Video Article

Simulating the Mechanics of Lens Accommodation via a Manual Lens Stretcher

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URL: https://www.jove.com/video/57162
DOI: doi:10.3791/57162

Keywords: Bioengineering, Issue 132, Lens Stretcher, Accommodation, Presbyopia, Biomechanics, Crystalline Lens, Modulus, Mechanical testing

Date Published: 2/23/2018

Citation: Webb, J.N., Dong, C., Bernal, A., Scarcelli, G. Simulating the Mechanics of Lens Accommodation via a Manual Lens Stretcher. *J. Vis. Exp.* (132), e57162, doi:10.3791/57162 (2018).

Abstract

The goal of this protocol is to mimic the biomechanics of physiological accommodation in a cost-efficient, practical manner. Accommodation is achieved through the contraction of the ciliary body and relaxation of zonule fibers, which results in the thickening of the lens necessary for near vision. Here, we present a novel, simple method in which accommodation is replicated by tensing the zonules connected to the lens capsule via a manual lens stretcher (MLS). This method monitors the radial stretching achieved by a lens when subjected to a consistent force and allows for a comparison of accommodating lenses, which can be stretched, to non-accommodating lenses, which cannot be stretched. Importantly, the stretcher couples to the zonules directly, and not to the sclera of the eye, thus only requiring the lens, zonules, and ciliary body rather than the entire globe sample. This difference can significantly decrease the cost of acquiring donor cadaver lenses by about 62% compared to acquiring an entire globe.

Video Link

The video component of this article can be found at https://www.jove.com/video/57162/

Introduction

Accommodation is the process by which the human eye is able to dynamically adjust the shape of its crystalline lens to see objects at far or close distances in sharp focus. Accommodation is an intrinsically biomechanical process. Upon neural stimulus, the ciliary muscles produce a force onto the ciliary body and to the zonule fibers that attach to the circumference of the lens capsule[1,2]. While there are different theories behind the biomechanics of accommodation, the most widely accepted is the Helmholtz hypothesis. According to the hypothesis, the lens is in a natural stretched state, corresponding to the thinnest shape of the lens which is optimal for the focus of distant objects. To change focus to closer objects, the ciliary muscles contract and the zonular fibers are relaxed. In turn, the lens thickens, increasing the anterior and posterior surface curvatures. This corresponds to an increase in dioptric power which is necessary for near vision, therefore, a shorter focal length[1].

The ability to accommodate is compromised over time via a condition named presbyopia. Affecting everyone by age 50, presbyopia makes the eye unable to dynamically change focus from far to close distances[3]. To combat presbyopia, current methods are passive including corrective lenses and bifocals. While increasing one's ability to focus on close objects at few planes, such passive treatments cannot restore the dynamic focus ability of the lens[4,5]. In order to treat presbyopia efficiently, or possibly prevent it, there is an ongoing need to better understand accommodation.

To study lens accommodation, a number of devices have been developed to simulate the phenomenon *ex vivo*[4,6,7,8,9]. Spinning disks were first introduced to monitor the stretching of the lens via centrifugal forces[8]. To more faithfully replicate the phenomenon, lens stretching devices were gradually introduced and innovated. Using a lens stretcher, Manns *et al*. characterized the force required to accommodate the lens while correlating such to lens power and equatorial diameter[9]. Current understanding is that the lens stiffens with age, resulting in a reduced change in lens shape in response to an equal force from the ciliary body[3,10,11,12].

Current lens stretchers often involve a complex setup, implementing electronics and programmable stretching rates, and requires the entire cadaver eyeball[6,7,10,13]. This requirement increases the cost per experiment to over $500.00 per eye and decreases sample availability. Here we present a method to replicate lens accommodation at low cost as the eye posterior totals around $200.00. While less sophisticated than many devices used today, the technique is much more cost effective and adoptable without compromising results. This method is centered around a manual lens stretcher (MLS) depicted in **Figure 1**, and uses a unique clamping system on the zonular fibers and a radial twisting method to expand the diameter of the lens. The physiological accuracy of the protocol is validated by the findings of Bernal *et al*., who studied the pathway by which the anterior and posterior zonular fibers are connected to the lens capsule[14]. Using the design of custom shoes which only require the lens, zonule, and ciliary body, we aimed to study lens biomechanics by replicating physiological accommodation.

