathology, accessing patients with naturally occurring central retinal lesions (Cohen et al., 2003; Gerrits & Timmerman, 1969; Valmaggia & Gottlob, 2002; Zur & Ullman, 2003). These studies have exclusively examined participants diagnosed with age-related macular degeneration, a slow degeneration of photoreceptors in the central visual field, or with retinal scars secondary to toxoplasmosis, an intraocular infection that destroys patches of retinal tissue. Therefore, any defects caused by these conditions were inherently heterogeneous in nature as scars and degenerated areas form without any particular pattern. The present study took advantage of the homogeneity of MHs, which create a consistently localized and circular central defect in the retina and leave peripheral areas intact.

Thus far, only one case study has been published on a detailed psychophysical evaluation of an untreated MH. The study was written by a physiologist who himself was affected by the condition (Burke, 1999; Davey, Ng, & Burke, 2004). Burke (1999) decided to investigate perceptual changes to his visual abilities, driven by his understanding of psychophysics and the unique opportunity to experience first-hand the effects of a MH. Even though he did not report his level of visual acuity, he did undergo a detailed examination of his abilities to perceptually fill in several stimuli, such as lines,

dots and annuli. His description of line stimuli is of special importance for the present study. Burke's MH had an approximate diameter of 1.5 degrees of visual arc, which was evaluated by the size of his absolute scotoma when fixating at the center of circular targets. He then repeatedly viewed lines of varying diameters at different eccentricities. The thickness of a line determined his ability to perceive its completion across the scotoma, while the positioning of the line determined its level of bending towards the center of the scotoma.

Unfortunately, a detailed assessment of Burke's MH with the use of OCT is not available. Furthermore, due to the low success rate in MH surgery at the time of his diagnosis, Burke chose not to undergo treatment of his condition and follow-up data on any perceptual improvements in his case are not available. He did eventually develop a MH in the second eye which was successfully treated but he did not undergo the same psychophysical assessment before and after his surgery (Davey et al., 2004). Burke's case study is written in the tradition of basic psychophysics where the same observer is presented with a stimulus that undergoes an array of changing parameters. The present study aimed to add to the assessment of perceptual changes due to MH by reversing this approach, in the tradition of applied psychophysics, where the same line-stimulus was presented to an array of patients with varying levels of macular damage.

Line-Stimulus

The assessment of perceptual filling-in has previously used stimuli that are circles (Burke, 1999; Komatsu et al., 1996; Sakaguchi, 2001, 2003), rings (Burke, 1999; Craik, 1966; Friedman, Zhou, & von der Heydt, 1999; Komatsu et al., 1996; Liu et al., 2004),

squares (De Weerd et al., 1998; De Weerd et al., 1995; Ramachandran & Gregory, 1991; Ramachandran et al., 1993; Reich et al., 2000; Welchman & Harris, 2000, 2001), gratings (Kawabata, 1983; Valmaggia & Gottlob, 2002; Zur & Ullman, 2003) or lines (R. J. Brown & Thurmond, 1993; Burke, 1999; Cohen et al., 2003; Craik, 1966; Fiorani et al., 1992; Gerrits & Timmerman, 1969; Zur & Ullman, 2003). Their contrast definition has been based on luminance (Burke, 1999; Reich et al., 2000), texture (Caputo, 1998; Craik, 1966; De Weerd et al., 1998; De Weerd et al., 1995; Kawabata, 1983; Spillmann & De Weerd, 2003; Welchman & Harris, 2001), motion (Welchman & Harris, 2000, 2001) or color (R. J. Brown & Thurmond, 1993; Friedman et al., 1999; Ramachandran & Gregory, 1991). However, the most common stimulus used by ophthalmologists to assess certain retinal lesions is a white line projected onto the retina. This is perceived by the patient against a dark background.

In 1969, Gerrits and Timmerman (1969) reported on the use of a narrow slit of light in the assessment of perceptual distortions in patients with central retinal scotomas. In the same year, Watzke and Allen (1969) published their article on the development of a simple test which now carries their names. The Watzke-Allen Test (WA) is performed by using a slit lamp to place a narrow vertical beam of white light across the fovea, after the pupil has been dilated. Patients are then asked what they see. The strip should be perceived as a continuous line if the macula is intact (negative WA). In the presence of macular pathology, other categorizations are possible: the line may be reported as broken (positive WA), distorted (metamorphopsia) or the patient may be non-responsive or unsure (equivocal).

Initially, this task was suggested for the evaluation of macular cysts and central serous choroidopathy (Watzke & Allen, 1969) and has since undergone transformations for use in the assessment of age-related macular degeneration (Zur & Ullman, 2003) and macular translocation (Stappler, Stanga, Groenewald, El Bably, & Wong, 2003). Moreover, its elegance and simplicity have made it most popular as a diagnostic tool in the assessment of MHs. The diagnosis of a full-thickness MH has been confirmed by the presence of a positive WA across several studies (Gurwood & Jones, 2001; Hikichi & Trempe, 1993; Ho, Guyer, & Fine, 1998; Hui & Guan, 2002; H. K. Kang, Chang, & Beaumont, 2000; Krasnik, Strmen, & Javorska, 2001; R. A. Scott et al., 2000; von Ruckmann, Fitzke, & Gregor, 1998; Wolf, Reichel, Wiedemann, & Schnurrbusch, 2003). Still, recurring inconsistencies in the responses to the WA have challenged its reliability and sensitivity. Previous work demonstrated that a clear positive WA may only be present in approximately 23% of full thickness MHs that were confirmed by OCT (Tanner & Williamson, 2000). Meanwhile, 77% of patients report some form of metamorphopsia or orientation-dependent WA.

From the psychophysical viewpoint, the lack of established parameters (luminance, size, display time) for the WA makes its interpretation difficult; however, the idea of using a line as a tool to evaluate the patients' perceptual experience of distortion or perceptual filling-in still holds promise. Based on previously reported line parameters used in the context of MH research (Burke, 1999; Martinez, Smiddy, Kim, & Gass, 1994; Tanner & Williamson, 2000; Wittich, Overbury, Kapusta, & Faubert, 2005), the present study utilized a vertical line that was defined by luminance contrast, with the approximate length of the macula and diameter of the fovea, and limited in its display time to 0.5 s.

By choosing size parameters that coincide with the anatomy of the macula and fovea, it was assumed that the image of the line would fall on the part of the retina that is generally affected by MH. The patients' perception of this line was used as an indicator of their ability to perceptually fill in this stimulus or to report any level of distortion/metamorphopsia they experienced before as well as after surgery.

The link between distortions and visual acuity in the investigation of structure-function relations in a sample of MH patients is the level of anatomical damage, created by the formation of a hole in the central retina. A classification of MH stages has been developed by Gass and has been widely used in the categorization and etiology of MHs (J. D. Gass, 1988, 1995). However, the development of the OCT has greatly influenced the way macular holes are presently diagnosed and classified (Altaweel & Ip, 2003; Hee et al., 1995). Whereas Gass' classification relies on the clinical impression by the ophthalmologist and a frontal view of the macula, the OCT scan provides a cross-sectional view of the retina.

Optical Coherence Tomography

The diagnosis of a MH has traditionally relied on the retinal specialist's ability to detect a small circular defect in the region of the macula by looking inside the eye of a patient using an ophthalmoscope. Different stages and sizes of MH, however, make this type of diagnostic technique unreliable and this has often resulted in misdiagnoses of, for example, lamellar or pseudo-holes as MHs (Martinez et al., 1994). The key problem in the diagnostic process lies in the fact that MHs are easily identifiable in a cross-sectional view but often misinterpreted from a frontal viewpoint, such as through the pupil. A cross-sectional image used to be available only in the context of histology by removing

and dissecting the affected eye; now, however, cross-sectional imaging of the retina *in vivo*, with the use of OCT, allows for easy and accurate diagnosis.

An optical coherence scan is based on interference patterns created by selectively reflected light (Michelson interferometry). A detailed technical review of OCT technology and its clinical application is available in the literature (Jaffe & Caprioli, 2004). A non-invasive laser beam is reflected off the retinal tissue and the resulting interference patterns create a two-dimensional image of the retina that resembles a sectional slide. The various colors of this image do not directly correlate with anatomical components of the retina but represent different layers of reflectivity. The resolution of these images depends on various factors, including the condition of the optical media, pupil diameter and patient cooperation.

The interpretation of OCT images for medical purposes requires substantial experience and training; however, the examination of structural characteristics is relatively straightforward and supported by software features in the analysis programs of the OCT. One such feature is the ability to manually place markers within an OCT image while the program extrapolates the distance between these markers in microns. This technique greatly facilitates the measurement of structural properties such as the minimum distance between the inner edges of a MH (Kusuhara et al., 2004), which is referred to as the MH diameter in the present study.

Hypotheses

In light of the reviewed information about visual acuity, perceptual distortions, their investigation and applicability to ocular pathology and the opportunity to access a participant pool with MH, the present study is divided into two major components:

Experiment 1: the psychophysical evaluation of visual acuity over time before and after MH surgery, and Experiment 2: the evaluation of perceptual distortions of a line stimulus before and after MH surgery, depending on pre-operative MH diameter, and its connection to visual acuity. The following hypotheses were addressed:

In the first experiment, it was hypothesized that rate of acuity recovery over time (linear and/or curvilinear slopes of acuity over time for each person) would differ significantly among individuals with smaller versus larger MHs, but more so in patients who previously had received artificial intra-ocular lens implants. It was predicted that individuals with smaller MH diameter and with already-implanted IOLs would recover function at the fastest rate.

In the second experiment, it was expected that MH diameter would determine the perceptual shape of a line stimulus before as well as after MH surgery. It was predicted that participants who have a larger MH diameter would perceive a broken line before surgery while participants with smaller holes would perceive some type of distortion or a thinned line. In addition, after anatomically successful surgery, individuals who had smaller MH diameters before surgery would perceive a solid undistorted line stimulus and would, thereby, have more successfully restored visual perception.

Finally, it was hypothesized that individuals who recovered from perceptual distortions by perceiving a solid line at the final follow-up would have significantly better visual acuity than those who reported residual metamorphopsia after successful MH surgery.

Experiment 1: Visual acuity

Method

The protocol was approved by the Institutional Ethics Review Board at the Sir Mortimer B. Davis Jewish General Hospital, Montreal, in accordance with the Canadian Tri-Council Policy Statement of ethical conduct for research involving humans.

Participants. Between June 2004 and August 2005, 31 patients of one retinal surgeon were diagnosed with MH. Of those, 24 were eligible to participate and were successfully recruited into the study. The sample consisted of 17 women and 7 men, ranging in age from 29 to 82 years. All patients were free of concomitant retinal disease, and were being treated by one retinal surgeon in the Ophthalmology Department of the Sir Mortimer B. Davis Jewish General Hospital, Montreal. All participants were scheduled to undergo 25-gauge transconjunctival sutureless vitrectomy surgery with gas tamponade (macular hole surgery). They all spoke English or French and were able to give informed written consent (see Appendix A).

Apparatus & Procedure. Participants were recruited by the researcher or a research assistant in the Ophthalmology Department the day of their diagnosis. The purpose and procedure of the study were explained. They were invited to arrive at the Ophthalmology Department 30 min before their scheduled subsequent appointment for Pre-Admission Testing (blood/urine tests and cardiogram, required by the hospital). Written informed consent was obtained and the participants underwent a series of three psychophysical tests as well as an OCT scan. All testing was done with the eye that was scheduled to undergo surgery while the other eye remained patched. After acuity testing, the OCT scan required the participants to have their pupils dilated. The identical testing

procedure was repeated on at least three separate occasions: pre-operatively on the day of the pre-admission exam and a minimum of two times post-operatively, when the patient returned to the eye clinic for a follow-up exam with the ophthalmologist. The testing intervals depended on the availability of appointments with the retinal surgeon as well as the time schedule and flexibility of the participants. This procedure allowed the participants to take part in the study without having to make additional trips to the psychophysics lab solely for the purpose of research. Because these participants were visually impaired for most of the study's duration, this arrangement proved to be useful for optimal data collection. Participants were tested under optimal artificial lighting conditions in an examining room in the Ophthalmology Department.

All participants were refracted with trial lenses before vision testing began, using the NIDEK Autorefractor ARK-760A (VisionMedical, Montreal, Quebec Canada). Acuity for the eye that was scheduled to receive surgery was determined in an otherwise dark room while the other eye was occluded. Snellen acuities were measured by an ophthalmic technician with projection charts (Project-O-Chart, American Optical Company, Buffalo, NY, see Appendix B) at a distance of 6 m (mean luminance 82 cd/m²). Standard retro-illuminated ETDRS and Landolt-C charts were presented by the researcher at a distance of 1 or 2 m to accommodate the acuity range of the patients (see Appendix B). The Landolt-C chart contained rings with gaps in 1 of 4 orientations (right, left, up, down). Black optotypes were displayed at full contrast on a white background (luminance 185 cd/m²). The luminance parameters fell within an acceptable range of previously established optimal values for eye-chart illumination (Sheedy, Bailey, & Raasch, 1984). Participants were encouraged to identify optotypes one by one in each

line while the experimenter scored correct responses. Testing stopped whenever a participant was unable to correctly identify five consecutive optotypes in a line. The same procedure was repeated on each follow-up testing session after MH surgery. For statistical analysis, acuities were expressed in logMAR.

