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A Proposed Method to Verify Physician Visual Estimation of Intraoperative Corneal Edema From Refractive Measurement Images During Cataract Surgery

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A Proposed Method to Verify Physician Visual Estimation of Intraoperative Corneal Edema From Refractive Measurement Images During Cataract Surgery

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ABSTRACT

A patient's resultant vision quality in a restorative Femtosecond Laser Assisted Cataract Surgery (FLACS) can be fine tuned via an intraoperative measurement of refractive power and axis of astigmatism in the aphakic state. Standard preoperative measurements often disagree with intraoperative measurements (Optiwave Refractive Analysis; Alcon, Inc.) on account of the inclusion or exclusion of posterior corneal curvature, leaving the ultimate lens selection to physician discretion. One additional suggested cause of disagreement is swelling at the corneal incision site. The following proposes a method to verify visual estimation of intraoperative corneal swelling from 2D gray-scale images collected during cataract replacement surgeries. Though sophisticated technologies employed in other refractive surgeries such as corneal pachymetry or optical coherence tomography (OCT) could accurately estimate corneal swelling, they are costly and time consuming to add to clinical practice. This method aims to establish the qualities of a good intraoperative image, and correlate physician-determined boundaries of edema with accurate intraoperative OCT measurements of corneal swelling. The relationship between these estimates and true measurements can contribute to better informing physicians whether noticeable bruising should change their weighting of intraoperative measurements when making an artificial lens selection.

CONTEXT & INTRODUCTION

The Cost and Incidence of A Cataract

The simple motivation of a cataract surgery is to replace a clouded, crystalline lens (cataract) with a powerful artificial prescription lens implant. Changes in the protein structure of the natural crystalline lens are age-related, and onset in most individuals' 40s, though typically only considered severe enough for surgical intervention later in life (Pescosolido et al. 2016). As part of an ongoing surveillance of population health (Vision Health Initiative), the Centers for Disease Control and Prevention conducted a literature review of the incidence of cataract in the U.S. population, finding that a cataract affects at least half of Americans over age 80 (2021). Sometime between those ages, cataract clouding becomes apparent and then severe enough for treatment. Treatment consists exclusively of a surgical intervention, suggesting a grave economic burden in cost-of-illness for the high incidence level of this disease state. A recent case study comparing the cost of cataract surgery in three different countries (normalized for purchasing power of the individual) found the costs borne by American patients to be approximately twice that of patients in two other countries. (Xue et al. 2021) In essence: a cataract is common, and expensive to fix. The frequency, cost and safety risks of this invasive procedure draw much attention to the accuracy and outcomes of the technologies and techniques employed during cataract surgeries. The technological advances mentioned in the following proposal (toric intraocular lens implant upgrades, femtosecond laser assisted incisions, intraoperative optical refractive aberrometry measurement, and software-based lens recommendation) currently bear additional costs to the patient on account of claims to superior vision outcomes and safety. These

technologies are opt-in procedure upgrades, and their outcomes and implementation are the subject of much controversy and evaluation in the ophthalmology literature.

The Aims of Modern Cataract Surgery

Embarking on any highly invasive procedure offers an unfettered opportunity to go beyond just treating the disease state, but also to fine tune and optimize other nearby accessible anatomies. In the case of lens replacement cataract surgery, visual imperfections due to the morphological failures of the nearby cornea (which are not corrected during surgery) can be counteracted by our choice of lens implant–two birds, one stone. A simple cataract lens replacement achieves its primary outcome with ease and consistency. Manual lens replacement surgery *restores* visual acuity for patients with a high success rate (80% or higher by any visual metric), and bears a very low risk of ending up with poorer resultant vision quality due to failure or complication (Norregaard et al. 1998; Steinberg et al. 1994). Manual surgery gets the job done well enough, but advancing techniques for lens selection and implantation offers major opportunities for the surgeon to *refine* secondary outcomes in postoperative vision results by correcting vision abnormalities not directly related to the cataract.

The replacement lens choice, amongst other corrective surgical incisions, has the potential to effectively reduce or eliminate a patient's need for prescription glasses after surgery. This is a very impressive outcome, and an expectation we want to get closer to guaranteeing for most individuals. This is especially true when we remember that the risks of undertaking this procedure are more complicated on the whole in our patient population due to risk factors related

to age, and age-related chronic conditions under management (Gaskin et al. 2017). The benefits to the surgery should be commensurate to that risk, and ever improving. This motivates the development of automations and techniques that improve or resolve these secondary visual problems.

The superiority of modern cataract surgery and all its combinatorial upgrades really lies in selling increasing degrees of (1) the quality and (2) the probability of improving the resultant *subjective* quality of vision, not just basic visual acuity (Skiadaresi et al. 2012; Roach 2013). Simply put, patients will pay for better results and they want it to be guaranteed. The problem is, a reported improvement in subjective quality of vision from patients is more difficult to achieve and to measure; relative to measuring our outcomes by demonstrating improvements in visual acuity from a baseline that is already severe functional impairment induced by cataract. By that logic, any implant will be better than nothing and our procedure will always be considered successful. Why measure ourselves this way, when we have the opportunity to aim for a vision quality that is better than it ever was? Modern technologies attempt to effect a good subjective result via faster, safer and more powerful implants. Minimally invasive surgical techniques (safety), measurements of power and irregularities that are ever more precise and accurate (probability/quality), and techniques for surgical correction of those irregularities (quality) are the bulk of the improvements to be made and sold. Verifications of these choice upgrade technologies are important as a means to advancing the quality and consistency of surgical results in the discipline. These verifications would also amount to a financial justification for cost equity and cost reduction upon demand, if the techniques are found to be accurate and effective. We must investigate their claims, and improve their methods to achieve these ends.

