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Handheld Image Acquisition with Real-Time Vision for Human-Computer Interaction on Mobile Applications

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Abstract

Many important diseases manifest themselves in the retina, both primary retinal conditions and systemic disorders. Diabetic retinopathy, glaucoma and age-related macular degeneration are some of the most frequent ocular disorders and the leading causes of blindness in developed countries. Since these disorders are becoming increasingly prevalent, there has been the need to encourage high coverage screening among the most susceptible population.

As its function requires the retina to see the outside world, the involved optical components must be transparent for image formation. This makes the retinal tissue, and thereby brain tissue, accessible for imaging in a non-invasive manner. There are several approaches to visualize the retina including fluorescein angiography, optical coherence tomography and fundus photography.

The Fraunhofer's EyeFundusScope (EFS) prototype is a handheld smartphone-based fundus camera, that doesn't require pupil dilation. It employs advanced machine learning algorithms to process the image in search of lesions that are often associated with diabetic retinopathy, making it a pre-diagnostic tool. The robustness of this computer vision algorithm, as well as the diagnose performance of ophthalmologists and neurologists, is strongly related with the quality of the images acquired.

The consistency of handheld capture deeply depends on proper human interaction. In order to improve the user's contribution to the retinal acquisition procedure, a new graphical user interface was designed and implemented in the EFS Acquisition App. The intended approach is to make the EFS easier to use by non-ophthalmic trained personnel, either in a non-clinical or in a clinical environment.

Comprised of several interaction elements that were created to suit the needs of the acquisition procedure, the graphical user interface should help the user to position and align the EFS illumination beam with the patient's pupil as well as keeping track of the time between acquisitions on the same eye.

Initially, several versions of rotational interaction elements were designed and later implemented on the EFS Acquisition App. These used data from the smartphone's inertial sensors to give real-time feedback to the user while moving the EFS. Besides the rotational interactional elements, a time-lapse and an eye indicator were also designed and implemented in the EFS.

Usability tests took place, after three assemblies being successfully implemented and corrected with the help of a model eye ophthalmoscope trainer. Also, a protocol for the different use-case scenarios was elaborated, and a tutorial was created.

Results from the usability tests, show that the new graphical user interface had a very positive outcome. The majority of users adapted very quickly to the new interface, and for many it contributed for a successful acquisition task.

In the future, the grouping of inertial sensors data and image recognition may prove to be the foundations for a more efficient interaction technique performed in clinical practices. Furthermore, the new graphical user interface could provide the EFS with an application for educational purposes.

Keywords: Fundus Camera, Diabetic Retinopathy, Graphical User Interface, Interaction Element, Pupil Alignment, Inertial Sensors

Resumo

Várias patologias importantes manifestam-se na retina, sendo que estas podem ter origem na própria retina ou então provirem de doenças sistémicas. A retinopatia diabética, o glaucoma e a degeneração macular relacionada com a idade são algumas dessas patologias oculares, e também as maiores causas de cegueira nos países desenvolvidos. Graças à maior prevalência que se tem verificado, tem havido uma aposta cada vez maior na massificação do rastreio destas doenças, principalmente na população mais suscetível de as contrair.

Visto que a retina é responsável pela formação de imagens, ou seja, pelo sentido da visão, os componentes oculares que estão localizados anteriormente têm de ser transparentes, permitindo assim a passagem da luz. Isto faz com que a retina e, por sua vez, o tecido cerebral, possam ser examinados de forma não-invasiva. Existem várias técnicas de imagiologia da retina, incluindo a angiografia fluoresceínica, a tomografia de coerência ótica e a retinografia.

O protótipo EyeFundusScope (EFS) da Fraunhofer é um retinógrafo portátil, acoplado a um *smartphone*, que permite a obtenção de imagens do fundo do olho, sem que seja necessária a dilatação da pupila. Utiliza um algoritmo de aprendizagem automática para detetar lesões existentes na retina, que estão normalmente associadas a um quadro de retinopatia diabética. Para além disso, utiliza um sistema de suporte à decisão, que indica a ausência ou presença da referida retinopatia. A fiabilidade deste tipo de algoritmos e o correto diagnóstico por parte de oftalmologistas e neurologistas estão extremamente dependentes da qualidade das imagens adquiridas.

A consistência da captura portátil, com este tipo de retinógrafos, está intimamente relacionada com uma interação apropriada com o utilizador. De forma a melhorar o contributo prestado pelo utilizador, durante o procedimento habitual da retinografia, foi desenvolvida uma nova interface gráfica de utilizador, na aplicação Android do EFS. A abordagem pretendida consiste em tornar o uso do EFS mais acessível, e encorajar técnicos não especializados a utilizarem esta técnica de imagem médica, tanto em ambiente clínico como fora deste.

Composto por vários elementos de interação, que foram criados para atender às necessidades do protocolo de aquisição de imagem, a interface gráfica de utilizador deverá auxiliar todos os utilizadores no posicionamento e alinhamento do EFS com a pupila do doente. Para além disto, poderá existir um controlo personalizado do tempo despendido em aquisições do mesmo olho.

Inicialmente, foram desenhadas várias versões dos elementos de interação rotacionais, sendo posteriormente as mesmas implementadas na aplicação Android. Estes elementos de interação utilizam os dados recolhidos dos sensores inerciais, já existentes no *smartphone*, para transmitir uma resposta em tempo real ao utilizador enquanto este move o EFS. Além dos elementos de interação rotacionais, também foram implementados um temporizador e um indicador do olho que está a ser examinado.

Após a implementação de três configurações com as várias versões dos elementos de interação, procedeu-se à realização dos testes de usabilidade. No entanto, antes desta etapa se poder concretizar, foram realizados vários acertos e correções com a ajuda de um olho fantoma. Durante o planeamento dos testes de usabilidade foi estabelecido um protocolo para os diferentes cenários de uso e foi criado um tutorial com as principais cautelas que os utilizadores deveriam ter aquando das aquisições.

Os resultados dos testes de usabilidade mostram que a nova interface gráfica teve um efeito bastante positivo na experiência dos utilizadores. A maioria adaptou-se rapidamente à nova interface, sendo que para muitos contribuiu para o sucesso da tarefa de aquisição de imagem.

No futuro, espera-se que a combinação dos dados fornecidos pelos sensores inerciais, juntamente com a implementação de novos algoritmos de reconhecimento de imagem, sejam a base de uma nova e mais eficaz técnica de interação em prática clínica. Além disso, a nova interface gráfica poderá proporcionar ao EFS uma aplicação que sirva exclusivamente para efeitos de formação profissional.

Palavras-chave: Retinógrafo, Retinopatia Diabética, Interface Gráfica de Utilizador, Elemento de Interação, Alinhamento da Pupila, Sensores Inerciais

Contents

List of Figures

List of Tables

Acronyms

AI	Artificial Intelligence
AMD	Age-related Macular Degeneration
API	Application Programming Interface
DM	*Diabetes Mellitus*
dp	Density-independent pixel
DR	Diabetic Retinopathy
EFS	EyeFundusScope prototype
EFS-App	EyeFundusScope Acquisition Application
FA	Fluorescein Angiography
FDA	Food and Drug Administration
FhP-AICOS	Fraunhofer Portugal Research Center for Assistive Information and Communication Solutions
FOV	Field-of-View
GUI	Graphical User Interface
HCI	Human Computer Interaction
HFE	Human Factors Engineering
HIARQ	Handheld Image Acquisition library with Real-time Quality Control Component
IE	Interaction Element
LED	Light-Emitting Diode
NIR	Near-Infrared
OCT	Optical Coherence Tomography
OECD	Organization for Economic Co-Operation and Development
SUS	System Usability Scale

SD-OCT Spectral Domain Optical Coherence Tomography

TD-OCT Time Domain Optical Coherence Tomography

Chapter 1

Introduction

1.1 Context and Motivation

This master thesis was held at Fraunhofer Portugal Research Center for Assistive Information and Communication Solutions (FhP-AICOS). In the last few years, Fraunhofer AICOS' researchers have developed a smartphone-based retinal imaging system, the EyeFundusScope (EFS) prototype, that can be used as an effective screening tool for retinal diseases. The combination of affordability, portability, easy transmission of images and other features of this retinal imaging solution provides a platform not only for in-clinic use but also for planning mass screening programs in Portugal and other low- and middle-income countries.

FhP AICOS primary goals are to improve patient access to early treatment, to empower non-experts to acquire retinal images and decrease the burden of screening actions on healthcare systems. Diabetic Retinopathy (DR), Glaucoma and Age-related Macular Degeneration (AMD), are some of the retinal conditions that pose a significant threat to public health and global economies.

The robustness of computer vision algorithms is strongly related with the quality of the images acquired. For the matter of the EFS solution, the automatic assessment of diabetic retinopathy, that is performed through the detection of lesions in the retina, can be greatly enhanced if retinal images also see some quality improvements. Apart from the different clinical environments, the consistency of handheld capture deeply depends on proper human interaction. The main limitations of the most recent mobile solutions for fundus photography are rooted in its hand-held nature: focusing and illumination beam positioning, and these can be time-consuming.

To tackle these challenges, real-time computer vision combined with inertial sensors on the smartphone is expected to provide crucial data for the study of dedicated Human Computer Interaction (HCI) during the capture.

The intended approach is to make the EFS easier to use by non-ophthalmic trained personnel, either in a non-clinical environment or in a clinical environment, like the emergency room where nurse practitioners may take action. Furthermore, the approach may prove essential in an educational environment, because it would allow an efficient monitoring, in real time, of the user's examination technique, during their learning process.

1.2 Objectives

The main purpose of this master thesis is to explore new methods of visualization and interaction, using the interpreted data provided by Fraunhofer research team gathered from camera and inertial sensors in the EFS. The ultimate goal of this master thesis is to study and implement a handheld image acquisition interaction element for Android, which uses the real time image and signal features already developed, to achieve the best acquisition possible.

The 4 principal objectives targeted are:

- Development of a Human Computer Interaction (HCI) abstraction layer with Graphical User Interface (GUI) workflows, to provide feedback to the user so that the alignment, perspective, focus distance and other constraints are achieved within accepted levels.
- Create a repository of recommended and avoidable GUI elements.
- Development of prototypes to explore and demonstrate new and efficient methods of visualization and interaction on the Fraunhofer's EFS prototype
    - Definition of interaction protocol for smartphone image capture of the fundus of the eye
- Plan and execute field tests

The development of the HCI abstraction layer with GUI workflows consisted mainly in the design of interaction elements (IEs) for Android. These consisted of two different groups: the rotational IEs and the indicators. While the rotational IEs purpose is to give the user feedback relative to the EFS positioning and alignment, the indicators were developed to make the retinal exam procedure more efficient.

The repository created was composed of several versions of different rotational IEs, and also indicators that were all placed in the fundus observation screen.

In order to demonstrate a new method of interaction on the EFS, the interaction elements were implemented in Android and a tutorial was created in order to explain the new interaction protocol. The rotational IEs used the data from the inertial sensors of the smartphone.

Finally, the interaction elements usability was evaluated through field tests. These usability tests were executed first by Fraunhofer researchers and later by nurse practitioners.

1.3 Overview

This dissertation is divided in 7 chapters. In this first chapter, the project is put into context, and the underlying problem and the expected objectives are presented.

Chapter 2 starts with an anatomical and physiological outline of the eye, followed by some of the retinal imaging modalities, and then the most prevalent retinal pathologies diagnosed through fundus photography. This chapter also introduces some of the most recurrent challenges users deal with when doing a handheld retinal exam. Lastly, the EFS prototype that was created by Fraunhofer is presented.

Chapter 3 presents the current state-of-the-art of mobile solutions similar to the EFS.

In chapter 4, the methodology used to design, implement and test the interaction elements is shown. Also the approach throughout each stage is explained.

Chapter 5, shows the results from each of the development stage as well as the results from the usability tests.

Chapter 6 presents three innovative ideas that might be implemented in the EFS. These may prove useful to expand the usability of the EFS in the context of non-trained personnel.

Finally, in chapter 8, the conclusion of this work is presented. It includes a brief summary of the results and problems encountered, and also some final considerations.

Chapter 2

Ophthalmological background

This chapter makes a cross-sectional analyses of the most important topics related to retinal screening. Its divided into four major parts: a brief study on the anatomy and physiology of the eye; an overview of the different retinal modalities and the most impactful retinal diseases; an introduction to hand-held image capture challenges; and lastly, the presentation of the Fraunhofer EFS.

2.1 Eye's anatomy and physiology

The eyeball itself is a hollow, fluid-filled sphere, of about 24 mm in diameter and with three main components: three tunics (layers) that form the wall of the eyeball; optical components that admit and focus light; and neural components, the retina and optic nerve (Figure 2.1). Apart from being a neural component, the retina is also part of the inner tunic. The cornea is part of the outer tunic as well as one of the optical components. [1]

2.1.1 Layers of the eye

There are three tunics that form the wall of the eyeball:

The outer fibrous layer is composed of two portions, the sclera and cornea. The sclera is the thickest layer and is made of fibrous connective tissue that is visible as the white of the eye, covering most of the eye surface. [2] The most anterior portion, covering the iris and pupil inside the eye, is the cornea, a modified sclera that is transparent and therefore admits light into the eye. As part of the focusing system of the fibrous tunic, the cornea also bends, or refracts, the entering light. [3]

The middle vascular layer consists of three regions—the choroid, ciliary body, and iris. The choroid is a highly vascular, deeply pigmented layer of tissue that absorbs light within the eyeball and thereby prevents it from being reflected inside the eye. The ciliary body is a thickened extension of the choroid, forming a muscular ring around the lens. It supports the iris and lens and secretes a fluid called the aqueous humor. The iris is the colored part of the eye and acts as an adjustable diaphragm that controls the diameter of the pupil, its central opening. [3] [4]

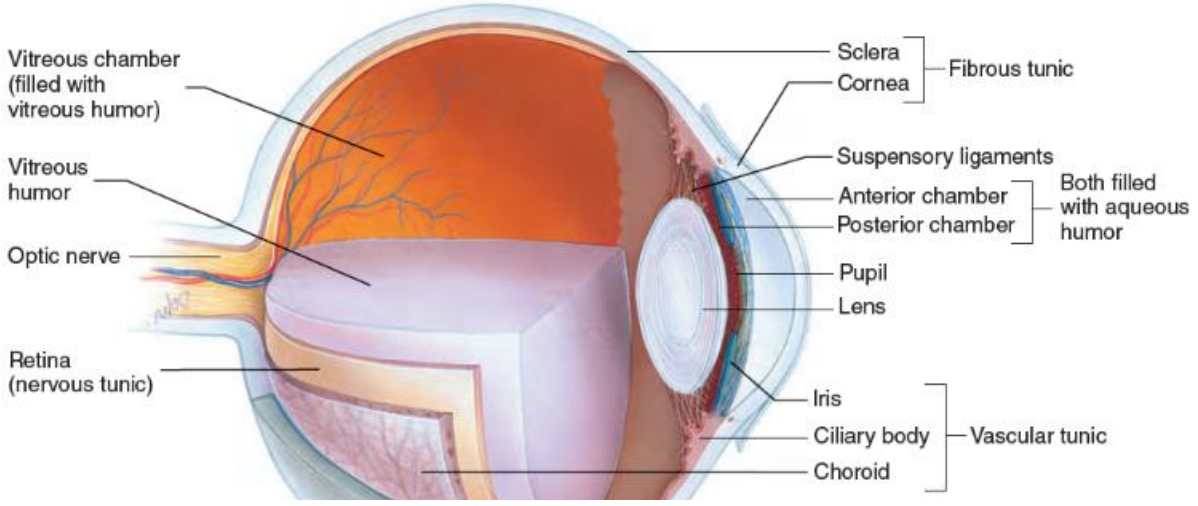


Figure 2.1 Sagittal section of the internal structure of the human eye. [4]

The inner layer consists of the retina, which internally lines the posterior five-sixths of the eyeball. The retina will be discussed in greater detail.

