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Abstract

The purpose of this study was to investigate the relationship between the stiffness of the material comprising the lens and the loss of accommodative amplitude with age. We used a validated mechanical model to determine the changes in the shape of the lens during accommodation and disaccommodation. The relative contribution of lens stiffness to loss of accommodative amplitude with age was determined by varying lens stiffness in the model. The changes in lens stiffness with age were based on the results of two recently published studies. In the first study we showed that lens stiffness increases exponentially with age, and in the second study we showed that there is a considerable stiffness gradient within the lens that changes with age. The results of both studies were incorporated in the mechanical model. The model showed that it is not the increasing stiffness of the lens with age, but rather the changing stiffness gradient that influences accommodative amplitude. The results show that the changing stiffness gradient in the lens may be responsible for almost the entire loss of accommodation with age.
6.1 Introduction

The ability of the young human eye to see objects far away as well as nearby has been the subject of scientific study for centuries. The most widely accepted theory on the mechanism of accommodation is attributed to Helmholtz (1855). However, the reason we lose the ability to accommodate with age has been subject to much debate. When we consider the aging eye, potentially all parameters that are involved in accommodation change with age, and virtually all of these parameters may be involved in the development of presbyopia (Atchison, 1995), leading some researchers to conclude that the cause of presbyopia is multifactorial (Weale, 1989, Gilmartin, 1995). In other studies attempts have been made to limit the potential causes of presbyopia to the most important ones. When human post-mortem lenses are stretched, the induced changes in shape decrease with lens age (Pierscionek, 1993, Pierscionek, 1995), and the decrease in power change appears to follow the decrease in accommodative amplitude with age (Glasser and Campbell, 1998). This indicates that the main causes of presbyopia may be found in the lens suspension system containing the zonular fibres, the capsular bag, and the crystalline lens matrix.

In recent years, the finite element (FE) method has been introduced as a useful tool with which to study the accommodative mechanism (e.g. Hermans et al., 2006, Weeber, 1999, Burd, Judge and Cross, 2002), and this method has increased our ability to identify the important parameters that may cause presbyopia. A parameter analysis, (based on data available up to 2003) indicated that increasing stiffness of the lens material (or loss of elasticity) with age has only a very limited impact on the development of presbyopia (Burd and Judge, 2003). More recently however, new data on the stiffness of the crystalline lens have become available from three studies, in which the mechanical properties of human lenses as a function of age were measured (Heys, Cram and Truscott, 2004, Weeber et al., 2005, Weeber et al., 2007). These studies revealed that the stiffness of the human lens increases exponentially with age. However, while these new data are not in conflict with earlier findings (Fisher, 1971), the exponential relationship has never been acknowledged. In two studies, the local dynamic mechanical properties within the crystalline lens were measured (Heys et al., 2004, Weeber and Eckert, 2004; Weeber et al., 2007). The results showed a large stiffness gradient in the lens, which changes with age. At a young age
the lens nucleus is very soft, but in old age the nucleus becomes very stiff. At the age of approximately 45, the stiffness is fairly uniform in the entire lens.

In this study, we use an FE modeling methodology that was validated by comparing the results of the model with in vivo measurements of an individual human subject (Weeber, Dubbelman and van der Heijde, 2003), and by comparing the results of the model with lens-stretching experiments (Weeber, 2003). The new data on stiffness were implemented in this validated model of accommodation. The model shows that the stiffness gradient in the lens, as an isolated factor, can almost fully predict the development of presbyopia.

6.2 Methods

In the present study, new data on stiffness were implemented in an FE model of accommodation. The geometry of the lens was obtained from in vivo measurements of the lens in the maximum accommodated state (Strenk et al., 1999, Dubbelman, van der Heijde and Weeber, 2005), and the mechanical properties of the tissues (lens, capsule and zonular fibres) were obtained from in vitro measurements of human eyes. Where the data were age-related, the values that were taken corresponded to a pre-presbyopic, 40-year-old person.

The purpose of this study was to determine the influence of changing lens stiffness on accommodative amplitude. Therefore, in the FE model, the lens stiffness (gradient) was the only parameter that was changed with age. In accordance with the Helmholtz theory of accommodation, the zonular fibres were stretched to achieve a state of disaccommodation. When comparing the results of different ages, the stretching force was assumed not to vary with age.