This is the motivation for the following verification.

One Verification in One Surgical Technology

We could investigate a number of verifications in measurement or technique for any one of the earlier cited surgical upgrades. A single advanced surgical technology may claim to contribute measurement and improvement to several dimensions of the surgical process and downstream results. This thesis builds upon prior research into the investigation of *one* confounding factor that may affect the value of *one* upgrade. The proposed experiment detailed in this paper is not carried out with the clinical data described, but is derived from a previously collected clinical data set. Proposed experimental aims and methods will be described in depth.

The technology we are looking to verify is called the Optiwave Refractive Analysis system (ORA, Alcon, Inc.), and it takes measurements of refractive power and axis of astigmatism via a light beam technique called wavefront aberrometry. ORA estimates the refractive (focusing) power of the eye by measuring micro changes in the movement of a light beam that is projected through the eye after the clouded lens has been removed, and calculates specific dimensions of visual irregularity (e.g. spherical power, cylindrical power, axis of astigmatism). The refractive power and axis of astigmatism measurements are only two values of many that can describe the strength and direction of visual irregularities present beyond the cataract-affected lens. They are directly related to prescription strength and lens placement of the intraocular lens implant (IOL). These intraoperative measurements will either confirm or contradict the prescription strength and suggested axis of the lens implant predicted by the

physician before surgery. Intraoperative aberrometry and preoperative biometry estimate the same variables (repeated measures), but often disagree. The difference between the intraoperative measurement and the preoperative measurement is that after the removal of the natural lens, ORA can also measure any irregular shape in the posterior corneal curvature of the eye–implying more accurate measurement estimations than preoperative biometry is capable of (Cionni et al. 2019). This disagreement results in a range of potential lens selections, and the final choice up to the discretion of the physician during surgery.

In previous research, we sought to determine whether bruising/swelling caused by the primary corneal incision and clearing of the lens demonstrates a patterned relationship with the magnitude of difference between intraoperative ORA measurements and preoperative measurements (Corley and Carmack 2020). Further, whether those differences correlated to a physician decision to change the resultant lens prescription from the preoperative prediction. More simply, would swelling during surgery make the intraoperative measurements significantly different, or less reliable? The investigation did not find statistical significance between the measurement disagreement and estimated size of wound edema. However, the retrospective analysis suffered a small sample size due to striking out certain image qualities, as well as some methodological concerns in accurately estimating and interpreting the extent of wound size edema from 2D gray-scale images collected from the ORA system.

Experimental Aims (Proposed)

The following method improves upon boundary selection and volume estimation of wound size edema from typical intraoperative images to support physician decision making in lens selection. The proposed experiment is motivated by the same questions as previous: does swelling at the incision site distort measurement during intraoperative aberrometry, and should that affect which repeated measure supersedes the other in suggestion of lens power/placement? This iteration of the experiment asks more specific methodological questions to verify the usefulness of these wavefront aberrometry images in clinical practice, such as: what are the best experimental methods to estimate corneal edema at the time of intraoperative measurement? Do estimations of the area of corneal edema from 2D intraoperative images correlate strongly enough to be a proxy measure for 3D volume of corneal edema? Given the same image and techniques, will a surgeon visually estimate corneal edema with some repeatability? Can we develop a severity rating for the presence of edema on these images?

Exploring sample images from the prior data set and processing them with image analysis software, a method is proposed herein to quantify corneal edema from ORA images. Supporting experiments are then proposed to verify the relationship between that estimation and its true values. The specific aims of the experiment are as follows:

- **Aim 1**. Establish the qualities of a good intraoperative image.
- **Aim 2.** Describe a method to calculate the 2D area of corneal edema.
- **Aim 3.** Determine the Lookup Table (LUT) contrast filters for which 2D measurements of corneal edema are most closely correlated with 3D volume measurements via corneal

pachymetry or optical coherence tomography (OCT).

- **Aim 4.** Estimate the relationship/consistency between 2D estimations of corneal edema demarcated by physicians and actual 3D measurements of corneal edema (volume)..
- **Aim 5.** Determine the standard error in physician annotation of the observable physical bruising boundary.
- **Aim 6.** Propose severity rating of edema with exemplar images.
- **Aim 7.** Describe and test the accuracy of physician determinations of severity of edema from novel intraoperative images, when trained on the proposed rating scale and exemplars.

The conclusions of the proposed experiment should establish best practices for experimentally estimating bruising via convenient optical wavefront aberrometry images produced during surgery. The accuracy of the relationships determined has the potential to inform physician intuition in visually estimating (‘eyeballing’) the extent of bruising before making a lens selection during surgery. Verifying whether these nonspecific images correlate to actual measurements of corneal swelling is the first step in determining whether noticeable bruising should change physician weighting of preoperative and intraoperative refractive power measurements. The implications of which could improve our understanding of the disagreement between these measurements, as well as post-surgical visual outcomes with better artificial lens selections (i.e. reducing pseudophakic refractive error) if bruising is determined to be a confounding variable in subsequent experiments.

