# Presbyopia and the Optical Changes in the Human Crystalline Lens with Age

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Lenses from 27 human eyes ranging in age from 10 to 87 years were used to determine how accommodation and age affect the optical properties of the lens. A scanning laser technique was used to measure focal length and spherical aberration of the lenses, while the lenses were subjected to stretching forces applied through the ciliary body/zonular complex. The focal length of all unstretched lenses increased linearly with increasing age. Younger lenses were able to undergo significant changes in focal length with stretching, whereas lenses older than 60 years of age showed no changes in focal length with stretching. These data provide additional evidence for predominantly lens-based theories of presbyopia. Further, these results show that there are substantial optical changes in the human lens with increasing age and during accommodation, since both the magnitude and the sign of the spherical aberration change with age and stretching. These results show that the optical properties of the older presbyopic lens are quite different from the younger, accommodated lens. © 1998 Elsevier Science Ltd.

Presbyopia    Accommodation    Spherical aberration    Crystalline    Lens    Age

## INTRODUCTION

According to the classical Helmholtz (1909) theory of accommodation, the eye is focused for distance when the ciliary muscle is relaxed. In this condition the zonule, which attaches to the equatorial edge of the lens, is held under resting tension to maintain the lens in a relatively flattened state. The act of accommodation causes a contraction of the ciliary muscle which reduces the ciliary body diameter and releases the resting zonular tension. This allows young lenses to undergo elastic recovery which causes an increase in the lens curvatures and an increase in lens power to enable near objects to be focused on the retina. When accommodation ceases, the ciliary muscle relaxes and returns to its unaccommodated configuration, the zonular tension is once again increased and the lens is pulled back into a relatively flattened state to increase the focal length.

Presbyopia (the age-related loss of accommodative amplitude) has been attributed to a multitude of age-related changes that occur in the eye. These can be broadly grouped into three categories: lens and capsule-based theories, which consider changes in the elasticity and compliance of the lens and capsule; geometric theories which consider changes in the geometry of the zonular attachments to the lens; and extralenticular theories which consider changes in the ciliary muscle and choroid (see Atchison, 1995 for a recent review).

Classically, presbyopia was alternatively attributed to an increased sclerosis of the lens fibers (Gullstrand, 1909), decreased ciliary muscle activity (Duane, 1922), or an inability of the capsule to mold the hardened lens (Fincham, 1937). In recent years, various reports and review articles have attributed presbyopia to changes in either individual aspects of the accommodative apparatus (e.g., lens visco-elasticity or ciliary muscle dysfunction) or as has become increasingly common, a combination of several age-related changes that occur in the eye. Weale (1962, 1963) introduced a multifactorial basis for presbyopia, but excluded lenticular sclerosis as a possible cause. The age-related loss of accommodation was attributed to decreased zonular tension resulting from continued growth of the lens (Weale, 1962) and the lenticular contribution to presbyopia was suggested to be due to a change in the ratio of lens capsular and lens matrix elasticities rather than actual sclerosis of the lens (Weale, 1962, 1963). The former claim is without experimental support and is no longer generally accepted since Farnsworth & Shyne (1979) showed that the distance from the ciliary body to the zonular insertion onto the lens does not change with increasing age. Weale (1963) provided no experimental evidence to support his claim that lenticular sclerosis does not occur, and his contention is not consistent with subsequent experimental findings (Fisher, 1971, 1973). Impedance cyclography

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has been used to measure ciliary muscle contraction and to show that it remains normal up to the age of 60 yr, again suggesting a lenticular basis of presbyopia (Swegmark, 1969). These findings have been criticized owing to the uncertainties of exactly what impedance cyclography measures. This stems, in part, from the observation that a given accommodative demand does not consistently produce the same impedance (Saladin & Stark, 1975). It has been suggested that impedance cyclography may actually measure blood flow rather than ciliary muscle activity (Saladin & Stark, 1975; Bito & Miranda, 1989). Substantial evidence for a purely lenticular basis of presbyopia comes from the experimental results of Fisher. Fisher (1969) showed that the elasticity of the human lens capsule decreases with aging and that human lenses subjected to rotational forces undergo an age-dependent decline in ability to be deformed (Fisher, 1971). These findings led to the suggestion that presbyopia is entirely due to changes in the lens, where a decreased molding pressure of the lens capsule failed to mold the increasingly elastic lens substance (Fisher, 1973). Fisher (1977) also showed that the human lens becomes increasingly resistant to the effects of stretching forces applied through the ciliary body/zonular complex. The relevance of these studies has been questioned, since it is not clear how Fisher's spinning and stretching of human lenses relates to the forces on the lens *in vivo*. The observations by Brown (1974) of an increase in lens curvatures with age and by Farnsworth & Shyne (1979) of an anterior shift in the zonular attachments onto the lens led to the suggestion that extralenticular factors result in a failure of the older lens to be held in an unaccommodated state. Presbyopia has, thus, more recently been described as a geometric disorder attributed to changes in the size and volume of the lens and the angle of zonular insertion onto the lens (Koretz & Handelman, 1988). The lack of experimental data and the speculated claims of altered zonular forces due to changes in the geometry of the lens/zonular complex based on the anatomical findings of Farnsworth & Shyne (1979) have prevented it from gaining general acceptance. A review by Stark (1988) re-emphasized the lens/capsular basis of presbyopia citing the work of Fisher (1969, 1971, 1977) and various other lines of evidence which suggest that ciliary muscle function remains normal throughout life. Among these are results from impedance cyclography and the observation that pupillary and accommodative vergence changes occur throughout life even after accommodation is completely lost. Since the stimulus response relationship remains close to unity in both young and older individuals for low accommodative amplitudes, the ciliary muscle activity is suggested to be normal for at least low accommodative amplitudes. While these factors may suggest that the ciliary muscle activity remains normal throughout life, they do not prove it. The potentially confounding results of impedance cyclography and subsequent evidence from monkeys for a decreased compliance of the ciliary muscle (Tamm *et al.*, 1992a; Poyer *et al.*, 1994) suggest a

possible loss of ciliary muscle function concurrent with the development of presbyopia. Bito & Miranda (1989) introduced the idea that presbyopia is an inability to "disaccommodate" the lens because of decreasing zonular tension with increasing lens growth throughout life. The apparent paradox that this raises (i.e., presbyopia is a loss of near vision rather than a loss of distance vision) is resolved in part by suggested changes in the gradient refractive index of the lens with age. This disaccommodation theory of presbyopia is without support from direct experimental evidence and it is heavily reliant on the suggested and still largely theoretical changes in the gradient refractive index of the lens. A more comprehensive multifactorial view of presbyopia, incorporating epidemiological, genetic, environmental as well as biophysical aspects, excluding the possibility of lenticular sclerosis, is presented in a review by Weale (1989). Although this review includes discussion of much new data published since his earlier reviews, once again no experimental evidence is provided to support the claim that lenticular sclerosis does not occur. In fact Weale cites his earlier *review* article on presbyopia as a *"demonstration"* that the human lens does not become sclerosed. A change in the refractive index gradient of the lens cortex has been suggested to be a substantial factor in the multifactorial contribution to the onset and progression of presbyopia (Koretz & Handelman, 1988; Pierscionek, 1993). This postulate is invoked to account for the apparent paradox which arises because presbyopia results in a loss of near vision despite increased lens curvatures (Brown, 1974). Although the expected changes in lens gradient refractive index have been shown to be theoretically possible (Smith *et al.*, 1992), the substantial obstacles involved in accurately measuring the gradient refractive index of the human lens and its potential change with age have precluded experimental verification. Neider *et al.* (1990) have shown an age-dependent decline in the excursion of the rhesus monkey ciliary body/zonular complex during central stimulation. This work led to the observation that there is a declining responsiveness of the rhesus monkey ciliary muscle to pilocarpine stimulation that is reversed if the posterior attachment of the ciliary muscle is severed or if the ciliary muscle is isolated (Tamm *et al.*, 1992a; Poyer *et al.*, 1994). While these results do not preclude changes in the lens from occurring, they do not address the possible lenticular contribution to presbyopia or possible species differences in presbyopia. MRI studies have demonstrated the continued contractility of the human ciliary muscle throughout life (Strenk & Semmlow, 1995). However, the still relatively low resolution of this technique and the need for substantially more subjects in this preliminary study reduces the impact of this result. Pierscionek & Weale (1995a) speculate that because of the increased thickness of the lens and the anterior shift of the zonular attachments, presbyopia is a failure of the lens to be maintained in a flattened state. As with the disaccommodation theory, this idea is not given any support from experimental work and the authors do

not address the possibility that the increased thickness of the lens is a consequence of presbyopia, rather than a cause of it. Recent work has shown that the lens does become harder with increasing age (Pau & Kranz, 1991; Glasser & Campbell, 1996b). Some of these theories of presbyopia in relation to accommodation theory have been presented in a recent review by Atchison (1995).

Although some experimental studies of age-related changes in the optical properties of the lens do exist (see Pierscionek & Weale, 1995b), in general there is a paucity of experimental data on age-related and presbyopic changes in the optical properties of the human lens. Although many theories on the causes of presbyopia have invoked changes in the make-up of the lens (such as would be concurrent with a change in the refractive index of the lens), relatively few studies have directly measured the age-related optical changes in the lens. Surprisingly, even Fisher, despite his significant experimental evidence for a lenticular basis of presbyopia, made little mention of the optical changes in the lens with age. Fisher's work does not, for example, include data for the accommodated and the unaccommodated lens focal lengths or data showing lens focal length as a function of age—data that must have been available from his measurements. His optical measurements were relatively crude and subjective and were made through a 4 mm aperture on all lenses. Therefore, changes in paraxial focal length and changes in spherical aberration of the lenses would be difficult to separate. It is interesting that despite the substantial physical evidence Fisher accumulated for the lenticular basis of presbyopia, he did not consider the full implications of his results by extending his findings to the optical changes that accompany the aging of the lens. Substantial evidence, however, does exist for the age-related deterioration of visual function. Visual performance losses are evident with increases in age-related light scatter in the eye (Westheimer & Liang, 1995). It is well established that there is a need to increase the power of the near addition lens (the "presbyopic addition") on top of the distance correction with increasing age (Hofstetter, 1949; Pointer, 1995). This optical aging has been attributed to the need for an increased magnification (Hamasaki et al., 1956) in the face of decreased visual acuity and decreased contrast sensitivity function (see Charman, 1989). However, a neural contribution has also been postulated to explain age-related losses in contrast sensitivity function (Elliott et al., 1990). In addition, cross-sectional studies of age-related changes in resting refraction show a drift towards hyperopia from about age 30 to 65 yr and then a drift towards myopia after age 65 yr (Slataper, 1950; Saunders, 1981) that has been attributed to growth and the forward movement of the lens (Bennett & Rabbetts, 1989). Concurrent changes in the corneal curvature have the opposite effect (Saunders, 1982). The myopization in later years was attributed to the increased prevalence of senile lenticular cataract (Slataper, 1950). Changes in spherical aberration with accommodation imply concurrent changes in the optics of the lens with accommodation. There are known

spherical aberration changes with age but concurrent changes in the cornea and anterior chamber make the lenticular contribution to this change less obvious. Thus, although documented visual deficits and refractive changes are known to occur with age, little is known about how the changing optics of the lens contribute to these age-related processes.

We have taken advantage of the natural tendency of the young human lens to become accommodated when the zonular tension is released to study how the optical properties of the lens change with accommodation and age. When a young lens is removed from the eye the forces that would normally hold it in a relatively flattened, unaccommodated state are removed and so it becomes accommodated. Using a partially dissected human eye preparation we have mechanically returned the lens to its unaccommodated state by increasing the zonular tension on the lens with an outward stretching force directed through the ciliary body in a manner similar to that described by Fisher (1977). We have substantially extended Fisher's findings by using a scanning laser beam to identify the optical changes that occur in the human lens with age and accommodation. The more sophisticated optical analysis than used by Fisher (1977), together with the mechanical stretching has provided substantial new evidence for optical aging of the lens. Preliminary findings have been reported previously (Glasser & Campbell, 1995, 1996a; Campbell et al., 1996).

## METHODS

### Tissue preparation

Human eyes were obtained from the Eye Bank of Canada, Toronto. All eyes had been enucleated within an average of 3 hr after death. Dissections of the eyes were begun within an average of 48 hr of death (a minimum of 9 hr and maximum of 120 hr). The majority of eyes were obtained after the corneas had been removed by the eye bank for corneal transplants. Eyes which had sustained damage to the ciliary body or lens during this process were not used. Twenty-seven eyes were used from donors ranging in age from 10 to 87 yr (ten pairs and seven unpaired eyes).