2.1.2 Optical components

The optical components of the eye are transparent elements that admit light rays, bend (refract) them, and focus images on the retina. They include the *cornea, aqueous humor, lens,* and *vitreous body*.

The cornea, from where the light first enters the eye, has been described already. The aqueous humor is a serous fluid secreted into a space between the iris and lens called the posterior chamber, and then it flows through the pupil forward into the anterior chamber, a space between the cornea and iris.

The light, after passing through the opening of the pupil, reaches the lens, a crystalline and biconvex structure that is composed of flattened, tightly compressed cells called lens fibers. The lens is suspended behind the pupil by a fibrous ring called the suspensory ligament which attaches it to the ciliary body. [1]

The portion of the eye located behind the lens is filled with a thick, viscous substance known as the vitreous humor that helps to maintain the shape of the eyeball and gives the retina an even surface for the reception of clear images. [4]

2.1.3 Neural components

The neural components of the eye are the retina and optic nerve. The retina is a thin transparent membrane attached at only two points—a scalloped anterior margin called the ora serrata (between the photosensitive posterior region of the retina and the non-photosensitive anterior region of the retina that continues anteriorly to cover the ciliary body and the posterior side of the iris), and the optic disc, where the optic nerve leaves the rear of the eye. The rest of the retina is held smoothly against the rear of the eyeball by the pressure of the vitreous body. [1] [5]

The retina is composed of two layers: an outer pigmented layer and an inner neural layer. The pigmented layer is composed by epithelial cells with melanin and it is immediately internal to the choroid and attached to it. Just like in choroid, melanin present in the outer layer of the retina absorbs stray light rays that pass through the inner layer, preventing reflection and scattering of light inside the eyeball. [4] The neural layer, that houses all of the photoreceptors and their associated neurons, is an extension of the brain responsible for receiving light rays and converting them into nerve impulses that are transmitted to the brain through the optic nerve. [6]

2.1.3.1 Organization of the Neural Layer

Three distinct layers of cells form the neural layer (Figure 2.2): photoreceptor cells, bipolar cells and ganglion cells - separated by two zones, the outer and inner synaptic layers, where synaptic contacts happen.

The outermost layer of the neural layer is composed of photoreceptor cells. These are the neurons responsible for the conversion of light into electrical signals and are divided in two types: rods and cones. Both photoreceptors contain molecules, called pigments that disassociate in response to light - photochemical reaction that produces action potentials in the optic nerve [4]. Rods are especially important when the light is dim. They detect movement but exhibit poor visual acuity. In addition, rods pick up contrasting dark and light tones, but cannot distinguish color [2]. Whereas cones are activated by high-intensity light and provide precise visual acuity and color recognition. Their pigments are called

photopsins. Some cones have a photopsin that responds best at a wavelength of 420 nanometers (nm), a deep blue light, others respond best at 531 nm (green), and still others at 558 nm (orange-yellow). The stimulation of various combinations of the three types results in color vision. [5]

Internal to the photoreceptor layer is a layer of bipolar cells. Rods and cones synapse with the dendrites of bipolar neurons, the first-order neurons of the visual pathway. There are far fewer bipolar neurons than photoreceptors and thus information must converge as visual signals are directed toward the brain from the stimulated photoreceptors. [5]

Ganglion cells form the innermost layer in the neural layer that is adjacent to the vitreous body in the posterior cavity. These are the largest neurons of the retina and the second-order neurons of the visual pathway. Most ganglion cells receive input from multiple bipolar cells. Their axons form the optic nerve. Some ganglion cells absorb light directly and transmit signals to brainstem nuclei that control pupillary diameter and the body's circadian rhythms. They do not contribute to visual images but detect only light intensity. Their sensory pigment is called melanopsin. [1]

There are other retinal cells, but they do not form layers of their own. Horizontal cells and amacrine cells form connections among rod, cone, and bipolar cells. Bipolar cells that carry rod signals do not synapse directly with ganglion cells, but only by way of amacrine cells [6]. Horizontal and amacrine cells play diverse roles in enhancing the perception of contrast, the edges of objects, and changes in light intensity.

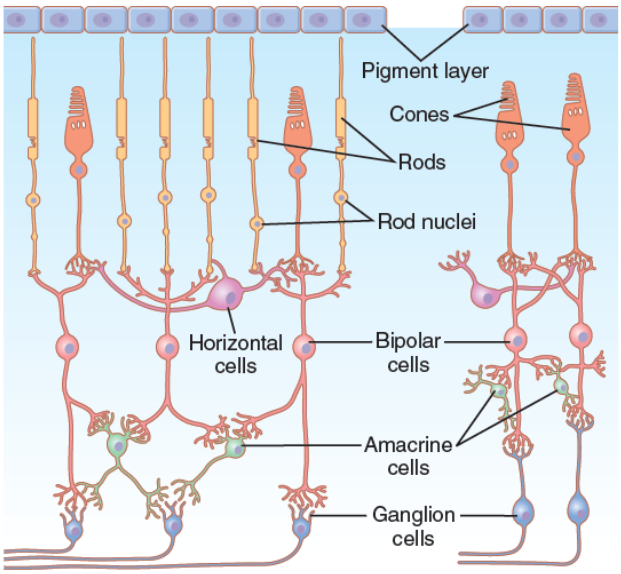


Figure 2.2 Neural organization of the retina, with the peripheral area to the left and the foveal area to the right (adapted from [5])

2.1.4 Funduscopic view

When the posterior region of the retina is examined with an ophthalmoscope, two major features can be observed: the macula and the optic disc (Figure 2.3). The macula is a small spot near the center of the posterior retina. [7]

In the center of the macula is a small depression, the fovea. This is the part of the retina where light is most focused when the eye is looking directly at an object. The fovea contains the highest

proportion of cones and almost no rods, making it the region responsible for the highest visual acuity. [1]

The optic disc is a white spot just medial to the macula, through which a number of blood vessels enter the eye and spread over the surface of the retina. This is also the spot at which axons of the ganglionic cells converge to form the optic nerve as they exit the eye and extend toward the brain [4]. The optic disc lacks photoreceptors, and consequently it is called the blind spot because there are no receptors to detect an image that might fall there.

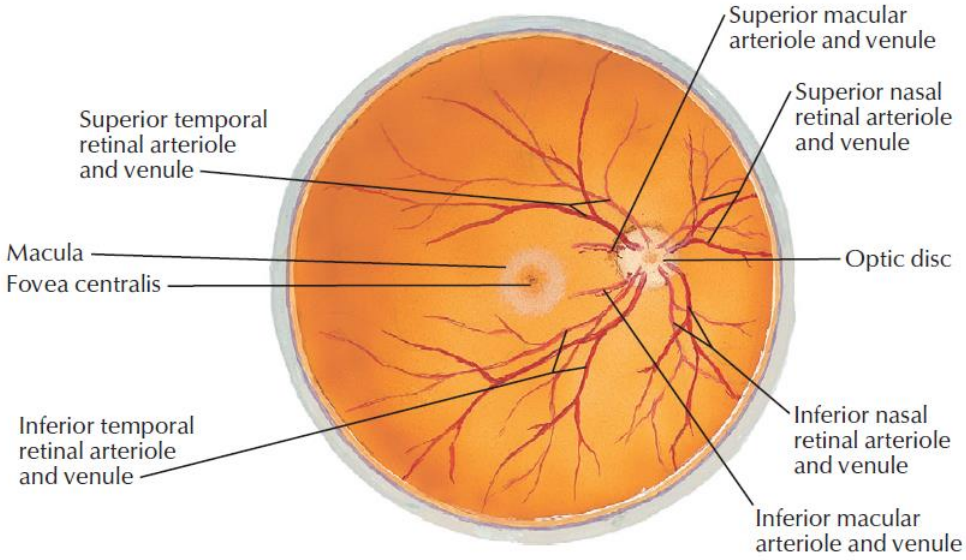


Figure 2.3 Right retinal vessels: funduscopic view [7]

2.2 Fundus examination in clinical practice

The ability to image the retina and develop techniques for analyzing the images is of great interest. As its function requires the retina to see the outside world, the involved optical components, previously mentioned, must be transparent for image formation. Thus, with proper techniques, the retina is visible from the outside, making the retinal tissue, and thereby brain tissue, accessible for imaging noninvasively. Because the retina's function makes it a highly metabolically active tissue with a double blood supply, the retina allows direct noninvasive observation of the circulation [8].

2.2.1 Ophthalmoscopy – Retinal imaging modalities

There are several approaches to visualize the retina including fluorescein angiography (FA), optical coherence tomography (OCT) and fundus photography, each having its own advantages and disadvantages.

2.2.1.1 Fluorescein Angiography

The FA is an exam that allows to study the characteristics of blood flow within retinal vessels and the choroid by assessing its functional integrity. This exam consists in administering sodium fluorescein into bloodstream that is primarily eliminated through the liver and kidneys within 24-36 hours via the urine [9]. The fluorescein is a non-toxic molecule that absorbs blue light (465-490 um) and emits a light within the yellow-green spectrum (500-600 um). After administering fluorescein, and using a dedicated fundus camera endowed with particular filters, it is possible to acquire a sequence of photographs showing the eye fundus and its vessels [10]. This enables a high-contrast image of the blood vessels and also highlights areas of damage where the dye escapes into the surrounding tissue.

Flow dynamics and related pathologies are revealed by capturing a timed sequence of images of the progression of the dye into the vessels. Fluorescein enters the ocular circulation via the ophthalmic artery 8 to 12 seconds after the administration, depending on the rate of injection and the patient's age and cardiovascular status. The retinal and choroidal vessels fill during the transit phase, which ranges from 10 to 15 seconds. The arterial phase of the angiogram occurs after the choroidal phase, with filling of the retinal arteries [10]. The arteriovenous phase begins with complete filling of the retinal arteries and capillaries and completes with laminar filling of the retinal veins. This phase, which usually occurs approximately 1 minute after dye injection, is considered the peak phase of fluorescence, where the most detail is evident in the fovea. [9]

The aforementioned process allows FA to diagnose macular edema, diabetic retinopathy (such as mycroaneurisms – Figure 2.4) and venous occlusions. Some complications may happen when using FA such as transient nausea, and vomiting [11]. The mydriatic desktop fundus camera (Figure 2.4) is the tool most commonly used for this technique, but scanning laser ophthalmoscopes and some specialized wide-field fundus cameras can also be used.

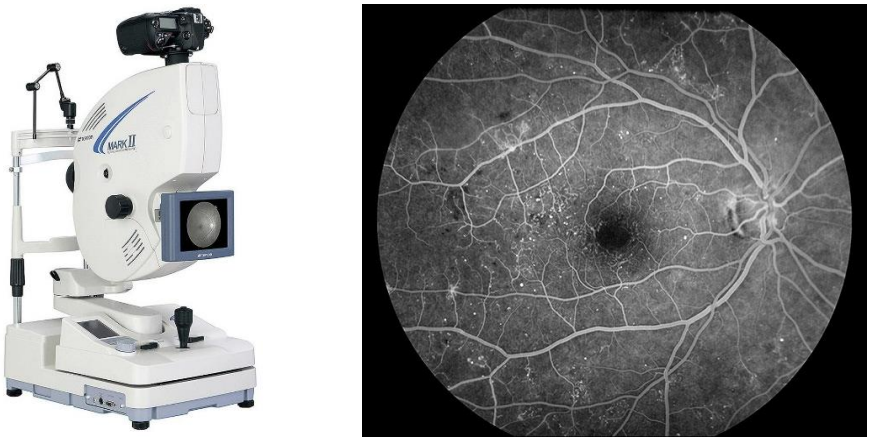


Figure 2.4 Left: Desktop Fundus camera (NW7SF Mark II). Right: Diabetic Retinopathy showed through Fluorescein angiography [11]

2.2.1.2 Optical Coherence Tomography

OCT is one of the most recent complementary exams used for diagnostic of retinal diseases, and consists on obtaining cross-section pictures of the retina with high resolution, using reflected infrared light [12]. This technique firstly introduced in 1991, utilizes a concept known as low coherence interferometry to create a cross-sectional map of the retina that is accurate to within at least 10-15 microns [13].

From its inception, OCT images were acquired in a time domain (TD-OCT) measuring the interference signal generated between reflections from a reference arm and a sample arm of an interferometer, where the eye is the sample. Time domain systems acquire approximately 400 A-scans per second that result from interference between the light reflected from the reference arm and the light backscattered from features in the retina located at different depths [14]. Backscatters are typically caused by differences in refractive index in transitions from one tissue to another. By collecting a series of laterally translated A-scans, a cross-sectional retinal image is created (B-scan).

Spectral domain technology, on the other hand, scans approximately 20,000-40,000 scans per second. SD-OCT is mathematically related to TD-OCT by the Fourier transform. This SD-OCT approach resulted in vastly increased imaging speeds as well as higher sensitivity when compared with TD-OCT [13]. This increased scan rate and number diminishes the likelihood of motion artifact, enhances the resolution and decreases the chance of missing lesions. Whereas most time domain OCTs are accurate to 10-15 microns, newer spectral domain machines may approach 3 micron resolution [14].

Figure 2.5 Cirrus HD-OCT 5000 from Carl Zeiss Meditec (SD-OCT system) [15]

Because OCT utilizes light waves, media opacities can interfere with optimal imaging. As a result, any pathology likely to reduce the transmission and reflectiveness of light such as vitreous hemorrhage, dense cataract or corneal opacities, limits the use of this technique [12].