IN-DEPTH BACKGROUND

Summarized in the prior section to contextualize the motivations of advancements in technologies for cataract surgeries, the following will detail the anatomy behind the aforementioned measurements (refractive power and axis of astigmatism), and the protocols behind lens implantation that prompt swelling.

The physical structures of the human eye are layered and cooperative in projecting an input image (visible light) onto the cells of the retina at the back of the eye to send to the brain. The individual function of any described sub-structure, and our measurement of that function, correlates to a sequential step of the passing or bending of that input light to focus the final image. Our measurements/rating of how well each inner ocular structure can refract light determine resultant vision quality. If we think of these inner structures as materials with ideal characteristics that we are quantifying on common numeric scales (e.g. diopters), we get a rough and intuitive understanding of where prescription lens values are derived from. We can compare these performance values between patients' unique physiologies and the ideal, and also between natural structures and their complementary artificial technologies (e.g. the artificial lens implant). Impaired function or altered characteristics of any one of the substructures in the human eye has unique effects on the clarity of our vision, which we describe with various medical diagnoses.

The anatomical structure affected by a cataract is the crystalline lens (or natural lens), and is that which we need to access surgically for artificial replacement. Its relative importance in resultant vision quality is high, surpassed only by the functional health of the innermost

‘detecting’ layer, the retina. The natural lens is located in the middle layer of the eye. (Appendix 1). Light processes through the eye towards the retina from the outer layer, the cornea, which bends incoming light through itself, then a fluid filled anterior chamber, then the aperture of the pupil, and finally onto the centrally located lens. The lens structure clearly and powerfully focuses this bent light onto the innermost retina. The characteristics determining the power of the lens and its contribution to resultant vision quality are two-fold, dependent on (1) the quality of its *transparency*, including the solubility of lens proteins and the orderliness of cortical lens fibers, and (2) proper accommodation of *shape* via strong ciliary muscle movements and softness/*elasticity* of the lens capsule (Ruan et al. 2020; Tripathi and Tripathi 1983; Appendix 2). These characteristics in part define the ideal, or emmetropic, eye–i.e. that which lacks refractive errors in either (1) refractive power or (2) accommodation.

The unique functional importance of the natural lens, compared to the similarly transparent and powerfully refractive cornea, lies in its accommodation abilities introduced above (American Academy of Ophthalmology).The lens plays a prominent role in how the eye deals with light at varying intensities and distances. It does so in coordination with inner structures upstream itself via changes in its morphology, or shape. Light occurring to the eye from far distances occurs less intensely, and more parallel to the eye than light from sources at close range, therefore less refraction/bending of the light at the lens is required to achieve a focal point. So the lens must change shape when perceiving near point objects to accommodate greater degrees of refraction for the close and angled light rays. It accomplishes this via vascular connective tissues called the ciliary body. (Aliancy and Mamalis 1995) A common and helpful analogy is to think of the biconvex lens shape as a lentil. The ciliary muscles prompt immediate

lens accommodation when they contract, reducing tension on the attached zonular fibers of the lens, causing the lens to thicken and round in shape. In this state, the lens is more exaggeratedly convex and powerful (Glasser 2010). When contracted, or plump, the focal length from lens to retina/focal point decreases (i.e. it is exercising more lens power), which allows nearer objects to come into clear focus. Perception at varied distances is also a function of the elasticity of the lens capsule. (Ziebarth et al. 2008). When ciliary muscles pull on the zonule fibers in the epithelial layer, the lens capsule and matter must conform in response to that tension. The softer and more pliable the layers, the more powerful and convex the refraction. It is well documented that the crystalline lens capsule and lens matter lose elasticity and become relatively stiffened in this accommodation as we age.

Irregularities in the structural characteristics of the lens (transparency and shape/elasticity) justify an artificial replacement surgery of the natural lens. When we understand that the function of the lens is compensatory and cooperative with other structures, we are also understanding that the resulting refractive power of the eye depends on the lens' relationships to other irregularities that are not necessarily resolved upon replacement. We return to the reasoning that the prescriptive power of our lens implant, and our chosen axis of placement are methodological opportunities to overcome the static irregularities in refractive power measured at points upstream of lens refraction.

Aberrations in the characteristics and function of the inner structures of the eye due to characteristic, morphological or biochemical causes are constantly being discovered, and attributed to known disease states even more frequently. Aberrations can be thought of as any

cause of visual irregularity. They happen when light is scattered instead of focused at one of the points of refraction. These irregularities drive resultant vision away from the ideal. Resultant image quality can be assessed at two points: the refractive quality of the image that makes it to the retina, and the perception of that image by the retina. The structures discussed herein address the refractive quality of the image that makes it to the retina, and concern any phenomenon that causes light scattering.There are several types of optical aberrations that can affect our vision. The natural lens has been shown to compensate for spherical aberrations and coma. (Berrio et al. 2010) Optical aberrations are typical of the aging process, and frequently imply the impaired function of the crystalline lens or its compensatory ability. For instance, the deterioration of the accommodation function explains the need for reading glasses as we age, pathologically called age-related presbyopia, or farsightedness (Xiang et al. 2021). Sources of aberration we are interested in are those that result in the pathological development of a cataract, but even more so we are concerned with auxiliary irregularities that can be corrected during lens replacement.