The eyes were placed in a dissecting dish filled with a balanced salt solution (human saline) with an osmolarity close to that of the vitreous (290 milliosmoles) of the following composition (g/l) NaCl 8.00, KCl 0.40, $Na_2HPO_4$ 0.10, glucose 1.00, Hepes 2.38, buffered with 8 ml of 0.5 M NaOH to a pH of 7.4. If present, the corneas were removed. The iris was removed and the ciliary body was separated from the sclera. The anterior sclera was cut away to expose the ciliary body and anterior choroid. A circumferential cut was made through the choroid at the region of the ora serrata to separate the anterior segment tissue from the posterior segment of the eye. The anterior segment tissue comprises the ring of ciliary body and ciliary muscle, the lens and the zonular complex. This anterior segment tissue, with the lens still

naturally suspended by the intact zonule, was then lifted free of the globe and a cotton swab was used to remove any remaining vitreous from the posterior surface of the lens. The tissue was removed from solution and positioned on a tapered post with a beveled hole in the top which matched the posterior curvature of the lens. The ring of the ciliary body was then gently pulled out over the edges of the taper to spread the ciliary body and choroid and to completely extend, but not stretch the zonule. The zonule was extended in this manner to ensure that when the ciliary body was glued to the stretching apparatus the zonular fibers were not flaccid but were extended without actually being stretched. This ensured that the lens did not sag or tilt when the zonule was in this unstretched state. The distance of separation of the eight arms of the stretching apparatus was adjusted to correspond to the diameter of the ciliary body and the eight arms were then glued to the ciliary muscle region on the anterior surface of the ring of the ciliary body.

*Stretching apparatus*

A specially designed and custom-built stretching apparatus was used to hold and stretch the tissue (Fig. 1). The design of this apparatus was similar to the apparatus used by Fisher (1977) for the same purpose. Our stretching apparatus consists of two 1/8th-inch-thick 2 1/2 inches diameter circular stainless steel plates, a base plate and a face plate. Each plate has a 1-inch diameter hole drilled through its center. A cuff in the hole in the face plate fitted into the hole in the base plate so the two plates were able to rotated concentrically against each other. Eight 1/16-inch-thick stainless steel arms were made to slide easily in eight radial grooves in the posterior surface of the base plate. The arms were held in place by screws passing through grooves in both plates. In the face plate, spiral grooves each subtended an arc of 90 deg such that as the screws were moved counterclockwise through the grooves as they also moved radially outwards. The screws passed through radial grooves in the base plate and screwed into the eight arms of the stretching apparatus holding the two plates firmly against each other. When the face plate was turned clockwise relative to the base plate the eight arms moved radially outward as the screws travel through the spiral grooves. Turning the face plate counterclockwise moved the arms radially inwards. A small section of millimeter graduated scale on one of the arms allowed the movement of the arms to be measured in 0.5 mm steps.

A drop of cyanoacrilate Super Glue was placed on the angled tip of each of the eight arms of the stretching apparatus. The angled tips ensured that, after being glued

to the arms, the orientation of the ciliary body remained close to that in the intact eye. Under a dissecting microscope the separation of the arms was adjusted to match the diameter of the ciliary body and the stretching apparatus was carefully lowered onto the tissue positioned on the tapered plastic post until the arms contacted the ciliary muscle region on the outer surface of the ring of the ciliary body (Fig. 2). When the glue had set, the tissue was lifted up off the tapered post. The lens remained naturally suspended by the zonule within the ring of the ciliary body tissue. In the unstretched state, the position at which the arms of the stretching apparatus were glued to the ciliary body, the zonule was extended but not stretched. In a young eye, this would be comparable with a lens in the accommodated state. The position of the graduated plastic ruler was noted and this was identified as the unstretched zero starting position. Since the zonule was extended in this position, although not stretched, the relatively small gravitational effect on the lens in solution would be unlikely to introduce any significant sag or lens tilt. When the face plate of the stretching apparatus was turned clockwise relative to the base plate the arms of the stretching apparatus moved radially outward, stretching the ring of ciliary body. This caused an increase in tension on the zonule which applied an outward force on the equatorial edge of the lens (Fig. 2). Turning the face plate counter clockwise relative to the base plate moved the arms of the stretching apparatus radially inward, back towards the unstretched zero stretch starting position.

The stretching technique that we have used, although similar to that used by Fisher (1977), differs in that it was designed to allow a far more sophisticated and comprehensive optical analysis of the lenses than Fisher's measurements. We used a thin stretching apparatus so that a scanning laser could be used in conjunction with stretching. This enabled more precise measurements of the optical consequences of the applied stretching force and of age-dependent optical changes of the lenses than Fisher was able to do using his subjective measure of best image focus. The use of a stretching technique similar to that employed by Fisher, together with the more systematic and accurate optical technique, has allowed us to substantially extend Fisher's results, representing more than a minor extension of Fisher's mechanical experiments.

*Scanning laser apparatus*

A rectangular Plexiglas chamber 8 cm long, 6 cm wide, 6 cm high and open at the top held the stretching apparatus in vertical grooves on the inside walls of the

FIGURE 1. Photographs of the stretching apparatus (a) and the human anterior segment tissue attached to the stretching apparatus before (b) and during (c) stretch. (a) Shows the back surface (base plate) of the stretching apparatus with the eight arms to which the ciliary body is glued in order to apply stretching forces to the lens. A small piece of millimeter graduated plastic ruler is fixed to one of the arms to measure the position of the arms. (b) The anterior segment tissue comprising the ciliary body, lens and zonular complex from a 54-year-old human eye is glued to the arms of the stretching apparatus. The ciliary body/zonular complex is in the unstretched state with the zonule extended but not stretched. A young lens without any stretching forces on it is in an accommodated state. (c) When the ciliary body is stretched the increased zonular tension applies an outward pull to the equatorial edge of the lens as the zonule is stretched. A young lens is pulled into a flattened, unaccommodated state during such stretching. Between the arms of the stretching apparatus, the stretching of the zonular fibers appears uniform.
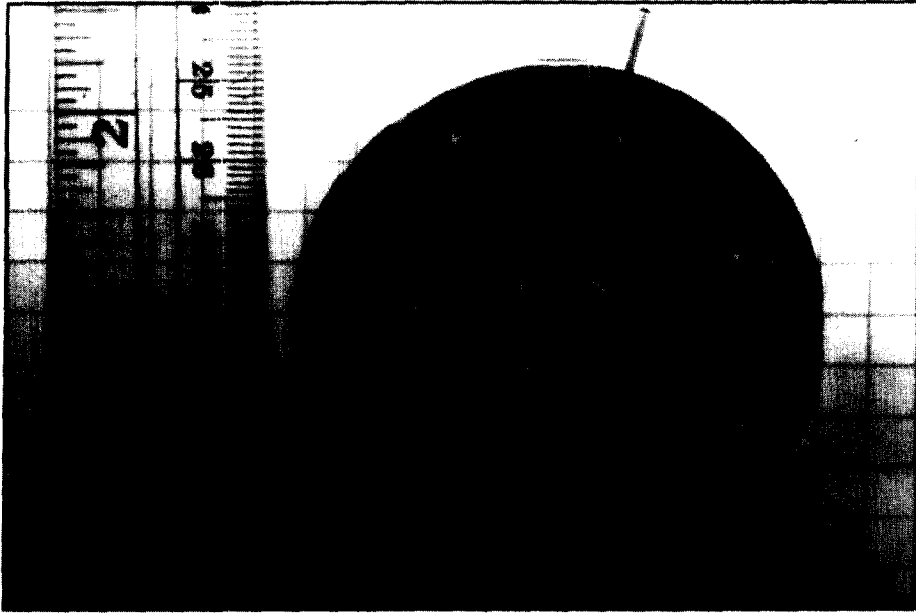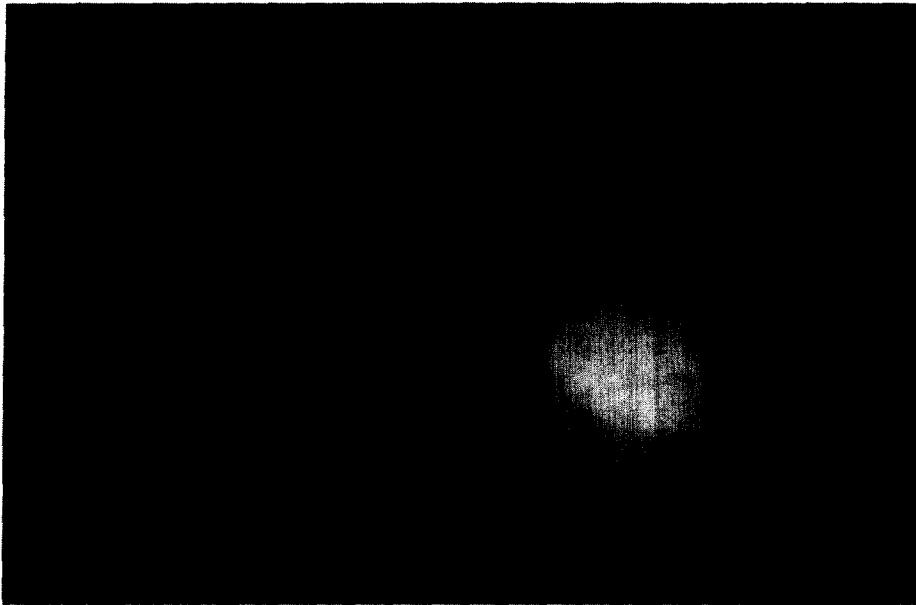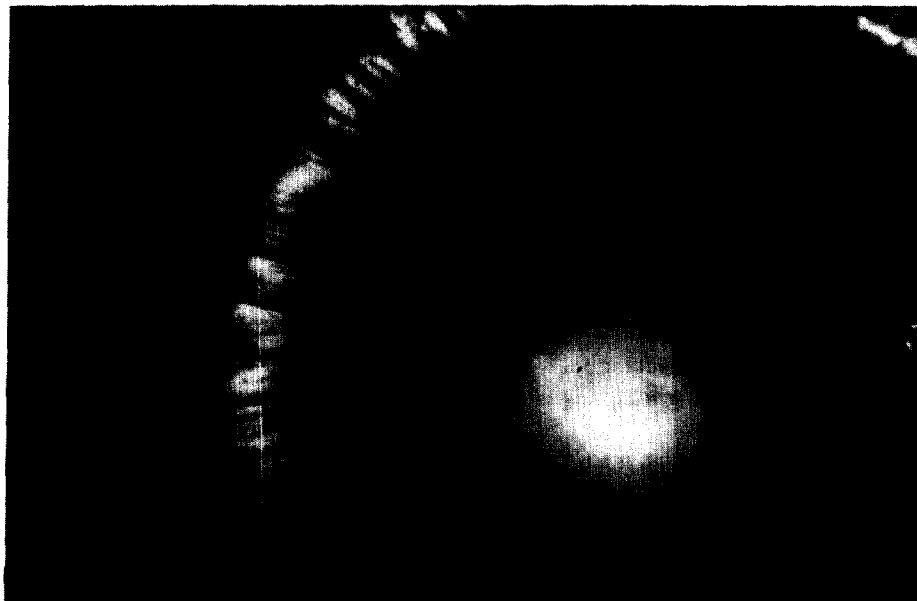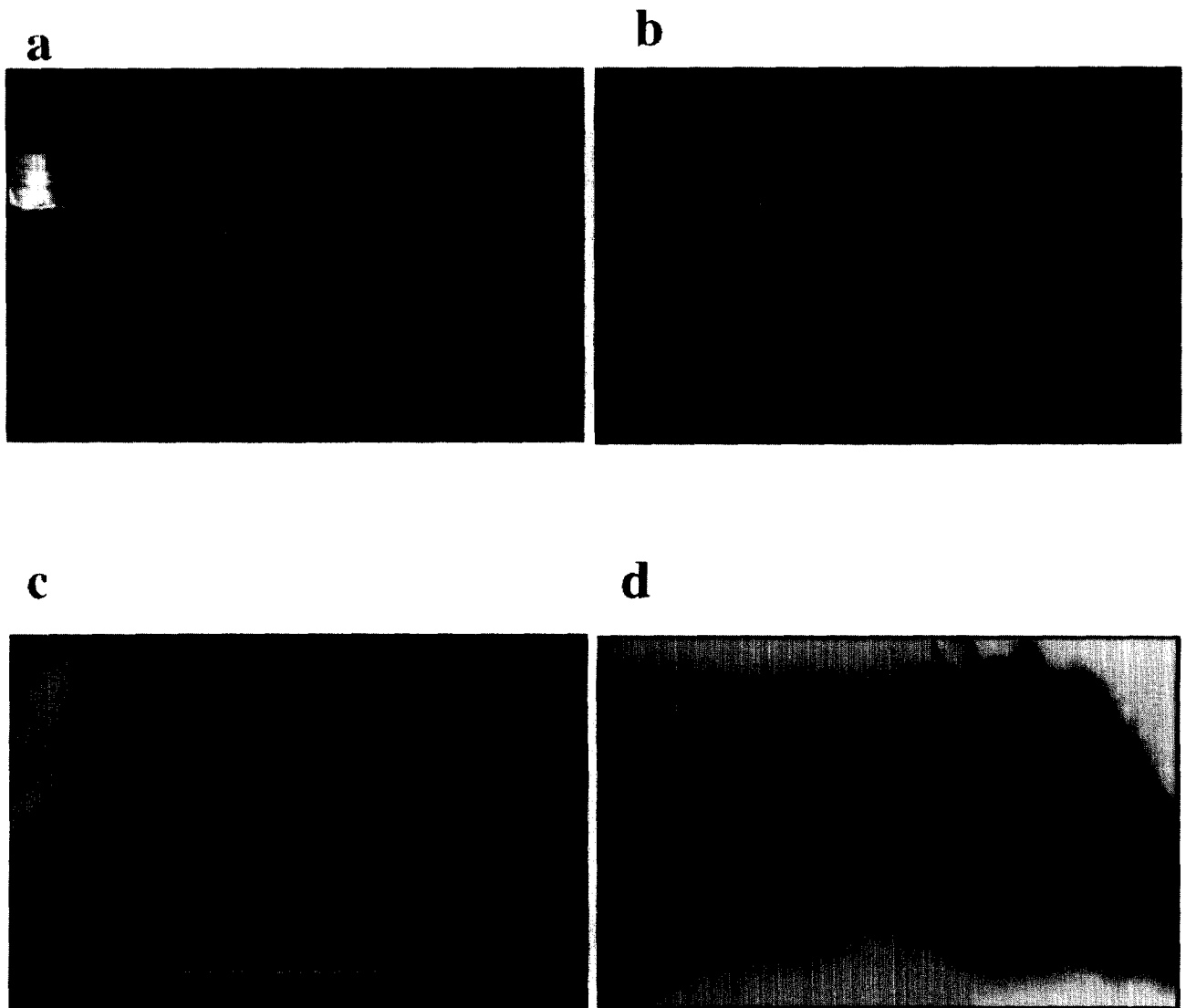
FIGURE 2. A series of photographs at increasing magnification of the partially dissected anterior segment tissue of a 34-year-old eye with a single arm of the stretching apparatus glued onto the ciliary body (a–c) and the ciliary body, zonule and lens from the eye of a 54-year-old without a stretching arm attached (d). Half of the ring of the ciliary body has been removed to see the cross-section of the ciliary muscle and ciliary body and associated zonular fibers suspended (but not stretched) between the ciliary body and the equatorial edge of the lens. The bent tip of the stretching arm is glued to the outer edge of the ciliary body using cyanoacrilate Super Glue. The orientation of the ciliary body is maintained at an angle similar to that which would occur in the eye *in vivo* (a and b). This maintains the normal orientation of zonular forces acting on the equator of the lens when the tissue is stretched. The ridges of the *pars plicata* can be seen on the inner aspect of the ciliary body (a, b and d). The location of the ciliary muscle (cm) between the tip of the stretching arm and the ciliary processes (cp) of the ciliary body (cb) can be seen in (b). The zonular fibers (zo) attach to the ciliary body all along the internal edge of the ciliary processes (c and d). There is considerable cross-over of the anterior and posterior zonular fibers near their attachment to the ciliary process: there are no distinct equatorial zonular fibers, but rather a uninterrupted group of fibers that attach to the anterior–equatorial region of the lens; a smaller group of zonular fibers attach to the posterior surface of the lens; some of the most equatorial of the zonular fibers attach to the more posterior aspects of the ciliary process; no zonular fibers attach to the anterior part of the ciliary muscle at the most anterior aspect of the ciliary process (c and d). The scale bar for (c) equals 1.0 mm.

