Ocular Cellscope

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This **Masters Project Paper** fulfills the Master of Engineering degree requirement.

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Masters of Engineering Final Report

Christopher Echanique

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This report covers some of the work done by the master's students on the Ocular CellScope Project. The methods and results of mobile application design will be emphasized because it was the work directly performed by the author.

Abstract

Globally, 314 million people are visually impaired, with 87% of this affected population residing in developing countries [1]. Glaucoma, macular degeneration, and diabetic retinopathy are all leading causes of blindness in the United States. These diseases require routine eye exams for their effective diagnosis and management. Identifying eye diseases at an early stage is crucial to preventing the condition from worsening and causing permanent vision loss. However, the high cost of retinal imaging equipment is often prohibitive for many clinics around the world and many people forgo necessary eye exams. Thus, low-cost handheld retinal imaging tools which could be used at home, in a primary care clinic, or a pharmacy, would dramatically expand access to eye examinations. We present Ocular CellScope, a mobile ophthalmoscope device that leverages smartphone technology to effectively capture retinal images and manage patient records. Our system is the second design iteration of the existing prototype, addressing a number of usability issues associated with the lack of an integrated mobile application and ergonomically friendly design. It features an advanced optical lens attachment for the iPhone built with a custom illumination system. A mobile application has been designed to capture, store, and review retinal images, as well as record patient information. Our device is capable of producing high-quality retinal images comparable to that of high-end retinal imaging equipment currently on the market and is priced at a significant fraction of the price of current competitors.

Introduction

The diagnosis and monitoring of retinal diseases such as diabetic retinopathy, macular degeneration, and CMV retinitis has been a key focus in the field of ophthalmology. The use of medical equipment with retinal imaging functionality has been a significant factor in the diagnosis of these eye diseases. Since the introduction of such equipment in the late 19^{th} century, technical improvement of retinal imaging has been steady [1]. Retinal imaging devices known as fundus cameras are most commonly used in ophthalmology clinics to provide a full evaluation of a patient's retinal health. However, despite the extensive functionality of these devices, their limitations including cost, size, and accessibility have given rise to the emergence of different imaging methods that address some of these issues. These new advanced ophthalmoscopes aim to provide retinal imaging on mobile platforms at low costs, yet trade off the advanced functionality of traditional fundus cameras. The goal of Ocular CellScope is to bridge this gap between the functionality of fundus cameras and the low cost of mobile ophthalmoscopes that seems to be lacking in the competitive landscape. Our mobile phone-based device is the second design iteration of Ocular CellScope, which leverages the compact size, high-resolution camera, large data storage capacity, and wireless data transfer capabilities of current mobile devices to capture retinal images for diagnosis and monitoring. The features of Ocular CellScope challenge competing products on the market and our deployment of this device into the market of developing countries such as Thailand will help target a need for these low-cost fully featured retinal imaging devices.

Literature Review

The current gold standard in retinal imaging is the tabletop fundus camera. These stationary devices found in ophthalmology clinics offer a wide array of advanced features for imaging the fundus of the eye. Such features include high-resolution retinal images, non-mydriatic imaging, large retinal viewing space (45 degrees), software interface for file storage and image analysis, and advanced software functions like auto-focus, auto-stabilization, and image stitching. Dozens of fundus camera models have been introduced to the market. Among the most widely used devices are the Canon CR-2, the Centervue DRS, and the Nidek AFC, which offer their own set of features in addition to the ones above. The Canon CR-2 model offers digital filter processing to enhance screening exams, and low flash photography for improved patient comfort, and a lighter weight (33 lbs.) design for increased portability [2]. The Centervue DRS model also offers a fully automated design requiring minimal operator skill, web connectivity for image transfer to a network, and software features for auto-sensing, alignment, and focus [3]. The Nidek AFC is one of the most comprehensive devices in that it offers all of these features in addition to an "autostereo" feature, which provides a serial analysis useful for the diagnosis of diseases such as Glaucoma [4]. Despite the large number of advanced features available, fundus cameras suffer from several drawbacks. Cost is the primary limitation, with most of these devices ranging from $10,000-$20,000 per unit. This price point is significantly higher than other types of retinal imaging devices on the market. Also these devices are much larger and heavier than their mobile counterparts, requiring a stationary setup for patients to sit upright for exams. This can pose issues for sick and hospitalized patients. These drawbacks make it difficult to compete in a market focused on low cost mobile retinal screenings as well as limit its presence in markets of developing countries.