The following, step-wise techniques of FLACS can be thought of as having an orderly intention to access or segment layers of the eye with increasing depth until accessing the target layer: the natural lens (Ali et al. 2015). The surgeon will begin preparation for the operation with pupillary dilation and a topical anesthesia. Then, suction docking of the LenSx allows for clear imaging of the depth of each layer of the eye, called anterior segment imaging. Taking this extra assistive step to measure the optical depths for the individual ensures precise incisions, limits risk to damage of the iris, and also risk of posterior capsular ruptures. Corneal and limbal relaxing incisions are planned and adjusted, and the femtosecond laser is delivered to make a circular cut called an anterior capsulotomy, followed by pie slice cuts called phacofragmentation.

These incisions guide the surgeon in the next steps. The surgeon then manually removes the clouded cataract lens using an ultrasonic probe (phacoemulsification) to break up lens tissue and suction it out. This is called nuclear disassembly and cortical cleanup. At this point, intraoperative wavefront aberrometry measurements referred to in this methodology would be confirmed before lens implantation. At this point, trauma to the corneal tissue has initiated the onset of corneal swelling at the incision site, and may be visualized by the aberrometer. After confirming measurements of refractive power and axis of astigmatism, the surgeon makes an intraocular lens implant (IOL) selection, and implants it on the suggested axis.

EXPERIMENTAL METHODS (PROPOSED)

Corneal swelling tends to creep into the anterior measurement field of the intraoperative aberrometer. There is no prior methodology noted in the literature estimating wound size edema from images taken during wavefront aberrometry. The following method suggests practices for estimating wound size edema from the imaged field of view of the aberrometer, and verifying whether this 2D area correlates with paired, reliable 3D measurements for volume of corneal edema.

Aim 1. Establish the qualities of a good intraoperative image.

First, we must establish the qualities of intraoperative images (Figure 1) that are suitable for our experimental analysis. All images of eyes that have undergone previous refractive surgeries (e.g. LASIK) shall be excluded from the data set. The qualities of a good image are

somewhat subjective, but most importantly the circumference of the standard capsulorhexis (4.7mm) must be imaged without significant deformities in curvature (Figure 2). The diameter of this measurement is the precise standard from which we will estimate the scale of the image during our measurement analysis. In such an image, we might observe a compressed or stretched incision boundary along different axes (Figure 3).

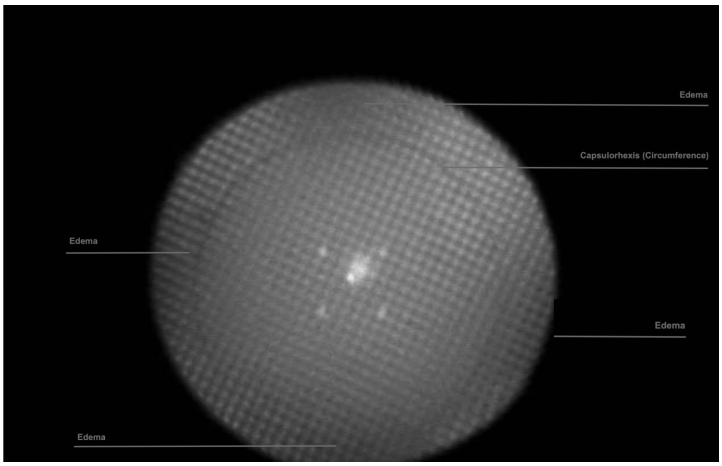

Figure 1. Intraoperative ORA image capturing the aphakic eye. Swelling at the corneal incision site indicated by shadowing anterior to the site of capsulorhexis, demarcated by the visible circumference. [Exemplar 1]

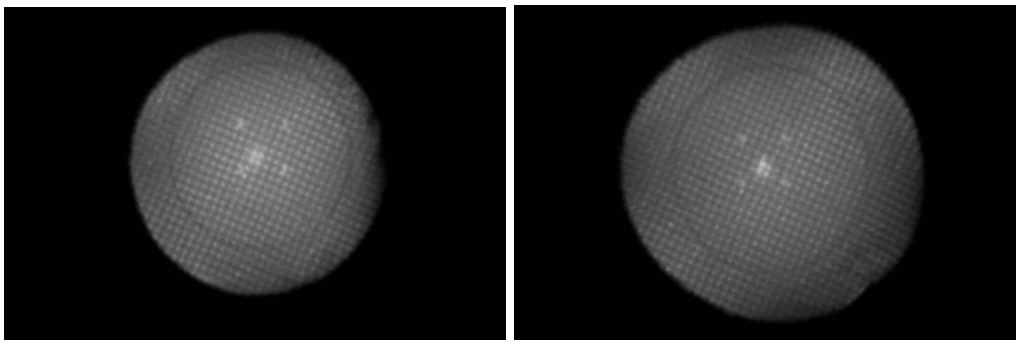

Figure 2. Two examples of intraoperative ORA images where acceptable, intact circumferences of the capsulorhexis. [left: Exemplar 2, right: Exemplar 3]