chamber, 2 cm from the front. The chamber was filled with human saline and one drop of white paint was added to cloud the solution slightly.

A scanning laser apparatus was used to measure the lens optical properties (Campbell & Hughes, 1981; Sivak *et al.*, 1986). A 5 mW HeNe laser beam (633 nM) was reflected off a mirror mounted on an X–Y stage in front of the chamber. The beam entered a clear glass window in the front of the Plexiglas chamber and passed through the

lens parallel to the optical axis. The horizontal position of the X–Y stage was controlled by a stepper motor through an AT computer to allow the laser beam to be scanned horizontally across the diameter of the lens. The vertical position of the X–Y stage could be changed manually to adjust the height of the laser relative to the lens. One video camera viewed the Plexiglas chamber from above and a second video camera viewed the chamber from the side. The outputs of both cameras were fed to a frame

grabber board (Oculus 300, Coreco, Inc. Quebec, Canada) in the AT computer. The laser beam was clearly visible in the clouded solution and could be imaged independently by either of the two video cameras. Although the anterior surface of the lens was obscured by the stretching apparatus, the posterior lens surface was clearly visible in the video images as it protruded behind the base plate of the stretching apparatus. A computer program was used to digitize the path of the laser beam before it entered the lens (the entrance beam) and after it exited the posterior surface of the lens (the exit beam). The program recorded the position of the posterior surface of the lens, the intercept and the slope of the beam (entrance angle) as it entered the lens and the intercept and slope of the beam (exit angle) as it exited the posterior surface of the lens. The stepper motor allowed the laser to be moved and positioned with an accuracy of approximately 12 $\mu$m, thus precluding any variability owing to inaccuracies in the instrumentation. The position of the posterior lens surface was recorded after each successive increase in stretch and was not seen to change.

From the image provided by the camera to the side of the chamber it was possible, through a manual adjustment of the height of the laser, to ensure that the scan was taken through a meridional section of the lens (a lens diameter) without any refraction of the laser beam in the vertical plane. The vertical position of the laser beam was manually adjusted while the software reported the angles of the entrance and exit beams. The laser beam was considered to be passing undeviated through the optical axis of the lens in the vertical plane when the angles of the entrance and exit beams, as reported by the computer, were judged to be similar.

The laser beam was then digitized by the camera mounted above the chamber to record the results of repeated automated horizontal scans of the lens. The camera magnification was calibrated prior to each experiment by digitizing a horizontal grid placed in the plane of the laser beam. The horizontal extent of the scan across the lens diameter was adjusted by first moving the laser until the beam just grazed the edge of the lens. This position was recorded as the start of the scan. The laser was then moved horizontally across the diameter of the lens by means of the stepper motor until it just grazed the opposite edge of the lens. This position was recorded as the end point of the scan. Each horizontal scan across the full diameter of the lens was done in 75 discreet steps with three repeated, independent digitizations at each step.

Two scans were initially done across the horizontal diameter of each lens while the ciliary body and zonule were in the unstretched state not applying any substantial outward pull on the edge of the lens. Each tissue was then incrementally stretched by increasing the diameter of the stretching apparatus in steps of 1.00 mm. New start and end points of the horizontal scan were identified at each edge of the now slightly stretched lens and the scan was repeated. This process was repeated at each of four

further increments in ciliary body diameter up to 5.00 mm. No attempt was made to measure the magnitude of the stretching forces applied to the lens, although from preliminary testing it was established that the ciliary body diameter could reliably be stretched by up to 5.00 mm from the start position without causing damage to the zonular fibers. Increasing the ciliary body diameter to 6.00 mm, however, caused some zonular fibers to break. Finally, after scanning the lens in the maximally stretched state, the stretching apparatus was returned to the unstretched starting position, and a final horizontal scan was done.

*Data analysis*

*Data recorded.* At each of the three iterations of the 75 positions of the scan across the diameter of the lens the stepper motor position, the slope and the intercept of the entrance beam and the slope and intercept of the exit beam were stored to disk for subsequently analysis. A second program was used to read in this data and to calculate a mean slope and intercept for the entrance and exit beams at each step by averaging the three iterations.

*Focal length measurement.* The intersection point of each entrance beam with its corresponding exit beam was calculated at each of the 75 steps in the scan (Fig. 3). These points represent the principle points or the principle plane of the lens (Sears, 1958). For each scan, the optical axis of the lens was identified as the beam passing through the lens in the horizontal plane with minimum deviation of the slopes of the entrance and exit beams. The distance along each exit beam from its principle point to its intersection with the beam representing the optical axis was calculated. The average of this distance from all the beams represents the mean focal length of the lens. The distance between these two points as the entrance beam approaches the optical axis is the paraxial focal length of the lens.

*Spherical aberration.* The spherical aberration of the lens was determined in the following manner: for each step in the scan an $(x, y)$ coordinate pair was recorded as the height from the optical axis at which the entrance beam is incident on the lens ($y$) and the distance along the corresponding exit beam from its principle point to its intersection with the optical axis ($x$) (light symbols in Fig. 3). The radius of each lens was normalized to +1.00. A fourth-order polynomial was fitted through all these $(x, y)$ coordinate pairs. The paraxial focal point of the lens, i.e., the focal point of the lens as the incident beam height approaches the optical axis (i.e., as $y$, the height of the incident beam tends to zero), can be calculated by solving the spherical aberration polynomial for a lens radius of zero. This is the constant term of the fourth-order polynomial.

The total spherical aberration of the lens is given by the formula:

$$SA = n'/\lambda_y' - n'/\lambda_0'  \tag{1}$$

where $n'$ is the refractive index of the vitreous (1.333), $\lambda_0'$ is the solution of the polynomial at the optical axis, and

$\lambda'_y$ is the solution of the polynomial at any height $y$ from the optical axis (Bennett & Rabbetts, 1989). Since the lens radius was normalized to +1, $\lambda'_{1.0}$ represents the solution of the polynomial at the edge of the lens. The angles of the exit beams are small enough relative to the focal length of the human lens that this provides an accurate measure of the spherical aberration. The focal length and the spherical aberration can be displayed graphically by reconstructing all the laser beam paths and their intersection points (Fig. 3).

### Visualization of the zonular fibers

In order to visualize and photograph the human zonule, several additional eyes of different ages were dissected to isolate the anterior segment tissue as described above. This tissue was then dropped briefly (30–60 sec) into chilled, 2% gluteraldehyde fixative to facilitate handling of the tissue. Two clean cross-sectional cuts were made through the ring of the ciliary body on opposite sides of the lens. One half of the ring of the ciliary body and the associated zonular fibers were separated from the lens by cutting through the zonular fibers. A semicircle of ciliary body and associated zonular fibers remained attached to the intact lens. A single detached arm of the stretching apparatus was glued to the ring of the ciliary body adjacent to the cut edge (using the same procedure as described previously) and this preparation was placed in human saline and photographed.

### RESULTS

### The zonule of the human eye

A partial dissection of the anterior segment tissues from several eyes has allowed a clear visualization of a cross-sectional view of the human ciliary muscle, ciliary processes and zonule (Fig. 2). We see that the zonule consists of a substantive anterior–equatorial group of zonular fibers and a diminutive posterior group. There is considerable overlap of these two groups as the individual zonular fibers course towards their attachment sites on the ciliary processes. The zonular fibers attach to the ciliary body all along the entire extent of the *pars plicata* of the ciliary processes. Many of the equatorial zonular fibers attach quite far towards the posterior of the ciliary processes, but no fibers attach to the anterior

aspect of the ciliary muscle at the anterior portion of the ciliary processes. At their attachment to the lens there is a separation of the anterior–equatorial group of zonular fibers from the posterior group in a 34-year-old eye [Fig. 2(c)], which is not evident in a 54-year-old eye [Fig. 2(d)]. No separation between the anterior and equatorial groups of zonular fibers can be seen, but rather this region of the zonule represents a continuous band of attachment to the lens. Even in a 54-year-old (presumably presbyopic with little or no accommodation) there remains a substantial attachment of the zonular fibers to the equator of the lens. The attachment of the stretching arm to the ciliary body [Fig. 2(a) and (b)] shows that the angle of the ciliary body relative to the lens is close to the expected orientation of the ciliary body *in vivo* prior to dissection. The stretching forces applied to the lens through the zonule would, therefore, also be in an orientation similar to that which occurs *in vivo*.

