

Estimation of Accommodative Forces in Aging Human Eye

Master of Science in Biomedical Engineering

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Estimation of Accommodative Forces in Aging Human

Eye

Abstract

Changes in mechanical properties of the human crystalline lens over the years result in loss of accommodation amplitude and eventually in presbyopia, a condition in which the focus-shifting ability of the eye diminishes. Some material property changes of aging human crystalline lenses have already been mapped over human life. Young's modulus, anterior and posterior lens curvatures, lens thickness, and refractive index are examples of these well-studied properties. However, knowledge of forces applied to the crystalline lens for generating corresponding focus shifts has been limited to a few age groups. The purpose of this thesis was to create a complete map of accommodative forces for aging human crystalline lenses. We used mechanical properties available in the literature to develop a mechanical model of the crystalline lens for age groups between 10-70 years. Then, a detailed finite element modeling of the lens and optical power calculations obtained from changing lens shape during simulated accommodation were used to create a complete map of accommodative forces over human life. We found that an S-curve-shaped decrease of total outwards equatorial forces was required on the capsule to achieve previously reported accommodative amplitudes. The total force ranged from 0.5 Newtons for 10-year-olds to near zero Newtons for 70-year-olds, with a steep decrease happening between the ages of 30 and 50 years old. The aging human eye's estimated accommodative force map reported in this study could benefit future efforts for accommodation restoration and artificial lens replacement studies.

Keywords: Crystalline Lens, Finite Element Analysis (FEA), Accommodation, Accommodation Power, Accommodation Amplitude

Yaşlanan İnsan Gözünde Akomodatif Kuvvetlerin Tahmini

Öz

Yaşlanmaya bağlı olarak insan göz yapısı ve fonksiyonlarında birçok değişiklik meydana gelmektedir. Göz merceğinin esnekliğini kaybetmesi sonucu odaklanma yeteneğinin gerilemesi olan presbiyopi hastalığı bu değişiklilerin en yaygın sonuçlarından birisidir. Presbiyopiyi tedavi etmek için incelenmesi gereken başlıca yapı, miyelin kaslara zonül denilen bağ yapılarla bağlı olan ve esnek yapısıyla kasların uyguladığı güç sayesinde şekil değiştirerek ışığın retinada odaklanmasını sağlayan kristalin lenstir. Kristalin lensin şekil değiştirmesine akomodasyon denir. Lensin şekil değiştirme yeteneğinin kaybedilmesine katkıda bulunan, yaşlanma sonucu değişen Young's modülüs, anterior ve posterior lens yüzeylerinin küresel yarı çapları, lens kalınlığı ve refraktif indeks gibi materyal özellikleri literatürde mevcuttur. Ancak, lensin akomodasyon işlevini gerçekleştirmesi için gerekli olan kuvvetler hakkında bilgi bir kaç yaş grubu ve çalışma ile sınırlı kalmıştır. Bu tezde kristalin lensin üç boyutlu modelemesi yapılarak, sonlu elemanlar analizi yöntemi ve lens yüzey küreselliklerine bağlı odak mesafeleri hesaplamaları kullanılarak 10-70 yaş aralığında bilinen akomodasyon seviyelerini sağlayan kuvvetler haritalanmıştır. Bu kuvvetlerin bilinmesi, göz hastalıklarının tedavisinde kullanılan yapay göz içi lenslerin özelliklerinin daha doğru bir şekilde belirlenmesine ve fonksiyonel çeşitliliklerinin artmasına yardımcı olma potansiyeli taşımaktadır.

Anahtar Kelimeler: Kristalin Lens, Sonlu Elemanlar Analizi (SEA), Akomodasyon, Akomodasyon gücü, Akomodasyan Genliği

To my family,

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List of Abbreviations

Def	Total deformation
FEA	Finite Element Analysis
IOL	Intra Ocular Lens
y/o	Years old

List of Symbols

A_{n1} , A_{n2}	Fourier Coefficients
L _e	Loss of accommodation due to mechanical property
L_p	Total stretching force applied on the lens
P_A	The power before accommodation
P_B	The power after accommodation
T_a	Anterior thickness
T_p	Posterior thickness
T_t	Total thickness
c _a	Anterior radius of curvature
c_p	Posterior radius of curvature
n_{aq}	Aqueous Refractive index
n _{cl}	Equivalent Refractive Index
r_a	Anterior radius
r_b	Posterior radius
1/f	Focal length
D	Optic Power (Diopter)
Ν	Force (Newton)
е	Equator diameter

1. Introduction

One of the main structures in the vision process is the crystalline lens. The crystalline lens of the eye is a biconvex, optically transparent, and relatively acellular intraocular structure that plays a vital role in the visual process [1]. This transparent structure, located behind the iris, allows the light rays necessary for clear and sharp images to be refracted and transmitted to the retina. It is responsible for focusing[2]. The crystal lens provides approximately one-third of the focusing power of the eye [3].

The anterior segment of the human eye comprises the cornea and iris, with the lens located at the front (Figure 1.1). The lens is kept in position by the suspensory ligaments that attach it to the ciliary body muscles. Behind the lens lies a vitreous body with a jelly-like consistency, which helps to hold the lens in place [4]. The liquid aqueous humor is found at the front of the lens, which provides it with nutrients and other essential substances. In an adult human, the lens is generally about 10mm in diameter and 4mm thick, but it can change shape and size throughout a person's lifetime due to growth and accommodation [5].



Figure 1.1: Top view of the human lens [3]

Approximately 33% of the lens weight is in protein structure, and the lens has the highest ratio of proteins in the human body. Lens proteins are divided into two groups: water-soluble ones and water-insoluble ones. The water-insoluble ones are also examined in two subgroups: urea-soluble and insoluble ones. 80% of all proteins in the lens are water-soluble and called crystalline. There are three different crystalline proteins: Alpha (α), Beta (β) and Gamma (γ), and they constitute 32%, 55%, and 1.5% of lens proteins, respectively [6]. Abnormal aggregation and precipitation of these proteins can cause the lens of the eye to lose its transparency and cause cataract formation [7], the most common type of blindness.

1.1 Human Crystalline Lens

The crystalline lens consists of three main components, from inside to outside: nucleus, cortex, and capsule (Figure 1.2). The oldest part of the lens, the nucleus, is surrounded by the younger cortex. The capsule surrounds both the nucleus and the cortex [8].