Structural Measure. After completion of all tests, participants' pupils were dilated with 2.5 % phenylephrine hydrochloride (Mydfrin, Alcon, Canada) and 1% tropicamide (Mydriacil, Alcon, Canada). After 20 min, the participants' eyes were scanned with the Optical Coherence Tomograph (OCT 3; Carl Zeiss Meditec Inc., Dublin, CA, USA, see Appendix C). This scan was performed on the day of diagnosis, as well as on each follow-up testing day. Participants fixated on the center of a line pattern in the scanner display. An optical signal was reflected off the retinal tissue. Differences in the reflectance pattern were translated into a cross-sectional image of the macula area (see Figure 1). The specifications of this technique have previously been described in detail (Jaffe & Caprioli, 2004). Six scans at different orientations to the horizontal (30, 60, 90, 120, 150 and 180 degrees) were taken per eye and the clearest image was analyzed independently by the investigator and a research assistant. The Stratus OCT program determined the diameter of the macular hole, based on manually placed markers, and its software expressed the diameter in microns. Macular holes and surgical outcome of closure were categorized by a combination of the parameters established by Kang, Ahn and Ham (2003) as well as Tornambe, Poliner and Cohen (1998). The anatomical condition of the fovea was categorized by the edges of the macular hole being flat or elevated and the hole being open or closed. All test results were recorded on a score sheet and a copy was made available to the participants upon request. Total duration of

each session, including pre-experimental preparation time, did not exceed 30 min. After the scan, participants were seen by the retinal surgeon, as part of their regular treatment.

Results

General Descriptors. Participants were recruited between June 2004 and August 2005. During this 14-month period, 31 patients received a diagnosis of MH; of these, 24 were interested and eligible to participate in the study. One patient developed a MH in the second eye during the study period; therefore, the analysis included 25 eyes of 24 patients. The sample consisted of 7 men and 17 women with a mean age of 71.0 years ($SD = 7.7$) at the time of recruitment. Follow-up time ranged from 3 months to 1.5 years, with a minimum of three testing sessions per participant. Pre-operative data were collected within 2 weeks before surgery. Three eyes experienced failed initial MH surgery (MH remained open with flat edges), two of which underwent an unsuccessful second surgical intervention.

Acuities were expressed in the traditional Snellen fraction and then transformed into logMAR units (log to the base 10 of the Minimum Angle of Resolution). The formula used has previously been described by Rosser, Laidlaw and Murdoch (2001), whereby the inverse of each fraction is divided and the logarithm is taken [e.g. $\log (20/20) = 0$; $\log (40/20) = .30$]. The conversion of “counting finger” to logMAR units followed previously established transformation guidelines (Holladay, 1997). Pre-operatively, ETDRS acuities ranged from 0.38 to 1.28 logMAR units (20/48 to 20/382) with a mean of 0.67 (20/92). Landolt-C acuities ranged from 0.40 to 1.68 (20/50 to 20/962) with a mean of 0.85 (20/140). Snellen Acuities ranged from 0.54 to 2.00 logMAR units (20/70 to Counting Fingers). A total of 327 acuity measures were taken, ranging from 6 to 22

per eye. The complete data for each participant are displayed in Appendix D and a summary of pre-operative patient characteristics is displayed in Appendix E. Average MH diameter at the time of diagnosis was 419.0 microns ($SD = 174.5$) with a range from 199.0 to 905.0 microns. Using average anatomical parameters of axial length (Cornsweet, 1970), MH diameter could be converted into degrees of visual angle (dva), with a mean diameter of 1.54 dva ($SD = .63$), and ranging from .70 to 3.3 dva. Pearson's correlation coefficients are displayed in Table 1.

Hierarchical Linear Modeling. In the evaluation of recovery rate over time, only the 22 eyes with anatomically successful treatment were included. For the purpose of comparison, however, an additional model, including the three eyes with failed surgery, is presented at the end of the Results section. The analysis of acuity change over time using HLM (HLM for Windows, Version 6.01h) allows for the division of variability in the data into within- and between-subjects components. The intra-class correlation coefficient (ICC) is an indicator of the percentage of variability in the data set that is due to differences between subjects. The ICC is calculated by dividing the amount of between-subjects variance (represented by a value known as *tau*, τ) by the total of the between- and the within-subjects variance (within variance is represented by a value known as *sigma squared*, σ^2). In a multi level analysis one can assess the percentage of variance that has been accounted for in the between and within components by computing the proportional decreases in the values of σ^2 (within subjects) and τ (between subjects).

In the multilevel analysis that was performed, information nested within the individual is contained in the Level 1 model. In the present study, the variables at Level

Table 1. Pearson's correlation coefficients for pre-operative variables

	MH Diameter	Snellen	ETDRS	Landolt-C
MH Diameter	-	.50*	.80**	.72**
Snellen		-	.46*	.59**
ETDRS			-	.92**
Landolt				-

* $p < .05$, ** $p < .01$

1 were *time* and *time*², in order to assess linear and curvilinear rates of change. Time was measured in the number of weeks following surgery. The outcome variable *acuity* was composed of all three acuity measures (Snellen, ETDRS and Landolt-C) simultaneously. Therefore, slopes and intercepts for acuity over time were based on multiple measures at each time point. This approach is conceptually similar to a repeated measure and was employed for the purpose of increasing the reliability estimate within the analysis. It must, therefore, be clarified that the dependent variable of *acuity* in the present study is an amalgamation of three separate acuity measures.

Level 2 data: Information about particular individuals (patient characteristics) was contained in Level 2 data. Variables at Level 2 were MH diameter (in microns, as measured by OCT), lens status (coded as “0” for natural lens and “1” artificial intra-ocular lens implant (IOL) prior to MH surgery), and status of the surgical outcome (coded as “0” for failure, “1” for anatomically successful treatment with natural lens, and “2” for success with IOL). Level 2 variables were used to predict intercepts and slopes observed in the Level 1 model

Sequential Hierarchical Linear Models. The first model (unconditional) was used to estimate the amount of variance contained within versus between subjects in the outcome variable *acuity*. The analysis revealed that σ^2 represented 70.7 % of variability within subjects while τ represented 29.3 % of variability between subjects. Intercepts differed significantly among individuals (see Table 2), indicating that pre-operative acuity varied among participants, $p < .001$. The reliability estimate for this model was .83. Slopes were not evaluated in this model.

Table 2. Results for the Unconditional Model with Acuity as Outcome Variable

	Coefficient	<i>SE</i>	<i>t</i>	<i>df</i>	<i>p</i>
Intercept	.56	.04	14.28	21	< .001

The second model estimated the amount of within subjects variance that could be explained by adding *time* (linear effect) and *time*² (curvilinear effect) in the equation as predictors. The ICC indicated that 30.0 % of the variance within subjects was accounted for by the passage of time alone. This value translates into 21.0 % of the total variance in the data set. The reliability estimate for this model was .88. Coefficients are displayed in Table 3.

The final model examined to which extent variation in the Level 1 parameters was related to the level 2 variables. MH diameter and lens status were added as Level 2 predictors for intercepts and slopes of Level 1 equations (see Table 4). MH diameter was a significant indicator of pre-operative acuity (intercept) but was not associated with acuity changes over time (slope). Lens status was not a significant indicator of pre-operative acuity; however, rate of acuity recovery over time differed significantly between individuals with natural versus artificial lenses. The reliability estimate for this model was .90. The results of this model are displayed in Figure 2, where *acuity* is graphed as a function of time. The graphing program within HLM combined data from all participants in order to create curvilinear representations of the acuity change over time. Data for participants were collapsed and represented by the 25th and 75th percentile for MH diameter.

For the purpose of comparing acuity change in failed versus successful MH surgery, an additional model was created in which functional recovery rate for three groups was evaluated. Independent of MH diameter, all 25 eyes were assigned to one of three groups: failed surgery, successful surgery with natural lens, and successful surgery with previously implanted IOL. The reliability estimate for this model was .82. Group

Table 3. Results for the Model including *time* and *time*²

Predictor	Coefficient	<i>SE</i>	<i>t</i>	<i>df</i>	<i>p</i>
Intercept					
Intercept	.73	.04	18.39	21	<.001
Time Slope					
Intercept	-.02	.002	-8.06	288	<.001
Time Squared Slope					
Intercept	< .001	< .001	3.67	288	.001

Table 4. Results for the Model including Level 2 Predictors

Predictor	Coefficient	<i>SE</i>	<i>t</i>	<i>df</i>	<i>p</i>
Intercept					
Intercept	.46	.11	4.18	19	.001
MH Diameter	< .001	< .001	2.39	19	.03
Lens	.09	.09	1.08	19	.29
Time Slope					
Intercept	< .02	.01	-2.37	282	.02
MH Diameter	< .001	< .001	.66	282	.51
Lens	-.03	< .001	-4.00	282	< .001
Time Squared Slope					
Intercept	< .001	< .001	1.54	282	.12
MH Diameter	< .001	< .001	-.84	282	.40
Lens	< .001	< .001	3.61	282	.001

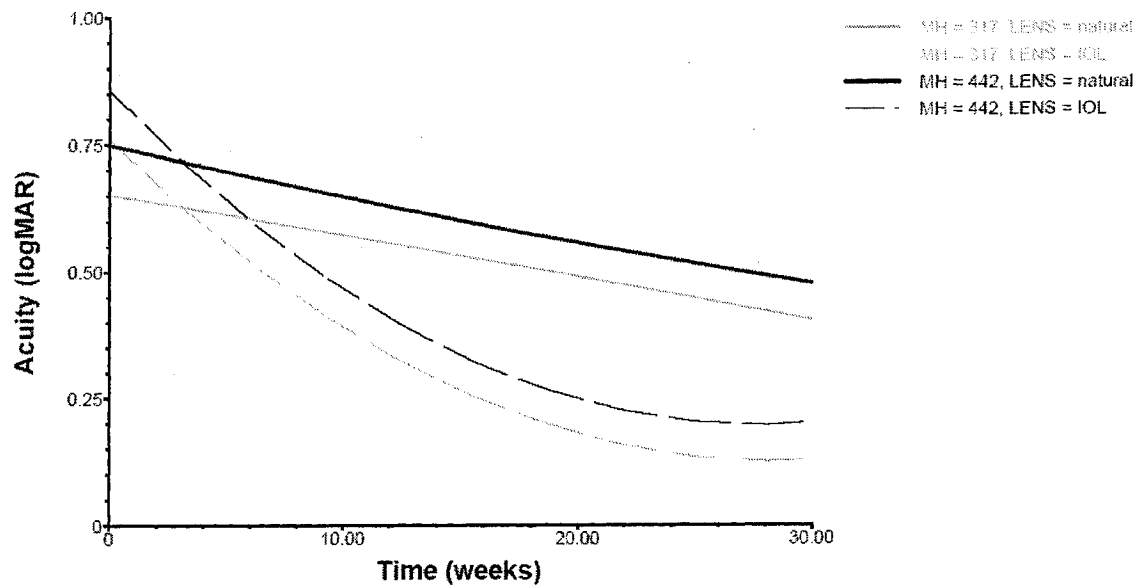


Figure 2. Acuity as a function of time. Grey indicates the 25th percentile of MH diameter while black indicates the 75th percentile. Solid lines represent patients with their natural lens while the dotted lines represent the group with intra-ocular lens implants.

membership was a significant predictor for slope of recovery, however, not for intercept (see Table 5). Acuity did not change over time in patients with failed surgery, but did improve with both successful treatment groups (see Figure 3).

Discussion

Intercepts (acuity before surgery). Consistent with previous studies, MH diameter was a significant predictor of pre-operative visual acuity (Nakabayashi, Fujikado, Ohji, Saito, & Tano, 2000; Sjaarda, Frank, Glaser, Thompson, & Murphy, 1993a). Patients with larger MHs were more impaired in their ability to recognize optotypes on three different eye charts (Snellen, ETDRS, and Landolt-C). This finding is, in part, explained by the necessity for these patients to fixate eccentrically. Furthermore, acuity is impaired by the dislocation and misalignment of photoreceptors immediately around the MH (Jensen & Larsen, 1998; Sjaarda et al., 1993a). Light is unable to optimally stimulate cones at the edge of the MH, as the directional sensitivity of photoreceptors (Stiles-Crawford effect) is disturbed. Previous work by Sjaarda et al. (Sjaarda et al., 1993a; Sjaarda, Frank, Glaser, Thompson, & Murphy, 1993b) described this reduced functional ability. Therefore, visual function in the presence of MH is characterized by the absolute size of the scotoma at the centre, surrounded by a relative scotoma in the area immediately around the MH. Lens status was not a significant predictor of pre-operative acuity. This finding is not surprising because it was expected that, before surgery, natural lenses were free of cataract, similar to clear artificial implants.