### Focal length measurements and accommodation

The mean focal length of all beams passing through the lens was first measured while the lenses were in the unstretched state [Fig. 3(a, c) and Fig. 4(a)]. The younger lenses have shorter mean focal lengths than older lenses. This reflects the tendency of the younger lenses to become accommodated in the absence of zonular tension. For the group of lenses used in this study (ages 10–87 yr) there is a significant linear ($r^2 = 0.800$; $P < 0.001$) increase in unstretched mean focal length with increasing age of the form:

$$\text{Focal Length} = \text{Age} \times 0.401 + 34.675. \quad (2)$$

A significant linear ($r^2 = 0.832$; $P < 0.001$) increase of similar form is found if the lens paraxial focal length (defined above) is plotted as a function of age:

$$\text{Paraxial Focal Length} = \text{Age} \times 0.515 + 25.928. \quad (3)$$

If the group of lenses is arbitrarily divided at 50 years of age, there is no statistical difference between the slopes of the focal length vs age relationship for lenses less than 50 (prepresbyopic) and lenses greater than 50 years of age (presbyopic).

When the mean focal length is measured in the lenses in the maximally stretched state (at an increase in ciliary body diameter of 5.00 mm), lenses younger than 50 years

FIGURE 3. Diagrams showing the reconstruction of a single scan on an unstretched 10-year-old lens (a); the same 10-year-old lens when the ciliary body diameter is stretched by 5 mm (b); and an unstretched 66-year-old lens (c). In each case the dark symbols (to the left) identify the intersection points of the entrance and exit beams showing the principal plane of the lens. In general, these points lie within the lens, however, near the optical axis where the slopes of the entrance and exit beams are similar, small deviations result in large variations in the location of these intersection points. The optical axis of the lens (the laser beam that passes through the lens with minimal deviation) is identified by the dark horizontal line through the middle of each scan. The light symbols (to the right) mark the horizontal position ($x$), where each exit beam intersects the optical axis and the corresponding vertical position ($y$), where the entrance beam is incident on the lens. A forth-order polynomial was fitted through these points to show the pattern of the spherical aberration of the lens. The larger single black symbol on the optical axis indicates the mean intersection point of all the exit beams with the optical axis (the mean focal length). The unstretched 10-year-old lens (a) has a relatively short mean focal length 34.39 mm (38.76 D) and a scan diameter of 7.09 mm. When stretched (b), the mean focal length increases to 57.69 mm (23.1 D) and the lens diameter increases to 8.66 mm. The 66-year-old unstretched lens has a mean focal length of 54.22 mm (24.59 D) and a diameter of 8.33 mm. Note that when the 10-year-old lens is stretched [from (a) to (b)] the focal length of the lens and the diameter of the lens increase, the principal plane and the spherical aberration are slightly disrupted, and the magnitude of the spherical aberration is reduced without a change in sign (see also Fig. 8). Each of the images has been expanded more in the vertical axis than in the horizontal axis.
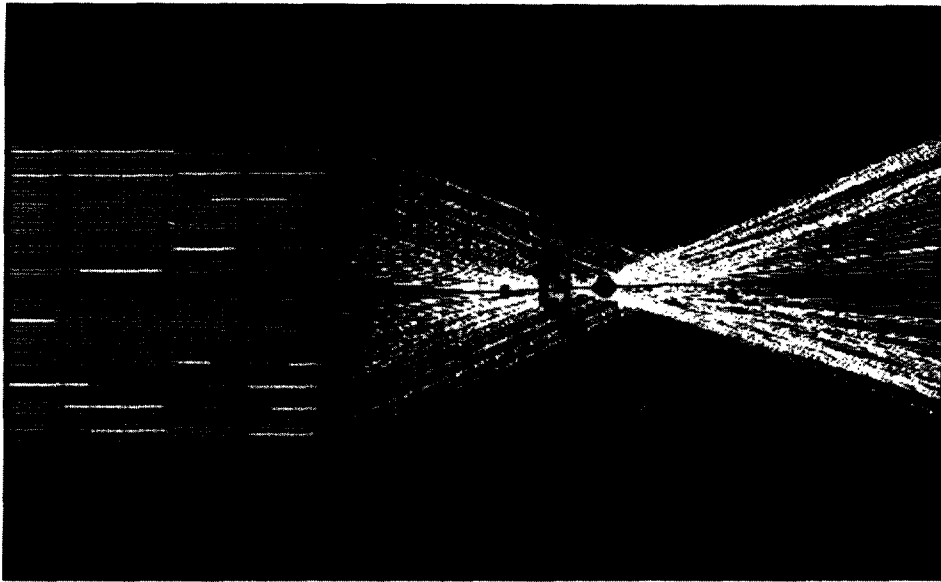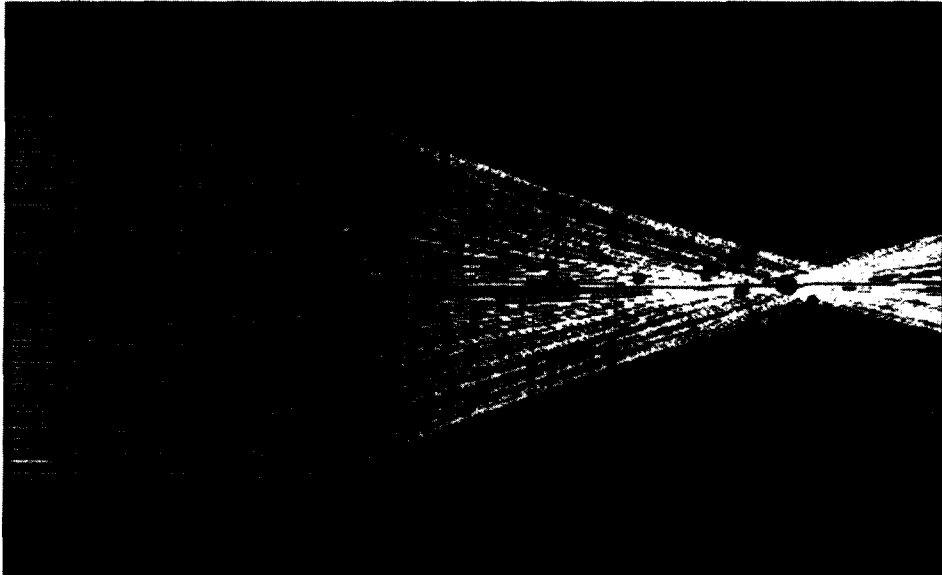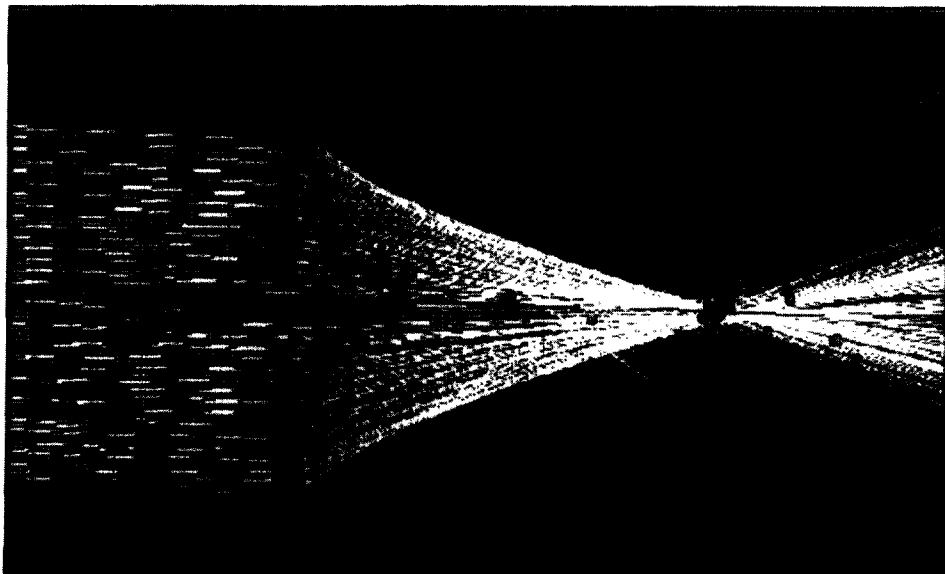
of age undergo substantial changes in focal length with stretching [Fig. 3(a, b) and Fig. 4(a, b)], while lenses over the age of 50 yr do not undergo any change in focal length with stretching. For lenses less than 50 years of age the slope of the regression line of stretched focal length vs age is negative, although not significantly different from zero. However, the positive slope of the

**(a)**



**(b)**



**(c)**



regression line for the lenses over the age of 50 yr is significantly different from zero and is very similar (not significantly different) to the slope of the regression equation for the unstretched lenses [Fig. 4(a)]. The intersection point of the two regression lines in Fig. 4(b) is at 58.32 yr.

After stretching, when the ciliary body diameter is returned to the unstretched state and the focal length is again measured, it is essentially identical to the focal length measured before any stretching forces were applied [Fig. 4(c)]. The relationship shows a good linear correlation ($r^2 = 0.980$), a slope close to one (0.948) and an intercept relatively close to zero (4.48). This verifies the integrity of the lenses and demonstrates that the lenses were not irreversibly altered through the stretching process. The younger lenses, which do show changes in focal length with stretching, return to their unstretched focal length, and the older lenses which have not undergone any change in focal length are unchanged.