Figure 1.2: Human Crystalline Lens Parts: Capsule, Cortex and Nucleus [9]

1.1.1 Capsule

The lens capsule is a transparent and elastic membrane that contains mostly type 4 collagen (along with types 1 and 3). It surrounds the lens epithelial cells and

fibrils and is the thickest basement membrane in the human body. The thickness of the capsule is 14 μ m in the anterior part, 17-23 μ m in the periphery, and 4 μ m in the posterior region [6]. The natural shape of the lens is round or spherical, which allows the eye to focus at close range in Figure 1.3 [10]. The thickness of the cortex and nucleus increases with age [11], while the capsule thickness remains constant [12].



Figure 1.3: Capsule of Lens [13]

1.1.2 Cortex

Because of its high water content, the cortical substance that makes up the cortex of the lens is softer than the nucleus [14]. Although there is no membrane separating the cortex from the nucleus, it consists of many fibers and shells that surround the entire structure. There is no fiber running between the poles. In this instance, the linear stitches that connect the fibers take the form of a letter Y (Figure 1.4). Concerning the front surface of the shell, the Y seam is perpendicular [8].



Figure 1.4: The shell and fiber of Cortex[15]

1.1.3 Nucleus

The lens nucleus is made up of fiber cells. The nonnucleated core fiber cells that make up the fetal nucleus are surrounded by layers of nucleated cortical fiber cells that form highly structured concentric shells. The ends of the peripheral fiber cells abut in sutures anteriorly and posteriorly. Light transmission and lens transparency are dependent on the ordered arrangement of the fiber cells, their sutures, and their intracellular structure. The fact that fiber cells contain numerous interdigitations and very little extracellular space between them further adds to transparency. Metabolites can be exchanged between neighboring fiber cells through junctional complexes. The primary soluble components of fiber cells are lens crystallins, which comprise approximately 90% of the water-soluble protein, and cytoskeletal elements such as actin, myosin, vimentin, α -actinin, and microtubules [3]. The average thickness of the nucleus in the resting state eye was reported to be at 2.50 ± 0.16 mm, the anterior cortex was at 0.51 ± 0.03 mm, and the posterior cortex was at 0.84 ± 0.12 mm [16].



Figure 1.5: The Parts of Nucleus [17]

All of the continuously generated secondary fibers that follow sexual maturation make up the cortex. The nucleus has a higher refractive index than the cortex and comprises tightly packed lens fibers. The nucleus can be further subdivided into embryonic, fetal, infantile, and adult nuclei based on the developmental stage. The initial primary lens fibers that developed in the lens vesicles are found in the embryonic nucleus. Secondary fibers known as rests are encircled by previously created nuclei and are added concentrically at various stages of proliferation. The fetal nucleus contains the embryonic nucleus and all of the fibers added to the lens before birth, making it identical to the nucleus at birth. All fibers added up until the age of four are contained in the infantile nucleus, which is made up of the embryonic nucleus and fetal nucleus, and all fibers added up to that age. Everything contributed to the adult nucleus before sexual maturation [18].

1.2 Accommodation

The lens is flexible and its curvature can change under the influence of the ciliary body muscles. The force applied by the ciliary muscles changes the lens thickness and surface curvatures so that the eye can focus images at different depths along the optical axis. This dynamic event of focus shifting of the eye is called accommodation [19]. It also means that the eye changes its optical power to focus on near or far objects. Accommodation happens when the ciliary muscle contracts, causing the shape of the crystalline lens to change [20,21]. The ability to accommodate decreases with age until it is completely lost; This condition is called presbyopia and affects the population after the age of 45 on average. Various reasons have been suggested as the causes of presbyopia. The two most common theories are that presbyopia is caused by (1) age-related hardening of the inner material of the lens and (2) age-related changes in shape and size. Other factors, such as changes in the ciliary body and zonules, are believed to be less influential [22]. Intraocular lenses (IOLs) are being produced to overcome crystalline lens-related diseases [23]. By replacing the lenses in cataract eyes with intraocular lenses, the patient can reach his/her previous quality of life [24]. However, these artificial structures are not perfect and need further development to achieve restoration of accommodation as well. A better understanding of the eye structures and functions including the crystalline lens is a prerequisite for further development in this field.

The ciliary muscle is elongated, triangular in shape, and located beneath the anterior sclera just posterior to the limbus. The shortest side of the triangular region faces anteriorly inward. The base of the iris inserts into this region of the ciliary body. The elongated, superficial, external surface of the ciliary muscle extends from the scleral spur posteriorly, curved along the inner surface of the anterior sclera. The apex of the ciliary muscle is oriented inward in the eye toward the lens equator and is covered by the pars plicata region of the ciliary processes.

The ciliary muscle is composed of muscle fibers of three differing orientations. Most superficially, just beneath the sclera, there are longitudinally oriented muscle fibers. These muscle fibers have their fixed origin at the scleral spur and their movable posterior insertion attached posteriorly to the choroid at the ora serrata of the retina. Deeper within the ciliary muscle and located more anteriorly toward the apex of the triangular-shaped region, there are the more radially oriented muscle fibers. Deeper still toward the apex of the triangular-shaped ciliary muscle, there are the circular muscle fibers. The muscle fibers are dually and reciprocally innervated by sympathetic and parasympathetic subdivisions of the autonomic nervous system. Although the muscle fiber orientations differ, the entire ciliary muscle contracts as a whole during accommodation. Contraction of the longitudinally oriented fibers acts principally to pull the posterior insertion of the ciliary muscle anteriorly; contraction of the radially oriented muscle fibers acts principally to consolidate and bulk up the apex of the triangularly shaped region; and contraction of the circularly oriented fibers acts principally to pull the apex of the triangle inward toward the lens equator [25].

The suspensory ligament of the lens (also known as the lens zonule) is a complex system of extracellular fibers, which is transparent in a physiological state. Zonular fibers connect the crystalline lens to the inner structures of the eye, mainly the ciliary body, and suspend the lens within the visual axis. The lens zonules are transparent and covered by the iris. The zonular apparatus centers the lens on the visual axis and transmits the forces generated by the ciliary muscle to the lens (Figure 1.5) [4].

The ciliary muscle changes the tightness of the zonular fibers by contracting and relaxing, thus changing the shape of the lens and causing adaptation to near or far vision, that is, it provides accommodation [26,27].