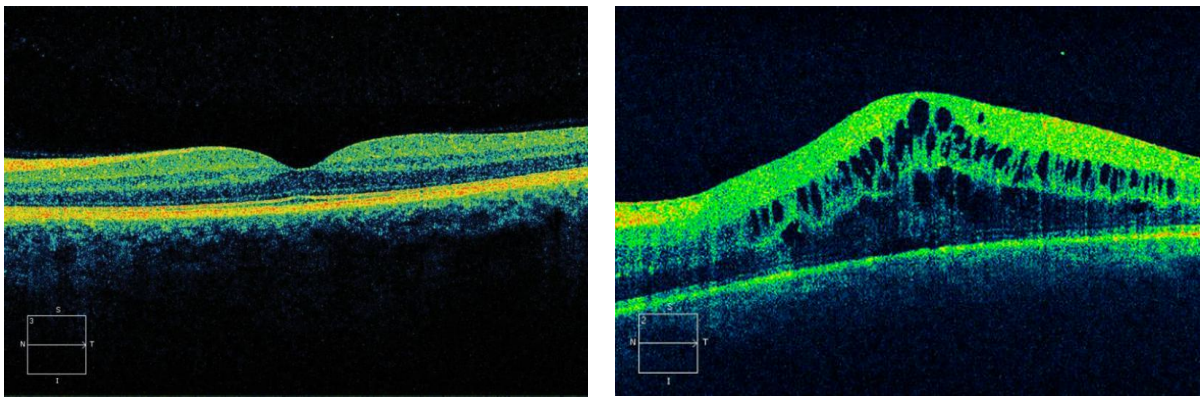


Figure 2.6 Left: Normal Retina OCT image. Right: Macular Edema [16]

2.2.1.3 Fundus Photography

Since the invention of the ophthalmoscope in 1851 by Hermann von Helmholtz, visualization of the posterior segment of the eye by ophthalmologists has undergone dramatic improvements [17]. Obtaining photographs of the posterior segment of the eye has always been challenging because illumination of the posterior segment is required simultaneously with visualization of the ocular structures by the photographer [18]. The first reliable fundus camera was introduced by Carl Zeiss and J.W. Nordensen in 1926, and this allowed for documentation of ocular fundus structures. This camera provided a 20º field of view (FOV), but it wasn't until years later that the Carl Zeiss Co. set a 30º FOV as the standard in ocular fundus photography [19]

Fundus photography, like the FA exam, generates a two-dimensional (2D) image of the interior three-dimensional (3D) surface of the eye, and is performed with a system that consists of a specialized low-power microscope and an attached camera. Most commonly, the retina is illuminated by white light and examined in full color. However, the imaging light can be filtered to remove red components, creating a red-free image with improved contrast of retinal and choroidal blood vessels and other structures [20].

Currently, standard fundus photography provides a 30º to 50º image of the retina, and with recent advances this FOV is achieved without the need to dilate the pupil (no mydriasis). This modality is widely available, so it is extensively used for clinical trials and for diabetic retinopathy screening in primary care settings, identifying pre-symptomatic stages where treatment interventions can protect sight. It is also used routinely in a variety of other ophthalmic conditions such as glaucoma and age-related macular degeneration where serial monitoring is used to pick up growth or changes inherent to each condition [21]. Moreover, as several studies have shown, non-mydriatic fundus photography by non-ophthalmic trained personnel is a clinical alternative to direct ophthalmoscopy in the emergency department, which is usually performed by emergency physicians. [22] [23] [24] In these sequential studies, 350 patients were photographed by nurse practitioners after approximately 30 minutes of training. Inclusion criteria included a chief complaint of headache, acute focal neurological deficit, acute vision change or a diastolic blood pressure of at least 120 mm Hg. Phase I of the FOTO-ED study found that non-mydriatic fundus photography identified over 80% of the previously unknown relevant findings that were missed during routine emergency department evaluations. [23]

In order to provide a view of the retinal periphery, which is the site of pathology in many ocular diseases, multiple images may be manually overlapped to create a montage, such as when the 7 standard 30º FOV fundus images are combined to create a 75º FOV, as Figure 2.7 illustrates [25].

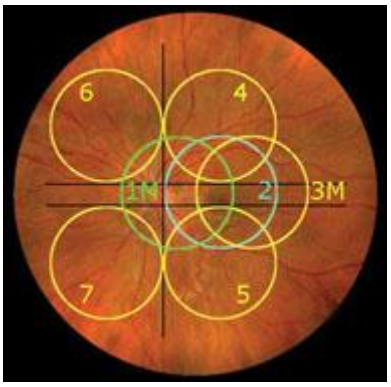


Figure 2.7 Diagram illustrating the extent of field of view of the ocular fundus with seven standard fields [25]

The conventional fundus camera used to capture a retinal image is commonly called desktop fundus camera (Figure 2.4). This type of device offers good-quality images but some constraints like its bulkiness, and the fact that is office-based and technician dependent, besides being of high cost, makes screening programs less viable for the entire population, especially in remote rural settings, where access and affordability is of utmost importance.

The most recent advances in microfabrication, optics, digital sensors and image processing have radicalized retinal photography by supporting the development of progressively smaller, therefore more portable, and more powerful imaging devices. Their integration into wireless networks facilitates secure image transmission for teleophthalmology applications. These developments brought various low-cost handheld fundus cameras that proved to be the best option for retinal image acquisition in resource-limited settings [20].

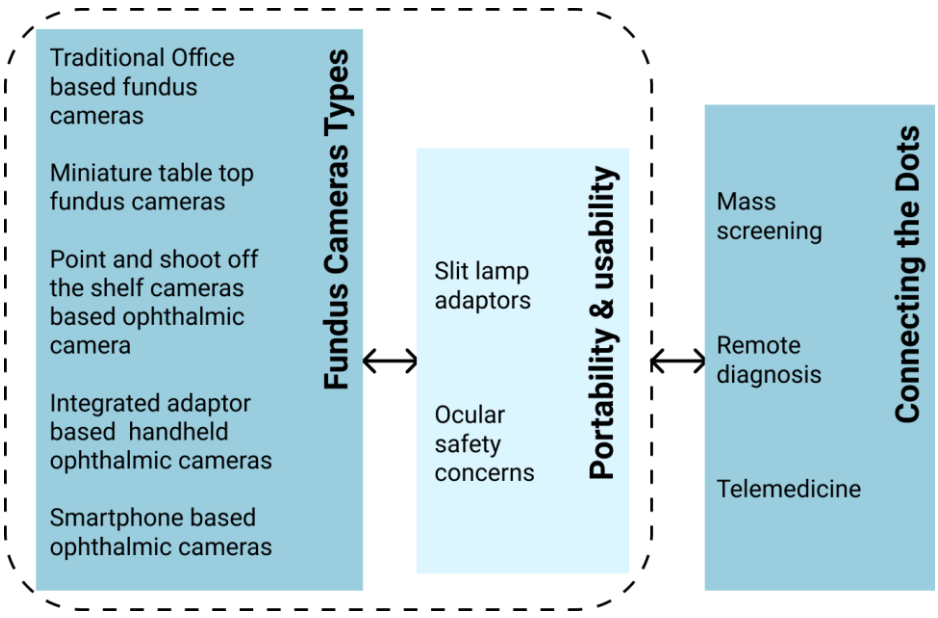


Figure 2.8 Flowchart depicting evolution and scope of retinal screening and fundus photography. Adapted from [20]

Some of the popular handheld prototypes, including some commercialized devices that will be presented in the next chapter, attach external optics to a smartphone to capture and store fundus images, allowing to substantially reduce the cost and increase the portability of the retinal imaging device.

Nevertheless, there are some drawbacks of handheld fundus cameras that include smaller field-of-view and lower image quality when compared to desktop fundus cameras [26]. Besides, in a limited resources framework the lack of well-trained clinicians and specialists indicates an urgent need for on-site automatic diagnostics and decision-making, as always been desired in healthcare cost containment. Improvements in telecommunications and smartphones are two remarkable breakthroughs that have made ophthalmic screening in remote areas a realizable possibility.

Inclusion criteria for the latter include a chief complaint of headache, acute focal neurological deficit, acute vision change or a high diastolic blood pressure.

2.2.2 Possible pathologies diagnosed with retinal imaging

Many important diseases manifest themselves in the retina, both primary retinal conditions and systemic disorders. For instance, diabetic retinopathy is a complication of diabetes mellitus, hypertensive retinopathy is related to systemic hypertension and pathologies of the retinal vascular network can be related to stroke and cardiovascular disease.

A brief overview of the most prevalent diseases that can be studied via imaging techniques, especially fundus photography follows.

2.2.2.1 Diabetic Retinopathy

Diabetes mellitus (DM), commonly referred as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. Regarding the prevalence of diabetes, the Organization for Economic Co-operation and Development (OECD) report of 2017 estimates that Portugal had 9,9% prevalence rate in adults in 2015 [27]. This value is above the 7% OECD35 average (Figure 2.9)

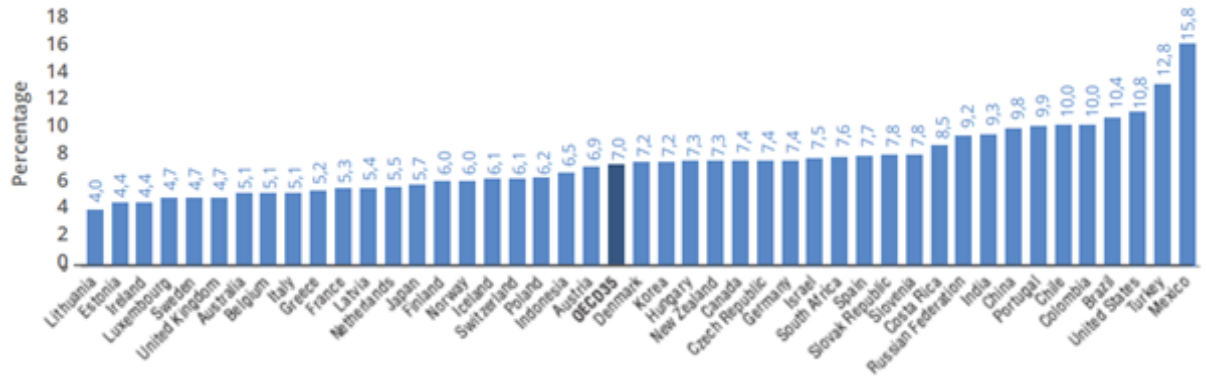


Figure 2.9 Prevalence of Diabetes in adults per country in 2015. Age 20-79 with DM1 and DM2 [27]

The prevalence and incidence of diabetic retinopathy is related to the type, duration and treatment of diabetes (insulin or not), with some systemic factors like hypertension and the control of glycaemia in the first stages of the disease. When this condition occurs, the diabetic patient will experience cumulative changes to his retina, ultimately leading to blindness. “The incidence of

retinopathy is rarely detected in the first few years of diabetes, but the incidence increases to 50% by 10 years, and to 90% by 25 years of diabetes" [27].

Macular edema is the most frequent cause of vision loss among patients with non-proliferative diabetic retinopathy, and it can appear on an early stage of this condition. The natural course of the disease follows different stages of the pathological picture: presence of microaneurysms on the retinal capillaries, increase of vascular permeability, vascular occlusion, appearance of new capillaries and fibrous tissue on the retinal surface and optic disc, vitreous hemorrhage and retinal detachment. [28] [29].

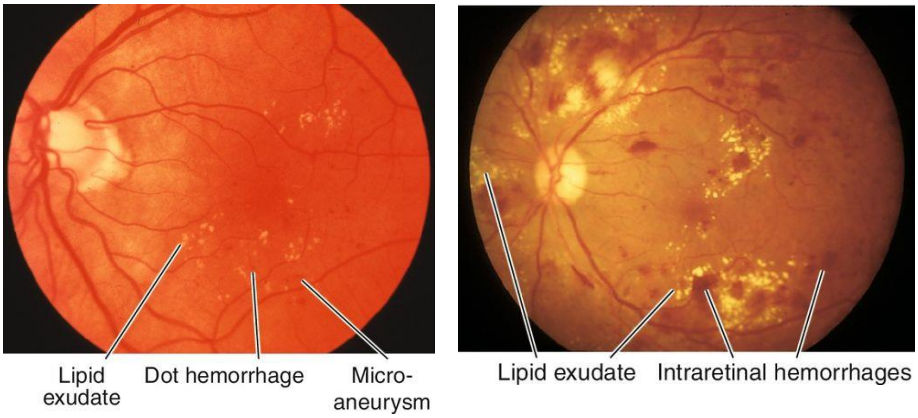


Figure 2.10 Left side: Moderate non-proliferative diabetic retinopathy with intraretinal hemorrhages, microaneurysms, and lipid exudate. Right side: Severe non-proliferative diabetic retinopathy with extensive hemorrhages, microaneurysms, and exudates [30]

The asymptomatic profile of the initial progression and the high effectiveness of early treatment have motivated the implementation of extensive screening programs covering the diabetic population, in which images of the patient retinas are acquired and subsequently analyzed by an expert [29]. In 2016 the National Program for Diabetes together with the Health Regional Administrations did the first report on diabetic retinopathy screening programs, which concluded that the number of screened diabetic patients increased 32% in comparison to the previous year (Figure 2.11).