Slopes (rate of functional acuity recovery over time). The analysis indicated that the shapes of recovery curves for acuity were curvilinear. Acuity improved more rapidly in

Table 5. Results for the Comparison Model

Predictor	Coefficient	<i>SE</i>	<i>t</i>	<i>df</i>	<i>p</i>
Intercept					
Intercept	.90	.10	8.80	23	.< .001
Group	-.10	.08	-1.24	23	.23
Time Slope					
Intercept	< .001	.005	.19	321	.85
Group	-.01	.004	-3.25	321	.002
Time Squared Slope					
Intercept	< .001	< .001	-1.06	321	.29
Group	< .001	< .001	2.41	321	.02

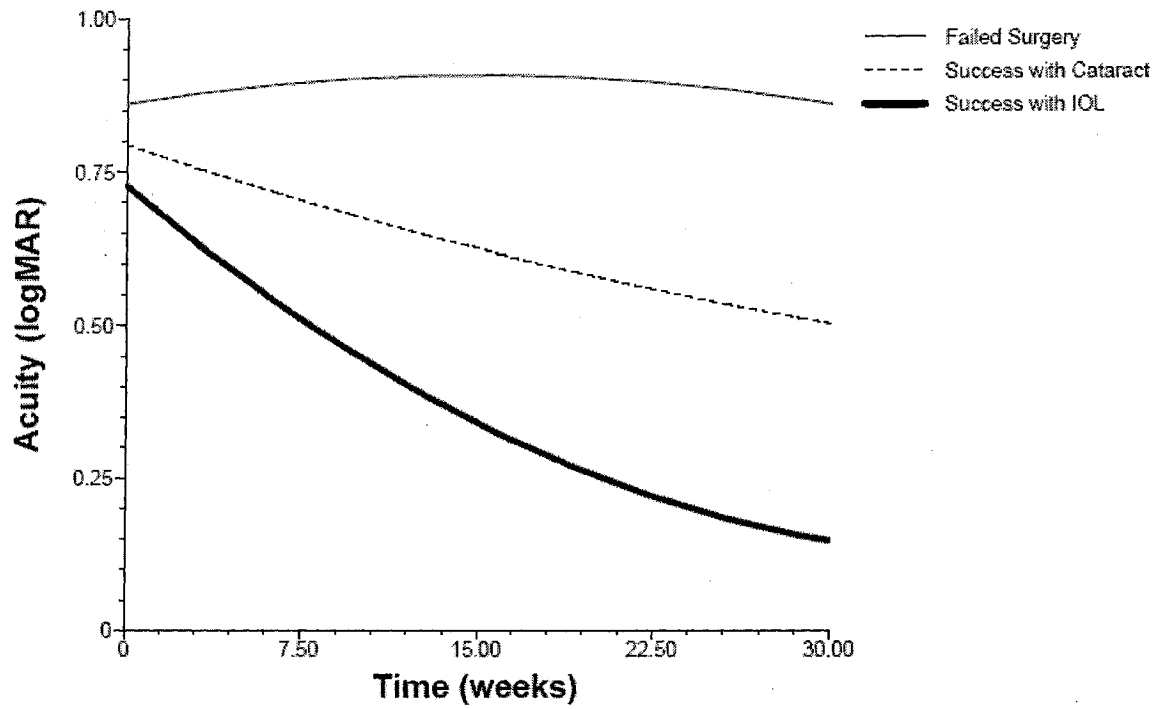


Figure 3. Acuity as a function of time. The thin line represents acuity in patients whose treatment failed, while the dashed line indicates acuity recover for patients with their natural lens and the thick line represents recovery in the group with intra-ocular lens implants.

the initial period after surgery, with the most notable change occurring during the first 6 months after the treatment (see Figure 2). This finding is consistent with a previous report by Leonard et al. (1997) who demonstrated continuous functional recovery for up to 4 years. Their report, however, merely supplied partial data on recovery over time, as only mean and median acuity values were given at 5 time points over 4 years. Standard deviations or standard errors were not reported. In addition, their results seemed “too good to be true” as the sample means continuously improved while the sample size shrank from 93 participants before surgery to 7 at the 4-year follow-up.

Leonard et al.’s data indicated that the recovery rate of acuity after MH surgery was indeed not linear and depended on the presence or absence of cataract. Unfortunately, very little information was provided about changes in acuity during the key time-period of the initial 6 months following surgical treatment. The present study was able to fill this void with its detailed analysis within this specific time span. Furthermore, Leonard and colleagues combined their results for all participants, independently of MH diameter. The present study was able to examine recovery rates based on the level of preoperative damage to the retina.

Pre-operative MH diameter was not a significant predictor of post-surgical recovery rate for acuity. This becomes especially clear when comparing the recovery curves for patients with previously implanted IOLs. Independently of MH diameter, acuity improved with time and at comparable rates; however, due to the differences in initial acuity, patients with larger MHs were unable to recover to the same level as patients with less damage. In previous reports, this difference in functional outcome has commonly been described as the percentage of patients that achieve acuities better than

20/40 or 20/70 (Bopp, Lucke, & Hille, 1997; Hikichi & Trempe, 1993; Kwok, Lai, Man-Chan, & Woo, 2003; Leonard et al., 1997; R. A. Scott et al., 2000; Sheidow et al., 2003; Smiddy, Feuer, & Cordahi, 2001), or the number of lines gained on a chart, based on their pre-operative MH stage (Dori, Thoelen, Akalp, Bernasconi, & Messmer, 2003; C. A. Gass, Haritoglou, Schaumberger, & Kampik, 2003; Ip et al., 2002; H. K. Kang et al., 2000; S. W. Kang et al., 2003; Krasnik et al., 2001; Kwok et al., 2003; Tranos et al., 2004; Wolf et al., 2003). This approach to reporting results is often complex and confusing. Furthermore, it masks any information about *recovery rate* and does not allow for detailed examination of the process of recovery as it only focuses on the final outcome. The present results indicate that the actual time point, at which this outcome is measured, matters considerably and can only be made apparent with growth-curve analysis.

Experiment 2: Line Distortion

Method

Participants. The second experiment involved the same participants as Experiment 1. Both experiments were conducted in parallel within the same timeframe.

Apparatus and Procedure. Perceptual distortions were evaluated after the acuity measurement but before pupils were dilated for OCT scans. The Line-Resolution Test, developed by the Faubert Perception Lab in the School of Optometry at the University of Montreal, was displayed on a Toshiba 2060CDS portable computer (Toshiba, Markham, Ontario, Canada) with liquid crystal display (LCD). The stimulus was a vertical line pattern (see Figure 4). Its luminance distribution was the fourth derivative of the Gaussian function. The width of the line was measured in standard deviations (SD) of this function, whereby the width was set at ± 4 SD from the center of the line. Peak luminance at the center was 130 cd/m^2 and the line display had the same mean luminance (33 cd/m^2) as the grey background on which it was presented. It was expected that participants would be unable to fixate on a central target, because their foveas did not function properly. Therefore, an incomplete fixation cross indicated the area in which the line was to be displayed (see Figure 4). This approach has been applied in previous work with MH patients (Bellmann, Feely, Crossland, Kabanarou, & Rubin, 2004; Davey et al., 2004; Wittich et al., 2005).

The parameters of this particular narrow-band line stimulus were chosen because the specified luminance distribution is resistant to blur. This choice was necessary to compensate for scatter which could be created when light passes through the optical media, specifically with early signs of cataract in the lens. The line contained no sharp

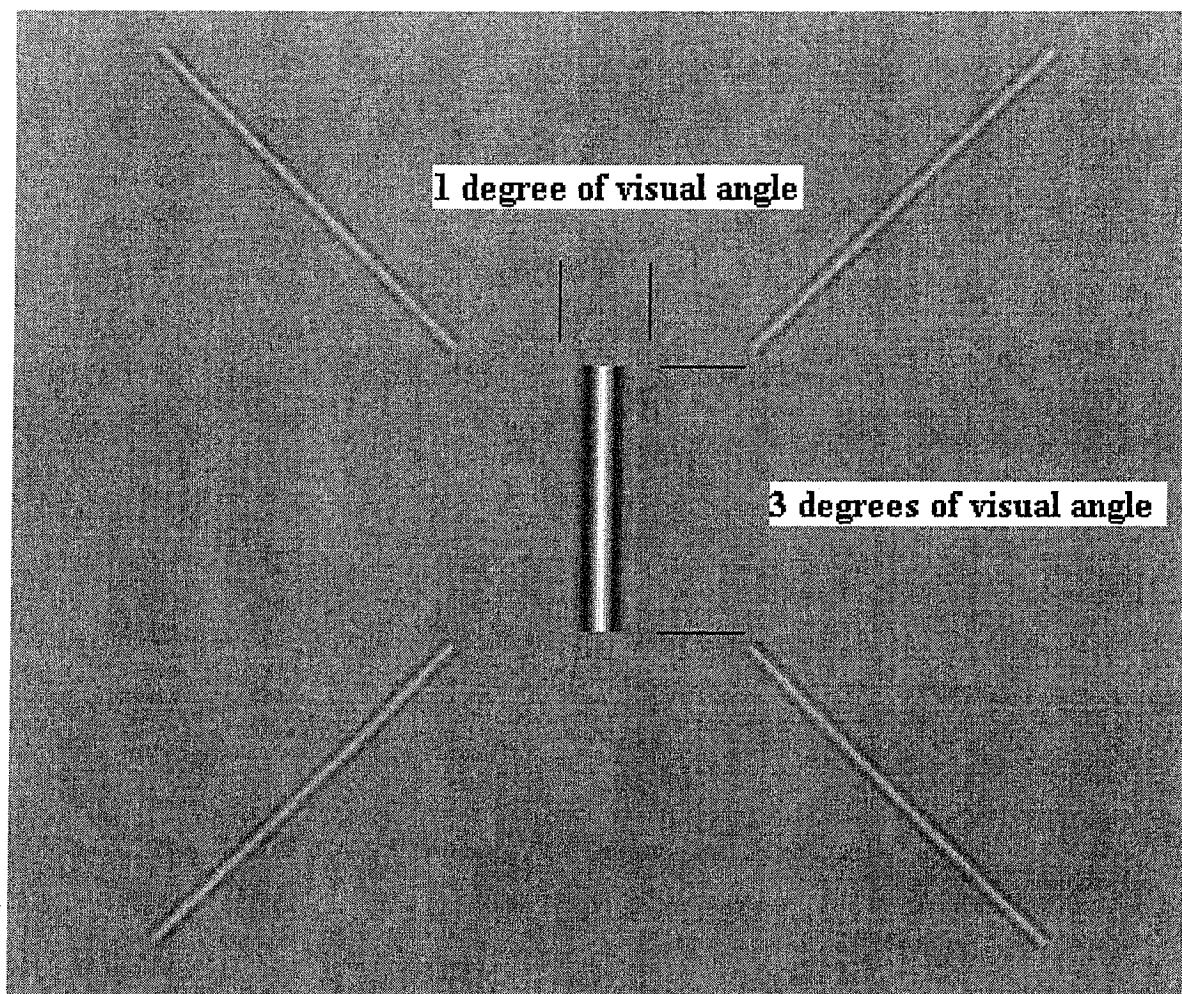


Figure 4. The Line Stimulus at the center of the incomplete fixation cross forms an image that is three degrees of visual angle long (diameter of the macula) and one degree wide (diameter of the fovea).

edges which would also be affected by scatter. The display of this line on a LCD screen was not cause for concern as the stimulus only contained first-order information (luminance) and was presented at above-threshold levels with regard to brightness and display time.

Before testing began, a display was shown to the participants that contained six possible categories of the line test (solid, bent right, bent left, small central hole, thinner center, broken, see Figure 5). They were able to view this display with their healthy eye and were instructed that they will be choosing from these categories during the testing procedure. Participants placed their heads in a chin rest and the screen display was positioned at a 90-degree angle to the participants' viewing direction. They were instructed to focus on the spot where the two diagonal lines would intersect. The test stimulus was presented five times, for 500 ms at each trial. After each presentation, the participants chose among the six possible categories and were asked which one most closely represented what they saw. If the available choices were insufficient, participants were encouraged to draw what they saw.

Results

Line Perception. Pre-operative perceptions of the line stimulus as a function of MH diameter are displayed in Figure 6 ($n = 25$). Participants' line perceptions before surgery did not depend on preoperative MH diameter. Due to the distribution of eyes among perceptual categories, only descriptive statistics were possible. When grouping these participants' perception of the line into symmetrical (solid, thinned, small hole, broken) versus asymmetrical categories (bent right or left), 19 (76%) eyes reported symmetrical perception of the line.

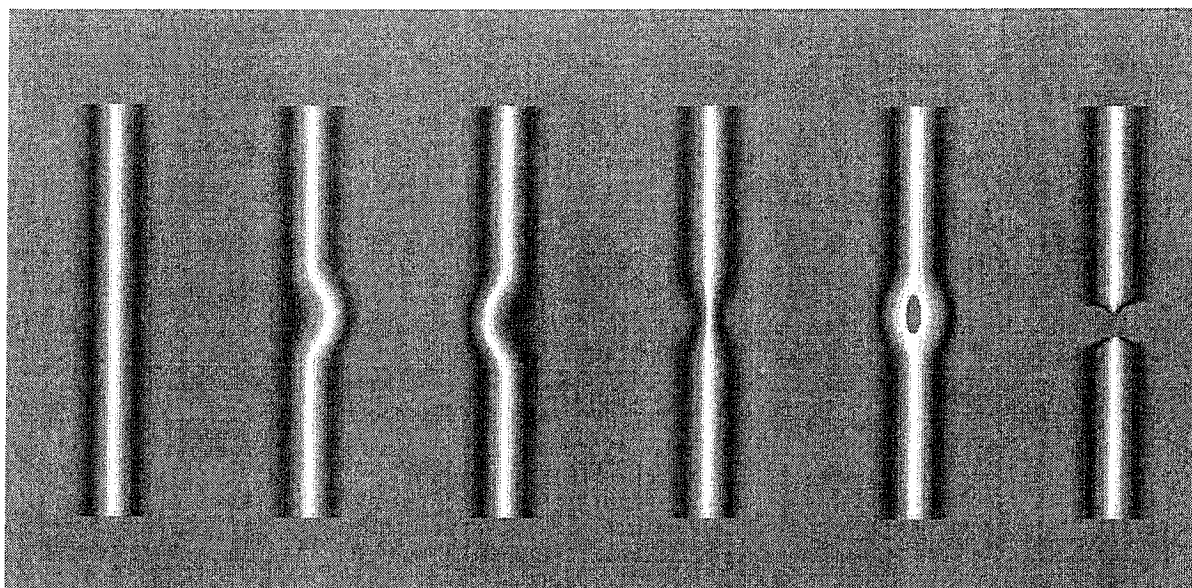


Figure 5. Categorical scoring options presented to participants for perception of the Line Stimulus.