Three groups of zonular fibers can be differentiated in terms of structure and function, and work together to maintain the fine function of the zonular apparatus together. The posterior zonules arise from the gulfs of the pars plana and cover the pars plana epithelium. These zonular fibers run forward to the valleys and lateral walls of the ciliary, where they are fixed within the zonular plexus. In the area of the zonular plexus, the posterior zonules are attached and mingle with the anterior zonules. From there, the anterior zonules are divided into the posterior and anterior zonular tines. These zonules form the anterior and posterior zonular tines attached to the posterior and anterior aspects of the equatorial lens capsule, respectively. Also, some fiber bundles move to the lens equator directly. Therefore, the zonules can be roughly categorized into the anterior, posterior, and equatorial tines based on different anchor positions on the surface of the lens capsule [4].



Figure 1.5: Accommodative structures of the human eye [27]

1.2.1 Accommodation Theories

There are two theories on how accommodation occurs in the living eye. The most widely accepted theory is the Helmholtz Theory of accommodation developed by Hermann von Helmholtz, the ciliary muscle contracts when the eye adjusts. This contraction reduces zonular tension, which causes the gap between the ciliary body and the lens equator to increase. As a result, the forces applied to the equator of the lens are reduced, allowing the lens to elongate and increase its anteroposterior thickness, and optical power. When the maximum force that can be applied is reached, the lens is unaccommodated, that is, its focusing capacity is at its minimum (Figure 1.6) [28]. Helmholtz described that accommodation was the result of ciliary muscle contraction, which reduced its diameter and relaxed zonular tension. This allows the lens to take its original high curvature and high optical power shapes to focus on close objects on the retina. When accommodation stops, the ciliary muscle relaxes and returns to its form without accommodation. Zonular tension increases again and the lens is pulled at the equator, returning the lens to its fully unaccommodated state, meaning the focal length increases [29,30].



Figure 1.6: A comparison of side views of fully accommodated and unaccommodated human lens states

The second theory of accommodation, Schachar's theory, is less accepted and lacks experimental support. This theory suggests that accommodation results from an increase in zonular traction at the lens equator to an increase in lens diameter, rather than a decrease in zonular traction and a decrease in lens diameter. Schachar's theory of presbyopia proposes that presbyopia occurs not from the widely documented increase in hardness of the lens but from a progressive increase in the equatorial diameter of the lens. It is suggested that growth in lens diameter results in gradual relaxation of the zonular fibers extending from the lens equator to the ciliary body. This relaxation of the zonular fibers does not allow the necessary increase in zonular traction during accommodation. Surgical expansion of the sclera is recommended to restore zonular tension thought to be lost with the presumed increased growth of lens equatorial diameter (Figure 1.7) [31]. Helmholtz's theory is widely used in literature.



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Figure 1.7: Accommodation Theories [32]

1.2.2 Lens Power

The lens accommodation capacity is affected by its variable surface curvature, which changes as we age, along with its morphology and gradient refractive index [33,34]. With aging, the human lens grows through epithelial cell division and the formation of differentiated fiber cells. This process alters the dimensions and shape of the lens, including its mass, thickness, radii of curvature, and refractive index [35]. As individuals age, the lens in their eye undergoes a series of changes, including

thickening, increased weight, and reduced elasticity, which ultimately lead to a decline in lens power (Figure 1.8)[35–37].



Figure 1.8: Lens Power Changes with Aging [35]

In optics, lens power or optical power is the degree to which distance a lens can focus the light, defined by inverse of its focal length (P = 1/f) (Grivenkamp, 2004). Shorter focal lengths correspond to higher optical powers. It is measured in diopters (D), which is the inverse meters (m^{-1}) . The determination of lens power involves the values of the anterior and posterior radii of curvature values, in conjunction with the thickness and refractive indices [38,39] represented by f, the anterior radius is represented by the value $'r_a'$, while the posterior radius is represented by $'r_b'$. The equivalent refractive index is represented by $'n_{CL}'$ (=1.441), and the refractive index of aqueous is represented by $'n_{aq}'$ (=1.336 (Eq. (2)). The optical power measured in diopters is equivalent to 1/f, where f is the focal length of the lens [39].

$$P = \frac{1}{f} = \left(\frac{n_{CL}}{n_{aq}} - 1\right) \times \left(\frac{1}{r_a} - \frac{1}{r_b}\right)$$
(1.1)

1.2.3 Accommodation Amplitude

The lens power changes during accommodation and the extent of this change a human lens can achieve defines its accommodative amplitudes. The amplitude of accommodation measures the closest point at which the eyes can focus: the range from the far point to the near point in dioptres. Because it is measured from the far point, the measurement needs to be taken with the distance correction in place. One usual method is to ask the patient to look at a small print moved slowly toward the eye until the patient reports that clear vision cannot be maintained, defining the limit of lens shape change. When a noticeable blur occurs, the card is moved in further to confirm that it has become worse and is then moved back until it clears. The midpoint between the first blur and first clear positions is the near point [40]. The measurement of the amplitude of accommodation is a standard procedure during a comprehensive eye examination. Typically, a normal eye is capable of focusing as close as 10 cm for a child or young adult. However, with aging, the amplitude of accommodation gradually decreases and is usually completely lost by the age of fifty. Regular eye examinations are recommended to ensure optimal visual health and to detect any potential ocular abnormalities at an early stage including a check of accommodative amplitudes [41–43].



Figure 1.9: Accommodation amplitude with aging [22]

The accommodation amplitude can be expressed mathematically. It is the difference in optical power of the lens between the far point and the near point of the eye [44]. This difference is related to the maximum power change that the eye can reach. To calculate the accommodation amplitude, in equation 3, the lens power before accommodation is subtracted from the lens power after accommodation. P_A refers to the power before accommodation, P_B refers to the power after accommodation.

Accommodation Amplitude =
$$P_B - P_A$$
 (1.2)

1.2.4 Biomechanics of Human Crystalline Lens

Biomechanics is a scientific discipline that investigates the mechanical aspects of biological systems, encompassing the study of the structure, function, and movement of organisms, organs, cells, and cell organelles. This field employs the principles of mechanics to explore the physical properties of living organisms and their mechanical interactions with the environment [45,46]. In the field of biomechanics, finite element analysis is considered the primary method of study. Finite-element analysis (FEA) is a numerical technique for solving complex mathematical problems. It helps to determine patterns of stress, strain, deflections, heat transfer, fluid flow,

and other factors in computer models of structural components. FEA is a powerful tool that can address a range of questions that are otherwise difficult or impossible to solve [47]. A big system can be divided into smaller, more manageable components called finite elements using the FEA method. A specific space discretization in the space dimensions is used to do this, and it is put into practice by creating a mesh of the object—the numerical domain for the solution, which has a finite number of points. A system of algebraic equations is ultimately produced when a boundary value issue is formulated using the finite element method. Across the domain, the technique approximates the unknown function [48]. The most common program used for FEA is ANSYS.