The dioptric change in optical power with maximal stretching is shown for all lenses in Fig. 5(a). The youngest lenses are able to undergo between 12 and 16 D of change in power, while the oldest lenses do not undergo any change in power. These data are plotted together with data from Duane (1912) showing the maximal and minimal amplitudes of accommodation, as measured using a push-up technique in over 1000 subjects. Fifth-order polynomials provide good regression fits to our lens data ($r^2 = 0.965$) and to an extended
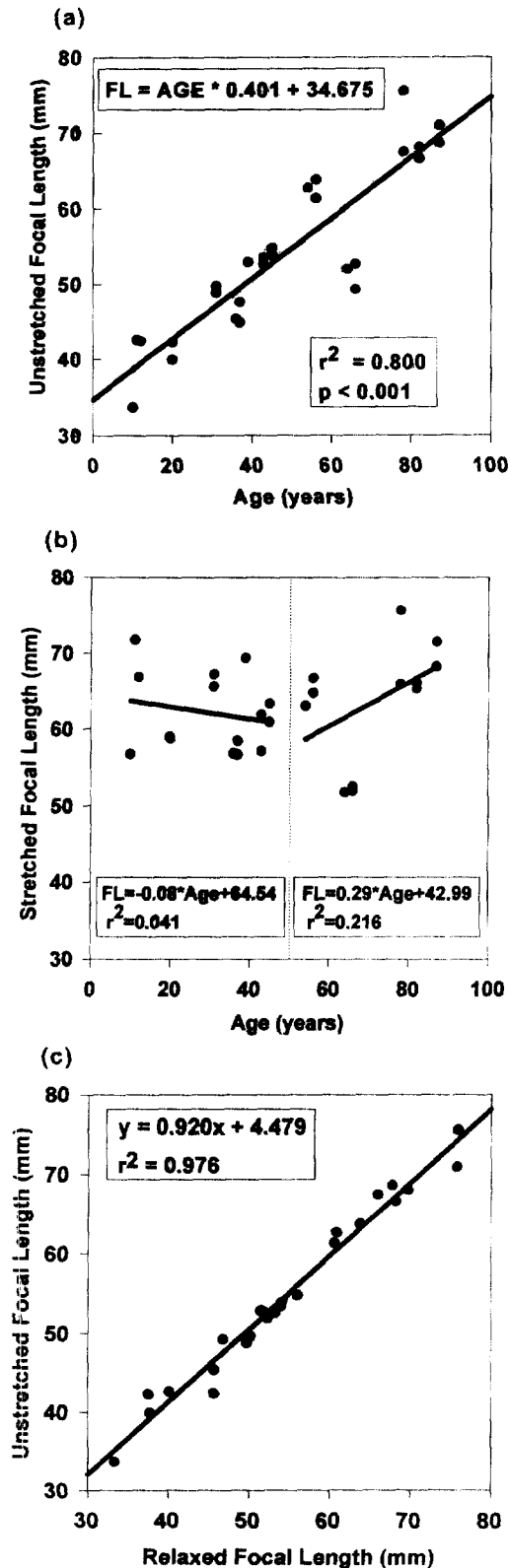
FIGURE 4. (a) Graph of the unstretched (accommodated) focal length of 27 human lenses as a function of age. This focal length is measured after the eye preparation has been glued to the stretching apparatus, but before any stretching tension has been applied. For the younger lenses (less than 50 years of age) which do undergo changes in focal length, the unstretched focal length represents the accommodated focal length. The remainder of the lenses (greater than 50 years), which undergo no changes in focal length on stretching, are of fixed focal length. (b) Graph of the maximally stretched focal lengths of 27 human lenses. The data have been divided into two groups roughly comprising a pre-presbyopic group (less than 50 years of age) and a presbyopic group (greater than 50 years of age). This division can be justified from the results of Hamasaki et al. (1956), which show that beyond the age of 52 yr there is essentially no accommodation. The slope of the linear regression line through the less than 50-year-old lenses shows a considerable decrease, and a reversal in sign, from the slope of the line in (a). This reflects the stronger change in focal length that the younger (10, 11 and 12) lenses are able to undergo, relative to the remainder of the lenses within this age range. The slope of the regression line through the prepresbyopic lenses is not significantly different from zero. The slope of the regression line through the presbyopic lenses is not statistically different from the slope of the regression line in (a). The similarity in the regression equations reflects the inability of the lenses within this age range to undergo changes in focal length with stretching. The two regression equations intersect at age 58 yr. This is a reflection of the age at which the amplitude of accommodation would reach zero for the lenses used in this study. (c) Graph showing the unstretched focal lengths measured prior to stretching versus the relaxed focal lengths measured after stretching the lenses. The regression line shows a significant linear relationship, a slope close to unity and an intercept close to zero. This indicates that the younger lenses, which are able to undergo changes in focal length, do return to their unstretched focal lengths, and the focal lengths of the older lenses remain unchanged. Thus, the stretching is well within the elastic limits of the lenses.
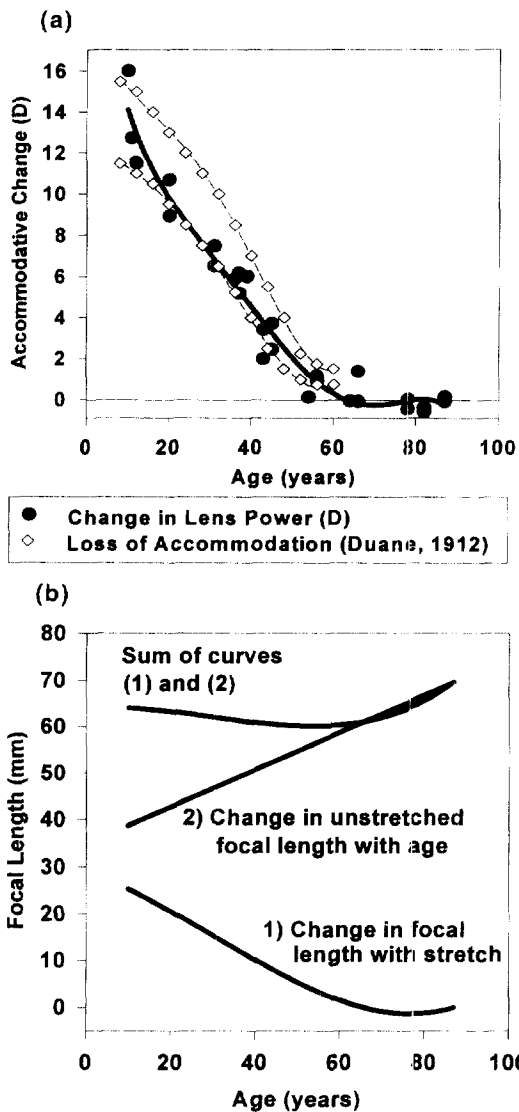
**(a)**



**(a)**



**(b)**



**(b)**



FIGURE 5. (a) Graph showing the maximal change in lens power for 27 human lenses as a function of age (filled symbols and solid line). For comparison, these data are plotted together with the maximum and minimum amplitudes of accommodation, as measured using a push-up technique (open symbols and dotted lines) (Duane, 1912). The magnitude of the change in lens power shows an age dependence similar to the change in accommodative amplitude. By roughly 58 years of age the lenses show essentially no change in focal length with stretching. The polynomial:

$$y = 23.7191 - 1.41131x + 0.0577x^2 - 1.3723 \times 10^{-3}x^3 + 1.5383 \times 10^{-5}x^4 - 6.3221 \times 10^{-8}x^5 \quad (6)$$

shows a good fit to the lens data ($r^2 = 0.965$). The difference (the residuals) between this curve and the fifth-order polynomial fit to the data from Duane (1922) ($r^2 = 0.998$) is not statistically different from zero (Mann–Whitney Rank Sum Test, $P = 0.881$). The negative values recorded for the older lenses are due to the reduced optical quality of some older lenses, resulting in random variations in focal length for successive scans. The equation relating accommodative amplitude and age crosses the y-axis at 58.25 years of age. (b) The change in lens focal length induced by stretch as a function of age (bottom curve) is plotted together with the unstretched lens focal length (middle curve). The sum of these two curves shows a continuous curve (top curve) relating stretched lens focal length and age. There is a gradual non-significant decrease in the unstretched lens focal length up to approximately age 60 yr and then a gradual increase beyond this age.
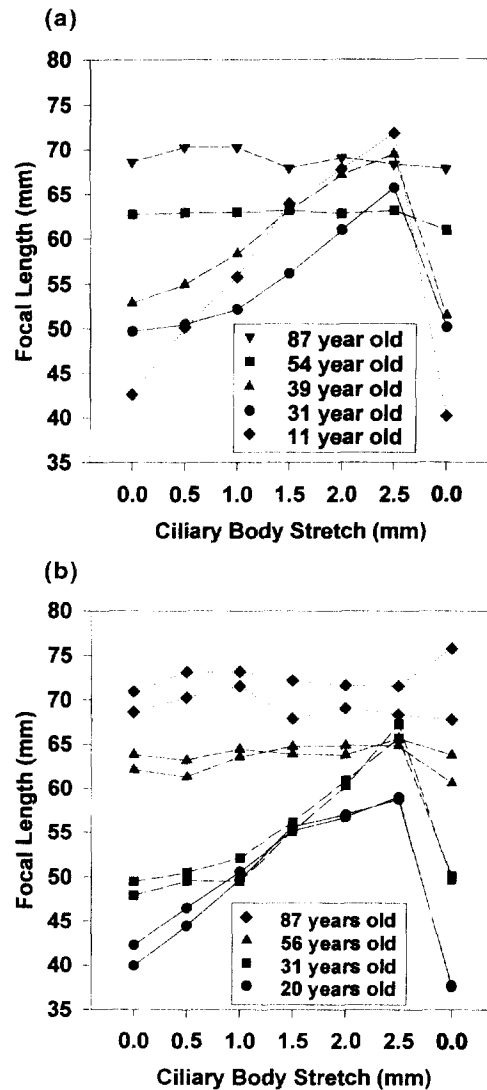
FIGURE 6. Graphs showing the extent of the change in mean focal length with stretching for five individual lenses (a) and for pairs of lenses from four donors (b). (a) Individual lenses, subjected to an increase in ciliary body diameter of up to 5.0 mm (an increase in ciliary body radius of 2.5 mm), show an age dependence in their ability to undergo changes in focal length. The starting unstretched condition (0.0 mm stretch) shows an age dependence of the unstretched focal lengths for these five lenses. The younger lenses (11, 31 and 39 years old) undergo changes in focal length with stretching, whereas the 54- and 87-year-old lenses show no change in focal length over the entire extent of stretching applied. After the stretching forces are released, the unstretched focal lengths of all lenses are essentially identical to the pre-stretch focal length. (b) With the exception of the 87-year-old pair of lenses, lens pairs from four donors show striking similarities in their optical changes with increasing stretch, to the extent that nonlinearities in the optical changes are evident in both lenses from each pair. The pre-cataractus 87-year-old lenses were of relatively poor optical quality and consequently repeated scans of the lenses showed some variability.

data set from Duane (1922) of the mean accommodative amplitudes for 4200 subjects ($r^2 = 0.998$) (data not shown). Our data from human lenses show that the age-dependent ability of the human lens to undergo changes in optical power falls within the range of accommodative amplitudes and that beyond about age 60 yr, the human lens can no longer undergo changes in optical power with

stretching. This agrees well with the gradual decline of accommodation in humans. If this change in lens power is expressed as a change in lens focal length [Fig. 5(b)] and the fifth-order polynomial is plotted on the same graph as the linear equation showing unstretched lens focal length, it is clear that adding these two curves provides a continuous relationship showing how the maximally stretched (unaccommodated) lens focal length changes with age. These data show that there is a small, gradual decrease in the focal length of the unstretched lenses until about age 60 yr, after which the lens focal length continues to increase.

The age-dependent ability of the lenses to undergo changes in focal length can also be seen by looking at changes in focal length of individual lenses over the full extent of the stretching forces applied (Fig. 6). A plot of five lenses of increasing age shows a gradually decreasing change in focal length with increasing stretch. The starting unstretched focal length of each of these lenses shows the same age-dependent increase shown in Fig. 4(a). For the three youngest lenses in which the focal length does change with stretch (11, 31 and 39-year-olds), the final unstretched focal length is essentially the same as the initial unstretched focal length, as shown in Fig. 4(c). The 54 and the 87-year-old lenses show no change in focal length over the entire extent of the stretch applied. The focal length of the 54-year-old lens remains fairly constant at each stretch position, while the 87-year-old lens shows some variability in the focal length measurements. This is largely due to the reduced optical quality in this pre-cataractus 87-year-old lens, which results in more variability between subsequent scans. This variability in focal length is only in the order of 1–2 mm.

Pairs of lenses from the same donor subjected to similar stretching forces show a striking similarity in the optical behavior of the lens pairs [Fig. 6(b)]. With the exception of the two 87-year-old lenses which show some independent variability owing to reduced optical quality as described above, the other lens pairs show almost identical responses to stretching to the extent that even the nonlinearities in focal length with stretch are similar between each of the two lenses of the pairs. For those lenses that do undergo changes in focal length with stretching, although the extent of the applied stretch is substantial, the curves are generally relatively linear over the full range of stretch applied, with no systematic evidence of asymptote.

## Spherical aberration

Figure 7(a) shows two fourth-order polynomial fits through the spherical aberration data from a 66 and a 10-year-old lens, both in the unstretched state. The 66-year-old lens shows uncorrected (positive) spherical aberration, while the 10-year-old lens shows over-corrected (negative) spherical aberration. The lens radii have been normalized to +1.0. In general, the fourth-order polynomials provide good fits to the spherical aberration data points. Because of the reduced optical quality of the 66-
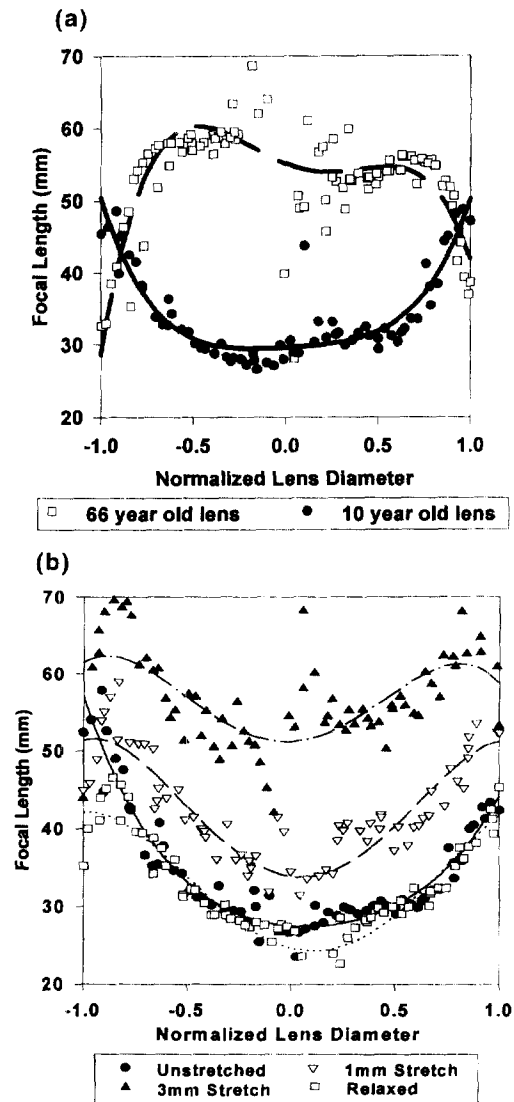


(a)

(b)

FIGURE 7. (a) Graph of the sign and extent of the spherical aberration in two lenses (66- and 10-year-old) lenses. The younger (10-year-old) lens shows over-corrected (negative) spherical aberration with the focal length increasing as the incident beam moves farther from the optical axis, while the spherical aberration of the older (66-year-old) lens is of the opposite sign. (b) The change in spherical aberration of the same 10-year-old lens as in (a) as a function of a change in ciliary body diameter. At each state of stretch, a fourth-order polynomial curve is fit to the spherical aberration data points. The two lower curves show the spherical aberration prior to stretching and then again once the stretching tension has been released after stretching. The magnitude of the spherical aberration decreases as the lens is stretched towards an unaccommodated state (increasing focal length). A higher-order polynomial may provide a better fit to the spherical aberration in the maximally stretched state, where some higher-order aberration has been induced near the edges of the lens.

year-old lens there is some variability in the intersection points of the more paraxial rays with the optical axis. Since the angle between the paraxial rays and the optical axis is very small, small variability owing to reduced optical quality of the lens can result in large deviations of these intersection points. The extent of the spherical aberration is calculated from Eq. (1) as the dioptric difference between the paraxial focus and the focus of the beams at the edge of the lens. The extent of the spherical

aberration, but not the sign, changes slightly with stretching in a young lens [Fig. 7(b)]. As the focal length increases with increasing stretch, the extent of the spherical aberration is reduced. When the lens is returned to the unstretched condition the spherical aberration curve is essentially superimposed on the curve obtained prior to stretching. Thus, the stretching has not caused

irreversible changes in the spherical aberration of the lens.