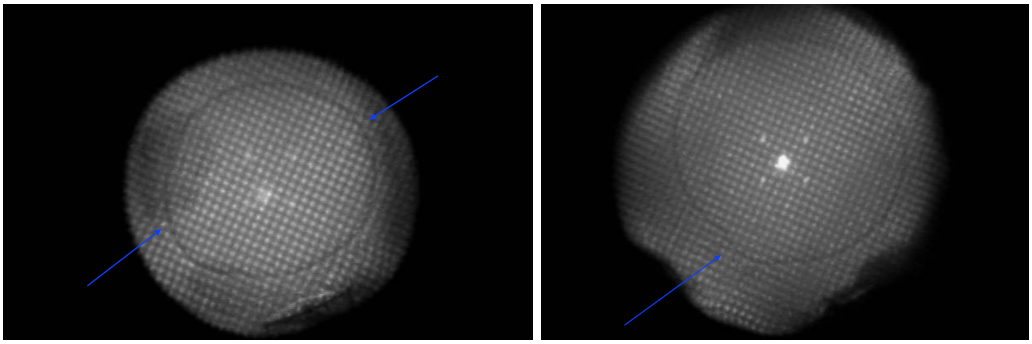

Figure 3. Two examples of intraoperative ORA images where unacceptable, deformed circumferences of the capsulorhexis are observed, specifically indicated by arrows. [left: Exemplar 4, right: Exemplar 5]

Aim 2. Describe a method to calculate the 2D area of corneal edema.

We can accomplish all of our image measurement and annotation tasks using an image analysis software designed for biological specimens: ImageJ. The field of view and magnification of each image changes between patients, therefore we must standardize the scale of our image via the known diameter of the capsulorhexis. The boundary of incision at the site of capsulorhexis is clear across image samples, allowing us to set an image-specific reference scale by measuring the diameter of capsulorhexis in the aphakic image in pixels marked by a straight line annotation tool (Figure 4). We can define each image's actual reference scale by setting the ratio of length of pixels measured across the image diameter of the capsulorhexis to the known 4.7mm diameter. For Exemplar 1, the scale is approximately 198.12 pixels per millimeter. An alternative to this measurement technique that may offer more accurate diameter measurement would be to fit a circle shape onto the circumference of the incision, and allow ImageJ to analyze.

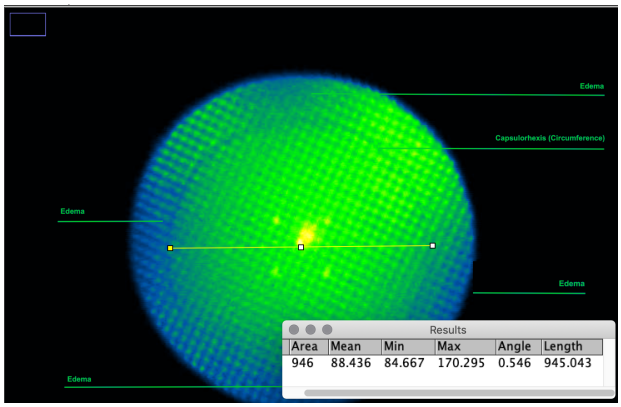

Figure 4. Diameter (pixels) of the capsulorhexis is measured using the ImageJ Analyze > Measure 'Length' function on a straight yellow line fitted onto the intraoperative image. [Exemplar 1]

After setting the scale of the image, we can estimate the 2D area of corneal edema. Corneal edema is represented in the sample intraoperative ORA images by a gradient of shadowing about the circumference of the capsulorhexis. There are several methods by which we can demarcate and measure the 2D area of the gradient, each for which it will be important to visualize the shadowing in high contrast. By applying various Lookup Table filters that assign a preset color value to corresponding gray scale values, we are able to first better distinguish the boundaries of edema in plain sight (Figure 5).