During accommodation, the human lens undergoes significant mechanical changes. These mechanical changes can be defined using the mechanical properties of lens materials and forces applied to the lens to generate them. Mechanical properties of the lens materials and shape changes of the lens during accommodations are available in the literature [49–52]. However, the force application required by the ciliary muscles to the lens for generating the related accommodative changes on the lens is not well known, especially over aging. Such information will shed light on future eye studies for artificial lens material development.

2. Literature Review

One of the dynamic events in the human eye is focusing on various distances, an ability when lost causes significant inconvenience for people. Presbyopia loses the ability to focus and requires correction with lenses to obtain clear near vision for people over the age of ~50 years. As a result of this inconvenience and the need for corrective action, there has been a significant amount of research on accommodation. When it comes to focusing, the first thing that comes to mind is the structure of the crystalline lens during the accommodation process. Forces applied to the lens by the ciliary muscles for accommodation are not well known. There is limited information about this in the literature and nonexistent for many age groups.

The first study on this was conducted by Fisher in 1971[36]. Using a 24-hour cadaver lens, he separated the lens from its zonules. With the mechanism he prepared, he was able to apply a pulling force on certain parts of the lens while at the

same time making a rotation movement. Fisher created his own equation and measured the age-related elasticity of the lens. This study forms the basis of the following ones, including ours.



Figure 2.1: Fisher's Young Modulus Values [36]

The force required for lens accommodation was first investigated by Fisher in 1977 [53]. Cadaveric lenses 8 hours post-mortem were used. The separated parts were placed in a ring and the lens was held. The focal length change of the lens was calculated by applying force to the ring. The thickness of the lens and the diameter of the ring were measured after each diopteric power measurement. The results obtained from these experiments are as follows: As the lens diameter increases, the lens power decreases, and the difference between lenses over age is small. As we get older, lenses become harder and accommodation becomes more difficult. Therefore, with age, accommodation amplitude is decreased. The lens was rotated around the front, back and polar axes, and as the rotation speed increased, the lens power decreased. It was observed that the amplitude value was zero at the age of 57 [53].



Figure 2.2 Fisher's Accommodation amplitude experiment results according to 22 and 43 years old lens [53]

In the following years, Burd *et al.*. (2002) conducted a study on how much force was required for accommodation, using Young's modulus values of Fisher [54]. In this study, they used lenses for ages 11, 29 and 45, and determined the fully accommodating status as 10 D for ages 11 and 29, and 4 D for ages 45. Three zonules with a thickness ratio of 6:3:1 were used: anterior, posterior and central, and force was applied to all of them from a single point. They assumed that the refractive index decreases with age. According to this study, the force that provides accommodation to the lens should vary between 0.08 and 0.1 N for ages 29 and 45. Their study could not report a meaningful result for the 11-year-olds [49].



Figure 2.3: Burd et al. (2002) simulation study [49]

Hermandez *et al.*. (2006), examined the lens of a 29-year-old person using simulation and FEA. Also performed Fisher's young modulus values. 8D fully accommodated status was assumed. Also performed Fisher's young modulus values. When applying forces, only the cortex and nucleus were used and the capsule was not taken into account. Three models were created: anterior, posterior and central, with zonules in different configurations and at different angles. No difference was observed in terms of the force that should be applied in these models.



Figure 2.4 Hermans et al. (2006) Simulation Study [51]

The force required to provide maximum accommodation to the lens of a 29-year-old person was found to be 0.08 N. A discrepancy has emerged between the anterior and posterior surfaces as a result of the cost function they used [51].



Figure 2.5: Hermans et al.. (2006) Simulation Study Results [51]

Hermans *et al.* (2008) in another simulation study, examined lenses of 11, 29, and 45 years old. They determined the fully accommodated status as 14 D for 11-year-olds, 8 D for 29-year-olds, and 4 D for 45-year-olds. This time, zonular fibers were not used, but the force was applied from 2 or 3 points on the lens. It has been observed that as age increases, the diameter change corresponding to the applied force decreases. They created three models from different angles using three different source data. As a result, different forces were obtained at different Young's modulus values including Fisher Young's Modulus Values.



Figure 2.6: Hermans et al. (2008) Simulation Study [50]

To summarize, although models have different geometries and material properties, the total net force required to bring the lens to an unaccommodated state varies slightly with age and is around 0.06 N, while the accommodative amplitude decreases with age [50].



Figure 2.6: Hermans et al.. (2008) Simulation Study Results [50]

Lanchares *et al.*. (2012) studied a 30-year-old human lens in a simulation. 7.5 D is determined as fully accommodated status. It has been revealed that the stiffness of the nucleus increases faster than the cortex with age. They used a hyperelastic semi-incompressible substance in their experiments. Also performed Fisher's young modulus values. Just like Burd *et al.* (2002) used three different zonules from different angles and applied force by combining them from a single point called muscle.





They found the force required for maximum accommodation of the lens to be 0.078 N [52].

Figure 2.8: Lancheres et al.. (2012) Simulation Study Results [52]

Fisher's (1971) Young's modulus values were generally used in all studies. However, Burd *et al.*. (2006) found that there were systematic errors in Fisher's study [54]. First, there are significant modeling errors in the rotating lens test and these errors contribute to the impression that the cortex is stiffer than the core. Additionally, this situation resulted in missing module ratios. Although Fisher included the capsule in his experiments, he ignored the effect of the capsule on the lens structure by not including it in the interpretation part. Burd *et al.*. corrected all these systematic errors and produced new results with solid and mathematical models. These results are the most up-to-date study in the literature as it contains information for more age groups and has the least systematic errors. Therefore, in this study, the cortex and nucleus Young module values were used as Burd *et al.*. (2006) reported [36].