6.2.1 Model geometry.

The FE model consisted of three structures: the crystalline lens, the capsular bag, and the zonular fibres. The geometry of the anterior and
posterior lens surfaces was based on the *in vivo* measurements made by Dubbelman et al. (2005) of the maximally accommodated lens. In accordance with these measurements, the lens surfaces were aspherical (Fig. 1). The lens equatorial diameter was taken from *in vivo* measurements of accommodated lenses (Strenk et al., 1999). The anterior and posterior surfaces were connected with a spherical fillet. The lens capsule was modeled as a membrane around the lens, with its thickness varying with position (Fisher and Pettet, 1972). The zonular fibres were schematically modeled according to Rohen and Rentsch (1969), Kaczurowski (1964) and Farnsworth and Shyne (1979). Details of the dimensions of the model are listed in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Crystalline lens</th>
<th>Capsular bag</th>
<th>Zonular fibres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior radius</td>
<td>8.59 Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior radius</td>
<td>5.00 Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiffness</td>
<td>varies (see text)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centre thickness</td>
<td>3.98 Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior pole thickness</td>
<td>13 x10^{-3} Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior pole thickness</td>
<td>3 x10^{-3} Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young's modulus</td>
<td>1.5 N/mm²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poisson's ratio</td>
<td>0.47 -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of anterior zonular fibres</td>
<td>100 -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter anterior</td>
<td>50 x10^{-3} Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of equatorial zonular fibres</td>
<td>50 -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter equatorial</td>
<td>40 x10^{-3} Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of posterior zonular fibres</td>
<td>135 -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter posterior</td>
<td>40 x10^{-3} Mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young's modulus</td>
<td>0.35 N/mm²</td>
<td></td>
<td></td>
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<tr>
<td>Poisson's ratio</td>
<td>0.47 -</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Table 1. Details of the FE model.*
Figure 1. Finite element (FE) model of the accommodative apparatus. The edited picture shows how the FE model was derived from Scheimpflug photographs of the in vivo human lens in the maximally accommodated state (Dubbelman et al., 2005, copyright Elsevier). The actual model geometry had aspherical lens surfaces and was based on the average of the right eyes of 65 subjects ranging in age from 16 to 51 years.

6.2.2. Mechanical properties.

For the mechanical properties of the capsular bag we used the Krag, Andreassen and Olsen (1996) measurements (elastic modulus at 10% strain). For the zonular fibres we used the data from van Alphen and Graebel (1991).

The mechanical properties of the crystalline lens were successively taken from Weeber et al. (2005), Weeber et al. (2007), and Fisher (1971). For the model having gradient stiffness, the lens was divided into concentric regions of equal stiffness. The number of regions was equal to the number
of stiffness measurements of the lens (Weeber et al., 2007). The 20-year-old lens has the lowest modulus in the lens center, and the 60-year-old lens has the highest modulus in the center. The 40-year-old lens combines an equal modulus in the center and at the equator with a higher modulus between the center and the equator (Fig. 2). All mechanical properties were assumed to be isotropic.

![Figure 2. FE model of the crystalline lens in which the stiffness gradient is implemented. The colors indicate the stiffness of the zones (Young's modulus). The number and size of the zones correspond with the locations at which the stiffness was measured on post-mortem human lenses (Weeber et al., 2007).](image)

6.2.3. Finite Element Analysis.

Because the system is symmetrical, only half of a lens cross-section was modeled. The model was entered in general purpose FE software (Marc Analysis 2003, MSC.Software Corporation, Santa Ana, CA, USA). The
effects of element types and density were described previously by Weeber and Martin (2001). Based on that experience, the current model (Fig. 2) was given 2689 incompressible elements for the lens and 169 shell elements for the capsular bag. To obtain a good modeling result of the gradient stiffness, the model includes a fine mesh throughout the entire lens. The calculations were geometrically non-linear. Two models were evaluated: 1) a model with a lens of uniform stiffness (Fisher, 1971, Weeber et al., 2005) and (2) a model with in which the lens stiffness is gradient (Weeber et al., 2007). Both of the models began with an analysis of the accommodative amplitude, based on the stiffness data of a 40-year-old lens: the tip of the zonular fibres was stretched to the point at which the lens diameter had increased by 7% (Wilson, 1997, Strenk et al., 1999), causing the shape of the lens to change and the surface curvatures to decrease. Subsequently, the dioptric power of the lens was calculated using the thick-lens equation, an equivalent refractive index of 1.422 for the lens and a refractive index of 1.336 for aqueous and vitreous. The force required for stretching the 40-year-old lens was recorded, and this value was applied as the imposed stretching force for the simulations of other ages of lens. Therefore, the increase in lens diameter during disaccommodation varied with age.