The normalized spherical aberration of all unstretched lenses shows a systematic increase from negative values below 40 years of age to positive values above this age [Fig. 8(a)]. The younger lenses show characteristic over-corrected (negative) spherical aberration with the paraxial rays focusing closer to the lens than the more peripheral rays, while in the older lenses the sign is reversed to produce uncorrected (positive) spherical aberration. When the lenses are stretched, both the slope and the intercept of the spherical aberration regression equation are reduced [Fig. 8(b)]. This is predominantly due to a reduction in the negative spherical aberration of the younger lenses with stretching, as seen in Fig. 7(b). Since the older lenses do not undergo any systematic optical changes with stretching, there is no systematic change in the spherical aberration of these older lenses with stretching. In the older lenses there are some changes in the coefficients of the fourth-order polynomial regression fits through the spherical aberration data points with successive scans. This is due to the reduced optical quality of the older lenses and it results in some nonsystematic variability in the extent of the spherical



**(a) For Unstretched Lenses**

SA = AGE * 0.394 - 15.675
$r^2 = 0.634$; $p < 0.001$

**(b) For Stretched Lenses**

SA = AGE * 0.298 - 9.765
$r^2 = 0.713$; $p < 0.001$
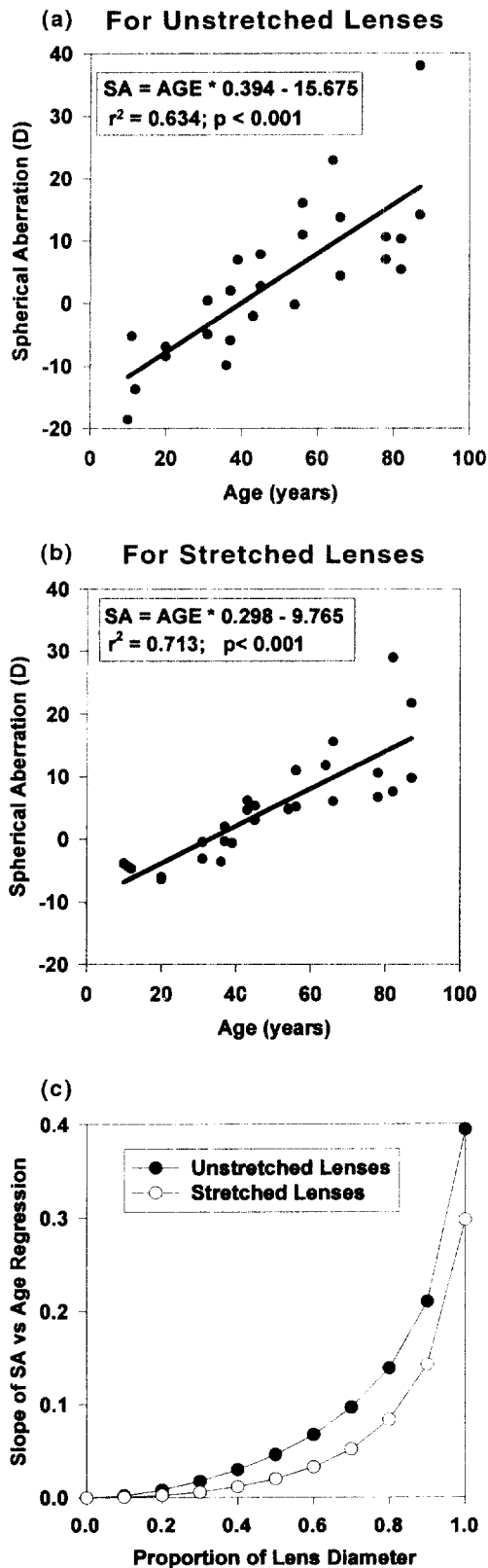
**(c)**

Unstretched Lenses
Stretched Lenses

FIGURE 8. Spherical aberration vs age for 27 human lenses in the unstretched (a) and fully stretched (b) states. The slopes of the spherical aberration regression lines as a function of the lens diameter for lenses in the unstretched and fully stretched states (c). The extent of the spherical aberration shown here reflects the difference in focal length between the paraxial focal length and the focal length at the full diameter of the lens. These graphs show substantially more spherical aberration than would be seen at normal pupil diameters of between 3 and 6 mm [see (c) below]. In the unstretched state (a) lenses younger than about 40 years of age show predominantly negative spherical aberration (over-corrected) and lenses older than this age show positive (under-corrected) spherical aberration. From the regression equation, lenses of 39.79 years of age would have zero spherical aberration. For the fully stretched lenses (b), both the slope and intercept of the regression equation are reduced. This reflects the reduction of the spherical aberration in the younger lenses during stretching [as seen in Fig. 7(b)]. From the regression equation for the stretched lenses, there is zero spherical aberration at 32.77 years of age. These data show that, in general, human lenses between the ages of 32.77 and 39.79 yr would be expected to undergo a change in sign of spherical aberration with stretching to become more positive. Note that the changes in slope and intercept of the spherical aberration between the unstretched and the stretched states are completely accounted for by the younger lenses, since the older lenses do not undergo any optical changes (in either focal length or spherical aberration) with stretching. The slopes of the spherical aberration regression equations are determined for different proportions of the full diameter of the lenses (c). The data points for the stretched and unstretched lenses at a diameter of 1.0 correspond to the slopes of the regression equations shown in (a) and (b). Both of the curves in (c) show that as an increasingly smaller proportion of the lens diameter is considered, the change in spherical aberration as a function of age is reduced. In other words, for lens diameters less than 50% of the full lens diameter there is only a small change in spherical aberration as a function of age. This shows that the change in spherical aberration as a function of age, shown in (a) and (b) above, is primarily due to the spherical aberration near the edges of the lens. This effect is accentuated for the unstretched lenses since the slopes of the regression equations are larger for all lens diameters. Although the regression equations fit to the spherical aberration at a diameter of 1.0 (a) and (b) are significant ($r^2 = 0.63$ and 0.71, respectively), the $r^2$ values for the regression equations decrease as a smaller lens diameter is considered.

aberration between successive scans, and hence also between the stretched and unstretched states.

The extent of the spherical aberration of each lens is predominantly determined by the strong spherical aberration near the edges of the lens. This is shown by considering how the slope of the regression line of spherical aberration as a function of age [Fig. 8(a and b)] changes with a change in the diameter of the lens considered. The slope of these regression lines changes as the proportion of the diameter of the lens considered changes [Fig. 8(c)]. For the full lens diameters ($x = 1.0$), the slopes of the regression equations for the stretched and unstretched lenses are those shown in Fig. 8(a, b). As the proportions of the lens diameters are decreased from 1.0, the age dependence of the spherical aberration rapidly declines towards zero. For proportions less than about half of the diameter of the lens there is little systematic age dependence of the spherical aberration. The dependence of the spherical aberration of each lens on the strong spherical aberration near the edges of the lens is also shown by considering the second- ($x^2$) and fourth- ($x^4$) order terms of the spherical aberration polynomial fit through the scan data as a function of age (graphs not shown). For the unstretched lenses there is a significant linear relationship for the fourth-order terms as a function of age:

$$\text{Fourth Order Term} = \text{Age} \times -0.955 - 1.666. \quad (4)$$

($r^2 = 0.478$; $P < 0.001$), but there is no significant relationship for the second-order terms ($r^2 = 0.119$; $P = 0.078$). Similarly, for the stretched lenses there is a significant linear relationship for the fourth-order terms as a function of age:

$$\text{Fourth Order Term} = \text{Age} \times -0.689 - 4.566 \quad (5)$$

($r^2 = 0.511$; $P < 0.001$), but there is no significant relationship for the second-order terms ($r^2 = 0.008$; $P = 0.653$). For both the unstretched and the stretched lenses, the regression line through the fourth-order terms vs age is a good predictor of the regression line through the sum of the second- and fourth-order terms vs age. In other words, essentially all age dependence of the spherical aberration of the lenses is accounted for by the fourth-order terms.

## DISCUSSION

### Use of human tissues

Owing to the uncertainties of obtaining human eyes and the scarcity of young donors, relatively few lenses between the ages of 0 and 30 yr were used. However, we feel justified in reporting these findings because of the relative scarcity of studies on human lens optics and because of the consistency of the results obtained. Further, in spite of the often lengthy delay between the time of death and the start of the experiments, we are confident that our results are not unduly influenced by the delay or by the prior removal of the corneas by the Eye Bank. In no cases did we observe a deterioration of the optical quality of a lens over the duration of the

experiments. On the contrary, one or two lenses, which at the start of the experiment showed questionable optical clarity, visibly improved after the lenses had remained in saline for 15 min or so. In one case, repeated measurements of an 82-year-old lens tested 120 hr after death showed no evidence of changes in spherical aberration, focal length or optical quality in measurements carried out over the subsequent 6 hr. An additional finding of this study is the remarkable optical resilience of the human lens. Animal lenses have been kept under organ culture conditions for prolonged periods of time (weeks) without significant deterioration of the optical quality (Weerheim & Sivak, 1992).

### Stretching methods

The stretching technique used to induce changes in focal length of human lenses is not ideal. Only eight arms apply the stretching force to the ciliary body, resulting in a potentially uneven distribution of force on the zonule. However, in spite of the gaps between the arms of the stretching apparatus there is, by visual inspection, a relatively uniform stretch applied to the entire zonule [Fig. 1(c)]. The tips of the stretching arms were angled to ensure that the orientation of the ciliary body and hence the direction of the zonular forces was maintained as close as possible to that occurring in the eye in vivo (Fig. 2). However, dissection and removal of the anterior segment tissue affects many other aspects of the accommodative system in the eye. There is a loss of the intraocular pressure normally present in the eye, a loss of the vitreous support against the posterior lens surface and the stretch applied to the ciliary body may not be of a physiological extent or orientation. All these factors will certainly influence the focal length of the lens before stretching, after stretching and the extent to which the focal length can be changed during stretching. The in vitro preparation and the mechanical stretching differ substantially from the in vivo accommodative mechanism in spite of our efforts to minimize the differences through the design of the stretching apparatus. The mechanical stretching results in a force directed radially outward at the equator of the lens, while in vivo, after an accommodative effort the force of the ciliary muscle may have a posteriorly directed component as well. While the in vitro measurement of human lens optics is no substitute for understanding the true optics of the lens in the intact eye under physiological conditions, it is the best we are able to accomplish with current technology, and has provided considerable insight and new information on the optical changes in the human lens. Caution should be employed in extrapolating such results to the living organ under physiological control. Where possible, we have drawn comparisons with data from more physiological optical measurements and in spite of the artificial stretching methods used, our results do agree well with established measures of accommodative amplitude and its decline with the progression of presbyopia. This is perhaps particularly remarkable since we have no information on the individual refractive error,

corneal power, ocular biometric data or other information which could influence the optics of the eye and the amplitude of accommodation *in vivo*. Even with an artificial radially directed zonular force are we able to demonstrate the inability of the older lenses to undergo accommodative changes. We argue that if we are exerting forces on the lens that are in a more radially directed orientation than occurs in nature, presbyopia should, if anything, be less evident in this preparation, in light of current extralenticular theories of presbyopia.