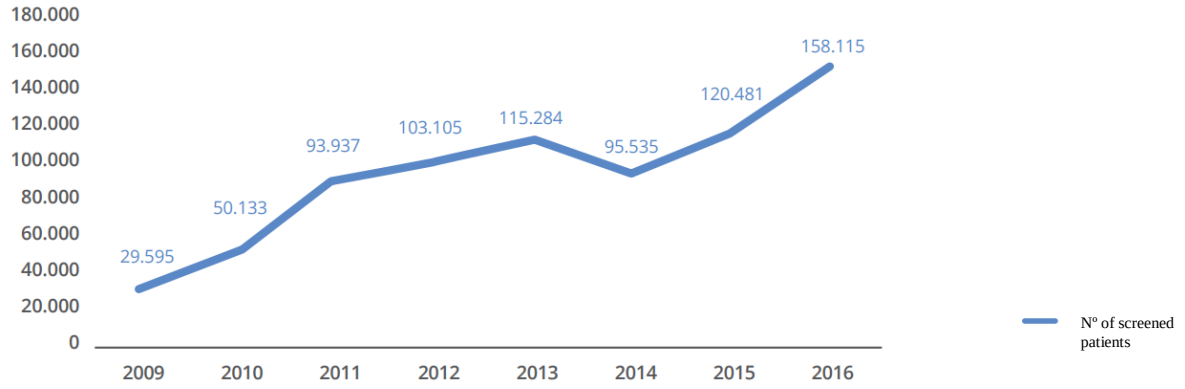


Figure 2.11 Screening evolvement for diabetic retinopathy in Portugal [27]

For the cases of proliferative DR or presence of macular edema, there are two different treatments that can performed. The laser photocoagulation procedure "dries" the neovasculature and also decreases the chance of vitreous hemorrhage and retinal detachment. On the other hand, the vitrectomy is used when there is a severe vitreous hemorrhage. The procedure itself is done by surgically

removing the neovasculature and the scar tissue, allowing the retina to return to its normal state. [28] [29]

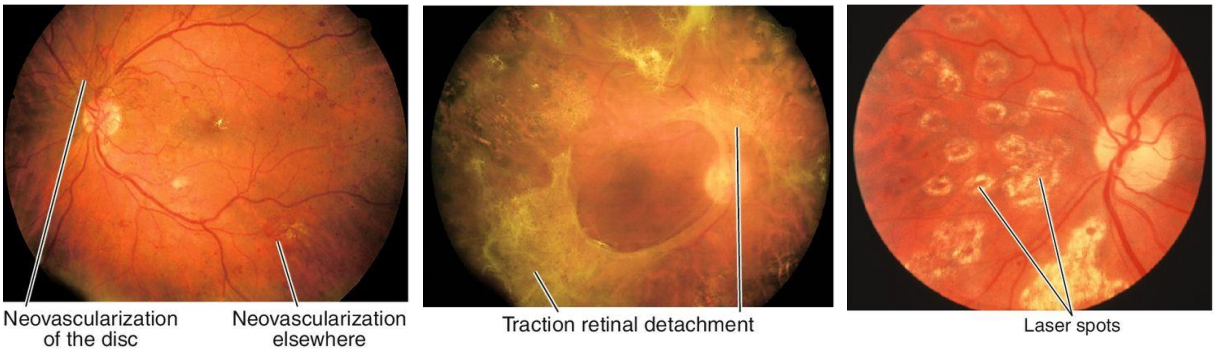


Figure 2.12 Left side: Proliferative diabetic retinopathy demonstrating florid neovascularization of the disc and elsewhere. Middle: Proliferative diabetic retinopathy demonstrating neovascularization, fibrosis, and traction retinal detachment. Right side: Laser spots demonstrating quiescent proliferative diabetic retinopathy following pan-retinal photocoagulation [30]

2.2.2.2 Glaucoma

It is estimated that around 150 thousand Portuguese suffer from Glaucoma, with an increase for the next years due to population ageing. Glaucoma affects 80 million people worldwide, and it's a progressive disease of the optic nerve, that if left untreated will eventually lead to permanent blindness. It's the second major cause of blindness and the first cause of avoidable irreversible blindness worldwide. Even in developed countries, only about 50% of the patients that suffer from Glaucoma are diagnosed and treated accordingly, because the majority doesn't show, at the initial stages, any visual alteration [29] [31].

Glaucoma is the generic denomination for a group of diseases where vision is lost due to damage to the optic nerve. The main risk factor associated with this condition is ocular hypertension [30].

As previously mentioned, aqueous humour flows from the ciliary body, through the anterior chamber and drains out of the eye via the trabecular meshwork. However, if this draining process becomes blocked, the aqueous fluid level within the eye can build-up, resulting in increased eye pressure. The normal interval of intraocular pressure in general population is 10-22 mmHg [5].

The ratio of the optic disc cup and neuroretinal rim surface areas, called cup-to-disc ratio, seen in funduscopic images, is an important structural indicator for assessing the presence and progression of glaucoma. The average value for cup to disc ratio is 0.3, any significant increase is a potential sign of glaucoma. This condition is typically treated with ocular pressure lowering drops, and in refractory cases through surgery [29].

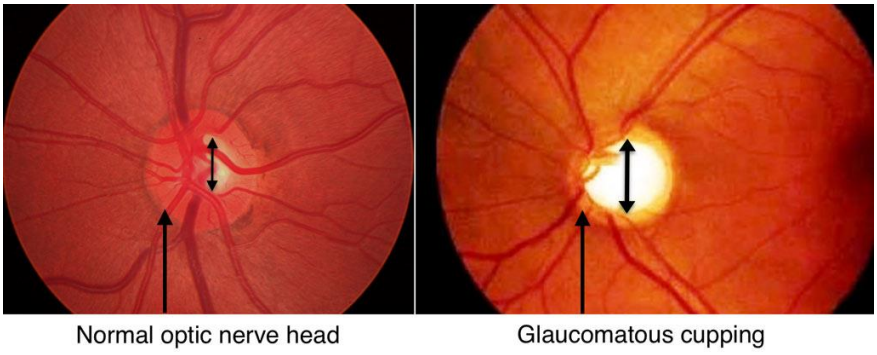


Figure 2.13 Left side: a normal optic nerve head has a thick outer ring of nerve tissue with a small optic "cup" centrally Right side:in the glaucomatous optic nerve, the outer ring is thin and the "cup" is larger, corresponding to the loss of nerve fibers [53]

2.2.2.3 Age-related macular degeneration

Age-Related Macular Degeneration (AMD) is a common eye condition and a leading cause of vision loss in developed countries among people aged 50 and older [8]. This is a multifactorial chronical disease that causes damage to the macula. Since the main risk factor is age, it is expected an increase of its prevalence in the western world.

Based on the prevalence among Caucasian populations in developed countries it is estimated that there are 384.000 cases in Portugal, being approximately 85% of those in an early stage of the disease [29]. In this sense, there is a major concern in implementing the AMD screenings in association with Diabetic Retinopathy Screenings, for a matter of resource managing.

There are two types of advanced AMD, affecting approximately 15% of the total cases: non-exudative or "dry" AMD and exudative or "wet". The dry form is more common and affects about 90% of patients in an advanced stage [32].

Dry AMD occurs when the light-sensitive cells in the macula slowly break down. This usually occurs in both eyes and patients may see a blurred spot in the center of their vision. Regarding the Wet AMD, new abnormal blood vessels start to grow in an area, such as the macula, where they are not supposed to be. These new blood vessels are very fragile and often leak fluid that can cause damage to the macula rapidly. These hemorrhages cause exudates that can be easily seen through a retinal exam. [8] [29]

Progression of dry AMD can be slowed in many patients through dietary supplements, while visual loss from wet AMD is treated with intravitreal administration of anti-vascular growth factor [8].

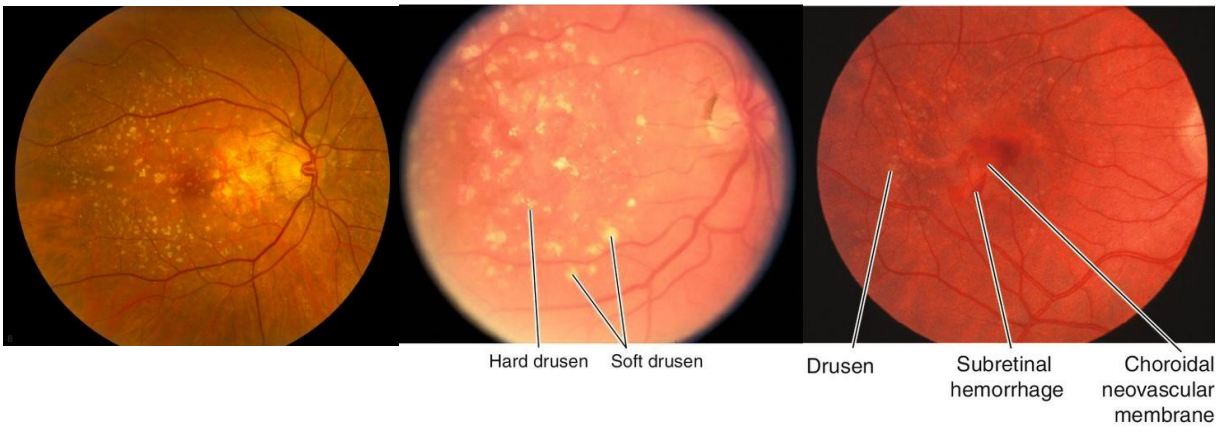


Figure 2.14 Left side: Picture of the fundus of the eye showing intermediate age-related macular degeneration [54] Middle: Dry, age-related macular degeneration demonstrating drusen and pigmentary changes. [30] Right-side: Exudative age-related macular degeneration demonstrating subretinal hemorrhage from choroidal neovascular membrane. [30]

2.3 Imaging Challenges

Image quality, especially in the field of medicine, has gained more attention, since insufficient quality in medical images can affect the clinicians' capacity to perform a correct diagnosis. Although quality assessment is a difficult and subjective task in any field, there have been several approaches published regarding fundus image quality.

The main limitations of the most recent mobile solutions for fundus photography are rooted in its hand-held nature: focusing and illumination beam positioning, which can be time-consuming. Although their performance is not yet assessed in comprehensive clinical trials, these devices show promising results.

Quality of fundus images is usually verified by the photographer in the acquisition moment, and in case of poor quality, where an adequate assessment of key features in retina is impaired, it should be retaken [33]. There are two main characteristics for a good quality fundus image:

- Positions (The macula and the optic disc are horizontally aligned in the middle)
- High contrast (The macula, optic disc, and vessels are all clear)

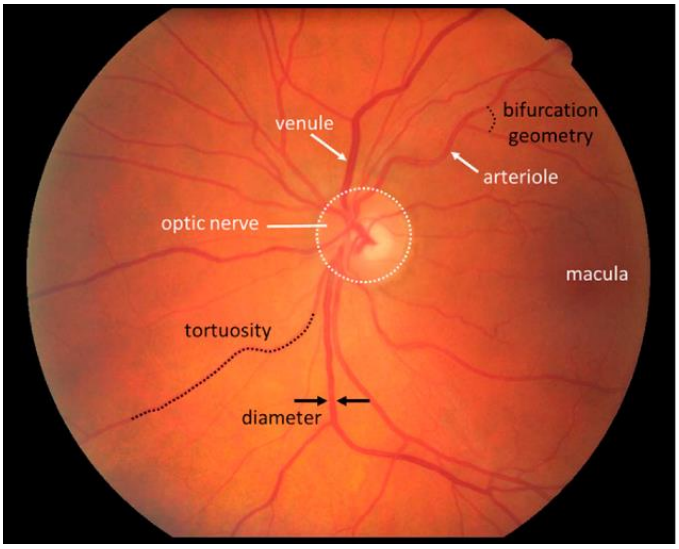


Figure 2.15 Features of interest in a fundus image. [21]

As explained by MacGillivray TJ et. al. the optic nerve head boundary provides a reference point for locating and quantifying other features of interest, and is therefore the first focus point of any retinal exam. Besides this, measurement of parameters such as the vessel diameter, bifurcation geometry and vascular tortuosity can reveal a suboptimal microvascular network in the retina, which in turn may be related to microvascular damage and an indicator of disease [21]. Hence, the need to provide a view of the retinal periphery, so that the full scope of the retina may be examined.

To capture a high quality fundus image, proper camera-to-eye distance and alignment should be maintained to avoid haziness and artifacts [33]. The camera settings, such as the ISO, Light intensity and exposure time, among others, are also of major importance to image quality, and they should be adjusted to a low light environment (where pupil diameter reaches the recommended size) avoiding

severe over- and underexposures [34]. Summarizing, the quality of fundus photographs is dependent on the photographer skills and experiences, the camera, the patient and the environment/setting.

When issues in quality exist, it may be difficult to identify the cause of artifacts in the photograph. Just like any multistep process related to hand-held image acquisition, each act within the procedure can compound possible errors. Since each error can produce a corresponding artifact, it is important to describe and catalogue fundus photo errors accordingly. The type of artifacts and their cause were introduced in 1984 by Patrick J. Saine at the Ophthalmic Photographer's Society, at the time with the use of a desktop camera [35].

More recently, several user manuals of handheld ophthalmic cameras, have highlighted the artifacts caused by misalignments and improper camera-to-eye distance. The Figures 2.16 and 2.17 (created using Figma - a web-based design tool) depict these failures, according to the manuals description and illustration [36].

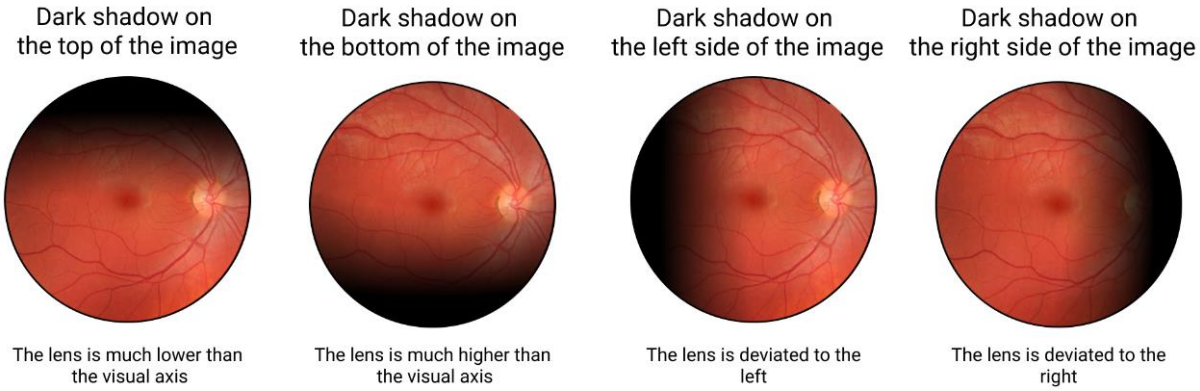


Figure 2.16 Right eye fundus with peripheral crescent artifacts, indicating position misalignment between the lens and the patients' pupillary aperture

The peripheral crescent artifacts shown in Figure 2.16, occur due to vertical and/or horizontal misalignment between the lens of the handheld device, i.e. the illumination ring and patient's pupillary aperture [37]. This is rectified by moving the camera in the same direction of the artifact. For instance, when a dark shadow appears on the top of the image, it means the lens is much lower than the visual axis and therefore the user should correct this by tilting or moving the device upwards.

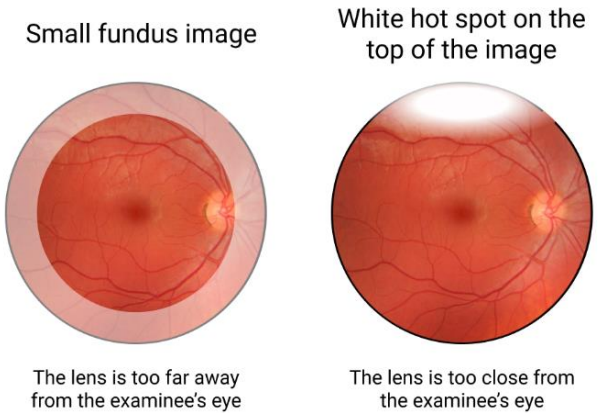


Figure 2.16 Right eye fundus with artifacts, indicating improper camera-to-eye distance

The artifacts shown in Figure 2.17 occur due to an improper camera-to-eye-distance. On the left-side we have a small fundus image, indicating the lens is too far away from the examinee's eye. As the image shows, the retina doesn't fully occupy the field-of-view expected. On the right side we see a

white hot-spot on the top of the image, indicating the lens is too close from the examinee's eye. This over-exposure artifact is due to the reflection of light caused by an excessive proximity.