6.3 Results

In the FE model that had uniform lens stiffness throughout the entire lens, and which used the stiffness data from Fisher (1971), the decrease with age was almost linear (Fig. 3). The change in lens power decreased from 6.9 diopters to 5.2 diopters between 20 and 60 years of age. With the Weeber (2005) data, the change in lens power decreased from 7.4 diopters to 3.4 diopters between 20 and 60 years of age.

When the gradient was introduced, the change in lens power decreased from 8.0 diopters to 0.4 diopters between 20 and 60 years of age. The decrease with age was non-linear, and accelerated between 40 and 55 years of age.
Figure 3. Change in the dioptric power of the lens as a function of age, based on the change in lens stiffness with age, according to three different studies. Dashed curve: based on change in the stiffness according to Fisher (1971). Dotted curve: based on the uniform change in stiffness according to Weeber et al. (2005). Solid curve: based on the change in stiffness gradient according to Weeber et al. (2007). In Fisher (1971) and Weeber et al. (2005), lens stiffness is represented by the value for the complete lens. In Weeber et al. (2007), the stiffness gradient was measured.

6.4 Discussion

In the model having uniform lens stiffness, an exponential increase in lens stiffness results in an almost linear decrease in accommodation (Fig. 3, dotted line). When the stiffness gradient of the lens is introduced, the model predicts an accelerated decrease in accommodative amplitude after the age of 40 years.

The calculated values can be compared with clinical values. Multiplying the change in lens power by 75% (Holladay et al., 1988) gives
an estimate for the resulting change in refraction of the total eye, the outcome of which is the objective accommodative amplitude. Fig. 4 shows results from the model with the gradient stiffness compared with the clinically measured objective accommodation obtained from 7 studies. To model the onset of presbyopia more accurately, the FE model with the stiffness gradient was also evaluated with 50- and 55–year-old lenses. Although the shape of the curve from the FE model is reasonably similar to the measured data, the model predicts the onset of presbyopia about 10 years later than was found clinically. This discrepancy could be due to shortcomings in the model and in the input data. On the other hand, it could indicate that more factors than were modeled in this study play a role in the development of presbyopia.

Figure 4. Accommodation as a function of age in 7 clinical studies and the predicted values from the mechanical model that includes a lens with a stiffness gradient. The studies are: Otake et al., 1993, Koretz et al., 1989, Hamasaki, Ong and Marg, 1956, Ostrin and Glasser, 2004, combined results of Ramsdale and Charman, 1989 and Hofstetter, 1965, Wold et al., 2003.

Clinical studies that involved larger populations have measured subjective accommodative amplitude (Duane, 1922, Ungerer, 1986). Subjective accommodative amplitude is significantly influenced by the
eye’s depth of focus. This effect can be quite large, with a magnitude that is dependent on the actual accommodative amplitude. To a great extent, this can be accounted for by correcting the subjective values for the influence of using a fixed target size (Atchison, Capper and McCabe, 1994, Rosenfield and Cohen, 1995). Fig. 5 shows the decrease in the accommodative amplitude with age according to two of the largest studies, each containing data on over 1000 subjects. In this figure, correction is made for a fixed target size. The figure also shows the decrease in accommodation, as predicted by the FE model with the stiffness gradient. The accelerated loss of accommodative amplitude after the age of 40 years as found in the FE model is also found in Duane’s curve (though to a much lesser extent). Ungerer’s curve shows an accelerated loss of accommodated amplitude after the age of 25 (Ungerer measured 351 subjects in the age range of 18 to 24 years).