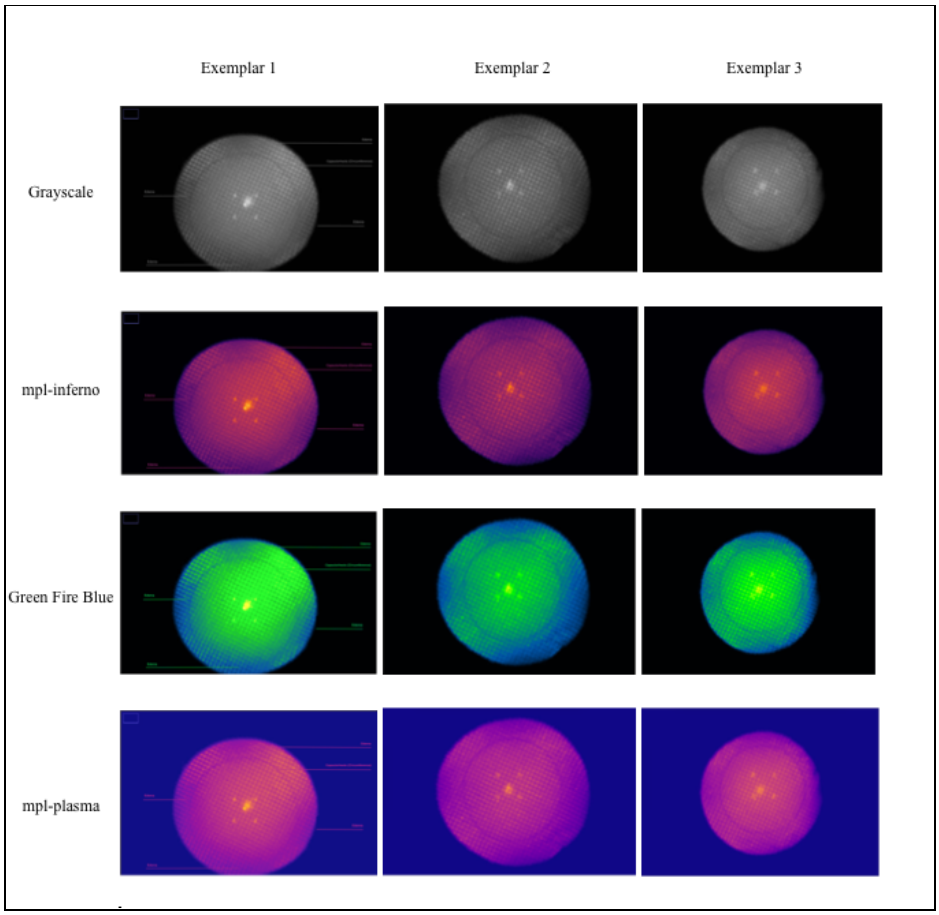

Figure 5. Acceptable intraoperative ORA images [Exemplars 1-3] filtered via several ImageJ LUT filters noted along the vertical, with original annotated grayscale images for reference in the first row. Shadowing representing the intensity of corneal swelling is better visualized by a high contrast filter.

From there, we may examine strategies for boundary demarcation and area selection. We will only measure shadowing anterior to the circumference of capsulorhexis. The shadowing representing wound swelling is not easily demarcated, but we can take advantage of the color scale LUT filters to set boundaries both by fitting shapes with manual annotation tools, as well as using automated tools to select areas based on color thresholds. In the following figure, three

types of manual area selection tools are demonstrated on Exemplar 1: freehand selection, multipoint polygon selection, and elliptical selection. They correspond to measured areas of 416.48mm (82513 pixels), 451.42mm (89436 pixels), and 548.67mm (108703 pixels), respectively. The marking of these boundaries for subsequent experimental aims will be physician-determined. Weaknesses observed in the usability of the selection tools included difficult handling with freehand selection, and nonspecific boundary overhang for elliptical selection. The multi select polygon tool appears to have the best handling in control over placement, and would be the manual technique of choice for the following proposed experiments. From multiple selections and measurements of shadowing about the image, we can estimate the 2D area of corneal edema as a percentage of the total field of view.

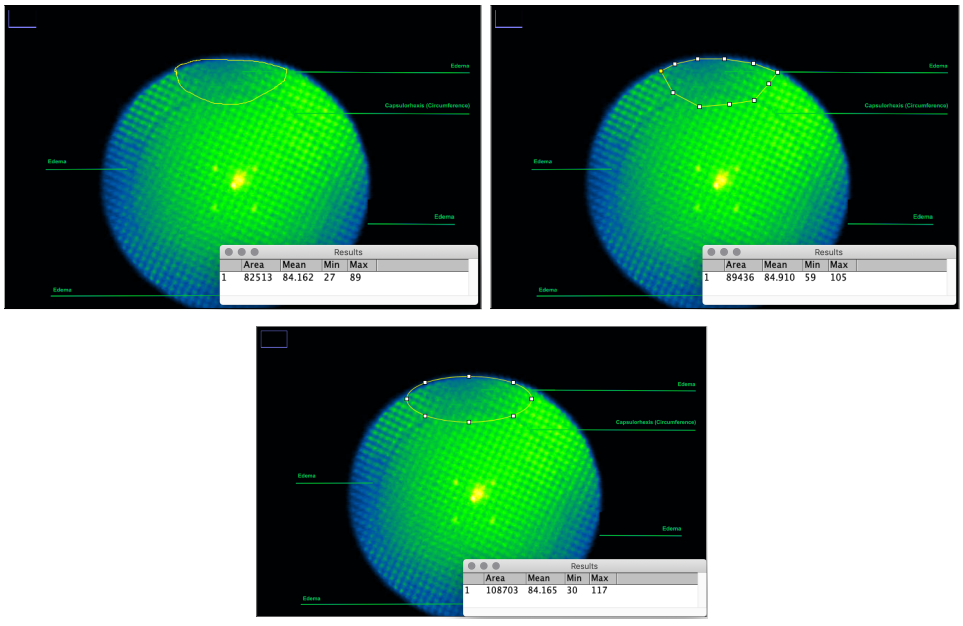

Figure 6. The high contrast boundary of wound edema at the upper vertex in the field of view is demarcated using freehand selection (upper left), multipoint polygon selection (upper right), and elliptical selection (bottom). Measurements of the selected areas are represented in pixels in the bottom right popup window. [Exemplar 1]

Thinking back to choices in LUT filters, the Green Fire Blue filter appears to show the most apparent boundary distinctions of corneal swelling across sample images (Figure 5). This distinctive appearance has utility insofar as one individual's experimental analysis, but it should be noted that specific color gradients may not be as distinctive to surgeons with certain forms of colorblindness in clinical practice nor in subsequent experiments measuring the accuracy or repeatability of boundary determination by physicians. To that end, we will examine more automated color threshold determinations.