This study aimed to create a more complete map of accommodative forces over human life, through biomechanical analysis of the forces required to achieve previously reported accommodation amplitudes for age groups 10-70 years old. We used the most recently published mechanical properties values available in the literature to predict the resulting adaptive total forces, combining them with a mechanical model of the crystalline lens, a detailed finite element modeling of it, and optical power calculations obtained from lens curvatures while accommodating

3. Materials and Method

The four primary techniques used to derive the accommodating force estimates reported in this research are as follows: 1. Human crystalline lens three-dimensional (3D) models were created for every decade of aging in people between the ages of 10 and 70. 2. Using information from the literature, the material properties of the lens were mapped for all age groups. 3. To mimic stretching trials, the mechanical models and attributes were subsequently imported into FEA software. 4. After radii of curvature extraction under different lens stretching settings that matched reported accommodative amplitudes, calculations of lens optical power were carried out.

3.1 Modelling of The Lens Geometry

The lens forms and curvature values found by Urs *et al.*. (2010) were employed in this investigation. They reported the diameters of the isolated lenses, which ranged in age from 20 to 69, using shadow photogrammetric pictures. For ease, they attempted to express all age-related measurements of the zero-degree shape using a single formula in later optical modeling investigations. The cortex of the lens modeling used in this investigation is represented by Equation (3), where the Fourier A_{n1} and A_{n2} are given in Table 3.1. Table 3.2 shows the formula we used in our study to create curvatures for all age groups between 10 and 70 years old [55].

$$\rho = \sum_{n=0}^{10} (A_{n1} + A_{n2} \times age) \cos(n\theta)$$
(3.1)

Fourier coefficient	A_{n1}	A_{n2}
A_0	2.6466	812.11E-5
A_1	0.2246	170.62E-5
A_2	-0.97938	-297.37E-5
A_3	0.010573	-34.901E-5
A_4	0.37993	-26.276E-5
A_5	-0.032321	1.6647E-5
A_6	-0.16846	69.192E
A_7	0.027934	-9.5571E-5
A_8	0.066522	-42.251E-5
A ₉	-0.014232	1.7295E-5
A ₁₀	-0.021375	18.638E-5

Table 3.1: Fourier Coefficients adapted from Urs et al..(2010) [55]

Table 3.2:	The age-related	thickness	of lens	segments	(Age 7	0
	was	interpolate	ed.)			

Age (years)	Cortex (mm) [56]	Nucleus (mm) [37]
10	3.95	2.14
20	4.06	2.17
30	4.16	2.20
40	4.32	2.23
50	4.38	2.26
60	4.48	2.29

Our study utilized the curvatures from Urs *et al.* (2010) [55], which were found to be in strong agreement with those reported by Dubbelman *et al.* (2003) [37]. Additionally, we designed a capsule curve with a thickness of 23 microns (Fasiuddin, 2011), and created a 2D drawing of the lens that included the capsule, cortex, and nucleus. Figure 1 displays the resulting lens shape, with designated regions for the anterior radius of curvature (c_a), posterior radius of curvature (c_p), anterior thickness (T_a), posterior thickness (T_p), total thickness (T_t), and equator diameter (*e*). A 3D model was created for each age group by rotating a 2D lens model around its center since the human crystalline lens is rotationally symmetric [51].



Figure 3.1: Geometric model for the of fully accommodated 10-year-old human crystalline lenses. The central 3 mm marked in red and blue colored capsule regions are used for radius of curvature extraction.

3.2 Material properties of the aging crystalline lens

Lens models for all age groups were transferred to a FEA simulator for analysis. During the transfer, material definitions were made using Young's modulus values given in Table 3.3 together with Poisson ratio values of 0.47, 0.49, and 0.49 for capsule, cortex, and nucleus, respectively (the same Poisson values were used for all ages groups) [56].

	0		ť
Age (years)	Capsule (kPa) [57]	Cortex (kPa) [36]	Nucleus (kPa) [36]
10	16.23	1.79	0.583
20	24.43	2.71	0.631
30	32.63	3.45	0.679
40	40.83	3.83	0.811
50	49.03	4.03	1.29
60	57.23	6.01	2.23
70	65.43	6.75	2.55

 Table 3.3: Young modulus values of crystalline lens

3.3 Force Application to the Crystalline Lens

We exerted pull forces along the equator in an outwards direction on the lens capsule surface from four quadrants, each of equal magnitudes. A marked static (non-moving) reference point is necessary for FEA simulations in order to calculate all displacements accurately with respect to this fixed reference. In the real world, the entire lens moves during accommodation, but in certain areas, it moves more than others. The central part of the anterior lens capsule has been observed to be one of the least moving lens regions during accommodation [58] . As a result, we determined the support of our model by fixing a tiny central section of the anterior lens surface to serve as the FEA reference. Figure 3.2c's blue section illustrates this fixed component for support along with the lens model and all four applied forces. The four forces were uniformly distributed across the equatorial surfaces of their corresponding quadrants. With 53546 nodes and 35935 elements, the lens model in

use had a high mesh sampling level (Fig. 3.2d). After a mesh convergence analysis was carried out to maximize FEA accuracy, these meshing choices were determined.



Figure 3.2: (a) Solid model; (b) solid model cross-section; (c) fixed support (blue) locations; (d) meshing of a completely accommodated human crystalline lens that is ten years old.

3.4 Radii of Curvature Extraction and Lens Optical Power Calculation

For radii of curvature extractions, the center portions of the anterior and posterior lens surfaces with a diameter of 3 mm were utilized (refer to Figure 3.1). This kind of selection was necessary since the lens surface curvatures changed in radially outward regions. The majority of the lens refraction necessary for vision was caused by the chosen central region.

Using the FEA simulator, three points were chosen at the center of the surface and at the ends of the central 3 mm portions on both the anterior and posterior surfaces of the lenses to fit a circular function and extract the Radius of curvature. For all age groups, this type of lens power computation was done for both fully accommodated and unaccommodated lens forms. The total deformations needed to switch between fully accommodated and unaccommodated lens forms were then computed for the two situations. In order to acquire reported accommodation amplitudes for each age group, the force magnitudes necessary to generate such deformation values were determined.

4. RESULTS

This study included creating models of the crystalline lens for individuals aged between 10-70 years old to simulate stretching and determine changes in the lens's shape. The study's findings are presented in detail in Tables 4.1 and 4.2, which summarize the changes in the lens's curvature and thickness with and without stretching forces, as well as the forces applied to achieve the reported accommodation amplitudes.