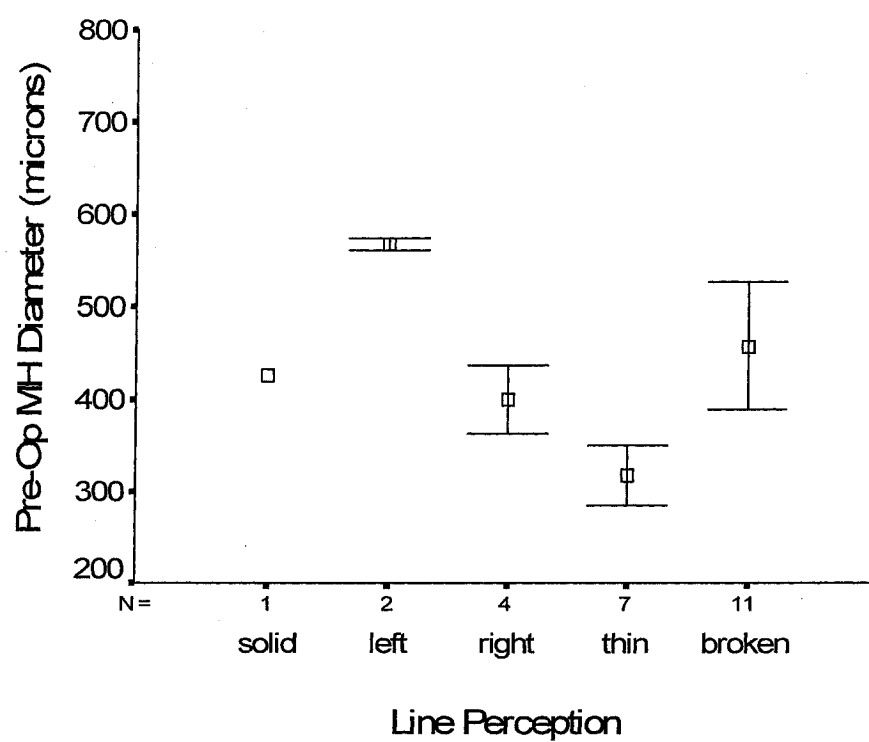


Figure 6. Line Stimulus perceptions preoperatively as a function of pre-operative MH diameter . Error bars represent one standard error from the mean.

Post-operative perceptions of the line stimulus at 1 to 3 months as a function of MH diameter for eyes with successful surgery are displayed in Figure 7 ($n = 22$). When classifying the perceptual reports into non-distorted (solid, $n = 13$) versus distorted (all other, $n = 9$) perception of the line, a statistically significant difference in pre-operative MH diameter became apparent, $t(20) = 2.04$, $p = .05$, $\eta^2 = .17$, observed power = .50. Eyes with larger MHs were more likely to retain residual metamorphopsia after successful closure of the defect.

After minimally 5 months of follow-up, post-operative perceptions as a function of MH diameter are available for 18 eyes and are displayed in Figure 8. When classifying the perceptual reports into non-distorted vs. distorted line perception, no statistically significant differences were found in pre-operative MH diameter, $t(16) = 1.47$, $p = \text{ns}$.

Metamorphopsia and Visual Acuity. The final analysis compared visual acuities on the ETDRS and Landolt-C charts between the groups of eyes with ($n = 9$) vs. without ($n = 13$) residual distortions at both time points. At 1 to 3 months, the groups did not differ significantly on either acuity measure, $t(20) = .06$, $p = \text{ns}$ for ETDRS and $t(20) = .08$, $p = \text{ns}$ for Landolt-C. At more than 5 months of follow-up, the same pattern was found, $t(16) = .53$, $p = \text{ns}$ for ETDRS and $t(16) = .51$, $p = \text{ns}$ for Landolt-C. Neither visual acuity measure at either time point was able to reflect the presence or absence of metamorphopsia.

Discussion

MH diameter did not accurately predict perception of a vertical line stimulus before MH surgery. The two key components in explaining this finding may be the

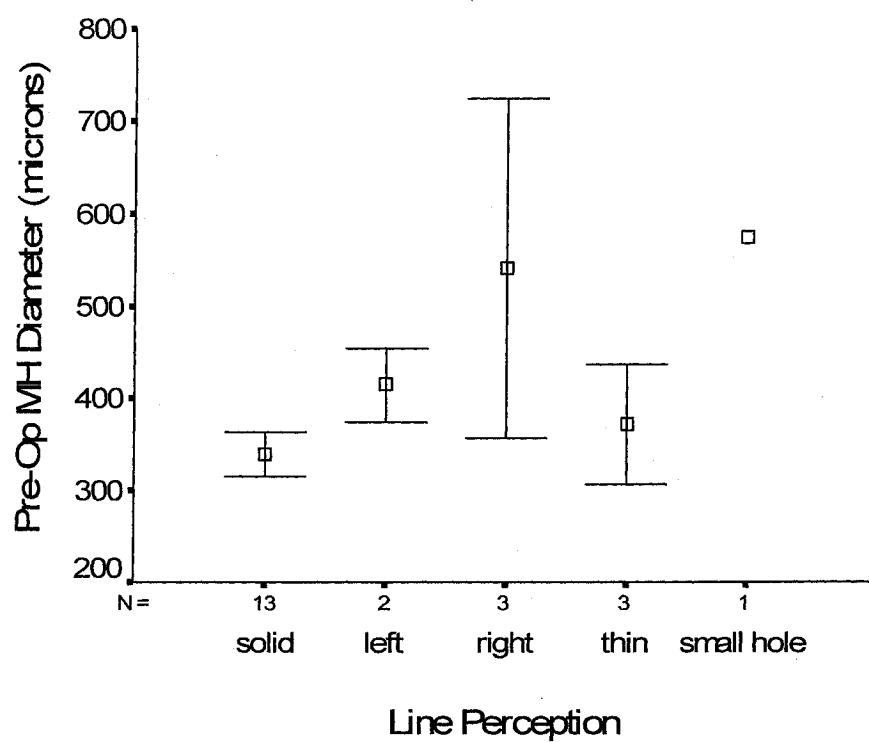


Figure 7. Line perception as a function of pre-operative MH diameter at 1 to 3 months post-operatively. Error bars represent one standard error from the mean.

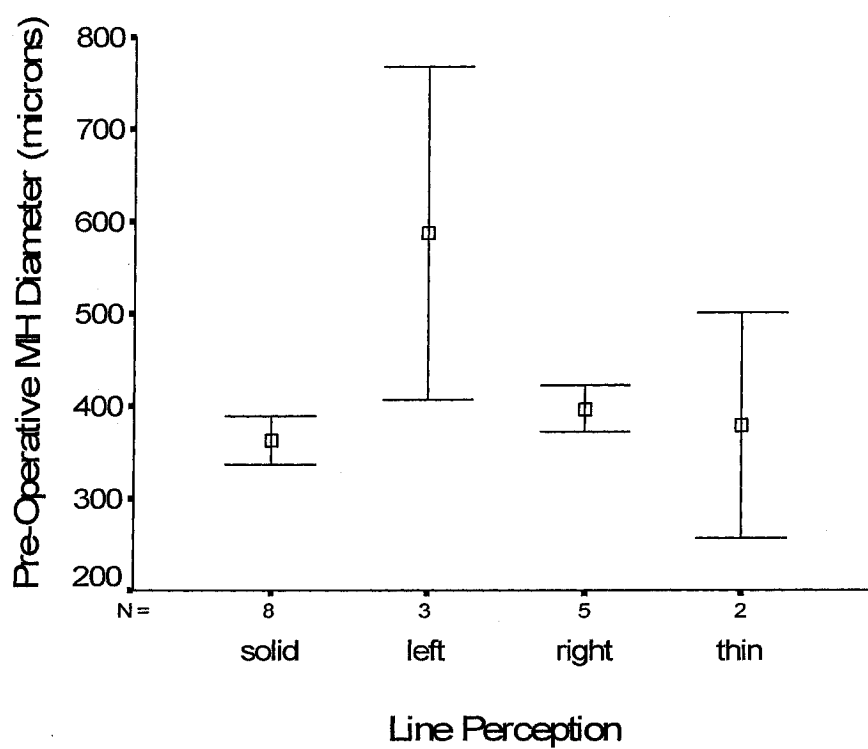


Figure 8. Line perception as a function of pre-operative MH diameter at more than 5 months post-operatively. Error bars represent one standard error from the mean.

choice of fixation target in the stimulus presentation as well as the fixation preferences of MH patients. Various forms of fixation targets have been used in the context of research involving patients with central scotomas (Bellmann et al., 2004). The most common challenges were related to fixation stability and to the ability to find the fixation target (Schuchard & Raasch, 1992). The choice of an incomplete fixation cross in the present study was based on its successful use in previous work with MH patients (Davey et al., 2004; Wittich et al., 2005). In addition, it was assumed that this type of fixation technique would result in placing the center of the line across the center of an absolute scotoma. This assumption may have been incorrect. Previous work by Schuchard and Raasch (1992) evaluated fixation stability in patients with central scotomas across different types of fixation targets. Their findings indicated that the technique of using peripheral retina for fixation information may not be as efficient as when using a small x, which resulted in more stable fixation. In addition, the authors pointed out that a peripheral target, such as the incomplete fixation cross in the present study, still resulted in fixation with the new preferred retinal locus. Even with specific verbal instructions, a large majority of their patients were unable to control their viewing direction in such a way that the center of their scotoma would fall on the fixation target.

When examining the perceptual reports after successful MH closure, it can be assumed that fixation has returned towards the center of the macula (Nakabayashi et al., 2000). At 1 to 3 months after successful surgery, 13 (59%) eyes perceived an undistorted line while 9 (41%) eyes reported residual distortions. The latter group had significantly larger MH diameter pre-operatively. These results indicate that the extent of residual metamorphopsia may depend on the amount of damage present before surgery. This

effect disappeared, however, after at least 5 months, indicating that some type of cortical reorganization may have occurred (Baker, Peli, Knouf, & Kanwisher, 2005) or that the healing process indeed continues in the long run after surgical intervention (Leonard et al., 1997).

The final question to be addressed was whether a link exists between the assessment of metamorphopsia and visual acuity. Contrary to the initial hypothesis, patients with residual distortions in their central visual field did not display differences on the acuity measures compared to patients who perceived the line stimulus to be undistorted. From the psychophysical perspective, this finding is intriguing as the use of this line test revealed perceptual distortions that otherwise remained unnoticed in the clinical setting which relies predominantly on visual acuity. In Ophthalmology, metamorphopsia in the context of MH is traditionally detected with the Amsler grid or the Watzke-Allen test (Burke, 1999; Saito et al., 2000). Both of these tests, however, are presented with unlimited display time and patients are given ample opportunity to scan the stimulus. It is possible that the parameters for the line test, specifically the limited display time of 500 ms, make this measure more sensitive in its ability to detect residual distortions in the central visual field (Wittich et al., 2005). It may, in fact, be sensitive enough to reveal distortions that are so minimal that they do not interfere with the ability to read an eye chart.

General Discussion

The present study addressed questions concerning the recovery rate of visual acuity in individuals with MH, as well as their perception of visual distortions. By considering both these functional aspects in parallel, it was possible to examine whether distortions influence acuity and to what extent these functional measures are influenced by structural damage to the retina.

The results of the first experiment indicate that the slopes of functional recovery rate over time depend on the lens status of the patient. Participants with previously implanted IOLs recovered function faster whereas patients with their natural lenses experienced slower recuperation. This delay can be explained by the onset of cataract within the first 6 to 12 months after surgery. In itself, this finding is not surprising, as several previous studies have indicated that the formation of cataract is a common post-surgical complication, again reducing patients' visual acuity temporarily (Benson et al., 2001; la Cour & Friis, 2002; I. U. Scott et al., 2003). In this phase, however, the functional impairment is due to opacity in the lens, secondary to the surgical procedure. Previous reports on the functional outcome of MH surgery excluded patients who developed cataract, or postponed the measurement of acuity until the lens had been replaced with an IOL (Leonard et al., 1997). It has even been suggested that functional outcome should generally not be evaluated until after cataract extraction has occurred (Pearce, Branley, Groenewald, McGalliard, & Wong, 1998). This approach was surprisingly mentioned in the context of patient satisfaction after MH surgery. The authors did not consider that patients do not just return to the ophthalmologist when a cataract has formed but often have to live with the developing impairment for a

considerable amount of time until the second surgery is scheduled. The present study was able to provide information about the experienced level of this impairment from the patients' point of view.

The investigation of acuity improvement after MH surgery focuses by definition on patients who underwent anatomically successful treatment. Yet, this desirable outcome is not always accomplished. The comparison analysis, that included patients with failed surgery, indicated that acuity neither improved nor worsened in cases where the treatment was not successful in closing the retinal defect. This finding forms an interesting addition to a previous report on acuity in patients who did not receive any treatment at all (Casuso et al., 2001). Unoperated MHs seem to progress until they stabilize, resulting in acuity of approximately 20/400 (6/120). The eyes in the present study where surgery failed, however, stabilized at acuity in the range of 20/200 (6/60). It could, therefore, be speculated that failure to close the MH but successful reattachment of the edges still results in better acuity and less eccentric fixation than no treatment at all.

The second experiment considered the occurrence of visual distortions. In order to explain the type of line distortions described by the participants before as well as after surgery, the question of fixation must be addressed in more detail. The inability to fixate at the center of a scotoma, using information from the peripheral retina had intriguing implications for the perception of the line stimulus. It was initially assumed that the peripheral fixation target would guide the participants' focus in such a way that the line would be viewed across the central scotoma. Unexpectedly though, participants may have used their new fixation area at the edge of the MH in order to fixate at the theoretical intersection of the incomplete fixation target. If that were to be the case, an

interesting perceptual change might have occurred as now the central absolute scotoma may not have fallen on the center of the line stimulus anymore but may have been moved off-center. Indeed, some of the participants mentioned that the distortions they perceived looked similar to the options in Figure 5, but were not at the center of the image that they saw. This observation leads to the question of where MH patients actually fixate with the affected eye. Previous work, using a Scanning Laser Ophthalmoscope (SLO), has indicated that, before surgery, patients fixate at or near the edge above the MH (Guez et al., 1998), and that fixation returns towards the central area of the macula after successful closure of the defect (Nakabayashi et al., 2000). As the majority of MH patients have been demonstrated to fixate with the area directly above the MH, the question of whether a line is perceived as distorted or not should be re-formulated into whether the line is perceived as symmetrical (fixation above the MH) or asymmetrical (fixation off to either side of the MH). Considering the results of the present investigation from this viewpoint, the percentage of patients with symmetrical line perception was in accordance with previous results (Guez et al., 1998), indicating that most do indeed experience symmetrical line distortions, probably due to fixation above the MH.