We were cautious to prevent the lens from sagging or tilting when the zonule was in the unstretched state by ensuring that the zonule did not become completely flaccid when the stretching tension was released. This was accomplished by ensuring that the zonule was extended, but not stretched, when gluing the arms of the stretching apparatus to the ciliary body. The camera to the side of the chamber allowed us to confirm that the laser beam was passing through the optical axis with minimal vertical deviation, thus ensuring that each scan was taken along a meridional section of the lens (across the full lens diameter). Since the optical properties of the older lenses were not seen to undergo *any* change with alterations in stretching, it is clear that they do not suffer optical effects from sagging or tilting. While it is true that the older lenses have a smaller circumlental space and so may be less susceptible to sagging, the circumlental space does still exist in even the oldest of eyes, and further, the older lenses are significantly heavier than the younger lenses and so may, in fact, be more susceptible to sagging owing to increased weight.

Although the ciliary body diameter was increased up to a maximum of 5.0 mm with stretching, all of this displacement is not conveyed to the lens. The ciliary body, choroid and the zonular fibers are all elastic tissues each with a lower modulus of elasticity than the lens and thus would themselves stretch. Much of the force generated by the increase in diameter of the stretching apparatus is therefore expended by the extension of these tissues. The horizontal extent of the scan is a good measure of lens diameter at each stretched state. For the three youngest lenses of ages 10, 11 and 12 yr, the lens diameter increased by 1.57, 1.04 and 1.04 mm, respectively with maximal stretching (representing an increase of 22, 12 and 13%, respectively of the unstretched lens diameter). In human eye specimens prepared for electron microscopy the extent of the circumlental space is in the order of 1.00–1.47 mm, depending on the age of the donor (Farnsworth & Shyne, 1979). Thus, a maximal increase in the lens *radius* by 0.5 to 0.78 mm is not unreasonable. Four further factors suggest the extent of the stretch was not unreasonable: (1) no zonular fibers are broken during the stretching; (2) the changes in lens focal length closely match accommodative amplitudes *in vivo*; (3) the stretching does not cause irreversible changes to the lens optics [Fig. 4(b)]; and (4) there is no asymptote in the change in focal length with stretching in the young lenses (Fig. 6). These factors suggest that the *optical* changes measured are physiological in nature and

magnitude. This is not to suggest that the magnitude and direction of our mechanically applied forces are the same as those that occur *in vivo*. Our results also suggest that younger lenses may have the capacity to undergo greater optical changes than those we have measured here since no systematic asymptote in the change in focal length was identified. To what extent this possible additional optical capacity is of physiological relevance is not known since we are unable to compare the forces that we have applied with the zonular forces that occur *in vivo* during accommodation. While it would have been technically feasible to measure the magnitude of the applied stretching forces, we would still have been unable to compare this force with physiological forces exerted on the lens during accommodation and relaxation of accommodation *in vivo*, since no such measurements exist and are beyond the scope of this work. Although Fisher (1977) has done theoretical calculations to deduce the force of contraction of the human ciliary muscle, they have yet to be experimentally verified.

## Comparisons with the work of Fisher

Despite the substantial evidence provided by Fisher for a lenticular basis of presbyopia (Fisher, 1969, 1971, 1973), numerous authors have subsequently proposed alternative theories for the development of presbyopia which contradict Fisher's findings or which have de-emphasized the importance of Fisher's results. While the methods employed by Fisher and ourselves can be criticized for the departure from the physiological process of accommodation, precise measurements of the optical and physical properties of the human lens are best accomplished through direct measurements on the lens. The primary emphasis of Fisher's (1977) lens stretching experiments were an attempt to deduce the force of contraction of the human ciliary muscle. We have, from our experiments, made no attempt to deduce the physiological changes in ciliary muscle function, but we have substantially extended the optical results reported by Fisher (1977) by using more sophisticated and objective techniques for measuring the optical properties of the lens. In spite of the differences in the optical methodology employed, both Fisher's (1977) work and our own show a striking similarity in the loss of the ability of the human lens to undergo changes in focal length and the decline in accommodative amplitude with age. While we have coincidentally used the same number of lenses as Fisher (1977), our lenses encompass a wider age range. Our optical measurements have substantially extended Fisher's findings in that we have described changes in resting focal length with age, changes in spherical aberration with age and changes in spherical aberration with stretching in the same group of lenses that we have shown a decline in the change in focal length with stretching.

## Accommodation and presbyopia

The results presented here are in complete agreement with classical theories of accommodation, which state

that the resting outward tension on the zonule maintains the lens in a relatively flattened state and that during an accommodative effort this zonular tension is released, allowing the young lens to undergo elastic recovery and become accommodated (Helmholtz, 1909). In our experiments, the outward tension applied to the lens pulls the lenses in a relatively flattened state and when the tension is released the young lenses become accommodated, thus decreasing the lens focal length (increasing the lens power). Our results disprove an recently proposed novel accommodative mechanism similar to one originally proposed by Tscherning (1904) (Schachar et al., 1995). This theory states that a ciliary muscle contraction *increases* equatorial zonular tension to paradoxically *increase* the power of the lens (Schachar & Anderson, 1995; Schachar et al., 1996). Presbyopia is then said to occur because the continued growth-related increase in lens diameter results in a gradual slackening of the zonular tension and an inability of the ciliary muscle to further increase zonular tension during accommodation (Schachar et al., 1995). If this theory were correct, then it is truly remarkable that by stretching human lenses we have produced optical changes that exactly match the magnitude and sign (direction) expected for accommodation in the human eye, and that we have demonstrated a declining ability of the lenses to undergo optical changes that exactly matches the age course of the progression of presbyopia. Further, the mechanism of this theory of ciliary muscle function (Schachar & Anderson, 1995; Schachar, 1996) depends entirely on the equatorial zonular fibers attaching to the most anterior aspect of the ciliary muscle and the complete separation of the equatorial zonular fibers from the anterior and posterior zonular fibers. From our observations, the structure and insertion of the zonule match the classical descriptions (McCulloch, 1954; Farnsworth & Burke, 1977). The zonular fibers of fresh human tissue attach all along the length of the ciliary processes with considerable overlap between the most anterior and most posterior zonular fibers [Fig. 2(c and d)]. No zonular fibers attach to the most anterior aspect of the ciliary processes and no separate and independent equatorial zonular fibers can be observed, as suggested by Schachar (1996).

The amplitude of accommodation, as measured using a push-up technique [Duane, 1912; Fig. 5(a)] indicates that at 60 years of age only 0.75–1.5 D of accommodation remain. This is due to depth of focus effects inherent in measuring accommodation using a push-up technique. Hamasaki et al. (1956) differentiate between true accommodative amplitude and depth of focus effects and have reported roughly 1.5 D depth of focus at ages between 51 and 60 yr. This is also very effectively demonstrated by Koretz et al. (1989), who measured accommodation in the same group of subjects using two independent techniques. Subjective reports of best focus through ophthalmic lenses resulted in at least 2 D of accommodation, even in the older presbyopic subjects, whereas the objective measurement of accommodative

amplitude using a Hartinger coincidence refractometer resulted in a 1.5–2 D lower accommodative amplitude for all ages and an absence of accommodation in all subjects over 50 years of age (Koretz et al., 1989). Fisher (1977) also recognized this distinction between different methods of measuring accommodation in relation to his *in vitro* measurements on human lenses. The curves from Duane (1912) can thus be "corrected" by subtracting 1.5–2 D of accommodation to correct for the depth of focus. Further, since the principle points of the lens are displaced from those of the eye and the principle points of the eye also move during accommodation, the change in refractive state from an unaccommodated to a fully accommodated *eye* is 20% less than the change in the power of the *lens* in a schematic eye model (Bennett & Rabbetts, 1989). Thus, to translate our measured changes in lens power to accommodative amplitude, the curve showing dioptric changes in lens power should be reduced by 20%. A fifth-order polynomial fit through our corrected lens data results in an accommodative amplitude within 0.5 D of zero by 58 years of age. This is also the age at which the two regression lines for stretched lens focal length less than 50 years old and stretched lens focal length greater than 50 years old intersect [Fig. 4(b)]. Thus, the measurements of accommodative amplitude from Duane (1912, 1922) and our measurements of change in lens power remain in relatively good agreement. Our *in vitro* measurements are in reasonably good agreement with the generally accepted age at which accommodative amplitude effectively reaches zero by about 52 years (Hamasaki et al., 1956; Koretz et al., 1989). From our results, it is clear that for lenses beyond the age of 58 yr, no amount of stretch can change the focal lengths, since they had undergone no change in focal length after an already considerable extension of the zonule. This result suggests that presbyopia in humans results from a loss in the ability of the lens to undergo changes in the focal length.

## The geometric theory of presbyopia

Our results provide experimental evidence against the hypothesis that changes in the zonular insertion angles onto the lens are a predominant factor in presbyopia. This geometric theory has its basis in the observation that the attachments of the zonular fibers undergo an anterior shift with increasing age (Farnsworth & Shyne, 1979). It has been suggested that because of these changes in geometry of the zonular fibers, presbyopia may result from either: (1) an inability of the ciliary muscle to release the zonular tension; or (2) a failure of the relaxing zonule to release the tension on the lens during an accommodative effort (Koretz & Handelman, 1986, 1988; Pierscionek & Weale, 1995a). We dispute the first hypothesis on the basis that we have completely stretched and relaxed the zonule through mechanical means. Since this causes changes in focal length of younger lenses but is without effect on the older lenses, it suggests that no amount of extension or relaxation of the zonule can cause a change in power of the older lenses. Although the mechanical

stretch may differ from the zonular forces *in vivo*, the artificial mechanical forces applied are the same for both the young and the old lenses. Thus, irrespective of the potential differences in our technique from the true accommodative mechanism, a lack of release of tension of the zonule is an unlikely cause of presbyopia. With regard to the second hypothesis we argue that the increased resistance (decreased compliance) of the lens (Fisher, 1971, 1973; Pau & Kranz, 1991; Glasser & Campbell, 1996b) may be a far more influential factor in the loss of accommodation than the postulated changes in zonular insertion angle. Additional experiments would be required to define the change in accommodation per unit release of zonular tension as a function of age.

It has been suggested that there is a change in the magnitude of the zonular force with accommodation in young lenses because of the change in thickness of the lens and the associated change in angle of the zonular fibers onto the anterior surface of the lens (Koretz & Handelman, 1982, 1983). This would predict a decreasing slope and possibly an asymptote in the change in focal length with increasing zonular stretch as the effective force applied by the anterior zonular fibers decreases as the lens flattens. Our data show no asymptote for the range of stretch we have applied to young lenses (Fig. 5), thus arguing against this geometric change in zonular force. Further, the zonule attached at the very equator of the lens represents a substantial proportion of the entire zonule, even in a 54-year-old [Fig. 2(c and d)]. The force provided by this equatorial portion of the zonule is independent of the thickness of the lens and would not change with a flattening of the lens. On the basis of our results, we believe that age changes in zonular insertion angle are an unlikely cause of presbyopia. Smaller increments in stretch might help to determine if zonular insertion angle is a partial factor in older lenses.

*The "disaccommodation" theory of presbyopia*

An alternative hypothesis for the cause of presbyopia (Bito & Miranda, 1989) suggests that, owing to the continued growth and the related increase in equatorial diameter of the lens and owing to changes in the zonular insertion angles with age, the resting zonular tension cannot be maintained. The absence of resting zonular tension causes the older lens to be accommodated because the lens cannot be pulled into its flattened shape. Presbyopia is then an inability to "disaccommodate", rather than a loss of accommodation (Bito & Miranda, 1989; Pierscionek & Weale, 1995a). Changes in the refractive index distribution of the lens are invoked to allow the older lenses to maintain a distance refraction by compensating for the increased lens curvatures (Bito & Miranda, 1989). This theory is unlikely since (1) our results show that among the older lenses the lens focal lengths do not, in fact, remain constant; (2) neither relaxing nor increasing the zonular tension can cause any change in the focal length of the older lenses: (3) our work and that of others has shown that the human lens becomes harder with increasing age (Fisher, 1971; Pau &

Kranz, 1991; Glasser & Campbell, 1996b); and (4) older presbyopic lenses cannot be considered to be in an accommodated form since the shape of the lens nucleus is quite different between young accommodated lenses and older presbyopic lenses and the thickness of the nucleus in the unaccommodated lens is constant over the entire adult age range (Cook *et al.*, 1994). Our optical results of changes in spherical aberration and continuing increases in lens focal length with increasing age, suggest that the older lens is similar to neither the younger accommodated nor the unaccommodated lens. Interestingly, we do find a constancy of focal length of unaccommodated lenses as a function of age, up to the age of presbyopia.