Figure 5. Accommodation as a function of age in two large clinical studies (Duane, 1922; Ungerer, 1986) and the predicted values from the mechanical model that includes a lens with a stiffness gradient. Dashed curve: clinical data according to Ungerer (1986). Dotted curve: clinical data according to Duane (1922). Solid curve: predicted data according to the mechanical model that includes a lens with a stiffness gradient. The clinical measurements were obtained with the ‘push-up’ technique, and the measurements in this graph are corrected for the influence of depth of focus according to the method described by Atchison et al. (1994).
The FE model closely resembles the test setup of stretching experiments (Pierscionek, 1993, Glasser and Campbell, 1998, Koopmans et al., 2003). In figure 6, the results of the stretching experiments were multiplied by 0.75 to convert their measured change in lens power to accommodative amplitude. The FE model correlates well with the stretching results, despite the fact that in the FE model, only the gradient stiffness changes with age and not the shape of the lens (curvature and thickness) nor the stiffness of the capsular bag. In addition, during the stretching experiments, the stretching force was undetermined, while the ciliary ring was stretched up to 4 mm.

![Figure 6](image)

**Figure 6.** Accommodation versus age according to the in vitro lens stretching studies of Glasser and Campbell, 1998 and Koopmans et al., 2003. The lens power changes of these studies were multiplied by 0.75 to estimate the effective accommodative amplitude. The results of the FE model with gradient stiffness are shown for three possible scenarios of the effective refractive index (ERI) of the crystalline lens: (1) with a constant, fixed ERI, (2) with an ERI that varies with age (Dubbelman and Van der Heijde, 2001) and (2) with an ERI that varies with age (Dubbelman and Van der Heijde, 2001), as well as with accommodation (Dubbelman et al., 2005).
In an additional experiment with the 60-year-old gradient stiffness model, we increased the force to such a high value that the lens stretched its diameter to the same extent as the young lens. Interestingly, while the zonular force was unrealistically high, the surface curvatures hardly changed. Thus, even when the lens was pulled very hard, the lens power did not change, so useful accommodation could not be achieved. We believe the underlying reason is that the lens nucleus is too stiff to change its shape, while the relatively soft cortex slides along the nucleus to the equatorial region without changing the lens curvature in the optical centre.

The mechanism of accommodation is complex and, as mentioned before, most of the tissues that are involved change with age. We used a model in which the stiffness of the lens was the only factor that changed with age. In this model, the change in stiffness gradient, as a single factor, almost fully accounts for the development of presbyopia, although over a slightly different time course. Clinical values of accommodative amplitude show a large variation (e.g. Duane, 1922, Koretz et al., 1989). Lens stiffness, which was also measured, shows a large variation (Heys et al., 2004, Weeber et al., 2005, Weeber et al., 2007). The limited number of lenses in lens stiffness studies may have resulted in a difference in the time course between model and clinical data. In addition, an obvious and important boundary condition in relation to the time course is the force that is applied by the zonular fibres to the lens. In our model, we chose for the force to be constant with age, but it is likely that there is at least some variation in force with age. It has been shown that the ciliary muscle stays active throughout life (Swegmark, 1969, Saladin, Usui and Stark, 1974), however, the force that is exerted onto the lens has not been measured. In vivo morphometric studies have shown that the movement of the ciliary body during accommodation is reduced with age, both with voluntary accommodation (Bacskulin et al., 1996, Strenk et al., 1999, Bacskulin et al., 2000), and with pharmacologically induced accommodation (Stachs et al., 2002). This may indicate that the exerted force is reduced with age. In vitro studies (Pardue and Sivak, 2000) are inconclusive, possibly due to the limited number of samples that have been measured.

Other factors probably play a role in the development of presbyopia. The gradient refractive index of the lens changes with age (Pierscionek, 1990, Moffat, Atchison and Pope, 2002, Jones et al., 2005), which may induce a loss of accommodative amplitude with age (Pierscionek, 1990).
The effect of a changing gradient refractive index is reflected by a change in equivalent refractive index with age (Garner, Ooi and Smith, 1998, Dubbelman and Van der Heijde, 2001). In addition, the equivalent refractive index was found to change with accommodation (Dubbelman, van der Heijde and Weeber, 2005). The change of equivalent refractive index with age and with accommodation have a similar effect in the model (Fig. 6) - the accommodative amplitude increases, especially for the younger lenses, while the influence on the time course of presbyopia is negligible.

An interesting topic for future modeling studies in this area would be the role played by changes in the geometry of the lens, as both the thickness and curvature of the lens increase with age (Brown, 1974, Goss et al., 1997, Dubbelman and Van der Heijde, 2001).

Acknowledgements.

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6.5 References