Protocol

The following protocols are accepted under the University of Maryland's Institutional Animal Care and Use Committee as well as the Institutional Review Board. The protocols follow federal, state and local standards, and the guidelines set out by the University of Maryland Policy on Biosafety.

1. Dissection of Eye Sample

1. **Obtain an eye sample from local slaughterhouse or tissue bank. If an entire eye globe is obtained, immediately extract the lens, attached zonules, and vitreous.**
   NOTE: The specific details described below pertain to both porcine and human eyes.
   1. Using disinfected surgical scissors and forceps, cut and remove all excess tissue surrounding the sclera.
   2. Firmly hold the eye on its side and, using a razor blade, make a small incision along the side of the eye 3 mm away from the cornea. Make the cut deep enough to have reached the vitreous inside the eye.
   3. Using scissors, carefully cut further along the incision around the circumference of the eye. Avoid puncturing the lens. A representative image is shown in **Figure 2A**.
   4. Once the outside circumference of the eye has been cut, remove the posterior tissue of the eye using forceps. Isolate the lens, zonules, ciliary body, and the attached vitreous with forceps. A representative image is shown in **Figure 2B**.
   5. Using the scissors and forceps, remove excess vitreous so the lens can lay flat on the MLS.
      NOTE: In cases of corneal transplant, the corneal button is used in surgery and the remainder of the globe is available for research purposes. However, this partial globe can still be used in the tissue preparation of the lens stretcher setup. If only the posterior is obtained, only perform step 1.1.4–1.1.5.
2. Disinfect all used equipment post-dissection in 15% bleach solution for 30 min.

2. Trial Assembly of the Manual Lens Stretcher

1. Insert the 10 mm shoe bottoms and the corresponding shoe tops into the bottom plate of the MLS so there remains a 5 mm gap between the back wall of the shoe indent and the shoe itself.
2. Align the top and bottom plates, snapping the plates together; the device is now in the unstretched position.
3. Insert the plates into the plate case and the stopper screw into the hole located on the side of the bottom plate.
4. Insert the plate case into the base and place the wrench into the aligned indents.
5. Twist the wrench clockwise until it reaches the stopping screw to contract the shoes, and twist back counter-clockwise to return the shoes to the original unstretched position.

3. Mounting of the Lens

1. Insert the 10 mm shoe bottoms into the bottom plate in the MLS so that a 5 mm gap between remains the back wall of the shoe indent and the shoe itself.
2. Using curved forceps, place the extracted lens face up on the middle of the bottom plate so that the shoes are supporting the lens over the central hole.
3. Snap the corresponding top of the shoes into place, clipping only the zonules and the vitreous. Visually ensure that the lens stays as centered as possible on the bottom plate.
4. Repeat Steps 2.3–2.4.

4. Measurement of the Lens

1. Place an imaging system directly above the apparatus in order to capture videos and pictures of the stretching process. Be sure to include a ruler in the frame of the picture to accurately size and scale images in post-processing.
   NOTE: Any suitable imaging system is sufficient for this step; here we use a 12 megapixel, autofocusing smartphone one foot from the sample.
2. Firmly yet smoothly, rotate the wrench in the clockwise direction to stretch the lens. **Figure 3** shows representative images at the unstretched and stretched state.
3. After photographing the stretched lens, rotate the wrench in the counter-clockwise direction to restore the sample to its resting state.
   NOTE: It is imperative that the measurement of the lens is performed in a timely manner in order to minimize the dehydration of the lens.
4. Clearly photograph the final resting state of the lens.