Of particular interest is the group reporting thinning of the line preoperatively, because, for them, the center should be perceptually missing. Patients seem to fill in the information, resulting in perception of a thinner line at the center. Saito et al. (2000) have previously attempted to explain this phenomenon by examining the perception of the Watzke-Allen Test. They assumed that the photoreceptors, though displaced, were functioning and that the line stimulated the edges of the MH. That cannot be the case in the present sample as calculation of the line width and MH diameters indicated that the

center of the line was not perceived because it was too narrow to be stimulating the edges of the MH in most patients (see Figure 9). This information must, therefore, be perceptually filled in at the cortical level.

The question of activity in the visual cortex in the presence of macular disease is difficult to approach as reports in the literature remain sparse and contradictory. It has been shown that functional magnetic resonance imaging (fMRI) is informative in patients with long-term macular pathology (Sunness, Liu, & Yantis, 2004). However, it remains unclear whether the cortical areas previously stimulated by the fovea remain active but now only process peripheral information (Baker et al., 2005), or if these areas become silent (Sunness et al., 2004). Some type of cortical reorganization may occur over time, yet, how long the required time span may be or how extensive the damage to the retina can be is not presently established.

The final component of the present study focused on the possible effect of distortions on visual acuity. It was hypothesized that the presence of residual distortions after surgery would be reflected in poorer acuity scores. However, this was not the case. The results indicate that the presented line test may be able to detect distortions that do not interfere with acuity measurement. This finding opens up speculations about the type of functional assessment that should be utilized with MH patients. Distortions are generally not quantifiable in the applied clinical context. From the patients' perspective, however, it is the presence of distortions that is more bothersome in their visual experience (Ellis & Baines, 2002; Ellis, Malik, Taubert, Barr, & Baines, 2000). Faces, for example, may appear distorted, making it more difficult to interpret expressions of emotions. From the perspective of structure-function relationships, it is intriguing that an

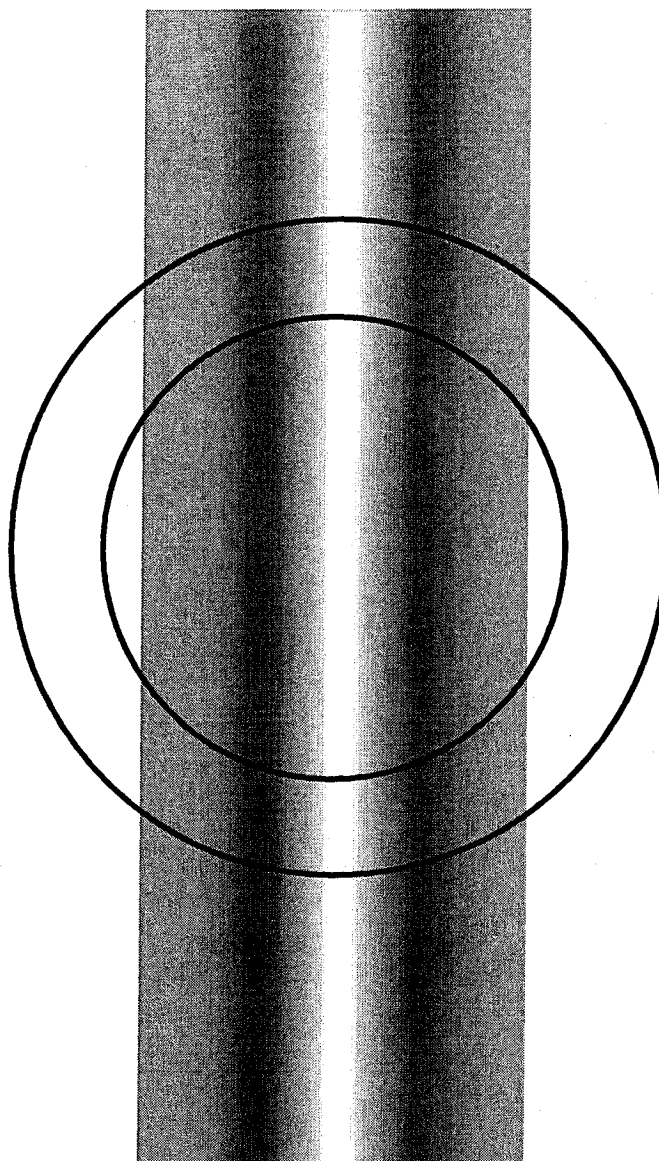


Figure 9. Schematic proportional representation of the mean MH diameter for perception of a broken line (outer circle) and a thinned line at the centre (inner circle). The area within each circle indicates the component of the line stimulus that is lost to perception due to the absolute scotoma within the MH.

anatomically restored retina looks structurally intact on an OCT scan and performs within an optimal range on recognition and orientation charts but is unable to perform equally well on a line distortion test. It is likely that this functional discrepancy will motivate future research regarding the restoration of structure *and* function after the occurrence of retinal disease.

In addition to the investigated hypotheses, the interaction with the participants revealed noteworthy information. The impairment due to cataract is generally expected by the ophthalmologist and MH surgery outcome is viewed independently by the retinal surgeon. For the patient, however, it is rarely clear that this decline in acuity is a normal consequence of the treatment. Many patients reported concerns that their MH may have re-opened or that the surgery failed. They were aware that they would require a second surgery for cataract removal but were generally unprepared for the impairment caused by the cataract. This type of response is consistent with previous reports about patient perceptions and level of understanding of common ocular pathology (Attebo, Mitchell, Cumming, & Smith, 1997; McCarty, 1997). In addition, the lack of appreciation by the ophthalmologist of the non-medical components in doctor-patient interaction have been shown to contribute to this type of insufficient communication (Pager & McCluskey, 2004).

The differences in recovery rate at the functional level give valuable insight into the patients' experience. Individuals who undergo MH surgery and who still have their natural crystalline lens at the time of treatment may require some additional information. Their recovery period will be longer, even though the initial surgery may have been anatomically successful. Patients are indeed informed prior to MH surgery that cataract

is likely to develop within 6 to 18 months after the initial surgical intervention. What is not necessarily clear to the patient is that this complication does not only entail a second surgery but that the cataract will perceptually extend the time period during which the patient will be able to achieve his or her optimal visual acuity.

It should be emphasized that the findings of the present study have to be viewed within the context of several limitations. Growth curve analysis relies on multiple repeated measures over time. By using HLM, it was possible to incorporate measures from three different eye charts in order to obtain the required number of repeated measures. The resulting outcome variable of *acuity*, however, does not directly translate into acuity as measured using one particular chart. This approach has both advantages and disadvantages. By utilizing several measures, it is possible to examine visual function in a more global way, specifically as recognition of letters and orientation detection of a ring are slightly different visual and cognitive tasks. The most disputable component may be the use of Snellen acuities; yet, it is exclusively this type of acuity that is available to the ophthalmologist who bases his or her clinical impression of function on this measure alone. Therefore, by combining all three acuities into one outcome measure, the resulting growth curves satisfy the scientific requirements of the psychophysicist while incorporating the clinically available information of the ophthalmologist.

In order to improve acuity measurement in patients with impending cataract formation, the use of a Potential Acuity Meter (PAM) may be desirable. This technique enables the researcher as well as the ophthalmologist to project an eye chart directly onto the retina using laser projection. With this technique, any clouding in the optical media

can be bypassed (Lasa, Datiles, & Freidlin, 1995). This method of measuring acuity has previously been used successfully with MH patients, however, it has been shown that its accuracy may depend on the level of acuity of the patient as defined by other measures, and that it may overestimate acuity compared to standard charts (Smiddy, Thomley, Knighton, & Feuer, 1994). In the present study, the differences measured in the presence or absence of cataract would disappear with the use of the PAM. These measurements, however, would no longer reflect the actual visual experience of the patient.

The evaluation of perceptual distortions and the display of the line test encountered a temporal problem. Patients were theoretically able to make saccadic eye movements across the line during the presentation of 500 ms. Under rigorous psychophysical testing conditions, display time would have to be limited to less than 150 ms. The choice of an extended display time was based on the logistics of applied psychophysical testing with a clinical sample of seniors. It must be pointed out that the participants in this study were recruited in the context of their medical treatment within an ophthalmology department. Their primary motivation for being present in the clinic was their visual impairment and their need for treatment by a retinal surgeon. Participation in a research project was not their primary concern or interest. The option of participating in a study that did not directly relate to the outcome of their individual treatment required extensive explanation. It was the goal of the research team to create a comfortable environment for the participants and to put them at ease with each task. By extending the display time to 500 ms, the task of “seeing” the line became less frustrating for these participants and they were less likely to discontinue the study. Additionally, by extending the display time, participants may have been able to compensate for fixation

instability, a common phenomenon in patients with macular damage (Bellmann et al., 2004). Therefore, by giving participants more time, they may be able to properly fixate and perceive the line stimulus with their most stable or comfortable fixation location.

The ideal solution for the problem of fixation instability and exact placement of the line stimulus on the retina would be the use of an SLO. With this technique, a camera and computer screen is connected to the ophthalmoscope, presenting real-time images of the retina to the researcher. The experimenter can then choose, on the computer screen, where on the retina a previously programmed image will be presented. The contribution of SLOs to research with MH has been invaluable, giving insights into fixation patterns (Guez et al., 1998; Hikichi et al., 2000; Nakabayashi et al., 2000), scotoma shape and density (Hikichi et al., 2002; Rohrschneider, Bultmann, Kruse, & Volcker, 2001; Sjaarda et al., 1993a, 1993b), as well as visually evoked potentials (Le Gargasson, Rigaudiere, Guez, Gaudric, & Grall, 1994).

Other investigations of visual function in MH patients have focused on psychophysical techniques such as binocular perimetry (Jensen & Larsen, 1998), spectral sensitivity (Kaur, O'Donaghue, & Murray, 2003), and spatial interval discrimination (Van Baelen, Claessens, Stalmans, & Wagemans, 2005). Each approach will no doubt continue to contribute to the understanding of visual function in patients with MH. In addition to these investigations of visual function, the assessment of structural changes in MH is progressing rapidly, specifically with the development of the next generation of OCT scans. It is now possible to obtain three-dimensional images at ultra-high resolution which allow for the examination of changes at the cellular level (Schmidt-Erfurth et al., 2005).

The present study was able to contribute to these investigations by demonstrating the patterns of functional recovery after MH surgery, with special focus on the key period of the initial 6 months after treatment. Future work in this area should carefully consider the time points at which function is assessed as the recovery process remains dynamic for several months after surgery. The evaluation of metamorphopsia in MH patients should be considered in addition to visual acuity. More sensitive measures, such as the presented line stimulus may be able to detect functional deficits that are subject to perceptual filling-in and may otherwise go unnoticed by clinically established measures. The research literature in both areas of acuity thresholds and perceptual filling-in has largely relied on healthy observers. Access to a sample of patients with MH provided a unique opportunity. It is questionable whether simulated deficits in younger individuals resemble the visual experience with disease-related vision loss. The key to a better understanding of the mechanisms involved in visual perception may, in part, lie in the evaluation of a visual system that is failing and adapting when affected by disease.

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Appendices

Appendix A1 – English Consent Form

Sir Mortimer B. Davis Jewish General Hospital
Department of Ophthalmology

Psychophysical Assessment of Anatomically Successful
Repair for Macular Hole and Perifoveal Detachment
with Macular Involvement

Investigator: W. Wittich

Consent Form

Introduction

We invite you to take part in this research study because it has been determined that you require surgery to improve your central vision. This study is being conducted under the direction of Dr. Overbury. You have the right to be informed about the procedures, risks and possible benefits of this study in order to decide whether or not you want to participate. Please read this consent form carefully and feel free to ask any questions.

Purpose of this study

The purpose of this study is to evaluate different types of tests used to measure central vision. Presently, the available testing techniques are adequate but we are constantly trying to improve their sensitivity. This project will help determine which of the 6 tests better evaluates improvements of your vision over time and may allow us to detect changes in your vision sooner. It is also the goal to better understand how changes in the structure of the eye affect how well we see.

Procedures

If you participate in this study, you will be asked to complete a series of five vision tests with only one eye. This will include reading letters on an eye-chart (1) as well as determining which way the letter C is facing on a similar chart (2). One test will require you to choose between two lines on a computer screen and decide which one is wavy and which is straight (3). We will also project a white strip of light into your eye and ask you if this strip has a gap or not (4). Afterwards, we will take a scan of your eye (5). This scan only takes a few seconds during which you will be looking at a red strip of light. For the last two tests we will need to dilate your pupil with drops. This is painless and not dangerous and the effect will disappear after about 2 hours. The first testing session will be before the surgery and will be repeated three to four months after the surgery and again each time when you return for your follow-up visits with Dr. Kapusta. Each session should not take longer than 40 minutes.

Version date: 2005/10/April

Sir Mortimer B. Davis Jewish General Hospital
Department of Ophthalmology

Psychophysical Assessment of Anatomically Successful Repair for Macular Hole and
Perifoveal Detachment with Macular Involvement

Investigator: W. Wittich

Risks and Benefits

All tests in this study pose minimal or no risk to you or your vision and are comparable to watching TV or reading on a computer screen. There will be no immediate direct benefit to you; however, you will be contributing to medical knowledge.

Participant's Rights

Your participation in this study would be greatly appreciated, but please be aware that you are not obliged to participate in this research study and you can withdraw at any time. Your medical care will not be affected in any way if you choose not to participate or withdraw from the study.

Confidentiality

All information collected will be confidential and, should the results be published, your name will not appear and your identity will not be revealed. In addition, at your request, a copy of the results will be provided to you.