Mobile ophthalmoscopes, on the other hand, have entered the market in recent years to provide a low cost portable alternative to expensive stationary fundus cameras. These devices can be categorized into two types: the standard ophthalmoscope and the mobile digital imaging ophthalmoscope. The standard ophthalmoscope is a handheld device with an optic lens and illumination used for simple viewing of the retina. One such device is the Keeler Standard Ophthalmoscope, which features an adjustable focusing lens, an aperture selection disc for dilated and undilated pupils, and a red-free filter for easy identification of retinal features [5]. These devices have the lowest costs on the market, with prices ranging from $100-$200 due to their simple design and basic functionality. However these devices are not as practical for retinal screening since they lack digital retinal image storing and thus require a trained physician to perform the exam and diagnosis. The second type of device mentioned is the mobile digital imaging ophthalmoscope, which categorizes our Ocular CellScope product. The newest of all types of retinal imaging device types available, this type has the least number of models on the market. The largest competitor to Ocular CellScope is the Welch Allyn iExaminer System. This system features a mobile PanOptic Ophthalmoscope with an iPhone adapter and integrated iExaminer App to capture, send, and store retinal images as well as record patient information [6]. The device has a 25-degree field of view and a patented anti-glare system to reduce unwanted glare in images and is valued at $1000. The ease of use, portability, and cost of this device make it practical for use in retinal disease screenings, however this systems faces a number of drawbacks. The main limitation is the 25-degree field of view it provides. Traditional fundus cameras offer 45 degrees, which is at times necessary for a complete diagnosis as some diseases depend on the outer regions of the retina. Also this system lacks a low-intensity illumination option for patient comfort during exams and offers no hardware controls or web connectivity in the iPhone application.

The Ocular CellScope device aims to address these limitations associated with both stationary fundus cameras and mobile ophthalmoscopes available on the market. The device provides an attachment to the iPhone similar to the Welch Allyn iExaminer system. However, the device’s illumination system will be fully integrated with the iPhone via Bluetooth to allow user control. The system also features a set of fixation lights to capture designed regions of the retina to provide a retinal field-of-view of approximately 55 degrees [1]. This is a drastic improvement from the 25-degree field of view offered by the iExaminer system. In addition, the mobile application allows the user to not only store patient information and retinal images but also upload this data to a web server for access by designated physicians. These added features will compete with the functionality of stationary fundus camera and existing mobile ophthalmoscopes, but at a price point on the order of $1000. The device will allow for a completely portable and inexpensive solution for retinal imaging that could be used both in the hospital setting and for community vision screening.

Methods

1. Initial Prototype

The initial Ocular CellScope prototype (shown in Figure 1) consists of a 3D-printed enclosure housing the optic lens and illumination system, which is powered by a 9V battery. A slot designed to fit the iPhone 4/4s models aligns the back camera of the iPhone with the optic lens of the device used to enhance the retinal image view. A switch on the back side of the device toggles power to the white LED of the illumination system and a knob adjacent to the switch controls the intensity of the light. Retinal images are captured using the native iPhone camera application while the light switch is powered on to illuminate the retina.

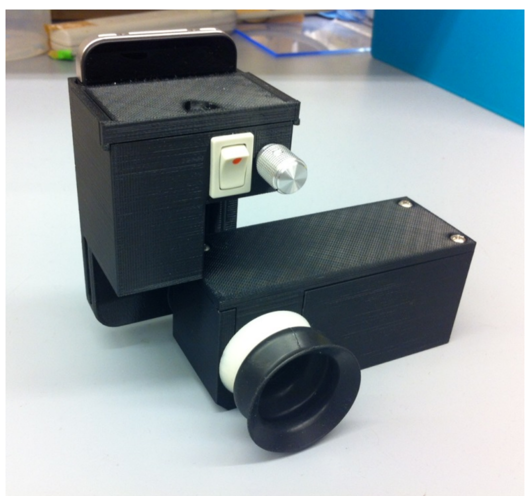


Figure 1. First Ocular CellScope Prototype

2. Prototype Feedback

Field-testing the initial Ocular CellScope prototype in Thailand unveiled a number of usability issues. These issues mainly stemmed from the lack of an integrated mobile application, which made common ophthalmologic screening tasks difficult for the clinical technicians using the device. The lack of a mobile application forced technicians to rely on the iPhone's native camera application to capture retinal images with the initial prototype. This approach was troublesome due to the fact that all images from the native camera application are stored in a centralized photo library on the phone, making it difficult to parse by patient. Technicians took images of the patient's paper medical record to mark the beginning of the retinal image set for that exam screening. They expressed frustration in trying to separate patient data for review. Additionally, the bulky nature of the prototype device made it difficult for technicians to operate with one hand. Since the native camera application required the user's touch to capture images, this led to awkward repositioning of the device during image capture and often times resulted in blurry images as clinicians readjusted. These poor quality images were also due to the inability to lock the iPhone camera's focus, causing the autofocus feature to result in nondeterministic image acquisition times. Furthermore, the technicians lacked a platform to digitally record patient information and link this to the set of acquired images.