Succinctly, an understanding of the factors that may affect non-mydriatic photographic quality in a real-life clinical setting can provide opportunities for improvements in camera design and personnel training which in turn could lead to improved photograph quality.

2.4 Fraunhofer's Eye Fundus Scope (EFS) prototype

Smartphone-based ophthalmic cameras, like the Fraunhofer's EFS prototype, emerged from the continuous development of the mobile phone hardware and the need to tackle certain limitations inherent with traditional retinal imaging devices. The application of these devices may have a major impact in clinical fundus photography in the upcoming years.

The EFS prototype is a self-contained mobile-based solution comprising automated and early detection of diabetic retinopathy with a low-cost optical attachment to an Android smartphone for retinal image acquisition. The automated analysis can provide a first assessment on the presence of DR by employing advanced machine learning algorithms to process the image in search of lesions such as microaneurysms and exudates, often associated with the onset of DR [38].

EFS technology aims to simplify, anticipate and increase the screening coverage, not only of DR, but also, Glaucoma and AMD among other retinal and systemic diseases. This is possible because it has a powerful image acquisition and pre-diagnostic tool that doesn't require pupil dilation. Its major goal is to facilitate patient access to early treatment and decrease the burden of screening actions on healthcare systems.

The EFS physical prototype consists of a device built through 3D printing with own industrial design and contains objective ophthalmic lenses, beam splitters for redirection and alignment of light, low energy LEDs, among other relevant elements to maximize comfort for the wearer and the quality of image capture of the retina. The most current version of the physical EFS prototype enables image capture with a wider FOV (about 45º), which allows for more clinically relevant information. In addition, it also has an infra-red light that is used to guide throughout the exam without any discomfort for the patient.

Figure 2.181 Assembled EyeFundusScope prototype

EFS enables the acquisition of retinal images through a mobile application running offline on the smartphone (EFS-Acquisition App). This application uses an Enhanced Camera API (Application Programming Interface) library, that allows low-level control of the camera parameters of smartphones with the Android operating system, to meet the advanced requirements of computational vision. This application also uses the Handheld Image Acquisition library with Real-time Quality Control

Component (HIARQC), which includes a set of operations that allow real-time measurement of parameters related to image acquisition quality, using data from the image sensors and inertial sensors of the smartphone. Both of these libraries were developed at Fraunhofer.

The various images can also be combined automatically for a broader view, through a process called EFS-Image Stitching.

The EFS-App is capable of not only detecting lesions associated with previously mentioned retinal diseases, such as microaneurysms and exudates but also to determine the diabetic risk level using a decision-support system [39]

After the first stages of image acquisition and quality filtering, the Decision-Support System that receives as input the results from microaneurysms detection and from the decision-tree that classifies the exudates [based on the approaches developed in (Costa et al., 2016) and (Felgueiras et al., 2016)] is executed, aiming at the separation between pathology-free and positive cases.

As previously seen, microaneurysms appear as small red dots in the retinal images and are the earliest sign of DR. This kind of lesion present specific characteristics in retinal images that are suitable for detection: small size (few pixels only) circular shape and hypo-intensity in relation to the background (Figure 2.19).

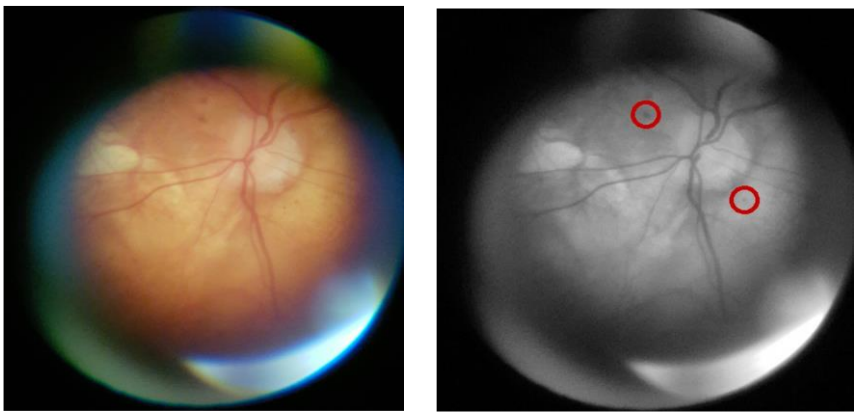


Figure 2.192 Retinal image with microaneurysms [39]

On the other hand, exudates are yellow structures that often appear in the retina as a result of the progression of DR. There are two types of exudates, soft and hard, which are accumulations of axioplasm and accumulations of lipid and protein in the retina respectively. These appear to be bright, reflective, white or cream colored lesions that indicate increased vessel permeability and an associated risk of retinal edema.

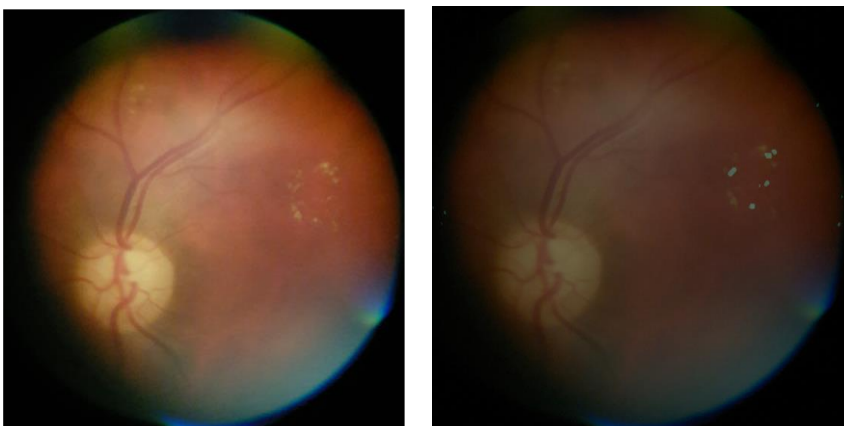


Figure 2.203 Retinal image with exudates. Right image highlights the área where the exudates are located [39]

In one of the most recent studies ('Mobile-based Risk Assessment of Diabetic Retinopathy using a Smartphone and Adapted Ophthalmoscope') a total of 80 patients were analyzed at Hospital Santo António, Centro Hospitalar do Porto. It was found that "the obtained images have enough information to provide feedback about Diabetic Retinopathy. However, sometimes it is complicated to provide feedback about all quadrants of the eye" without performing pupil dilation. Also, the time that each acquisition procedure took was very small, and the "classification results has shown that the usage of EFS may contribute for the reduction of the time-consuming task of image interpretation by specialists".

Chapter 3

State-of-the-art

Before creating and implementing a new GUI on the fundus observation screen of the EFS prototype, a study was made on what the current mobile solutions similar to the EFS have to offer in terms of specifications and user interfaces.

In the end of this chapter a table is presented, comparing the different handheld fundus cameras.

3.1 Visuscout® 100

Visuscout® 100 (Figure 3.1) developed by Zeiss (Oberkochen, Germany) is a handheld fundus camera with a compact and lightweight design. It is also a non-mydriatic device, with a precision autofocus system, allowing a clear fundus examination without the dilation of the patient's pupil.

This device acquires color, red-free and near-infrared (NIR) images (with a 40º FOV) that can be transferred to a PC or mobile device by WiFi. It has nine internal fixation LEDs built in, that help the correct alignment of the patients' pupil and also facilitates the capture of peripheral images. However, Visuscout® 100 is only suitable to examine patients that have at least a 3.5 mm diameter pupil [40].

In respect to the GUI, it has an adjustable diopter bar in the right-side of the screen and in the bottom left corner it has the internal fixation target display. The curved lines, on both sides of the fundus observation screen, indicate if the focus is appropriate or not, by changing its colors from red to green. In the bottom it has the illumination level indicator and also the focus mode indicator. In the top left corner it has the patient indicator and the still/video capture mode indicator.

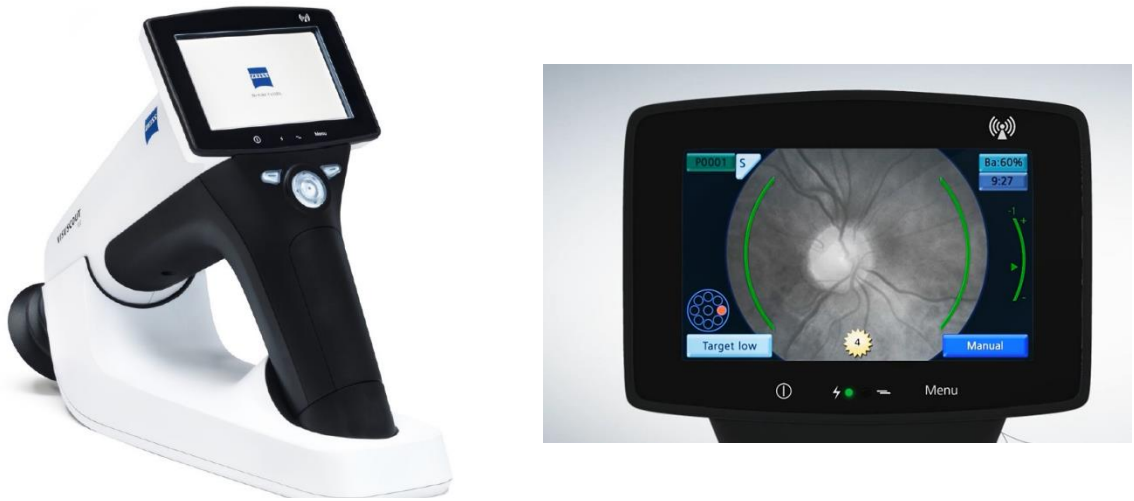


Figure 3.1 Left side: Visuscout® 100 from Zeis. Right side: Observation fundus screen in the Visuscout® 100 [40]

3.2 Volk Pictor Plus®

Pictor Plus (Figure 3.2) developed by Volk Optical Inc. (Mentor, Ohio, USA) is another non-mydriatic fundus examination device, with a 40º FOV. It allows the acquisition of both digital images

and videos of the retina, that can be transferred via WiFi or USB. The right imaging distance is about 2 cm, when the silicone support is compressed approximately half way down.

The 10 illumination levels and focusing (automatic or manual, diopter compensation -20D to +20D) can be adjusted to produce high-resolution reflection-free images and, beyond color images, it offers red-free images for better contrast. Pictor Plus is only suitable for the examination of patients with a pupil diameter of 3 mm or higher [41].

Its GUI is very similar to the Visuscout® 100.

Figure 3.2 Left-side: Volk Pictor Plus from Volk Optical Inc. Right Upper corner: Volk Pictor Plus observation fundus screen. Right lower corner: Volk Pictor Plus indicators from the observation fundus screen. [41]

3.3 Optomed Aurora®

The Optomed Aurora (Figure 3.3) developed by Optomed (Oulu, Finland), and launched in 2018, is intended for non-mydriatic fundus imaging, using infrared light for targeting the fundus and a flash of white light when an image (50º FOV) is taken.

This device, developed by the same company that launched the Smartscope PRO, includes as main features an autofocus system, diopter compensation (-20D to +20D), color, red-free and IR imaging, nine internal fixation targets for better peripheral imaging (the middle fixation target provides a macula-centred image) and WiFi/USB connectivity. The minimum pupil size indicated for the use of this device is 3.1 mm [42].

To move between the menu items, Optomed implemented the Optoroller. This rotational button is also used to change the focus mode (manual or automatic), select the diopter compensation (when in manual focus mode), the brightness level, the fixation target and the patients' menu. In this system the right/left eye selection is done after the image capture.

Figure 3.3 Left side: Optomed Aurora. Right side: Optomed Aurora fundus observation screen [42]

3.4 VersaCam™ α

VersaCam™ α (Figure 3.4) developed by Nidek Co., Ltd. (Gamagori, Japan) provides high quality digital imaging of the retina with a 45º horizontal FOV and a 40º vertical FOV. The auto-focus system allows easy image capture and the seven internal fixation LEDs equipped with the device facilitates the capture of peripheral images. Beyond autofocus, this device also has the option of manual focus. The acquired images can be saved on a SD memory card or transferred to a PC by a mini USB port [43].

As for the GUI, it has a focus alignment indicator (vertical bar) located on the right side, a left/right eye indicator located at the bottom corners, a fixation target indicator at the top right corner and a brightness indicator. It also as an effective zone indicator (dashed green rectangle) that is used to adjust an IR spot (reflection). Once the IR spot is located inside the effective zone an image with proper focus and without reflection artifacts can be captured.

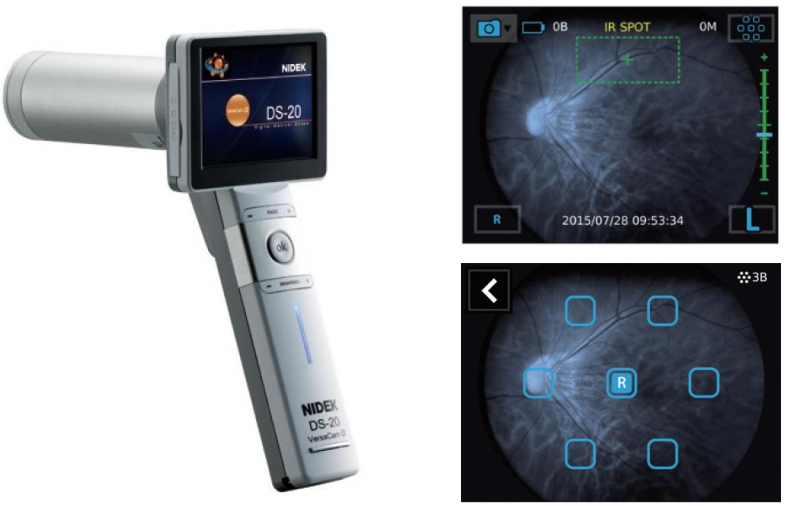


Figure 3.4 Left-side: VersaCam™ α from Nidek Co. Ltd.. Right top corner: VersaCam™ α observation fundus screen. Right bottom corner: VersaCam™ α internal fixation target display [43]

3.5 Horus Scope

Similar in specs and GUI, the Horus Scope (Figure 3.5) developed by JedMed (St. Louis, Missouri, USA) is a hand-held fundus camera that captures video and images (45º FOV). The built-in auto-focus technology helps to obtain quick and clear images of the fundus, through a non-mydriatic eye.