Questions

If you have any questions, you may contact the following individuals:

Researcher:	Mr W. Wittich (graduate student)	340 8222 # 4894
Supervisor:	Dr O. Overbury	340 8222 # 5211
Clinical Director:	Dr M. Kapusta	340 8284

If you have any questions regarding your rights as a research participant, you may contact the patient representative, Ms. Laurie Berlin, at 340 8222 ext. 5833.

Version date: 2005/10/April

Sir Mortimer B. Davis Jewish General Hospital
Department of Ophthalmology

Psychophysical Assessment of Anatomically Successful Repair for Macular Hole and
Perifoveal Detachment with Macular Involvement

Investigator: W.Wittich

Statement of Consent

► I have read and been told, the purpose, risks, possible benefits and alternatives of this project. I understand that my participation is voluntary and that I have the right to withdraw from the study at any time should I choose to participate. I understand that a copy of this signed consent form will be placed in my medical record and a copy will be given to me.

► I agree to take part in this research study.

Participant's Name

Signature

Date

Name of person obtaining
Consent

Signature

Date

Version date: 2005/10/April

Appendix A2 – French Consent Form

Hôpital Général Juif Sir Mortimer B. Davis
Département d'ophtalmologie
Évaluation Psychophysique de réparation réussie d'un trou maculaire
et de détachement perifoveal impliquant du macula
Investigateur: W. Wittich

Formulaire de consentement

Introduction

Nous vous sollicitons à prendre part à ce projet de recherche étant donné que vous subirez une intervention chirurgicale pour améliorer votre vision centrale. Cette étude sera conduite sous la direction du Dr Overbury. C'est votre droit d'être informé au sujet des procédures, risque et avantages possibles de cette étude et de décider, si vous désirez y participer. S'il vous plaît, veuillez lire ce formulaire de consentement avec soin et n'hésitez pas à poser des questions.

But de cette étude

L'objectif du projet est d'évaluer l'utilisation de différents tests utilisés pour mesurer la vision centrale. Présentement, les techniques de test disponibles sont adéquates, mais nous essayons constamment d'améliorer leur sensibilité. Ce projet aidera à déterminer lequel, parmi les 5 tests, évalue le mieux l'amélioration de votre vision avec le temps et pourrait nous permettre de détecter les changements de votre vision plus tôt. Cette recherche a aussi comme objectif de mieux comprendre les changements au niveau de la structure de l'oeil et comment cela affecte la façon dont nous voyons.

Procédures

Si vous participez à cette étude, vous serez invité à compléter une série des cinq examens de la vue avec seulement un œil. Cela inclura lire des lettres sur un tableau (1) ainsi que de déterminer l'orientation de la lettre C sur un tableau similaire (2). Un autre examen, sur un écran d'ordinateur, vous demandera de choisir entre deux lignes et de décider laquelle est ondulée et laquelle est droite (3). Également nous projetterons, dans votre œil, une bande de lumière blanche et nous vous demandons d'identifier si la bande est continue ou non (4). Par la suite, une lecture de votre œil sera prise (5). Pour faire cette lecture, vous devrez regarder une bande de lumière rouge, pendant seulement quelques secondes. Pour les deux derniers examens, nous aurons besoin de dilater votre pupille avec des gouttes. Cet examen est sans douleur et sans risque et les effets disparaissent environ 2 heures plus tard. La première série d'examen sera effectuée avant la chirurgie et sera répétée environ trois à quatre mois plus tard et répétée de nouveau lorsque vous reviendrez pour vos visites de contrôle avec le Dr. Kapusta. Chaque session ne devrait pas dépasser 40 minutes.

Version date: 2005/10/Avril

Hôpital Général Juif Sir Mortimer B. Davis
Département d'ophtalmologie

Évaluation Psychophysique de réparation réussie d'un trou maculaire et de détachement
perifoveal impliquant du macula

Investigateur: W. Wittich

Risques et Avantages

Les risques pour ces examens sont minimales pour vous ou votre vision et sont comparables à regarder la TÉLÉ ou lire sur un écran d'ordinateur. Vous n'aurez aucun bénéfice direct et immédiat de votre participation à cette étude, cependant, vous contribuerez à l'amélioration des connaissances médicales dans ce domaine.

Les droits du participant

Votre participation à cette étude serait grandement appréciée, néanmoins, soyez assuré qu'il n'y a aucune obligation de votre part et que vous pourrez vous retirer à n'importe quel moment durant le projet de recherche. Si vous choisissiez de ne pas participer ou interrompre l'étude, vos soins médicaux ne seront pas affectés en aucune façon.

Confidentialité

Les informations rassemblées seront confidentielles et advenant la publication des résultats, votre nom ainsi que votre identité ne seront pas révélés. Si vous le désirez, nous pourrions vous faire parvenir une copie des résultats.

Questions

Si vous avez des questions, n'hésitez pas à contacter les personnes suivantes:

Chercheur:	M. W. Wittich (étudiant d'honneur)	340 8222 # 4894
Directeur:	Dr O. Overbury	340 8222 # 5211
Directeur Clinique:	Dr M. Kapusta	340 8284

Si vous avez des questions concernant vos droits comme participant de recherche, adressez-vous à la représentante des droits aux patients de l'Hôpital général juif, Mm. Laurie Berlin, au 514-340-8222 poste 5833.

Version date: 2005/10/Avril

Hôpital Général Juif Sir Mortimer B. Davis
Département d'ophtalmologie

Évaluation Psychophysique de réparation réussie d'un trou maculaire et de détachement
perifoveal impliquant du macula
Investigateur: W. Wittich

Déclaration de consentement

► J'ai lu et compris, le but, les risques, avantage possibles et alternatives de ce projet. Je comprends que ma participation est volontaire et que j'ai le droit de me retirer de l'étude à n'importe quel moment si je devais choisir d'y participer. Je comprends qu'une copie de ce formulaire de consentement dûment signé sera placée dans mon dossier médical et une copie me sera remise.

► Je consens à participer à ce projet de recherche.