Patients being screened also issued a number of complaints with the device. Many patients expressed discomfort with the intensity and duration of the white LED upon image acquisition. The hard switch design of the illumination system made it difficult for technicians to rapidly turn the light on and off to simulate the speed of a camera flash, exposing patients to the intense white light for longer than tolerable periods. In addition, the asymmetric L-shaped design of the device obstructed the patient's face during retinal imaging of the left eye as part of the device enclosure extended toward the patient's nose.

3. Second Design Iteration

Hardware

The feedback obtained from technicians and patients has helped guide the redesign of the device hardware for the second prototype iteration of the Ocular CellScope device. The hardware redesign focuses on three main subsystems: the illumination system, the fixation light system, and the enclosure redesign. For the illumination system, a red LED is incorporated to allow technicians to focus on the retina between image acquisitions, allowing for improved patient comfort due to reduced retinal sensitivity. In addition, an external fixation light system is added to the hardware to provide patients with a region to focus their eyes during screenings and allow for a wider degree of retinal imaging space. Lastly the design of the enclosure is enhanced to provide a more ergonomic feel for both the technician and the patient.

Software

User feedback from the initial prototype has also inspired the creation of an iPhone application adapted for the device hardware and user. After an analysis of the competitive landscape for ophthalmoscope-based mobile applications, particularly the Welch Allyn PanOptic iExaminer application, this application has been designed to mimic a similar workflow for image acquisition and patient data storage. The application focuses on providing a structured workflow for the technicians to follow by allowing technicians to enter patient information, capture a set of retinal images for each eye, and persistently store this data on the phone for later access. Features have been added to mitigate the problem of poor quality images, such as locking the focus during image acquisition and capturing a series of images over short intervals, similar to that of the iExaminer application. The primary difference between the two is that the Ocular Cellscope application is integrated with the illumination and fixation light system through Bluetooth. This allows the phone to control the device's hardware components wirelessly and alleviating the burden of manual control, a feature that the iExaminer system lacks.

Results

1. Hardware Solutions

The first hardware design change in the next design iteration of the Ocular CellScope was the addition of red light focusing into the illumination system. The initial Ocular CellScope prototype uses three white LEDs to illuminate the retina. This type of illumination outputs light at a very high intensity, causing substantial discomfort in patients. Although white LED is necessary to capture full detail in retinal images, it is important to reduce the duration that the patient is exposed to this type of light in order to improve comfort. The use of red light for retinal focusing in between white light flashes during image acquisition can achieve this. Red light is much more comfortable for human eyes as they do not absorb red light as easily as other colors in the visible spectrum. An added benefit is that the use of red light minimizes the pupillary response, allowing the device to be used on dark-adjusted eyes, instead of requiring chemical dilation. Thus, three 655nm deep red Luxeon Rebel LEDs were added a single white LED in the original illumination system (see Figure 2a). This wavelength was selected because it is long enough such that the human eye is not very sensitive to it, but short enough such that it will still pass through iPhone camera infrared filters. Three high-powered LEDs were used so that sufficient red light would pass through the optical system to illuminate the eye with enough contrast for the camera to focus.

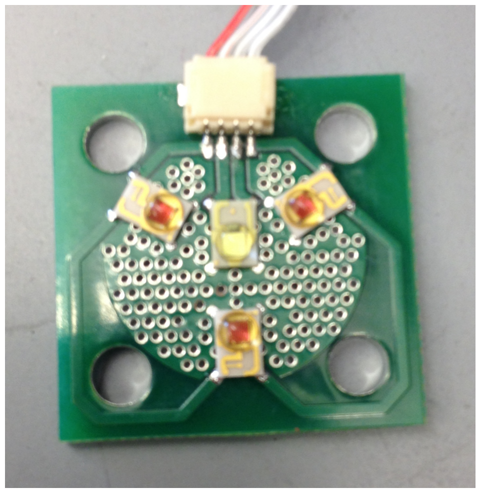


Figure 2. Illumination System with Red LEDs

Second, a fixation light system was implemented into the design. Fixation lights are small visible targets in the ophthalmoscope's viewing space where patients can fix their eyes during image capture. By adding five lights (four in each cardinal direction and one in the center), the device can provide visual cues to lock the patient's focus at strategic points in order to get sufficient coverage of the retina for diagnosis. This also ensures that the eye is not moving and causing motion blur in the images. Five 565nm green LEDs were selected for the fixation light system. Green was chosen because human eyes are highly sensitive to green, and it would contrast with red focusing illumination.