*Extralenticular theories of presbyopia*

In addition to previous work suggesting a lenticular basis for presbyopia (Fincham, 1937; Pau & Kranz, 1991; Fisher, 1973), the loss of accommodation has been attributed to numerous extralenticular age-related changes that have been documented in human and rhesus monkey eyes. With increasing age in the human eye there is an anterior shift in the attachments of the zonular insertion onto the lens (Farnsworth & Shyne, 1979) and there is a change in the orientation of the ciliary muscle (Tamm *et al.*, 1992b). In rhesus monkey eyes there are morphological changes in the ciliary muscle (Lütjen-Drecoll *et al.*, 1988a), a reduced responsiveness of the ciliary muscle to pilocarpine stimulation (Lütjen-Drecoll *et al.*, 1988b), and an increase in connective tissue within and adjacent to the ciliary muscle. The latter may cause a decreased compliance of the posterior ciliary muscle because when the posterior attachment of the ciliary muscle is severed (Tamm *et al.*, 1992a), or the ciliary muscle is isolated before stimulation (Poyer *et al.*, 1993), the ciliary muscle no longer shows an age-dependent declining responsiveness to pilocarpine stimulation. Our experiments do not address these changes, nor do they preclude their occurrence. Our results make it clear that in spite of these morphological changes, the changes in the lens alone can completely account for the progressive decline and the ultimate loss of accommodation in humans. Since these other age-related changes have been documented to occur with a time course matching the progression of presbyopia, we are left to speculate if they are a consequence of the same age-related processes that lead to changes in the lens, or the result of disuse of the ciliary muscle because of the inability to change the lens power, or if the loss of ciliary muscle function is, in fact, the cause of the decreased compliance of the lens. Perhaps it is possible that changes in the lens leading to the loss of compliance are a consequence of the reduced amplitude and frequency with which the accommodative musculature is able to flex the lens. It is equally possible, however, that the loss of lens visco-elasticity is brought about by environmental factors, with either a similar or different time course to the ciliary muscle changes.

*The lens paradox*

Presbyopia results in a loss of accommodation and

consequently a loss of near vision. Brown (1974) has shown through Scheimpflug measurements that in the unaccommodated, emmetropic eye there is an increase in lens curvature with age. Without other compensatory changes in the optics of the eye, this should cause an increase in lens power and a myopic shift in refraction, rather than the loss of near vision characteristic of presbyopia. The term "lens paradox" has been used to describe the fact that the distance refractive state of the eye is maintained with age in spite of the reported increasing lens curvatures (Koretz & Handelman, 1988). Changes in the refractive index distribution of the lens have been proposed to compensate for the progressive increase in lens curvatures with age (Koretz & Handelman, 1988; Pierscionek, 1990; Hemenger et al., 1995). Further, it has been suggested that such changes in the refractive index distribution may be an active mechanism of compensation to maintain lens power and refractive state in the face of the increasing lens curvatures (Koretz & Handelman, 1988; Pierscionek, 1993; Hemenger et al., 1995; Ooi & Grosvenor, 1995). The theoretical feasibility of changing the refractive index gradient to compensate for the increased lens curvatures has been shown (Smith et al., 1992; Hemenger et al., 1995). These studies have assumed that lens power and refractive state are maintained constant with increasing age. However, cross-sectional studies have demonstrated a hyperopic shift in refractive state after the age of 30 yr (Slataper, 1950; Saunders, 1981). Slataper (1950) alluded to the possibility of lenticular changes (either in the refractive index or zonular tension) to account for this hyperopic shift.

For the group of lenses used in this study there is a progressive decrease in the power of the stretched lenses after the age of 50 yr [Fig. 4(a, b) and Fig. 5(b)], rather than a maintenance of lens power. This suggests that previous hypotheses about the lens paradox are not entirely correct, and may be founded on incorrect assumptions. Since our results show that the lens focal length *increases* with aging rather than remaining constant, it cannot be argued that a change in the refractive index distribution is a mechanism of compensation for increased lens curvatures, since the compensation is poorly matched. It is just as likely that the lens curvatures may be increasing in an attempt to compensate for changes in the power of the lens, owing to an age-related decrease in the refractive index of the lens (Tamm et al., 1992b), or perhaps more likely still that the changes in lens curvatures and refractive index distributions are both simply coincidentally opposite effects of the same aging process that accompanies the continued growth of the lens.

*Spherical aberration*

Our analysis of spherical aberration considers the full diameter of the lens and weights the effects at the peripheral edges of the lens, much of which would normally be covered by the iris *in vivo*. Direct measurements of spherical aberration of isolated human lenses have been made previously with methodology similar to that used here, but little spherical aberration was found in the three human lenses of ages 16, 45 and 78 yr (Sivak & Kreuser, 1983). We have been unable to consider the biometric parameters of the eye, such as corneal curvature, anterior chamber depth, lens tilt, etc., all of which influence the optics of the eye and change with age, thus making comparisons with previous measurements of ocular spherical aberration difficult. Surprisingly, however, our measurements on lenses alone are in good agreement with the ocular observation that negative spherical aberration is most predominant in subjects less than 19 years of age (Stine, 1930), and with studies showing that up to 6 years of age, subjects had predominantly negative aberrations and over 35 years of age subjects had predominantly positive aberrations with an age-dependent increase (Jenkins, 1963). Three studies of changes in ocular spherical aberration with accommodation all report that the spherical aberration becomes more negative with accommodation (Koomen et al., 1949; Ivanoff, 1956; Jenkins, 1963). Our measurements of human lenses are in good agreement with this result. From his ocular measurements, Jenkins (1963), however, reported mostly positive spherical aberration in all but one of his young subjects (over the age of 8 yr) with a decrease in the aberrations (becoming more negative) with accommodation. Our measurements of young lenses (rather than the whole eye) showed negative spherical aberration, which became even more negative with increased lens power.

It is unclear how the spherical aberration of the lens and the spherical aberration of the eye are related. El Hage & Berny (1973) measured positive spherical aberration in the cornea of a single subject and showed that the lens compensates to reduce the spherical aberration of the whole eye. Millodot & Sivak (1978) showed that the aberrations of the cornea and lens are small and not usually of opposite sign. Most authors have measured a shape of the cornea which flattens in the periphery (Townsley, 1970; Kiely et al., 1982) and produces under-corrected (positive) spherical aberration (Bennett & Rabbetts, 1989). Our results of a change in sign of the spherical aberration of the lens with age, which differ from measured ocular values, could arise because a balance in age-specific spherical aberration for light incident from the cornea (i.e., with high vergence) will differ from that for light parallel to the optical axis. On the basis of our results we cannot conclude what, if any, the optical effects of the age change in spherical aberration of the lens are for vision. However, we have documented an additional age-dependent optical property of the lens that may be due to the changing refractive index distribution of the lens or the changing lens surface curvatures, or both. To what extent these optical parameters of the lens are influenced by age-dependent changes in the zonular forces on the lens is unclear.

Pierscionek (1993) has suggested that there may be age changes in the refractive index gradient of the cortex of the lens but not in the nucleus. This may be a possible

explanation for the change in spherical aberration with age, but it is unclear if this would account for the changes we have documented. The change in sign of the spherical aberration that occurs with age cannot be accounted for by the fact that the younger and older lenses are in different accommodative states. Although stretching the lenses changes the sign of the spherical aberration for lenses between the ages of about 32 and 40 yr, there are clearly inherent age-related differences in the spherical aberration (Figs 7 and 8). This age change in spherical aberration is also important in demonstrating that although the shape of the young accommodated lens may be similar to that of the older lenses (Brown, 1974), the optical properties are clearly different.

We think it unlikely that the age-dependent change in spherical aberration that we have measured is an artifact caused by the manner in which the lens is held in the stretching apparatus. While it is possible that the orientation of the zonular forces in our preparation is different from that which occurs physiologically *in vivo*, it is unlikely that this would substantially influence the spherical aberration. First, the spherical aberration of the older lenses is essentially unchanged, independent of whether the measurement was done in the stretched or unstretched state. Thus, in the older lenses, even a substantial zonular force on the lenses (nearly to the breaking point of the zonular fibers) cannot alter the spherical aberration. Subtle differences in orientation of the zonule such as may occur between our preparation and that in the eye *in vivo* are unlikely to have any substantial effect on the spherical aberration of these older lenses. Second, the same age-dependent trend in spherical aberration is clearly evident, regardless of whether it is measured in the stretched or in the unstretched lenses [Fig. 8(a, b)]. So even substantial changes in zonular force on young lenses, sufficient to cause substantial changes in focal length of these young lenses, do not significantly alter the age-dependent change in spherical aberration. During maximal accommodation, zonular tension is at a minimum in the eye and so subtle differences in the orientation of the zonular fibers are unlikely to cause substantial differences in spherical aberration from that which we have measured in the unstretched lenses. The changes in spherical aberration during stretching are more likely to be due to the specific deformation of the lens caused by the stretching.

*Gradient refractive index lens models*

Our *in vitro* results provide the first comprehensive descriptions of the kinds of optical changes that are likely to occur in the human crystalline lens *in vivo* with accommodation and age. These results demonstrate that information on lens thickness, curvature and focal length alone are insufficient to provide realistic gradient refractive index models of the lens. That the lens curvature increases with age (Brown, 1974), and that the lens focal length actually continues to increase in spite of this, demands that proposed models of the

gradient refractive index distribution within the lens predict the measured optical properties. No current schematic eye models consider age dependence, although studies have postulated that an age-dependent change in either the shape of the refractive index distribution or the value of the equivalent refractive index of the lens are required to compensate for age-dependent changes in optical elements of the eye (Smith *et al.*, 1992; Hemenger *et al.*, 1995; Ooi & Grosvenor, 1995). Other recent work has shown the need for reconsideration of an age-independent equivalent refractive index for the lens in childhood (Mutti *et al.*, 1995). In modelling the gradient refractive index changes in the fish lens as a function of age and growth, Kröger *et al.* (1994) demonstrated the importance of checking any postulated gradient refractive index against the measured optical properties. If accurate eye models or gradient refractive index distributions of the human crystalline lens are to be calculated in the future, it is essential that they include age-dependent parameters and that they are able to predict similar changes in focal length and spherical aberration as shown here, since these optical characteristics are highly dependent on the shape of the gradient refractive index profile used (Smith *et al.*, 1991).

## SUMMARY

1. The shortest focal length attainable by the human lens increases throughout life and this is attributable to both the loss of accommodative amplitude that accompanies the progression of presbyopia and to a continued increase in the focal length of the presbyopic lens.
2. The continued increase in focal length of the presbyopic lenses after 60 years of age could be caused by a decrease in the refractive index of the lens, an increase in lens thickness, or a change in the refractive index distribution within the lens. These changes would have to be of sufficient magnitude to override and surpass the opposing optical effects of the reported age-related increase in lens curvature (Brown, 1974).
3. The progressive increase in focal length of the unstretched lens provides a possible explanation for the hyperopic shift that is apparent in cross-sectional studies (Slataper, 1950; Saunders, 1981).
4. The human lens gradually loses the ability to undergo changes in focal length in response to mechanical stretching until approximately age 58 yr, after which no change in focal length can be produced via mechanically applied changes in zonular tension. This loss as a function of age corresponds well with the declining accommodative amplitude that characterizes the progression of presbyopia.
5. The decline in lens accommodative amplitude is independent of any changes that may occur in the ciliary muscle and associated choroid of the eye, and can be accounted for entirely by a declining ability

of the aging human lens to undergo optical changes in response to mechanical stretching.

6. There are dramatic changes in spherical aberration of the human lens with age. A reversal in sign from over-corrected (negative) to uncorrected (positive) spherical aberration occurs in unstretched lenses with increasing age. There are also smaller changes in spherical aberration of the lens as a function of accommodative state, in response to mechanically applied stretching forces.

7. If valid optical (schematic) eye models are to be used in the future, they will need to include age-dependent gradient refractive index lens models that predict the measured changes in focal length and spherical aberration with age. Without compliance with the results from empirical measurements such as those presented here, the models must be questioned for their validity and ability to accurately predict refractive state, presbyopic changes and changes in optical image quality with age and accommodative state.

8. Many current theories of the development of presbyopia are inconsistent with experimental data from Fisher (1977) and that presented here obtained from *in vitro* mechanical stretching of human lenses. Further experimental work is necessary to dispel many of the incorrect notions about the development of presbyopia and to identify those age-related changes in the eye that contribute to the loss of accommodative ability with increasing age.

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