Automated demarcation techniques are limited in their accuracy by the grid artifact overlayed on the image, preventing a true gradient effect for precise color threshold measurements. While using a Gaussian blur filter on the image could smooth this artifact, it may remove or distort information at the fine boundaries of edema. The raw aphakic image can still be processed with a finer distinction rule by applying a high contrast LUT filter distinctive to the viewer, converting the image to red-green-blue (RGB) and adjusting the boundary selection via the Color Threshold tool until we achieve best fit. This tool allows us to select every pixel satisfying our threshold rule for the color space based on RGB values (Figure 7), or alternatively, Hue, Brightness, and Saturation values (HBS). Though seemingly stronger as a measurement technique than strictly manual demarcations, the relative weakness of this measurement technique lies in viewer detection of the boundary, omitting areas due to the grid artifact, and potentially counting pixels within the boundary of the capsulorhexis.

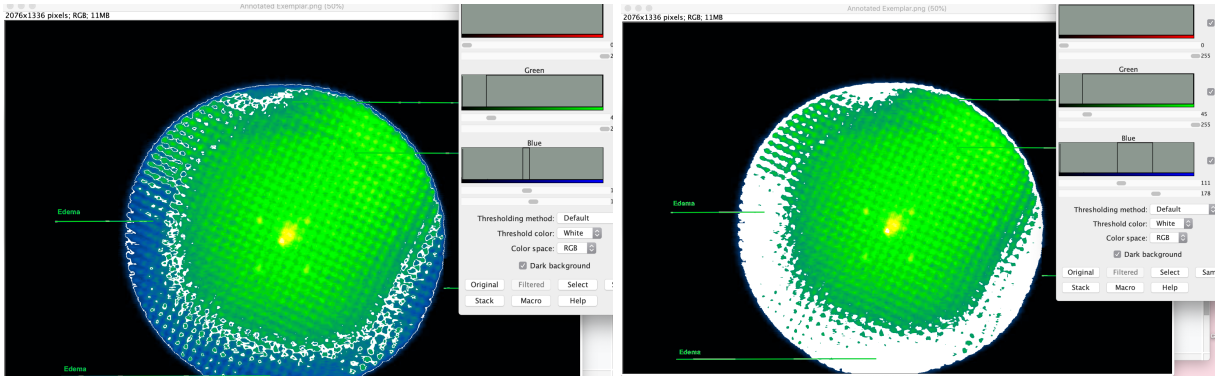

Figure 7. The high contrast boundaries of wound edema are demarcated by white color fill based on the RGB threshold selections in the popup. Areas of swelling are selected throughout the field of view (right), allowing for finer distinctions at the boundaries of shadowing via rules applied to every pixel (left). [Exemplar 1]

Aim 3. Determine the Lookup Table (LUT) contrast filters for which 2D measurements of corneal edema are most closely correlated with 3D volume measurements via corneal pachymetry or optical coherence tomography (OCT).

As previously discussed, sophisticated tools are available for intraoperative measurement of central corneal thickness. All of these measurement techniques are appropriate surrogates for direct measurement of corneal edema, each relying on assumptions about changes in various dimensions of tissue measurement (e.g. thickness, density) to draw conclusions about the extent of fluid swelling in the eye. Either pachymetric or optical coherence tomography (OCT) measurements of corneal volume shall be collected preoperatively, and again intraoperatively. Their absolute difference shall be calculated and considered an accurate proxy for volume of corneal swelling.

These precise measurements can be correlated with previously described 2D techniques for measuring corneal edema from these images to determine whether a strong relationship exists

between edema estimated from the nonspecific images, and that of a reliable measurement. The resulting correlations will be described between a single estimation of corneal edema via precise intraoperative techniques, and several estimations of corneal edema stratified by the LUT applied to the image, and one of the two techniques for measurement estimation described.

Aim 4. Determine the standard error in physician annotation of the observable physical bruising boundary.

It is also of importance to this experiment that a surgeon physician is able to replicate their own determinations of corneal swelling boundaries. Sample images provided by the ORA technology should be annotated by a group of physicians using the best practice determined via Aim 3, and estimated area of corneal edema shall be calculated and recorded for each image. The order of those same images should be randomized, and at a later time point, provided to physicians for repeated annotation. The standard error between their estimations should be calculated for each image. From those absolute differences, the average standard error of estimation shall be calculated for each surgeon individual, and also described across a group of physicians of similar experience level.

Aim 5. Estimate the relationship between 2D estimations of corneal edema demarcated by physicians and actual 3D measurements of corneal edema (volume).

The most important verification to support the proposed method is describing the relationship between the best combinations of techniques for methodological estimate of the area

of wound edema developed here, and the accurate measurements collected via pachymetry or optical coherence tomography. The strength and direction of this correlation shall determine the extent to which 2D images are good estimators of true corneal swelling during surgery.