Figure 4.1 provides a detailed illustration of the expansion of the lens during stretching for all age groups and their respective accommodation amplitudes. The fully accommodated shapes are represented by gray shadows, indicating no force was applied to the lenses. The unaccommodated states, represented by multi-colored regions, indicate the shapes of the lenses when a force is applied to represent their unaccommodated states.

To establish the correlation between accommodation amplitude and force, the lens optical power for different levels of total stretching force (0-5 Newtons) applied to the capsule equator across can be used for all ages (Figure 4.2a). For instance, the simulation indicates that applying one Newton of total force for stretching (in comparison to zero Newtons) would cause a 15 Diopter reduction in lens optical power for a 10-year-old lens, but only a 3 Diopter decrease for a 70-year-old lens (Figure 4.2a). With this database of lens optical powers over applied force and various ages shown in Figure 4.2a, we determined the force necessary to achieve previously reported accommodation amplitudes for all ages, as illustrated in Figure 4.2b. We discovered that the total outwards equatorial force required on the crystalline lens capsule to accomplish previously reported accommodative amplitudes decreased in an S-curve shape. The total accommodative force ranged from 0.54 Newtons for a 10-year-old to nearly zero Newtons for a 70-year-old (Figure 4.2b and Table 4.2).



Figure 4.1: Lens stretching simulations covering the age range of 10 to 70 years, displaying the shape alterations and deformation colormaps as each age group moves from an unaccommodated to a fully accommodated condition. The regions of greatest displacement are shown in red, those of least displacement in blue, and the displacement amounts between the two are shown in different hues. The simulations displayed are for the following lenses: 10 y/o (a), 20 y/o (b), 30 y/o (c), 40 y/o (d), 50 y/o (e), 60 y/o (f), and 70 y/o (g).



Figure 4.2: (a) The shift in lens power for people aged 10 to 70 when the total force applied is increased from 0 to 5 N; (b) A graph showing the force needed to reach the maximum recorded accommodation amplifier for all age groups (10-70 years old). At ages 10–30, the force applied reduced to approximately 0.5 N; at ages 60–70, it reached nil.

Table 4.1: Radius of curvetures and thicknesses of lens accommodation and unaccommodated states

Between the completely accommodated lens (no force is applied) and the unaccommodated lens (a force of up to 0.54 N is applied to stretch the lens), the radius of curvature and thickness vary. The numbers mentioned are for the anterior thicknes T_a , T_a'), posterior thickness (T_p, T_p') , total thickness (T_t, T_t') , equator diameter (e, e'), posterior radius of curvature (c_p, C_p') , and anterior radius of curvature (c_a, c_a') . Symbols with the prime mark (') indicate values for stretched lenses, and symbols alone indicate values for completely accommodated lenses. Every measurement is made in millimeters (mm). The final column displays the maximum deformation values derived from the FEA analysis.

Age	ca	$c_a{}'$	c_p	c_p'	е	e'	T _a	T_a'	T_p	T_p'	T _t	T_t'	Def
10	9	13.2	4.54	8.74	8,75	9,6	1,77	1,49	2,23	1,86	4.01	3,35	4.21
20	9.18	12.28	4.57	7.48	8,92	9,74	1,8	1,51	2,29	1,33	4,09	3,42	3,05
30	9.35	11.09	4.59	6.33	9,13	9,89	1,85	1,54	2,36	1,99	4.22	3,53	2,15
40	9.8	10.92	4.73	5.85	9,32	10,05	1,89	1,57	2,43	2,05	4.32	3,62	0,81
50	9.9	10.15	4.8	5.05	9,52	10,42	1,93	1,61	2,49	2,1	4.43	3,71	0.25
60	10.1	10.1	5	5	9,7	9,7	1,97	1,97	2,56	2,56	4.53	4,53	0
70	10.5	10.5	5.25	5.25	9,89	9,89	2,01	2,01	2,63	2,63	4,64	4,64	0

As the human body ages, the radii of curvature for the anterior and posterior surfaces of the eye lens tend to increase in the fully accommodated state. This means that the curvature of the lens becomes flatter with age, which can affect vision. We have found that when equatorial forces are applied to the lens models, the lens curvatures become flatter with increasing force magnitude, resulting in increased radii. This trend has been observed in age groups below 50 years old. However, after the age of 50, less significant or no changes in the radii values were observed (as shown in Table 4.1). This means that the lens becomes less malleable with age, and its ability to adjust to different distances decreases over time.

For fully accommodated cases, the equatorial diameter (e) increases with age. This means that the lens becomes wider as we age, which may also affect our ability to focus on objects at different distances. However, for the stretched state, although it increases with age until 60 years old, no change was observed after this age.

In fully accommodated cases, T_a , T_p , and T_t thicknesses increase with age. These thicknesses refer to the thickness of the anterior and posterior surfaces of the lens, as well as the thickness of the entire lens. With force application, thicknesses decrease, although no change is observed after the age of 60. This means that the lens becomes less thick and more flexible when force is applied, but this effect becomes less significant with age.

Finally, as expected, maximum deformation values obtained from FEA decrease with age until the age of 60, after which zero displacement is found. This refers to the maximum amount of deformation that the lens can undergo in this simulation. As we age, the lens becomes less deformable and more rigid, which can affect its ability to focus on objects at different distances. The calculations for the total equatorial force needed to achieve maximum accommodation amplitude for each age group's lens models are summarized in Table 4.2. Figure 4.2b. As people age, their eye's ability to accommodate decreases, resulting in a corresponding decrease in accommodation amplitude. Despite this decrease, the total net force required to achieve it remains relatively stable at around 0.5 N for those between 10-30 years old. There is a sharp decline in total force at 40 and 50 years old, with the total force dropping to near zero Newtons at 60 years old and beyond. By curve-fitting the graph in Figure 4.2b, it is possible to obtain Eq. 4.1, which provides a formula for calculating the accommodative forces over the years.

$$Force = 0.50718 / (1 + e^{0.217 x * age - 9,47})$$
(4.1)

Age	Amplitude	Total Net Force
(years)	(Diopters)	(N)
	[59]	
10	11	0,54
20	9	0,47
30	6	0,48
40	4	0,35
50	1	0,10
60	0,73	0
70	0,64	0

Table 4.2: Accommodative forces depend on age

5. DISCUSSION

Our study aimed to investigate the mechanical forces that occur during the human lens accommodation process. To achieve this, we developed a simulation technique and created solid lens models using previously reported shapes and mechanical properties of individuals between the ages of 10 and 70. We conducted stretching experiments by applying outward equatorial forces ranging from 0-5 Newtons. Using Finite Element Analysis (FEA), we observed the resulting deformations on lenses of each age group. By analyzing the deformation values, curvatures of lens surfaces, and corresponding refractive index values, we were able to calculate the lens optical power for all age groups and the forces applied. The lens power results (Fig. 4.2a) allowed us to observe the total force values required to achieve the reported accommodative amplitudes of the living human eye. We also mapped the total force on the lens for known accommodation amplitude values of all age groups. Our findings indicated that accommodative forces in the human eye decreased from near 0.5 N to near 0 N from 30 to 60 years old, respectively (Fig. 4.2b). Overall, our research provides valuable insights into the mechanical forces that affect the aging human lens during the accommodation process. This information can help in the development of treatments for age-related vision problems.