This device also includes seven internal fixation points, which help to aid the patient in ocular positioning, as well as a manual focus version but with lower FOV (40º). [36]

Its GUI is very similar to the VersaCam™ α.

Figure 3.5 Left side: Horus Scope from JedMed. Right-side: Ez Horus Scope observation fundus screen [36]

3.6 iExaminer™

The Welch Allyn iExaminer™ (Figure 3.6) turns the ophthalmoscope, firstly designed as a direct ophthalmoscope, into a mobile digital imaging device. It aligns the optical axis of the PanOptic™ ophthalmoscope to the visual axis of the iPhone camera to capture high-resolution pictures of the fundus and retinal nerve. The storage and display of images is done by the iExaminer app. The iExaminer is available for iPhone 4, 4S, 6, 6S, 6 Plus and 6S Plus [44].

Figure3.6 iExaminer from Welch Allyn [44]

3.7 Volk INview

The Volk INview (Figure 3.7) is a recent ophthalmic camera device, attachable to iPhone or iPod that allows the capture of wide-angle color images of the retina. The patient's pupil must be dilated, because it requires a minimum of 5 mm for pupil diameter, so this is a mydriatic device.

It requires the use of a mobile application (Volk INview mobile app) that automatically detects and selects the images with higher definition and more focused, acquiring images quickly and easily. Thanks to the dilated pupil, this device achieves a wide 50º FOV, allowing more retinal tissue to be visible in one image. The images are stored with patient data and can be easily exported to a computer. Volk INview is available for iPhone 5S, 6 and 6S and for iPod Touch (6th generation) [45].

Figure3.7 Volk INview from Volk Optical Inc [45]

3.7 FOP NM-10

The FOP NM-10 (Figure 3.8) is a non-mydriatic (above 3.3mm pupil size) smartphone enabled retinal imaging device created by Remidio. This ophthalmic camera, attachable to iPhone 6, 6S or 6S+, gives a FOV of approximately 45º and up to 10 times magnified view of the retina. Its photography modes include the standard color, red-free and NIR. It also includes as main features a manual and automatic focus adjustment, and a diopter compensation (-30D to 30D). [46]

Figure 3.8 Left side: Remidio FOP NM-10. Right side:Remidio FOP NM-10 observation screen [46]

The built-in smartphone app designed with cloud sync function enables remote view of images in a variety of telemedicine models. The software also offers advanced options including Image Montaging, Glaucoma Screening Assist and artificial intelligence (AI) based image analysis for automatic diabetic retinopathy detection.

Regarding the GUI, it has a mode changing slider (bottom right corner) to toggle between mydriatic or non-mydriatic imaging. In mydriatic mode only the white LED icon (bottom left corner) appear. In the non-mydriatic mode both the white and red LED icons appear, as figure 3.8 illustrates. It also visible an ISO, a Tone and an IR/White LED intensity indicators, allowing the user to quickly access the settings without leaving the fundus observation screen.

Table 1 State-of-the-art handheld fundus cameras

	FOV	*Pupil dilation*	*Illumination**	*Internal Fixation Points*	*Price/Cost*	*GUI elements***
Visuscout 100	40º	No (min. 3.5 mm)	IR and W	9	10000€	Diopter, IFP, Focus and Brightness
Volk Pictor Plus	40º	No (min. 3 mm)	IR, W and RF	9	10000€	Diopter, IFP, Focus and Brightness
Optomed Aurora	50º	No (min. 3.1 mm)	IR, W and RF	9	12000€	Diopter, IFP and Brightness
Versa Cam	40º	No (min. 3.5 mm)	IR and W	7	9500€	Diopter, IFP, Focus, Brightness and L/R
EZ-Horus Scope	40º	No	IR and W	7	9000€	IFP, Focus, Brightness and L/R
iExaminer	25º	No	W	0	-	-
VolkInView	50º	Yes (min. 5 mm)	W	0	1000€	-
FOP NM-10	45º	No (min. 3.3 mm)	IR, W and RF	0	7000€	M/N-M slider, ISO, Tone and IR/W intensity
EyeFundusScope	45º	No	IR and W	0	800€	-

* IR – Infrared light for alignment mode, W – White light for acquisition mode, RF – Red-Free images for better contrast

** IFP – Internal Fixation Targets display indicator, L/R – Left/Right eye indicator, M/N-M – Mydriatic or Non-mydriatic imaging indicator, IR/W – Infrared/White LED intensity indicators

Note: The estimated cost per EFS prototype unit in a production of 100 units (includes optical system, all electronics, smartphone adapter and mobile software) is 800€. At the beginning of this project the EFS fundus observation screen didn't have any GUI indicators. At the time the usability tests were concluded the EFS didn't have any internal fixation points.

Chapter 4

Methods

In this chapter the methodology used in the progress of this project is presented. It started with the designing of a wide variety of interaction elements (IEs), some of which, the rotational IEs, translate the data from the inertial sensors of the smartphone. After the design stage came the implementation of the IEs on the EFS Android App. Throughout the design and implementation stages, several tests were performed in an ophthalmoscope trainer which allowed for several readjustments and modifications. The last stage was the validation with field tests, so that several users could try the new GUI that was implemented. An interaction protocol for smartphone image capture of the fundus of the eye was developed simultaneously to the testing stage with the ophthalmoscope trainer, and was later carried out in the field tests.

As JoAnn T. Hackos et.al. stated, “Understanding how people interact with technology and studying how user interface design affects the interactions people have with technology is the focus of human factors engineering (HFE) and usability engineering (UE)” [47].

4.1 Interaction Elements Design

The main purpose on creating new interaction elements is to make digital retinal photography an easier learning task, and at the same time encouraging any personnel to perform adequate digital photography in a matter of hours. The focus in the development of an HCI abstraction layer with GUI workflows, is to provide feedback to the user so that the alignment, perspective, focus distance and other constraints, inherent to retinal imaging, are achieved within the accepted levels.

In order to create a GUI that is the starting point to a new interaction technique, developed between the user and the EFS, there is a need to consider the foundations of handheld fundus photography. The objective is to avoid common user errors related to incorrect alignment and positioning of the retinal imaging device, as presented in chapter 2, by translating the data from inertial sensors into rotational IEs.

The design of all IEs was done using Figma, which is a web-based design tool with real-time collaboration. Since there is no software to download and all work was saved automatically to a shared space in the cloud, it was easy to share the progress in the design and to discuss the updates.

4.1.1 Handheld camera movements

As many other projects currently being developed at Fraunhofer, the usage of inertial sensors is considered a great improvement for real-time biofeedback applications. The first step before creating any rotational IE is to deconstruct and label every movement inherent to a hand-held device, like the EFS. There are 5 types of movements that we can clearly identify when using any hand-held device, each of them are shown in Figure 4.1.

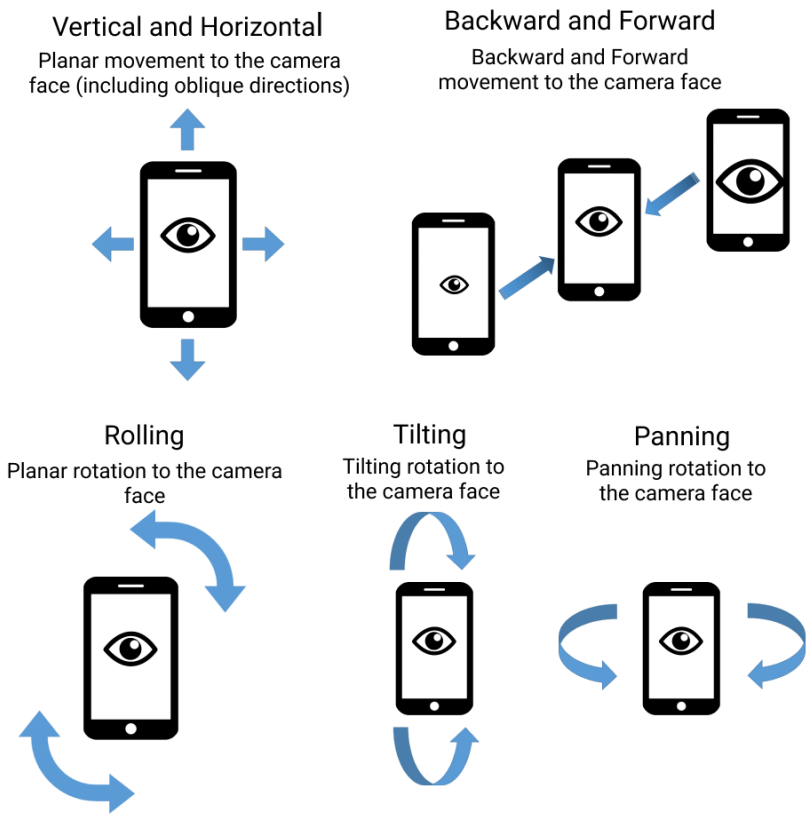


Figure 4.1 Identification of Handheld movements

There are three movements in which the inertial sensors can provide meaningful data: the planar rotation to the camera face (rolling), the tilting rotation to the camera face and the panning rotation to the camera face. These movements, if successfully translated into interaction elements in the fundus observation screen, can be an innovative interaction technique for alignment and positioning of the EFS.

4.1.2 Inertial sensor based Interaction Elements

Inertial sensor based IEs were created in order to give the user a proper indication of the handling of the smartphone. The 3-axis were taken into consideration and to determine which of them are the most appropriate to correct the alignment, while the acquisition takes place, usability tests that are described later in this chapter were executed. In order to better differentiate each rotation in respect to the camera face, the same nomenclature given in cinematography was used, as shown in Figures 4.1 and 4.2.

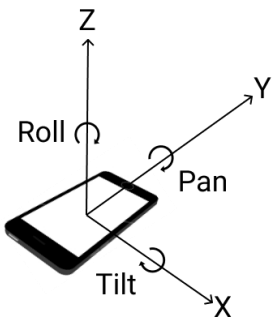


Figure 4.2 Smartphone Sensors axis

4.1.2.1 Roll Interaction Element

The Roll IE, related to the Z-axis of the Cartesian coordinate system was created in order to assure that the smartphone is properly aligned with the typical vertical position of the patient. By standardizing the orientation of all acquired images, it should allow an easier detection of the quadrant on which the lesions appear.

In order to better illustrate the Roll IE, three different versions were designed. Before reaching the final versions that were later implemented each in a different Android App several changes were made throughout. The first sketches for each of these versions are shown in Appendix 1. Later they were redesigned, to better suit the requirements of the EFS, as well as its functionality and purpose.

The most important characteristics were its size, colour and position. Since the alignment is done using NIR light and in a clinical environment there should be almost no other source of light, it was required that all IEs stayed out of the region which the retina is visible on the observation screen. This was done by roughly measuring in density-independent pixel (dp), the size of this region.

Version A

The version A Roll IE is a simple circle with four indicators (up, down, left and right) to help the user keep track of the position of the smartphone. The approximate diameter of the component is 374 dp which is the area occupied by the retina in the fundus observation screen. Two colors, green and red, were chosen to indicate if the prototype was aligned or misaligned respectively.

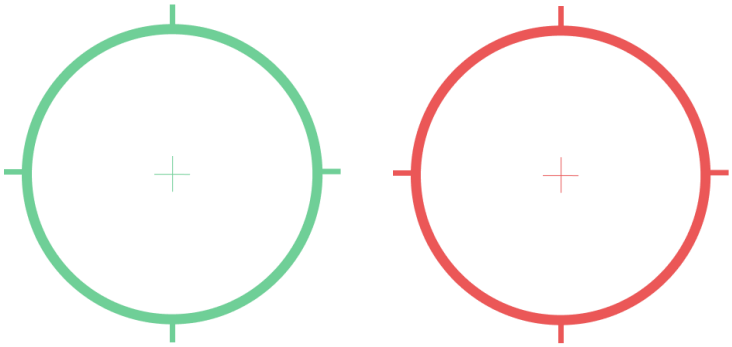


Figure 4.3 Version A of Roll IE. Left side: green circle indicating proper alignment. Right side: red circle indicating misalignment.

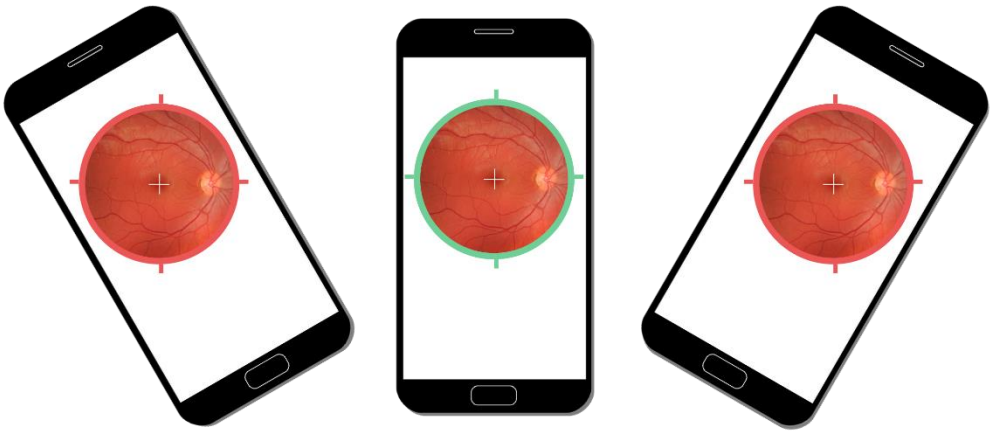


Figure 4.4 Version A. Correct illustration of the behavior of the Roll IE according to the position of the smartphone. 30º, 0º and -30º respectively.

Version B

The version B Roll IE, is comprised of a circle with seven indicators, placed at 0º, 30º, -30º, 60º, -60º, 90º and -90º. The 0º indicator is an inverted triangle with no filling. These indicators and the circle are "fixated" to the fundus observation screen, meaning that they won't change its position. In order to illustrate the rolling, an inverted triangle shape component was created, with a brighter color that should function as a pointer rotating around the "static" circle component.