Aim 6. Propose severity rating of edema with exemplar images.

If a significant relationship exists between the 2D estimates of corneal edema and the more accurate 3D measurements, exemplar images should be gathered and categorized by severity in the incidence of wound swelling. These general groupings should correlate to thresholds informed by measured wound size edema.

Aim 7. Describe and test the accuracy of physician determinations of severity of edema from novel intraoperative images, when trained on the proposed rating scale and exemplars.

The usefulness of this methodology on its own rests on the resultant ease and veracity with which a surgeon might identify the severity of intraoperative wound edema from a simple visual assessment of the 2D intraoperative images. To verify this, a test must be performed to determine the efficacy of the severity rating system itself in assisting physicians during surgery. The test would compare an experienced femtosecond laser cataract surgeon with some counterfactual. The ideal counterfactual for this group of surgeons would be inexperienced surgeons trained on the surgical methodology and severity rating. The literature indicates that procedural efficiency is lower among physicians inexperienced with FLACS technologies, even

if postoperative vision results remain comparable (Pittner and Sullivan 2017). Therefore, such a group of resident physicians could be an effective control group to measure the effects of training via visual based severity ratings. Their group has comparable physiological expertise, but enough relative inexperience to verify the value of these severity ratings in clinical practice.

DISCUSSION

The motivations for estimating corneal edema in prior literature regarding cataract replacement patients relates largely to postoperative complications and patient satisfaction. Measurements take place well after onset of edema, most often post-surgically. This paper offers a methodology to more rigorously process images that are available from cataract replacement surgeries assisted by intraoperative wavefront aberrometry, imaging the onset of corneal edema. The method establishes best practices for analyzing images taken from wavefront aberrometry in a novel way to estimate corneal wound edema. Further, it verifies which technique choices (color filters, measurement tools) are true to the real values of intraoperative corneal wound swelling. Verifying consistency in the wound boundary estimation amongst surgeons confirms reproducibility, and gives reason to develop a severity rating that can be implemented in the clinical setting.

Development and improvement upon novel estimations from these images underpins the validity of future attempts to correlate visualized intraoperative corneal wound swelling with any choices, techniques or outcomes during FLACS. Further, a verification of the method proposed herein against reliable pachymetry or tomography estimations in small, supporting experiments

could broaden the tools available for intraoperative wound estimation for future experimental purposes in clinical data sets/settings lacking multiple measurement technologies.

The conclusions of the proposed experiment would establish best practices for experimentally estimating bruising via convenient optical wavefront aberrometry images produced during surgery. The accuracy of the relationships determined has the potential to inform physician intuition in visually estimating ('eyeballing') the extent of bruising before making a lens selection during surgery. Verifying whether these nonspecific images correlate to actual measurements of corneal swelling is the first step in determining whether noticeable bruising should change physician weighting of preoperative and intraoperative refractive power measurements. The implications of which could improve our understanding of the disagreement between these measurements, as well as post-surgical visual outcomes with better artificial lens selections (i.e. reducing pseudophakic refractive error).

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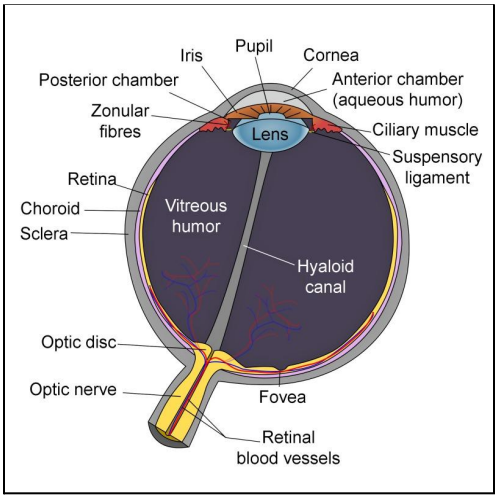
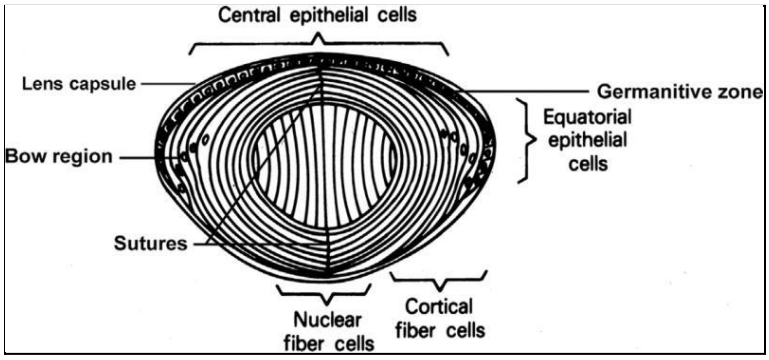
APPENDIX



Appendix 1. "Schematic of eye anatomy including the optic disc, optic nerve, fovea, sclera, choroid, vitreous humor, hyaloid canal, retina, zonular fibers, iris, pupil, cornea, ciliary muscle, and suspensory ligament." (Omari 2021)



Appendix 2. "Overview of the Lens" (Hejtmancik and Shiels 2015)