The human eye is a remarkable and intricate organ capable of adjusting its optics to focus on objects at varying distances. Accommodation, the process that enables us to focus on both near and far objects, involves changes in the shape of the lens. The ciliary muscle that surrounds the lens contracts, causing it to change shape and increase its refractive power. Prior research has attempted to estimate the forces required for this accommodation process. However, very few studies have been conducted on living human eyes, and previous research papers [49–52]have reported

varying total force values for young lenses. This study sought to investigate the estimated accommodative forces in living human eyes, with a particular focus on young lenses. The study's results demonstrate that the total force values for young lenses differ from those previously reported. For example, this study reports a value of 0.48 N for a 30-year-old eye, while the previous three studies reported a value near 0.1 N [49–52]. This indicates that our findings of total force applied to the lens to achieve the known accommodation amplitudes in young lenses (10-30 years old) is approximately 5 times higher than previously reported. These findings are significant as they provide new insights into the accommodative process of the human eye. They may also have implications for the diagnosis and treatment of certain eye conditions, as well as the development of new technologies for correcting vision.

FEA techniques are commonly employed to simulate the behavior of complex mechanical systems. However, the precision of these techniques is directly impacted by the accuracy of the mechanical properties used for the materials being analyzed. To achieve a realistic representation of the actual process, it is necessary to use precise values for mechanical properties, including Young's modulus. For an accurate FEA investigation of accommodative forces, one crucial mechanical property of the lens is Young's modulus. Prior studies relied on Young's modulus values reported by Fisher et al.. (1971) [54], but more recent research by Burd et al.. (2006) showed significant discrepancies in these values due to systematic errors in Fisher *et al.*'s (1971) study[36]. Our study utilized the updated and accurate Young's modulus values reported by Burd et al.. (2006) to achieve a more realistic FEA investigation of accommodative forces. This approach revealed a 5 times larger accommodative forces discrepancy between our study and the previous three studies, highlighting the critical role of using recent and precise mechanical properties data. In summary, for FEA techniques to be accurate, they require the use of precise mechanical properties values. The use of up-to-date and accurate values, such as those from Burd et al. (2006) for Young's modulus, is crucial for achieving a realistic representation of the process. Our study contributes to the advancement of FEA techniques for investigating accommodative forces by using the latest and most accurate data available[36].

The discrepancy in the reported accommodative forces can be attributed to two main factors. The first factor is the difference in the properties of the materials used between the previous studies and our current study. The previous studies used Young's modulus values of Fisher et al.. (1971) and other material properties that are different from those used in our study [54]. These differences in material properties can affect the results of the Finite Element Analysis (FEA) simulation, leading to discrepancies in the reported accommodative forces. The second factor is the differences in the implementation of the FEA simulation, specifically in meshing choices and applied boundary conditions. The previous studies used different meshing choices and boundary conditions than those used in our study. When we applied the boundary conditions used in Hermans et al. (2006) and the material properties used in Fisher et al. (1971), we found total accommodative forces of 0.23 N for a 30-year-old lens[51]. This force value is less than half of the force results of the current study and closer to theirs. Moreover, when Burd et al.. (2006) applied forces to the lens via three zonules, they used an asymmetric model for FEA[36]. In such models, material properties and boundary conditions must also be applied asymmetrically for more precise modeling. However, their choice of fixed support point was not ideal for such asymmetrical applications. To avoid such accuracy losses, our model avoided any asymmetric force applications and fixed support points. When a mesh convergence analysis was performed using oversized mesh elements, approximating the estimated meshing of previous studies, a decrease in the reported accommodative force values was observed. Although the mesh element size and number of nodes used in previous studies are not reported, the significant leap forward in FEA software and computational power since the previous studies led us to think that the number of nodes and elements used in this study was significantly higher than theirs. Such higher numbers of nodes and elements combined with a smaller mesh element size resulted in a more optimal modeling and higher accuracy of force magnitude detection. In conclusion, the discrepancy in the reported accommodative forces between our study and previous ones can be attributed to differences in the FEA modeling implementation, specifically in meshing choices and applied boundary conditions. The differences in material properties used in previous studies and our study can also affect the results of the FEA simulation, leading to discrepancies in the reported accommodative forces.

The data presented in Figure 4.2a demonstrates a loss of accommodative force, which raises the question of whether the stretching force applied to the lens by the zonules over time contributes to the loss of accommodation amplitude, in addition to the stiffening of the lens. To investigate this, we used our simulation results, combined with the known accommodation amplitude profile over time presented in Figure 5.1. By using the lens optical power results under various total force levels for all age groups, we generated a hypothetical accommodation amplitude graph over time under the assumption that the total stretching force on the lens remained constant at 0.5 N even after the age of 30. Figure 5.1a (blue line) shows the hypothetical plot, representing the change in accommodative amplitude over time obtained by our simulations using an assumed unchanged accommodative force of 0.5 N for all ages. If this assumption were correct, accommodation would have preserved an amplitude of 4 D, 3D, and 2 D at the ages of 50, 60, and 70 years, respectively. Figure 5.1a also shows the actual measured change in accommodation amplitude over time on the same plot (red line). By comparing the two, we marked the regions depicting the lost accommodative amplitude for both conditions. Our findings suggest that the loss of accommodative amplitude over time cannot be fully explained by the stiffening of the crystalline lens. While changes in the mechanical properties of the lens alone, if the total stretching forces remained constant over time, could not account for all of the accommodation amplitude loss, the unaccounted part of the lost accommodation amplitude after the age of 30 may be explained by diminishing stretching force application on the lens. Figure 5.1b shows the lost amplitude over time due to changes in two factors: 1) shape and mechanical properties changes (elasticity) of the lens (Le) and 2) decreased stretching forces applied to the lens (Lp). Our simulation results indicate that for the first 30 years, the loss of accommodation appears to be mainly (~5D) due to changes in the shape and mechanical properties of the lens. However, after the age of 30, decreasing accommodative forces also have a significant contribution (1D for 40, 3D for 50, 3D for 60, and 2D for 70 years old) to the accommodation amplitude loss. In conclusion, our study suggests that the loss of accommodative amplitude over time is a complex phenomenon that cannot be explained solely by the stiffening of the lens. The changes in the mechanical properties of the lens and the decrease in stretching forces applied to the lens both contribute significantly to the loss of accommodation

amplitude over time. These findings may have important implications for the development of treatments to mitigate age-related changes in accommodative function.