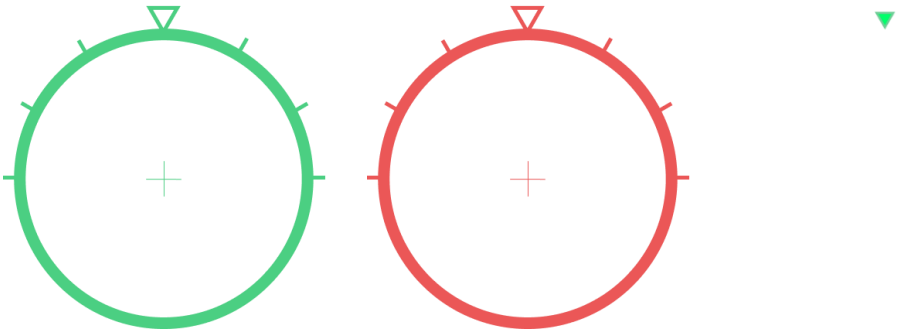


Figure 4.5 Version B of Roll IE. Left side: green circle indicating proper alignment. Middle: red circle indicating misalignment. Right side: pointer

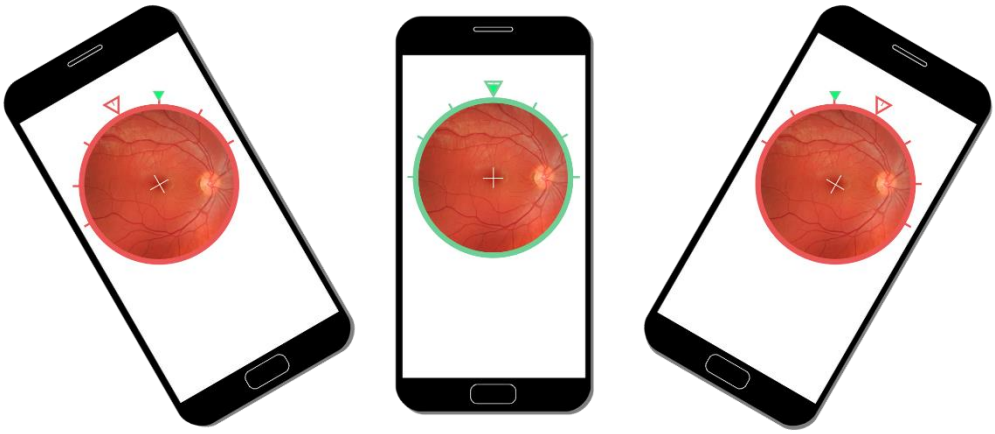


Figure 4.6 Version B. Correct illustration of the behavior of the Roll IE according to the position of the smartphone. 30º, 0º and -30º respectively.

Version C

The version C Roll IE, like the previous one, also includes two different components: a white circle with 4 indicators, which is "fixated" in the fundus observation screen and a pointer (rotating component). The 4 indicators, located up, down, left and right, act as a referential, and are used to align the pointer, which is a straight line that spins when the angle shifts.

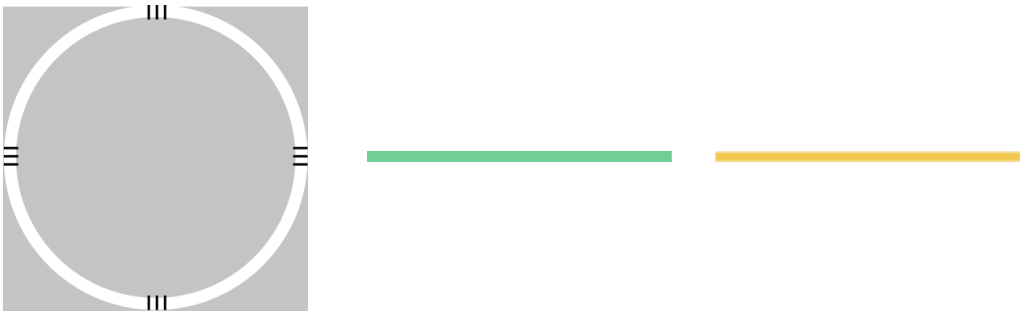


Figure 4.7 Version C of Roll IE. Left side: white circle alignment. Middle: green pointer indicating proper alignment Right side: yellow pointer indicating misalignment.

All 4 indicators are composed by 3 small black lines, and should help the user to stabilize the smartphone. In order to achieve an adequate vertical position, the pointer should maintain contact with the 2 indicators located at the left and right side of the circle, changing its color from yellow to green. Between the upper and lower line of these indicators, the user has a small interval (app. 6º) in which the pointer is green.

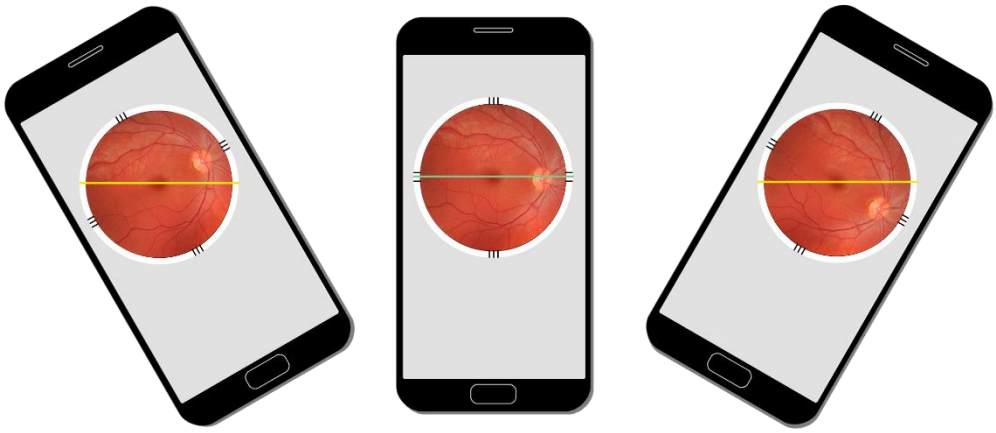


Figure 4.8 Version C. Correct illustration of the behavior of the Roll IE according to the position of the smartphone. 30º, 0º and -30º respectively.

4.1.2.2 Pan Interaction Element

Panning defines itself as a rotation around a vertical axis which causes the field-of-view to move horizontally. This is where the traditional term of *panorama* comes from. Therefore, the Pan IE, related to the Y-axis of the Cartesian coordinate system, was created in order to assure that the smartphone is directly positioned in front of the patient eye. This should help the ophthalmic lenses inside the prototype to be inline with the patients' pupil.

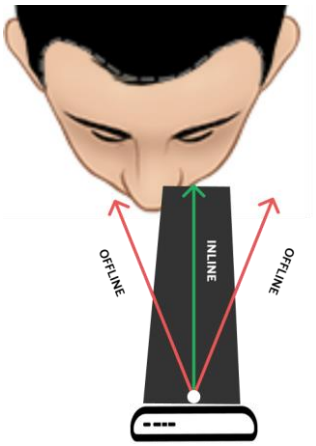


Figure 4.5 Illustration of the possible deviations caused by panning.

In order to better illustrate the Pan Rotation, three different IEs were designed. Just like the Roll IEs, before reaching the three final versions that were implemented in the EFS App, several changes were made throughout its development. The first draft for this interaction elements can also be seen in the last sketch of Appendix 1.

The same pallet of colors used for the Roll IEs is used for the Pan IEs . This should help blending all the interaction elements together, creating a sense of what is correct and what type of motions should be avoided.

Version A

The version A Pan IE consists of two different components: an elliptical box, which acts as a background, and coloured arrows that indicate to the user if the smartphone is deviated to the left or to the right. Otherwise, if the smartphone is correctly aligned, a green circle should appear instead of the arrows. The colour and position of the arrows indicate the level of deviation.

Figure 4.6 Left side: Grey elliptical box used as background. Right side: Colored arrows and green circle, which will indicate the Pan rotation

Version B

The version B Pan IE consists of a colored box as a background on which colored vertical lines appear indicating the user if the smartphone is deviated to the left or to the right. The color of these lines is the same as the box, making it more perceivable for the user to acknowledge the degree of deviation.

Figure 4.7 Left side: colored boxes Right side: colored lines

Version C

The version C Pan IE consists of a colored box, similar to the previous version, which also changes the color accordingly to the position of the pointer that flows left or right. Also, just like the previous version, the box changes its color accordingly to the pointer, making it easier for the user to perceive it.

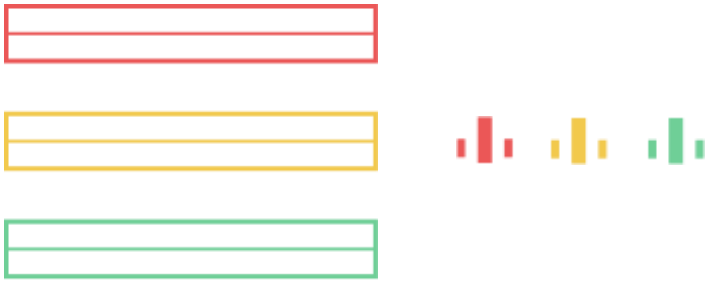


Figure 4.8 Left side: coloured boxes Right side: colored pointers

The behavior of the 3 versions previously presented according to the position of the smartphone is shown in the Figure below.

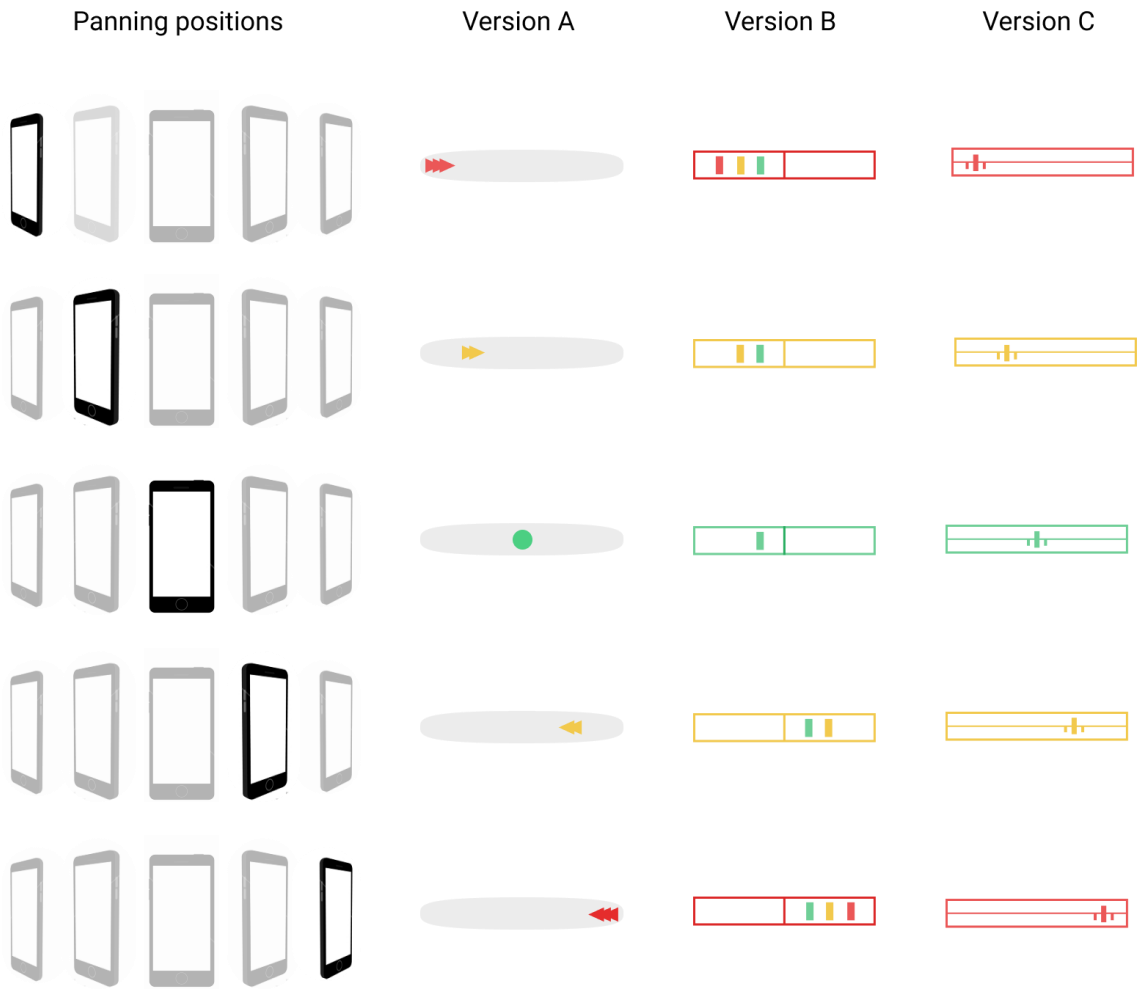


Figure 4.9 From left to right: Panning positions of the smartphone; Version A feedback according to each position; Version B feedback according to each position; Version C feedback according to each position

4.1.2.3 Tilt Interaction Element

Titling defines itself as a rotation around a horizontal axis going through the camera perpendicular to the lens, which moves the field-of-view up and down. There is a neologism word *vertorama* which essentially means a *vertical panorama*.

The Tilt IE, related to the X-axis of the Cartesian coordinate system, will indicate when the smartphone is lower or higher than the visual axis. The purpose is to guide the user to keep the lenses levelled with the examined eye.

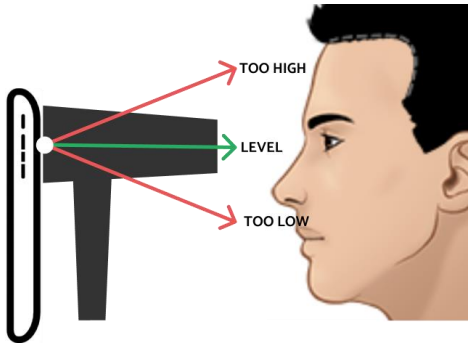


Figure 4.14 Illustration of the possible deviations caused by Tilting.

Just like the Rolling and Panning IEs, three different versions were tested to give the user feedback for the Tilting IE. Since the Tilting motion is essentially a vertical Panning, the components used for the Panning motion were redesigned for a "vertical reading", using the same pallet of colours.