Third, the form factor of the device needed to be streamlined. The old model enclosure is awkward to handle, at times requiring the technician to use two hands to operate. This disrupts the workflow of retinal imaging, especially when technicians need a free hand to operate the phone or open the patient's eye. Also the asymmetric L-shaped design of the original enclosure is shaped sometimes blocks the patient's eye when the other eye is being imaged. The new Ocular CellScope enclosure (shown in Figure 3) has a simplified ergonomic design inspired by standard ophthalmoscopes, making is easier to hold with one hand and more natural for technicians to operate. In addition, the external light switch and light intensity knob control have been removed in this new design, since the illumination will now be control through the mobile application interface.

Figure 3. Redesigned CellScope Enclosure

2. Software Solutions

The mobile application has been designed to provide technicians with a convenient way of acquiring patient data and an improved interface for acquiring high quality retinal images. Since the device enclosure has been designed to house the iPhone 4 and 4s models, software development has been targeted to these two platforms, though the mobile application is forward compatible with iPhone 5/5s/5c models to allow for future upgrades.

Patient Data Model

Technicians need a convenient way of recording and storing patient data at the beginning of each exam. This data should be accessible when the application is closed and revisited. To achieve this, a database management system is required to ensure persistent storage of data between application uses. Apple provides two main platforms for data persistence: SQLite and Core Data. SQLite is a library for relational database management known for its speed and reliability, especially in handling sizable sets of data. Core Data, on the other hand, is an object relational mapping system that interfaces with SQLite, yet allows for the direct manipulation of high level objects as opposed to raw relational data [7]. The main drawback here is the performance costs in dealing with large sets of data. However, since technicians will not be handling considerably large sets of patient data locally on the phone, the Core Data framework is preferable for the purposes of this application.

To model the patient exam information and associated images, entities were created using the Core Data framework. Each entity is essentially an object in Objective C containing a set of attributes associated with it, and these attributes are assigned a specific type depending on the kind of data being held. Figure 4 illustrates the entities, attributes, and entity relationships used for this application. An "Exam" entity has been created with a set of attributes corresponding to the patient's name, identification number, the date of the exam, and notes to record during the screening. Similarly, an "EyeImage" entity has been created with metadata for the image, including the type of eye (left or right) and the fixation light triggered to capture the image. The "Exam" entity shares a one-to-many relationship with the "EyeImage" entity, as the logic follows that one exam contains multiple images associated with it.