Nom du participant

Signature

Date

Nom de la personne obtenant le
consentement

Signature

Date

Version date: 2005/10/Avril

Appendix B1

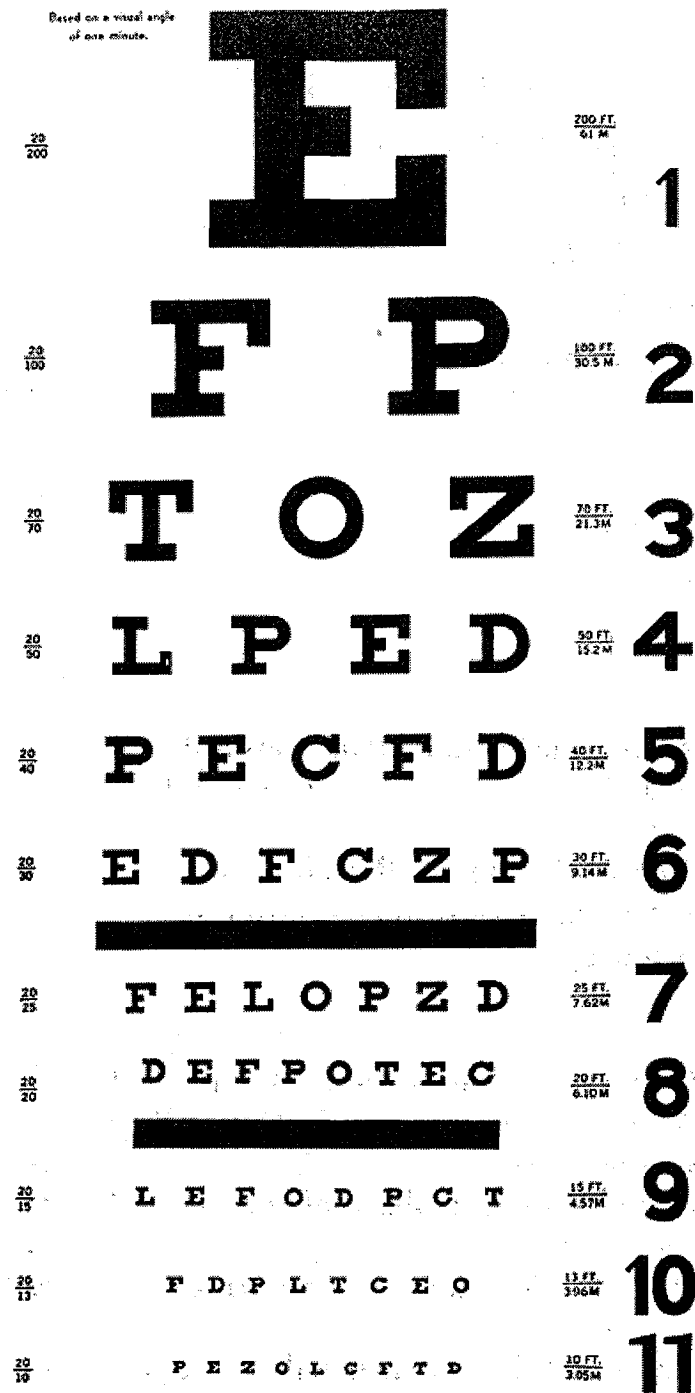


Figure B1a Snellen Acuity Chart

Appendix B2

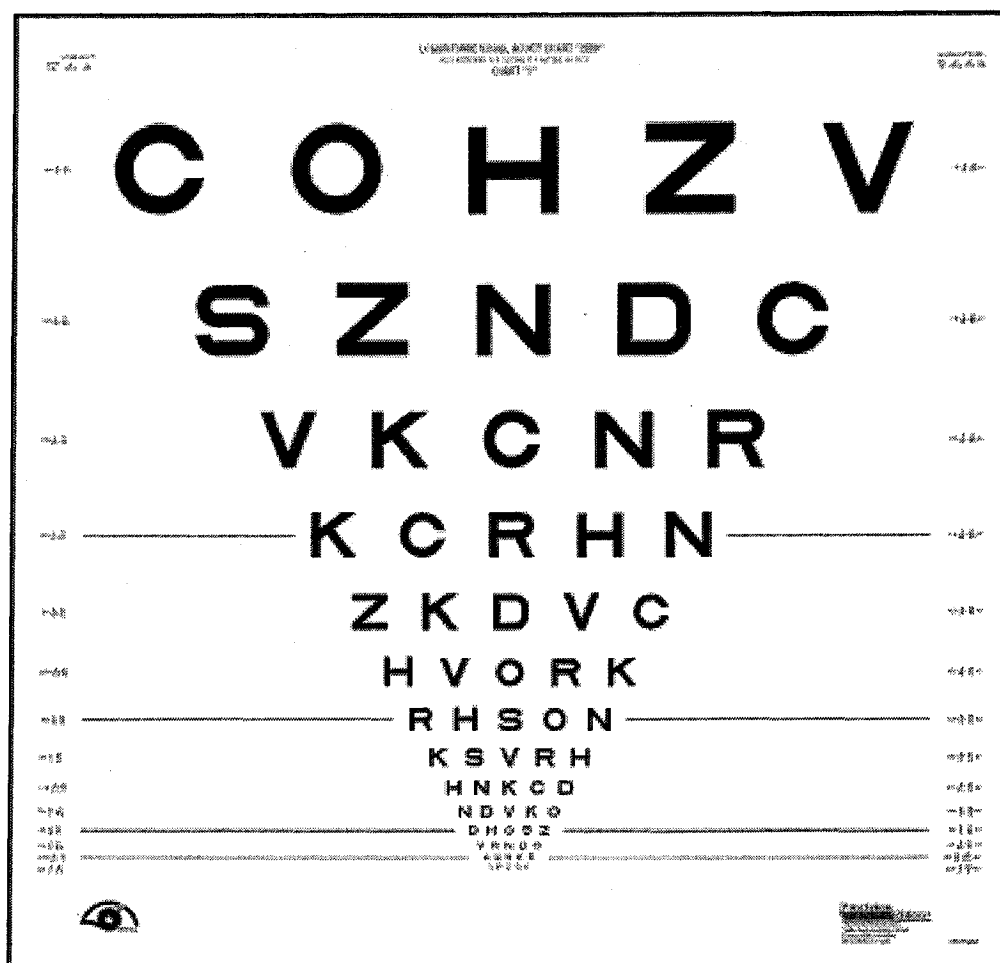


Figure B1b. ETDRS Acuity Chart

Appendix B3

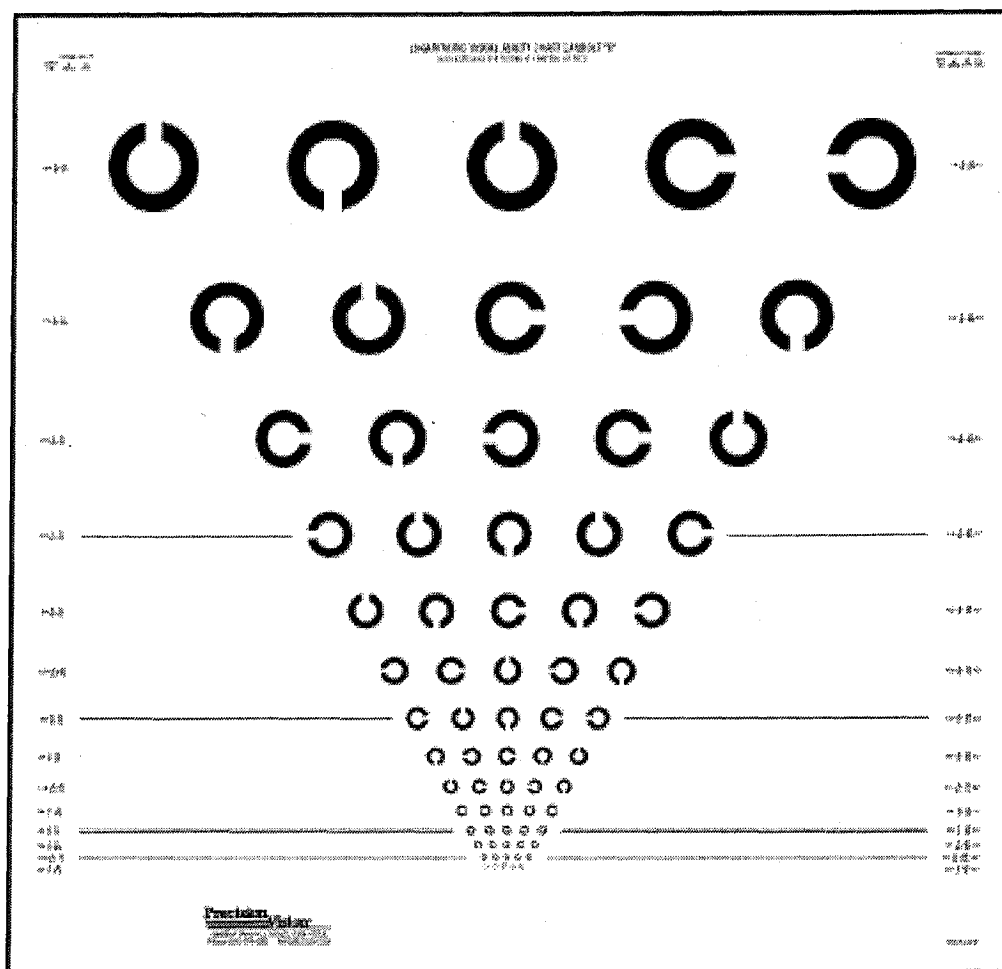


Figure B1c. Landolt Ring Acuity Chart

Appendix C – OCT Scanner



Figure C. Optical Coherence Tomograph,

Appendix D 1. Patients with Failed Surgery

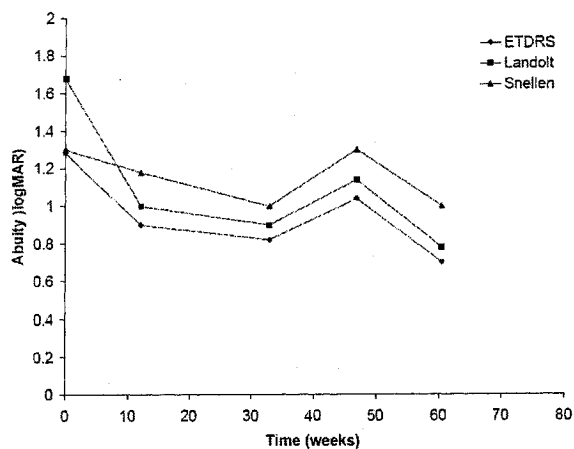


Figure D1a. Acuties as a function of time for patient 02

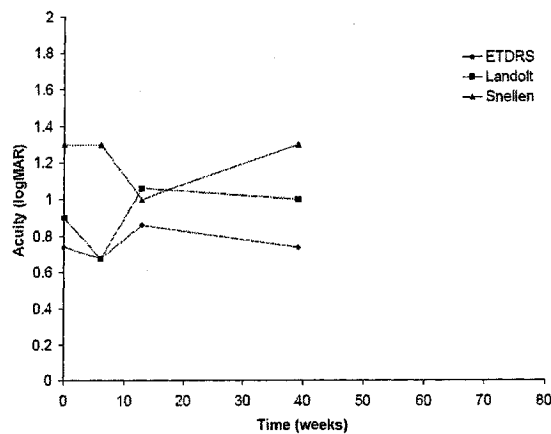


Figure D1b. Acuties as a function of time for patient 11

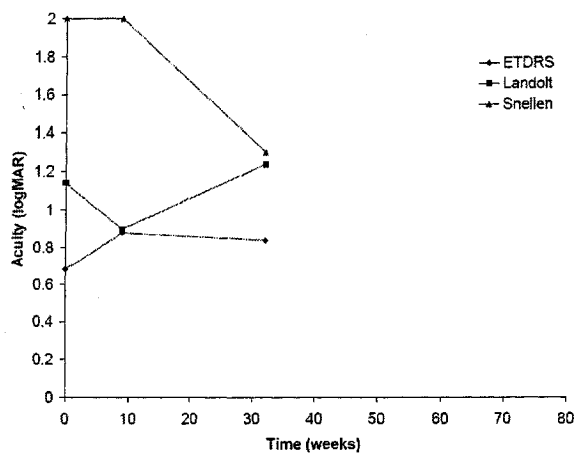


Figure D1c. Acuity as a function of time for patient 27

Appendix D 2. Patients with natural lens

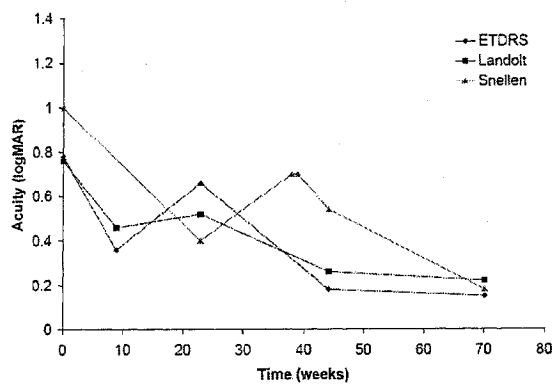


Figure D2a. Acuity as a function of time for patient 1

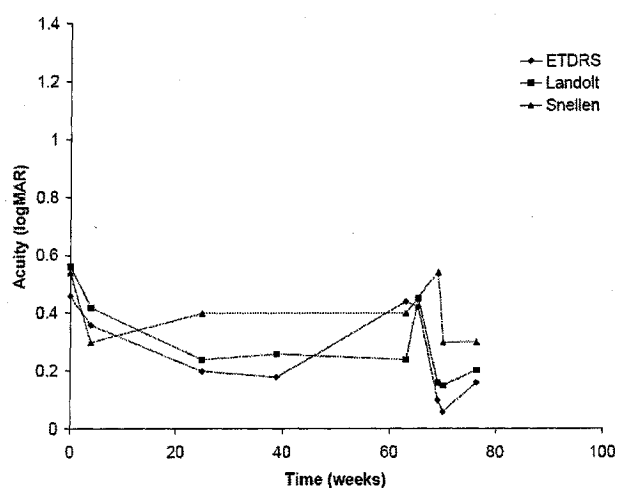


Figure D2b. Acuity as a function of time for patient 3

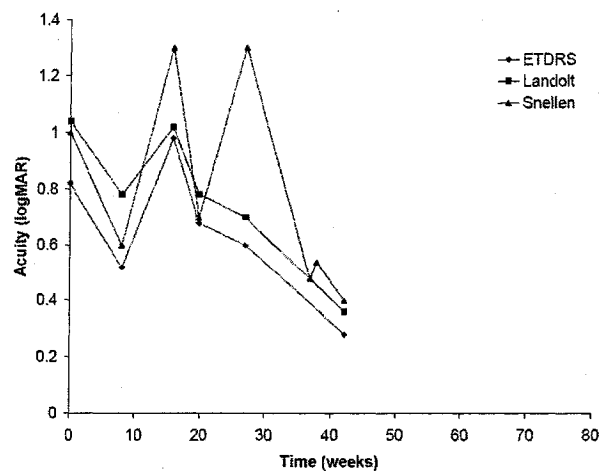


Figure D2c. Acuity as a function of time for patient 5

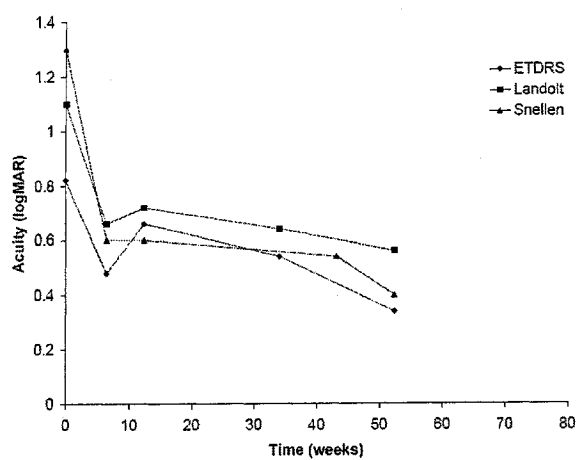


Figure D2d. Acuity as a function of time for patient 6

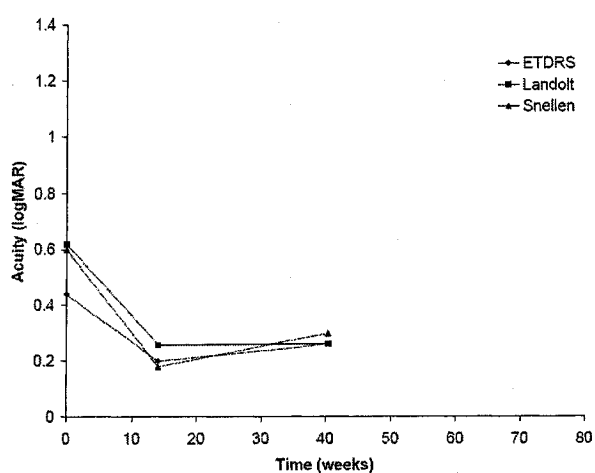


Figure D2e. Acuity as a function of time for patient 14

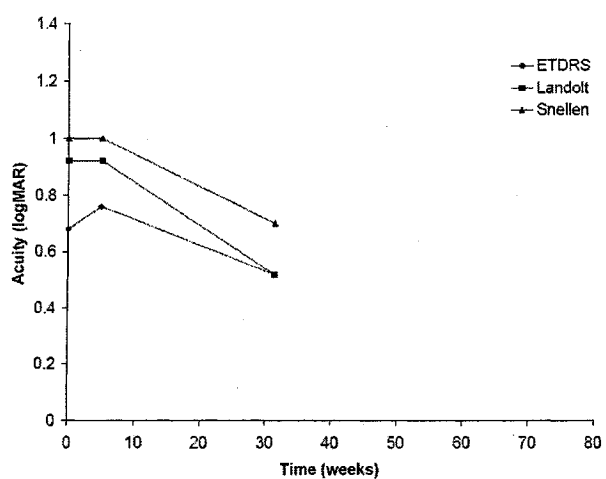


Figure D2f. Acuity as a function of time for patient 15

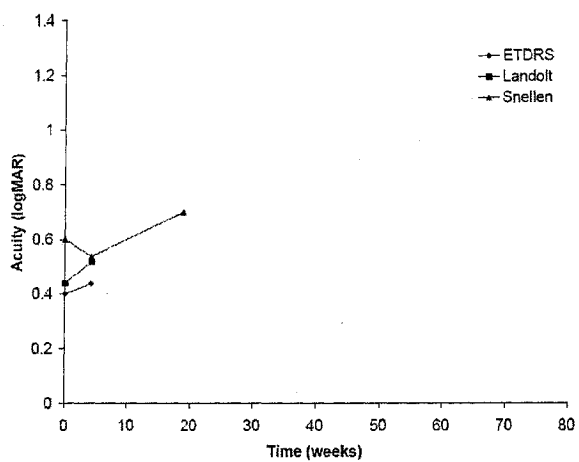


Figure D2g. Acuity as a function of time for patient 16

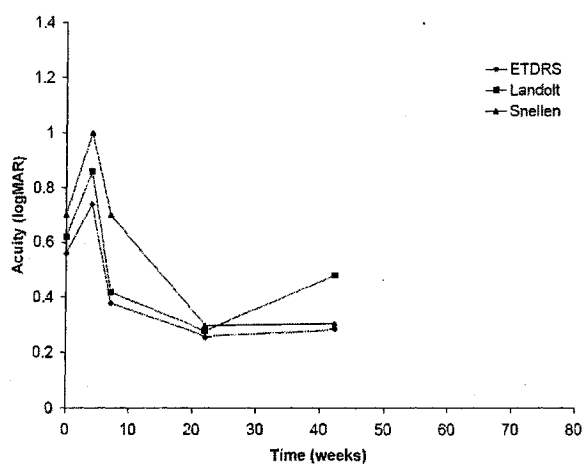


Figure D2h. Acuity as a function of time for patient 17

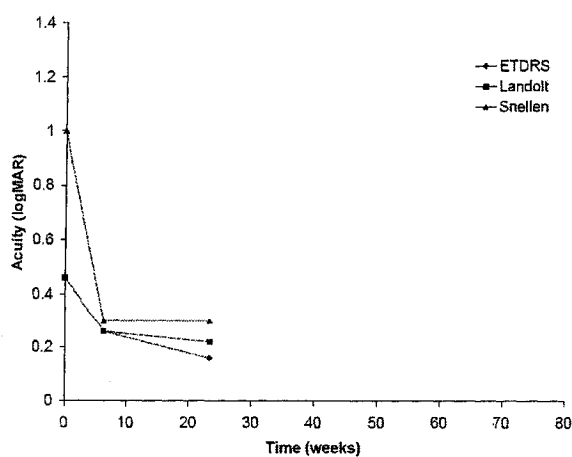


Figure D2i. Acuity as a function of time for patient 18

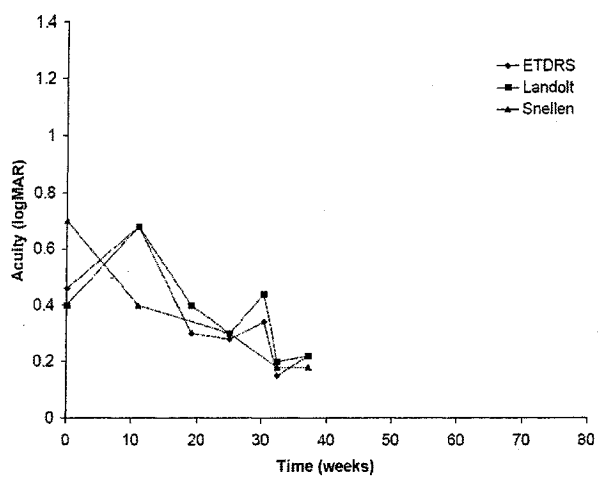


Figure D2j. Acuity as a function of time for patient 19

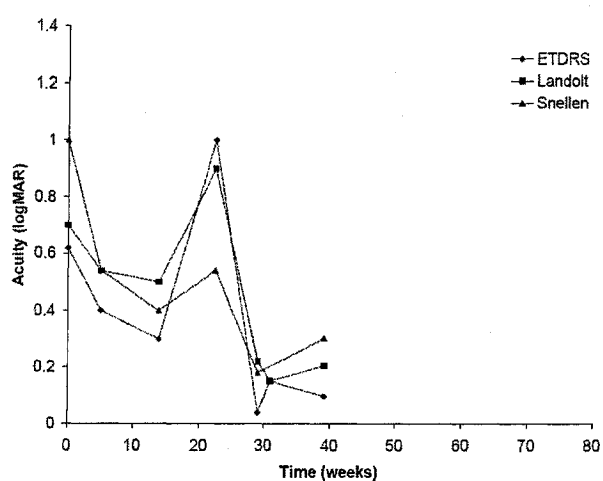


Figure D2k. Acuity as a function of time for patient 20

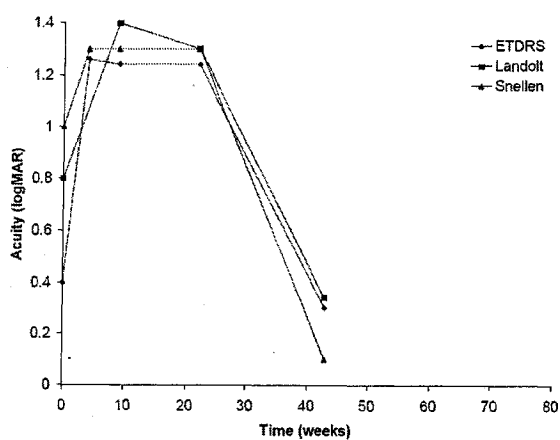


Figure D2l. Acuity as a function of time for patient 22

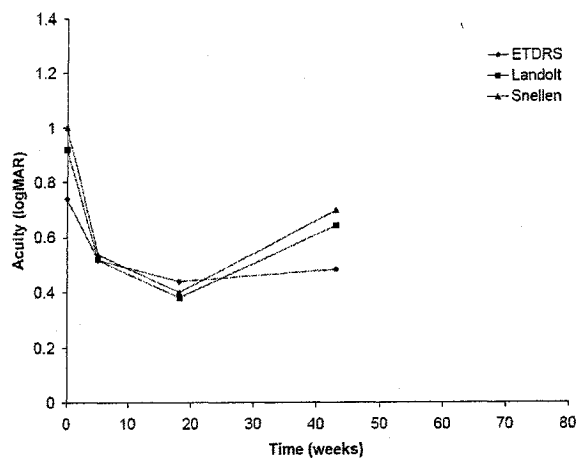


Figure D2m. Acuity as a function of time for patient 23

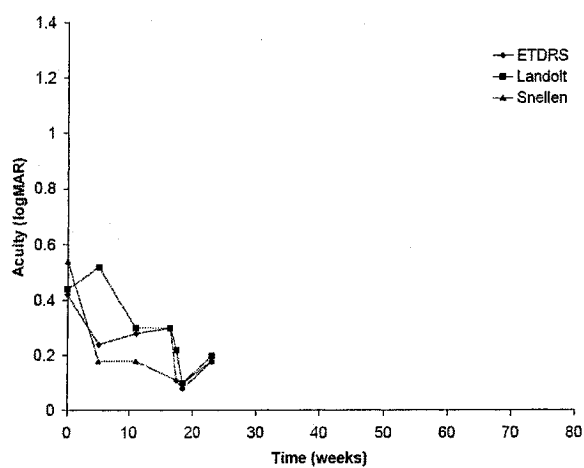


Figure D2n. Acuity as a function of time for patient 29

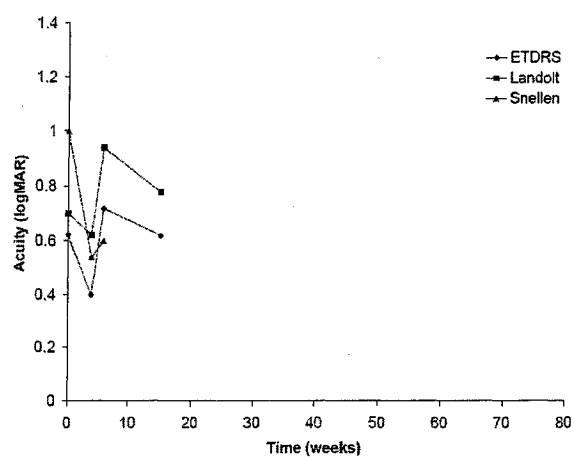