5. Data Analysis

1. Upload the image to ImageJ and, use the "point" feature to select at least 40 points around the circumference of the lens as shown in **Figure 4A**. Use the "Analyze" → "Measure" option to yield the location of each selected point.
2. Fit (using software *e.g.* MATLAB) the location points in order to yield a radius and chi-square of the fit as shown in **Figure 4B**. Convert the pixel radius and error into metrics using the photographed ruler.
3. Perform paired two tailed t-test to comparing an individual lens before and after stretching from the MLS.

Representative Results

Porcine eyes, a common sample for studying presbyopia via lens stretching[4,15], were obtained, (n = 10) from a local slaughterhouse and this protocol was used to observe the accommodation ability of the lenses. **Figure 5A** shows the comparison of the porcine lens before and after stretching via the MLS. There was an average 0.19 ± 0.07 mm increase in lens radius when stretched (p <0.001), equating to a 4.2 ± 1.62% increase from the original radius. Accommodation is correlated with lens elasticity, therefore, the radial difference between unstretched and stretched position suggest the ability to accommodate. We found a consistent increase in lens radius post-stretching, which is in agreement with similar studies[16,17]. The consistency and relatively low deviation within the study further validates our protocol.

This protocol allows for the comparison of both accommodating and unaccommodating lenses. The greater radial difference between its unstretched state indicates a greater ability to accommodate. To further validate the protocol, we observed human accommodation abilities as a function of age. We tested a 21 year-old and a 60 year-old human eye (The National Disease Research Interchange, Philadelphia, PA). The results, as shown in **Figure 5B**, indicated a decrease in ability to accommodate with age. The 21 year-old lens radius increased by 0.22 ± 0.13 mm or 5.2% upon stretching compared to the 0.0059 ± 0.099 mm or 0.14% increase of the 60 year-old lens. It has been shown that human lenses progressively lose the ability to accommodate with age[3]. These results demonstrated a smaller difference between stretched and unstretched radius of the 60 year-old lens compared to the 21-year-old lens, indicating a loss of accommodation ability. The older human lens demonstrating a decreased ability to stretch is in agreement with similar studies on accommodation as a function of age[8,18,20].

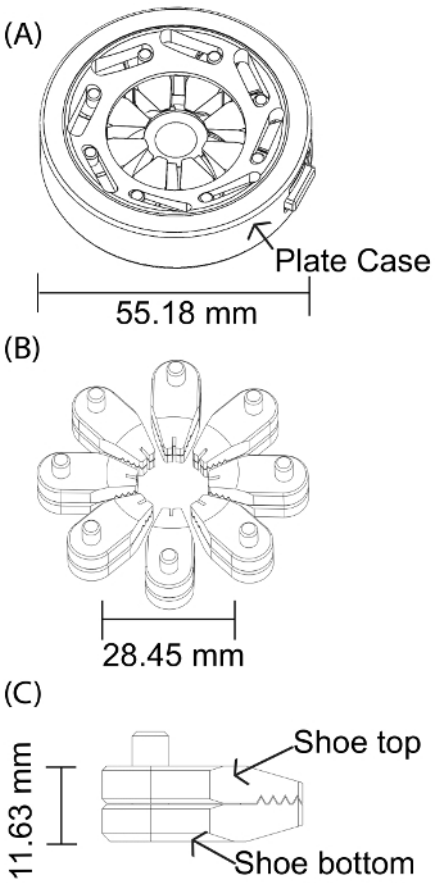

Figure 1: Schematic of the manual lens stretcher. (**A**) The assembled components of the MLS, including the shoes, plate case, upper plate, and bottom plate. (**B**) Representative diagram of the shoes radially connected to the sample. (**C**) Clamped shoe in which the zonules (not pictured) are attached and stretched. Please click here to view a larger version of this figure.