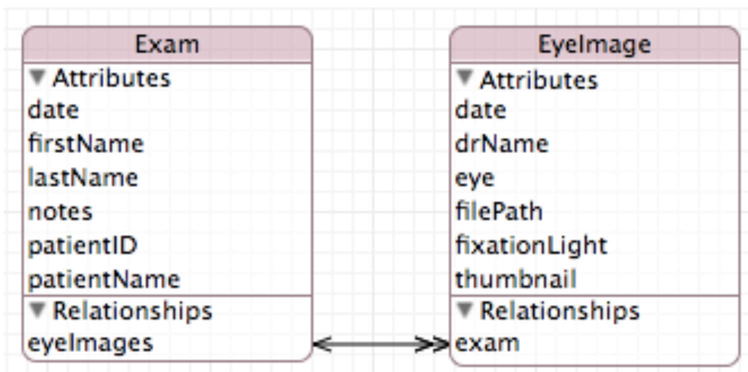


Figure 4. Core Data Model Graph

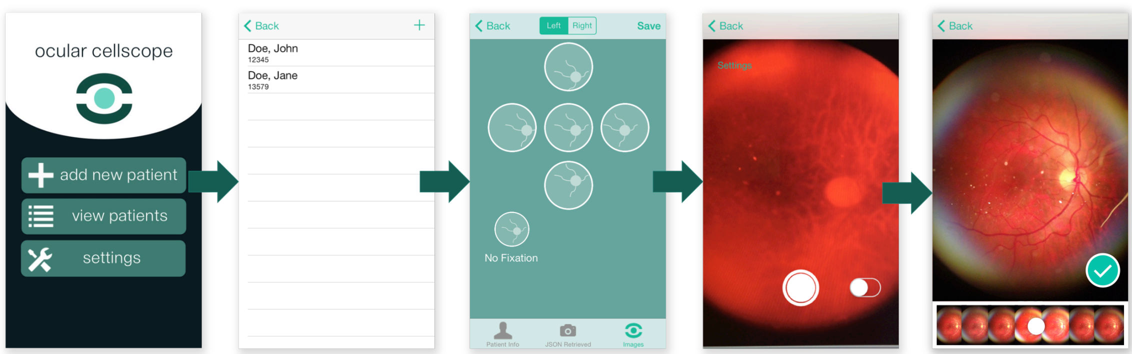
It is important to note that the raw image data is not being stored in the data model but rather a file path to this image data. While the Core Data framework supports the storage of this raw data within attributes, this approach is not good practice due to the size of these high-resolution images. To ensure efficient memory usage and performance, these images are stored on the phone using Apple's Asset Library framework and accessed with the file path saved in a given instance of the "EyeImage" entity. Lower resolution thumbnails, however, are stored in the data model and used to display miniature thumbnail images used for icons in the interface.

Image Acquisition

One of the biggest concerns expressed by the technicians using the initial prototype was the inability to acquire high quality retinal images. The native camera application on the iPhone placed limits image acquisition by forcing technicians to snap each individual retinal image as they held the device with both hands. The autofocus feature further impeded image capture as the camera refocused with slight movements, resulting in nondeterministic image capture times and thus blurry images. Furthermore, the custom lens of the device causes images to be rotated and mirrored when viewed on the iPhone screen. This made repositioning the device a challenging task as movements had to be interpreted in an inverted manner. Also the application did not provide a way to revert these inverted images into their original state.

The goal of the image acquisition feature was to design a simple tool to capture retinal images that is tailored to the needs of the technician. Apple provides two frameworks associated with image capture to achieve this. The UIImagePicker framework manages customizable user interfaces for taking pictures and video [8]. This method is essentially a black box, abstracting much of the camera controls from the developer. For this reason, the second method, the AVFoundation framework, is preferred as it provides more low-level controls of the camera device such as focus and exposure lock and callback functions for the instant an image is captured.

The procedure for image acquisition has been designed as follows. When the user selects a fixation light placeholder on the images tab of the new exam view, the application segues to the image capture view. Here the phone attempts to connect to the Ocular CellScope device hardware via Bluetooth. When a connection is made, phone sends a signal to the Bluetooth device to trigger the corresponding fixation light and the low intensity infrared light for retinal illumination. The capture button at the bottom of the screen initiates the image acquisition. In order to provide robustness of the system in the presence of movement by the user, the application captures a series of images spaced by a given time interval. At the start of each image in this series, the phone sends a Bluetooth command to briefly turn off of the infrared and fixation light and trigger the white flash illumination. After all retinal images have been captured for the given fixation light, the application enters an image selection view where the user can then review and select the images to save. Figure 5 below demonstrates this workflow.



(a) (b) (c) (d) (e)

Figure 5. CellScope Application Workflow: (a) Main screen, (b) patient table view, (c) fixation light selection view, (d) image capture view, (e) image selection view

Conclusion

We present the Ocular CellScope, a mobile ophthalmoscope device that leverages smartphone technology to effectively capture retinal images and manage patient records. Our system is the second design iteration of the existing prototype, addressing a number of usability issues related to the hardware subsystems and the lack of an integrated mobile application. It features a custom illumination system with red light focusing for improved patient comfort along with a fixation light system to provide a systematic approach for full-range retinal imaging. A mobile application has been designed to capture retinal images and record patient information, as well as control with device hardware components.

The fixation light system, illumination system, enclosure redesign, and mobile application have all been implemented as described in the previous sections. The full integration of the system has yet to be completed and tested as some of the ordered hardware components required for integration have not yet been delivered at the time of this report. Once all hardware parts are acquired, each subsystem will be assembled and integrated into a full device unit. This unit will be evaluated for its effectiveness in acquiring retinal images, the quality of the retinal images, and the usability of the device itself.

Future work on the Ocular CellScope device involves testing the device in clinical trials to determine its effectiveness in a practical setting. Feedback obtained from technicians and patients using the device could inspire additional modifications to this new prototype. Also a number of software features will be considered in the next steps of the device design. Adding a feature for technicians to upload patient information to a web server for ophthalmologist access will allow for remote diagnosis of potential eye diseases in patients. To improve the potential for quick onsite diagnosis of eye diseases, the use of computer vision to automatically characterize retinal images by their health condition will also be considered in future iterations of the device.

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