Figure D2o. Acuity as a function of time for patient 30

Appendix D 3. Patients with artificial lens

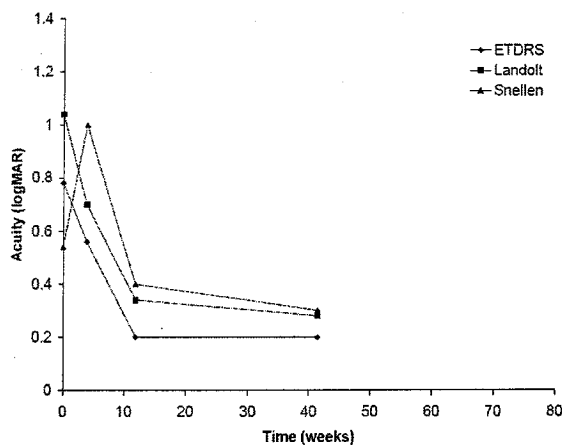


Figure D3a. Acuity as a function of time for patient 12

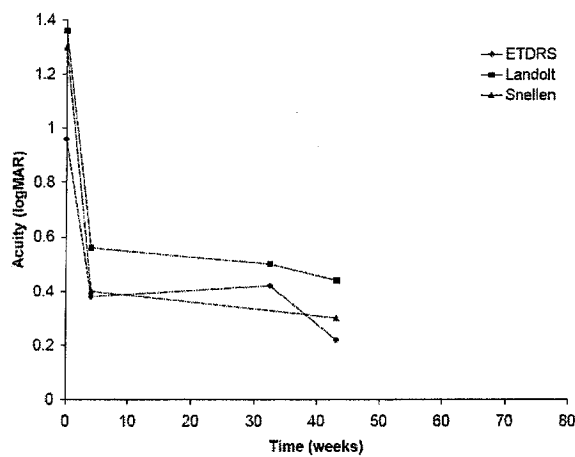


Figure D3b. Acuity as a function of time for patient 13

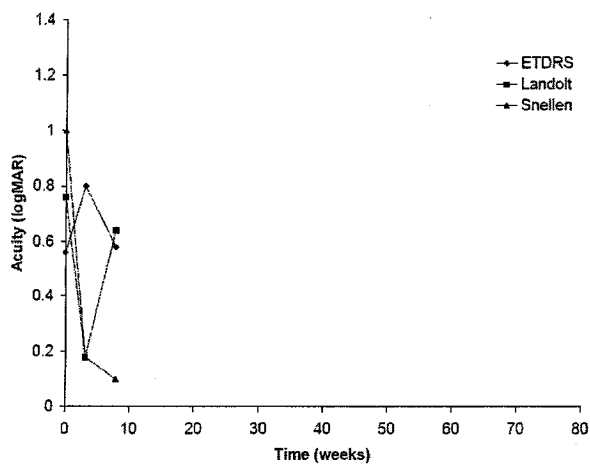


Figure D3c. Acuity as a function of time for patient 21

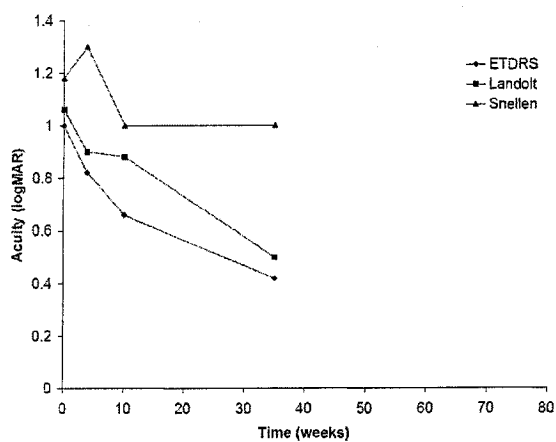


Figure D3d. Acuity as a function of time for patient 25

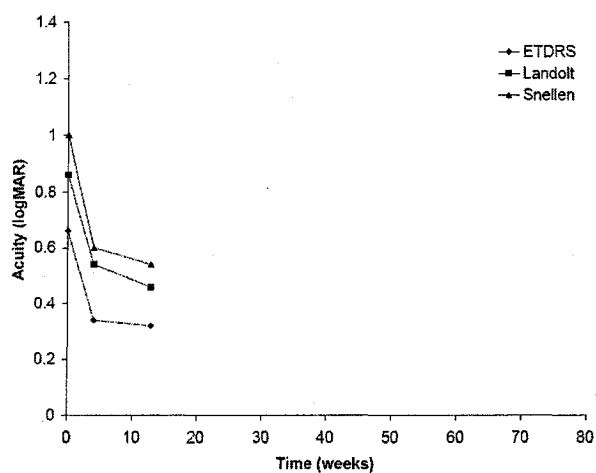


Figure D3e. Acuity as a function of time for patient 26

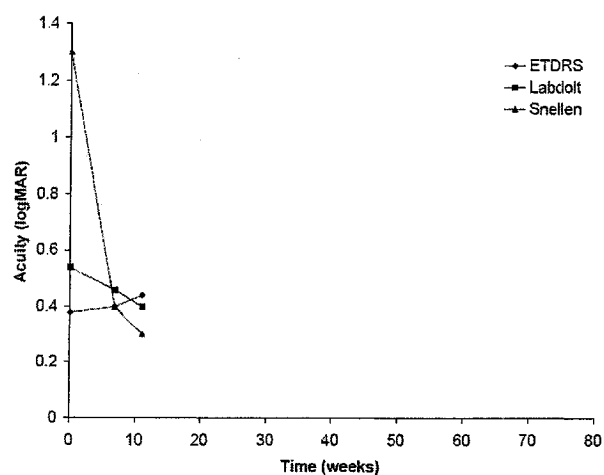


Figure D3f. Acuity as a function of time for patient 28

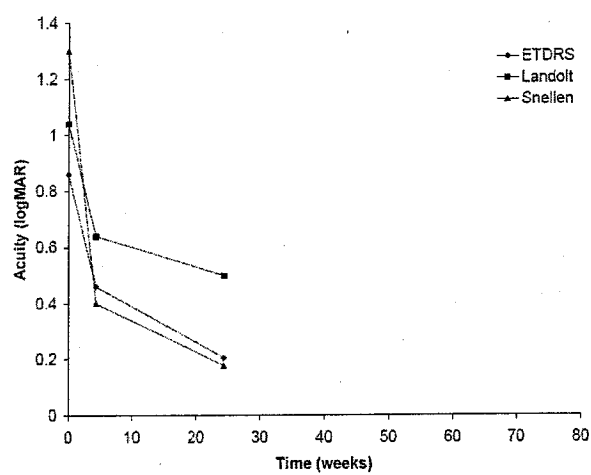


Figure D3g. Acuity as a function of time for patient 31

Appendix E – Pre-operative patient descriptors

ID	Gender	Age	MH diameter (microns)	MH diameter (dva)	ETDRS Pre-Op	Landolt- C Pre-Op	Snellen Pre-Op
1	M	82	392.5	1.5	0.78	0.76	1.00
2	F	82	879.0	3.2	1.28	1.68	1.30
3	M	62	280.5	1.0	0.46	0.56	0.54
5	F	69	386.5	1.4	0.82	1.04	1.00
6	F	67	573.5	2.1	0.82	1.10	1.30
11	F	78	425.0	1.6	0.74	0.90	1.30
12	F	66	436.0	1.6	0.78	1.04	0.54
13	F	64	374.0	1.4	0.96	1.36	1.30
14	F	78	255.5	0.9	0.44	0.62	0.60
15	F	74	455.0	1.7	0.68	0.92	1.00
16	F	67	199.0	0.7	0.40	0.44	0.60
17	F	60	317.5	1.2	0.56	0.62	0.70
18	M	29	355.0	1.3	0.46	0.46	1.00
19	F	81	349.0	1.3	0.46	0.40	0.70
20	F	64	442.5	1.6	0.62	0.70	1.00
21	F	67	280.5	1.0	0.56	0.76	1.00
22	F	53	324.0	1.2	0.40	0.70	1.00
23	F	74	474.0	1.8	0.74	0.92	1.00
25	F	73	905.0	3.3	1.00	1.06	1.18
26	F	76	337.0	1.2	0.66	0.86	1.00
27	F	71	560.5	2.1	0.68	1.14	2.00
28	M	75	324.0	1.2	0.38	0.54	1.30
29	F	81	355.0	1.3	0.42	0.44	0.54
30	M	71	230.5	0.9	0.62	0.70	1.00
31	M	73	499.5	1.8	0.86	1.04	1.30

Appendix F – List of Acronyms

ANOVA	Analysis of Variance
cd/m ²	candelas per square meter
dva	degrees of visual angle
ETDRS	Early Treatment of Diabetic Retinopathy Study
fMRI	functional Magnetic Resonance Imaging
HLM	Hierarchical Linear Modeling
ICC	Intra-Class Correlation Coefficient
IOL	Intra-Ocular Lens
LCD	Liquid Crystal Display
logMAR	logarithm of Minimum Angle of Resolution
MH	Macular Hole
OCT	Optical Coherence Tomography
PAM	Potential Acuity Meter
SLO	Scanning Laser Ophthalmoscope
WA	Watzke-Allen Test