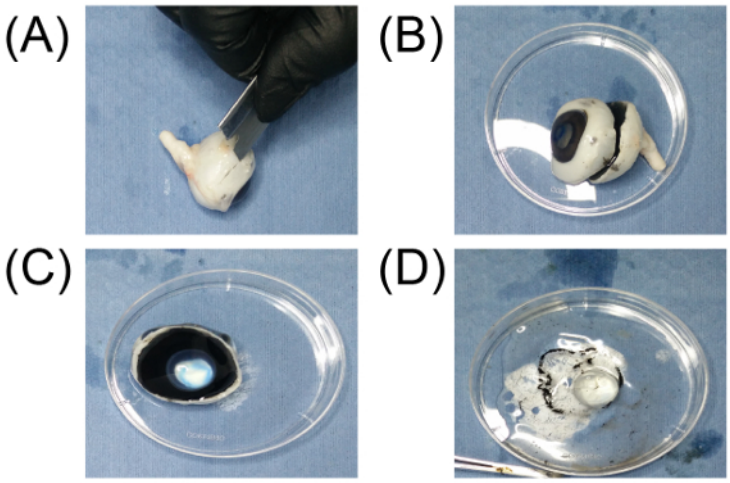

Figure 2: Representative images of dissection protocol. (**A**) The eye sample has been gathered and the first incision along the globe will be made approximately 3 mm from the cornea. (**B**) The eye globe has been correctly cut around its circumference. (**C**) The posterior sclera has been entirely separated from the globe**.** (**D**) The lens, vitreous, zonules, and ciliary body have been isolated from the globe. Please click here to view a larger version of this figure.

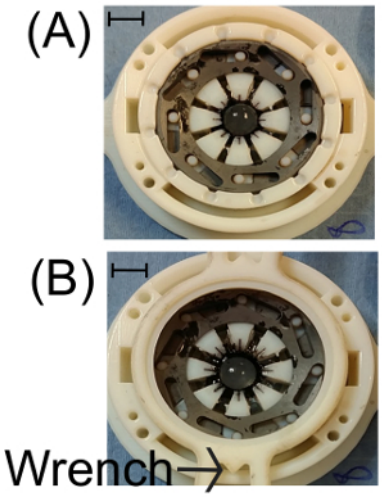

Figure 3: Representative image of the unstretched and stretched lens via the MLS. (**A**) The lens is held within the device, prior to wrenching, in its unstretched position. (**B**) The device is radially turned via the wrench, as the lens is stretched into its elongated position. Scale bar = 10 mm. Please click here to view a larger version of this figure.

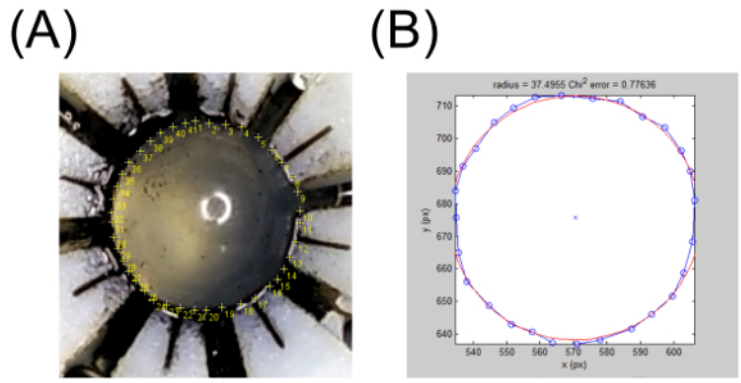

Figure 4: Representative images from the data analysis of lens samples. (**A**) 50 selected points were selected on the circumference of the lens sample using ImageJ software. (**B**) The calculated radius was 37.4955 pixels, and the chi-squared value of the fit was 0.77636 pixels. These results will change from lens-to-lens, and the pixels must be converted to metric units using the photographed ruler. Please click here to view a larger version of this figure.