Figure 5.1: Change in accommodation amplitude over years from literature (adapted from [59] and change in simulated accommodative amplitude over years for a hypothetical case of total force applied to the lens of 0.5 N remaining constant for all ages (blue color line) (b) Loss of accommodation due to mechanical property changes of the lens (L_e , blue line) and due to decreased total stretching force applied on the lens (L_p , orange line).

Although simulation studies are a popular method for modeling biological tissue, they do have some limitations. One such limitation is the assumption that the material properties of ex-vivo biological tissue are not significantly different from those of living tissue. Essentially, this means that the tissue's properties are assumed to remain constant even after it has been removed from the living organism. In this

study, the researchers relied on mechanical material properties obtained from previous literature. They assumed that these properties were representative of the actual properties of the living eye, even if they were measured ex vivo. Essentially, they used data from previous studies to inform their own research. However, it is important to note that there may be differences between the mechanical properties of living human lenses and post-mortem lens tissue used for measurements in the literature. Such differences could be a potential source of error in the results reported in this study. Therefore, while the researchers attempted to use the most accurate and representative data available, they acknowledge that there may still be some degree of error in their results due to the limitations of their assumptions.

For this investigation, we utilized a technique of applying four external forces to extend the lens capsule outwards across the entire linear equatorial surface of each quarter. We found this method to be a sensible compromise between mirroring the actual force geometry exerted by numerous zonules and our chosen four-force geometry used on each quarter of the lens' complete equatorial line. This approach enabled us to keep the simulation straightforward and viable. For subsequent simulations, increasing the number of forces applied to the lens and having more subregions smaller than a quarter would aid in achieving more precise force estimations. Dividing the lens into smaller components and applying autonomous forces on each component would also reduce the geometrical underestimation errors of the forces.

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Appendices

Appendix A

Codes used for lens modeling

```
%% Nominal values for isolated human lenses from the
paper: Urs, Ho, Manns
% and Parel, 'Age-dependent Fourier model of the shape of
the isolated ex vivo human
%crystalline lens', Vision Research 2010
%for Age = 1:100
Age = 70;
A0=2.6466+(8.12E-03)*Age;
A1=0.2246+(1.71E-03)*Age;
A2=-0.97938-(2.97E-03) *Age;
A3=0.010573+(-3.49E-04)*Age;
A4=0.37993+(-2.63E-04)*Age;
A5=-0.032321+(1.66E-05)*Age;
A6=-0.16846+(6.92E-04)*Age;
A7=0.027934+(-9.56E-05)*Age;
A8=0.066522+(-4.23E-04)*Age;
A9=-0.014232+(1.73E-05) *Age;
A10=-0.021375+(1.86E-04)*Age;
i = linspace(1,1000,1000);
     phi = 2*pi()/1000;
     theta = i*pi()/1000;
     rho(i) = A0 + A1.*cos(theta) + A2.*cos(2.*theta) +
A3*cos(3.*theta)+...
```

Appendix B

Publications from the Thesis

Conference Papers

1. İnsan Gözünde Accomodative Kuvvetlerin Modellenmesi

Turhal Caliskan, L. N., Cıklacandır, S., Kocaoğlu, O. P., (2024, May). İnsan Gözünde Accomodative Kuvvetlerin Modellenmesi. 8th International Students Science Congress 2024

Journal Articles

1. Accommodative Forces in Aging Human Eye (under peer review)

Turhal Caliskan, L. N., Cıklacandır, S., Kocaoğlu, O. P., (04 April 2024). Accommodative Forces in Aging Human Eye. *American Journal of Ophthalmology*.

Projects

1. İnsan Kristal Merceğinin Modellenmesi Ve Sonlu Eleman Analizi (in the publishing phase)

Turhal Caliskan, L. N., Cıklacandır, S., Kocaoğlu, O. P., (September 2023). İnsan Kristal Merceğinin Modellenmesi Ve Sonlu Eleman Analizi. *Izmir Katip Celebi Universitesi Bilimsel Araştırma Projeleri Koordinatörlüğü*. Project Number: 2023-TYL-FEBE-0033

Curriculum Vitae

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2022–2024	İzmir Kâtip Çelebi University, Dept. of Biomedical Enginnering	
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Work Experien	ce:	
2020 - 2021	Chil Tıbbi Malzemeler (R&D Engineer)	
2020	Siemens Healthineers (Intern)	
2019	Metrosan Tıbbi Cihazlar (Intern)	
2019-2020	Nailtronics (Voluntarily Intern)	

Publications:

1. Estimation of Emotion Status Using IAPS Image Data Set

Yeşilkaya, B., Güren, O., Bahar, M. T., Turhal, L. N., & Akan, A. (2020, October). Estimation of emotion status using IAPS image data set. In 2020 28th Signal Processing and Communications Applications Conference (SIU) (pp. 1-4). IEEE. DOI: <u>10.1109/SIU49456.2020.9302223</u>

2. Accommodative Forces in Aging Human Eye (under peer review)

Turhal Caliskan, L. N., Cıklacandır, S., Kocaoğlu, O. P., (04 April 2024). Accommodative Forces in Aging Human Eye. *American Journal of Ophthalmology*.

3. İnsan Gözünde Accomodative Kuvvetlerin Modellenmesi (in the publishing phase)

Turhal Caliskan, L. N., Cıklacandır, S., Kocaoğlu, O. P., (2024, May). İnsan Gözünde Accomodative Kuvvetlerin Modellenmesi. 8th International Students Science Congress 2024.