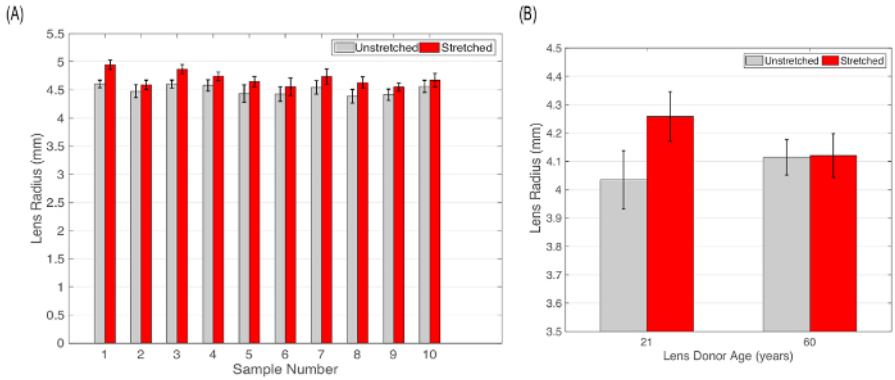

Figure 5: Lens radius before and after stretching via the manual lens stretcher. (**A**) The unstretched and stretched radii of 10 porcine lenses subjected to the MLS. (**B**) Representative graph of the measured radii of two human lenses, 21 years-old and 60 years-old, before and after manual lens stretching. The error bars in both part (A) and (B) represent the reported error in fitting the perimeter of the lens. Please click here to view a larger version of this figure.

Discussion

We have devised a novel method to provide an accurate and efficient way of studying the accommodation ability of the lens by utilizing a dual-piece clamping mechanism to couple the stretcher to the sample. During accommodation, the lens relaxes, and the diameter decreases in response to relaxation of the zonular fibers[1,2,4,19]. The method focuses on this phenomenon by clamping and controlling the tension of the zonular fibers. For this reason, critical care must be taken to clamp the zonules within the shoes to accurately simulate physiological lens accommodation. To ensure proper clamping, the lens should rest flat against the center of the bottom shoes with minimal vitreous attached. Additional care should be taken while wrenching to ensure equal radial stretching is performed around the circumference of the lens. If the lens stretching appears to be nonequivalent, or if the zonules become detached from the clamps, the sample must be remounted if possible.

Similar lens stretching protocols are currently being implemented to study accommodation and presbyopia[4,6,7,9,12]. However, these protocols are generally complex and expensive, requiring intricate machinery and software programming. Additionally, these techniques require entire eye samples at over $500.00 per experiment which further decreases widespread adoption. Our protocol increases feasibility by replacing the machine-programming with a manual lens stretching system and sample availability by only requiring a fraction of the sample. The needed posterior of the eye costs significantly less at $250.00 per experiment. However, there are some limitations associated with our protocol. As previously mentioned, misalignment of the lens or unequal zonule tension will result in an inapplicable stretching. Additionally, the wrenching force applied is not measured and thus relies on the consistency of the user to prevent unclamping or tearing of the zonules. If the zonules were to tear, the sample must be discarded as the MLS shoes would not be able to sufficiently clamp. Future efforts will focus on quantifying the applied force to ensure consistency and physiological relevance. In addition, the protocol involves the stretching to be increased until halted by the stopping screw. The stretching cannot, therefore, be altered or varied between samples and rather displays a binary fully stretched or unstretched state.

Preventing or innovating treatment for presbyopia is a focal point of ocular research, as the condition is currently inevitable and untreatable. However, the biomechanics of accommodation and presbyopia are not fully understood. The presented protocol allows for an accurate simulation of lens stretching during accommodation while requiring less sample material, device construction, and time. By increasing availability, the method allows for more laboratories to observe and study the biomechanics of lens accommodation.

Disclosures

AB has ownership interest in Bioniko Consulting LLC.

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