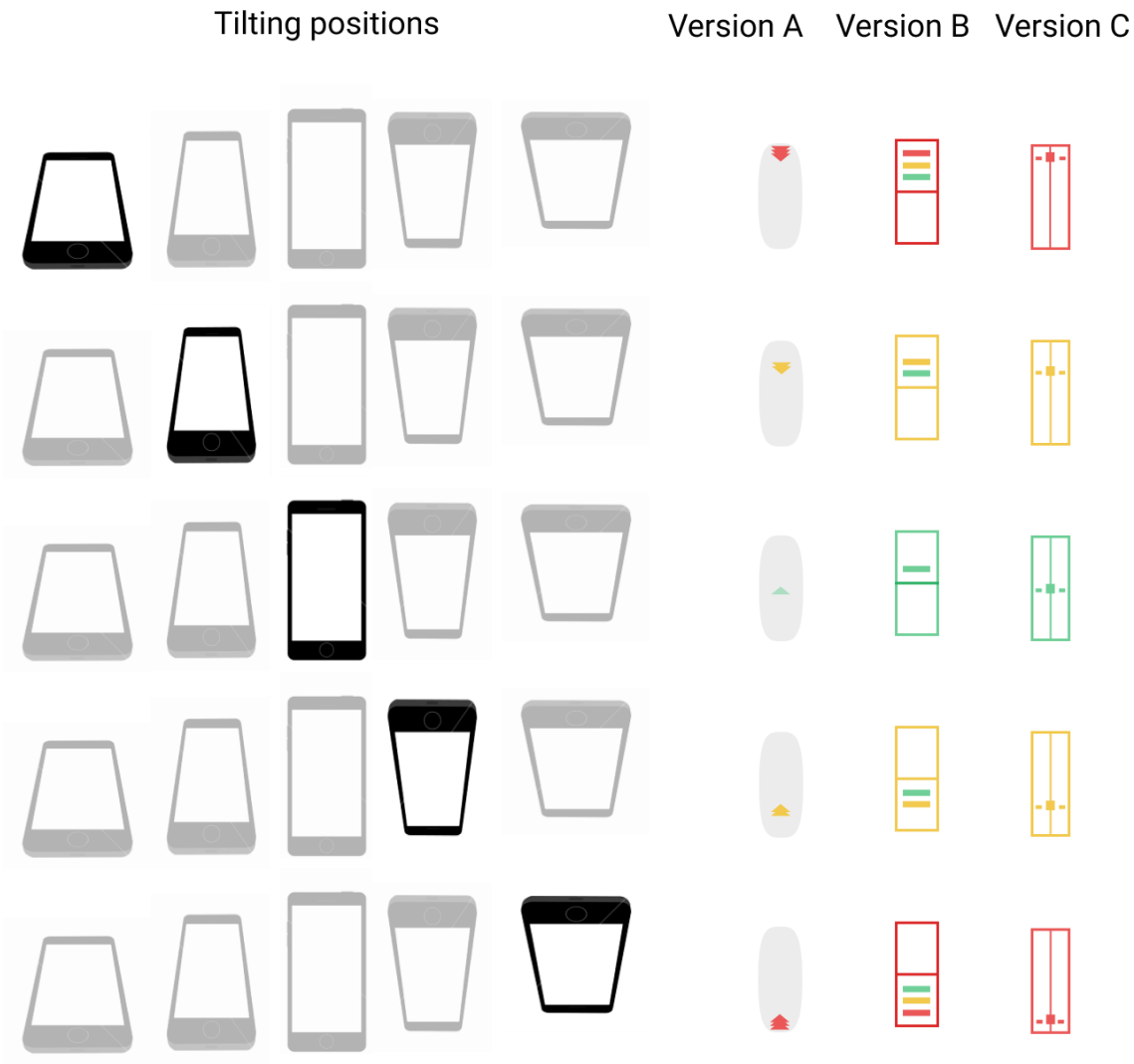


Figure 4.15 From left to right: Tilting positions of the smartphone; Version A feedback according to each position; Version B feedback according to each position; Version C feedback according to each position.

4.1.3 Indicators for fundus observation screen

Just like the rotational IEs that were previously presented, there are at least two other components that may prove to be useful in the fundus observation screen. These are the time-lapse IE, and a Right eye/ Left eye indicator. Although the Roll, Pan and Tilt IEs directly influence the way the user interacts with the EFS prototype in regards to its position and alignment, the time-lapse and the eye indicator should facilitate the exam procedure.

4.1.3.1 Time-lapse Interaction Element

A time-lapse IE, working as a timer, was created so that the user has the correct perception the time it should take between acquisitions of the same eye. If several acquisitions are taken in a short period of time, the patient's pupil is probably going to constrict making it more difficult to see the retinal tissue. The interphotographic interval that shows to be suitable is around 30 seconds. This should be quick enough for the whole exam to last 5 minutes balancing image quality and patient comfort, as shown by Lamirel C. et al [22].

The component used for the time-lapse IE is a dashed circle. It should be positioned inside the Roll IE without compromising the region of interest, that is where the retina appears.

The Figure bellow depicts the 9 stages of the interphotographic interval. Starting with a complete grey circle in the instant a photograph is taken, followed by an animation where each segment changes color, in a clockwise fashion, until the full circle is blue.

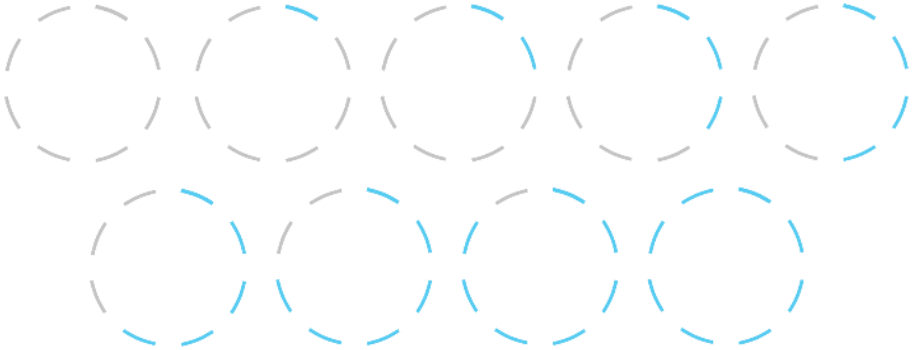


Figure 4.16 Representation of a full time-lapse between acquisitions on the same eye. Full grey circle being the first stage, and the full blue circle being the last stage

4.1.3.2 Right and Left eye indicator

Besides the time-lapse IE, an indicator of which eye the user should examine was implemented on the fundus observation screen. This component suits the EFS prototype exam workflow, since that for each patient, the user should always select which eye is going to be examined, and the pictures taken will be stored accordingly.

A real time scenario for the use of the EFS prototype would be the screening of numerous patients in a short period of the time, and for that matter the user is constantly changing from eye to eye for each patient. An indicator on the fundus observation screen should prove useful, in order to avoid mistakes or leaving the observation screen to double-check which eye is being examined at the time.

This indicator is comprised of two components, one for the left-eye, positioned on the right side of the fundus observation screen, and other for the right eye, positioned on the left side of the fundus observation screen. This positioning is easily explained since for the user point of view, the right eye of the patient is on its left side, and the left eye of the patient is on its right side. The eye being examined will be highlighted with a blue box while the other eye will remain in a grey box.

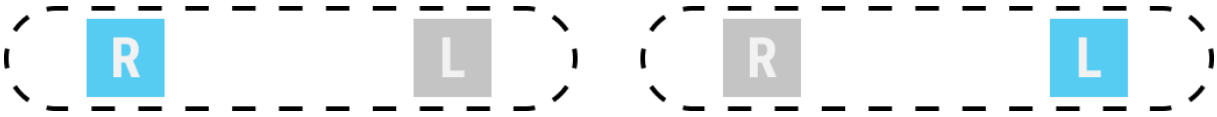


Figure 4.17 Right eye and left eye indicators. On the Left side, a blue R and a grey L indicate the right eye is being examined. On the right side, a grey R and a blue L indicate the left eye is being examined.

4.1.4 Tutorial

For the purpose of Usability Tests and for all the new users that want to handle the EFS prototype and learn the correct positioning and alignment, a Tutorial, as seen in the Figure below, was created explaining the basic principles inherent to a good acquisition.

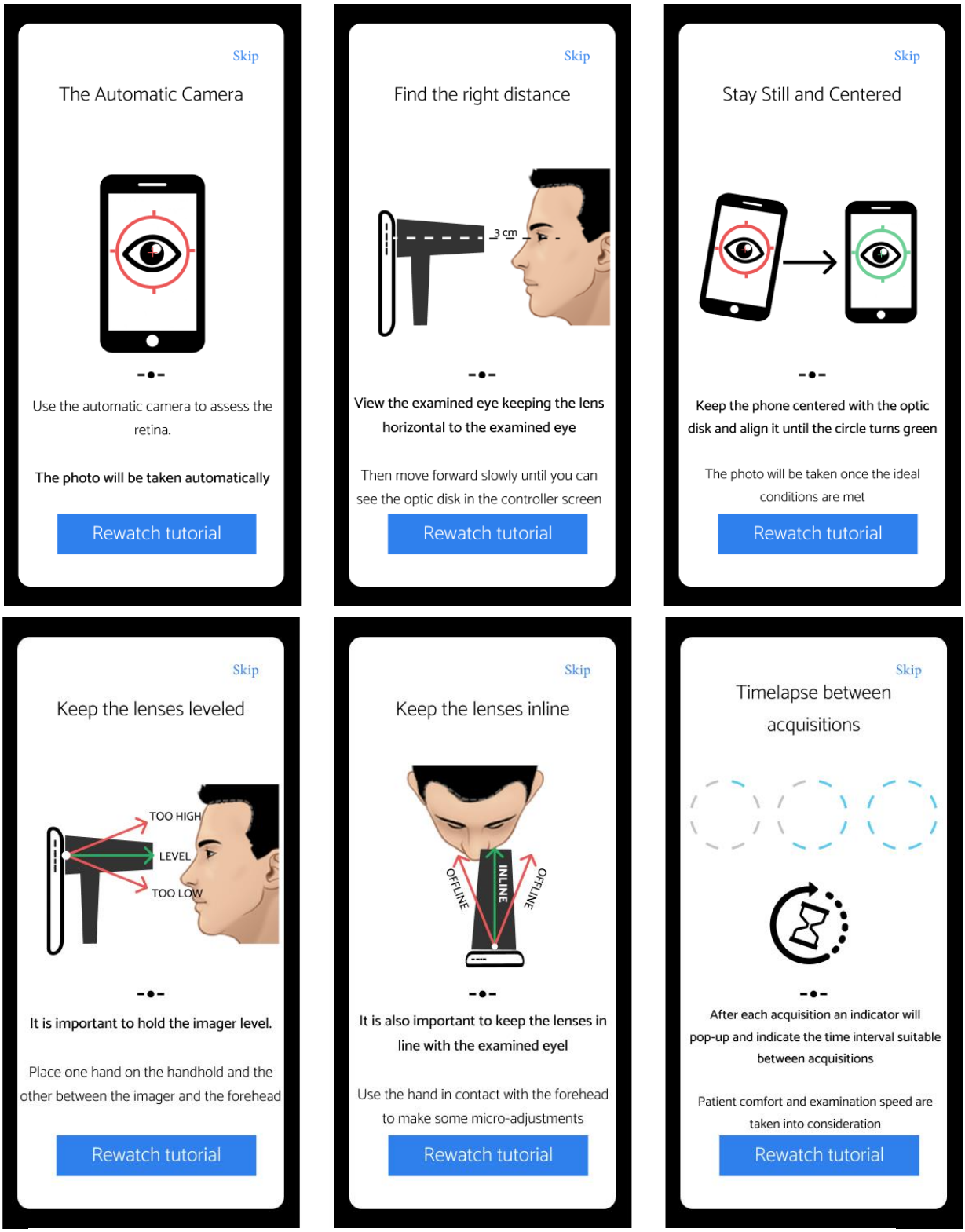


Figure 4.18 Tutorial slides presented in the Usability tests

In the first slide of the tutorial, “The Automatic Camera” is presented to the user. The photo acquisition will occur automatically once the EFS-Acquisition App is able to recognize retinal structures, such as the macula, the optic disc or retinal vessels. At the time the Usability Tests took place, only the manual acquisition mode was available, by pressing a button on the 3-D printed handhold.

The second slide of the tutorial, “Find the right distance”, explains the user how to achieve the best focus distance, first by keeping the lens horizontal to the examined eye and then moving forward until retinal structures are perceivable, at around 3 cm distance.

The third slide, “Stay Still and Centered” illustrates the use of the Roll IE by correcting the smartphone’s position. Also emphasizes the need to keep the smartphone still and centered before acquisition.

The fourth and fifth slide, “Keep the lenses leveled” and “Keep the lenses inline” respectively, alert the user for the importance of avoiding deflections in regard to the Tilting and Panning movement. It also explains the user how to better hold the prototype, by placing one hand on the handhold and the other between the imager and the forehead of the patient, and using the latter for micro-adjustments.

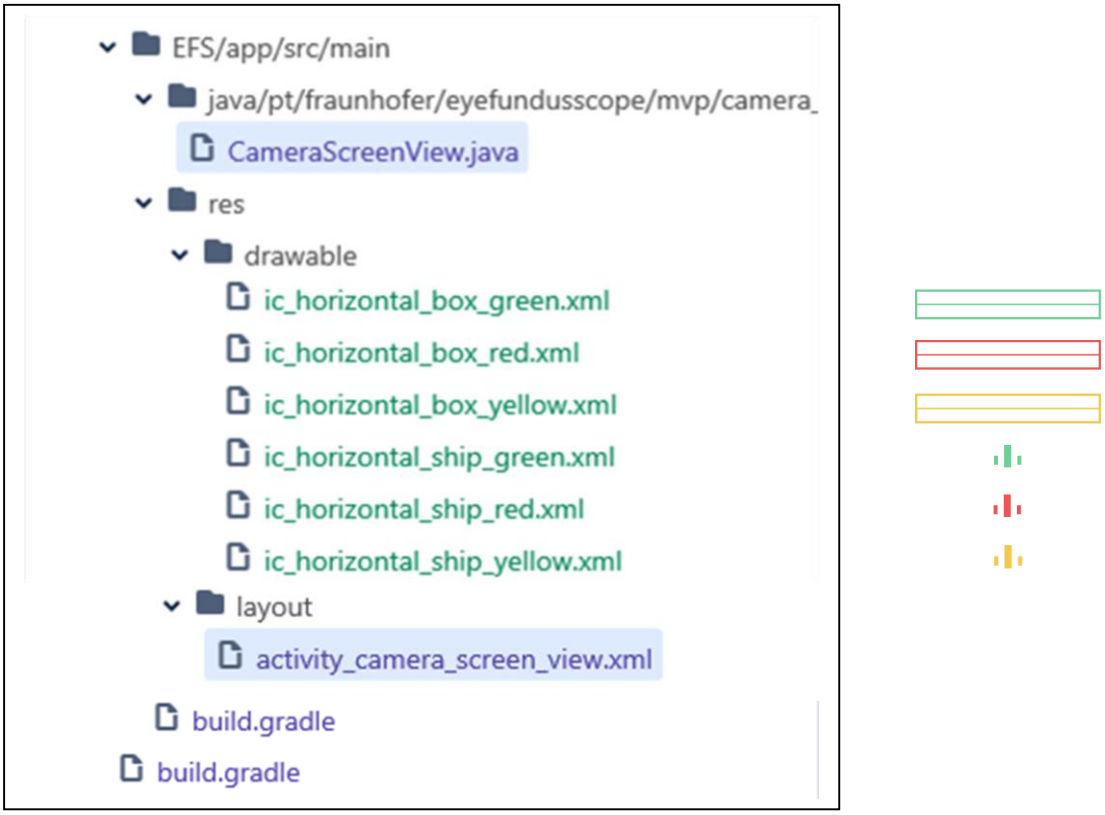
The last slide, “Time-lapse between acquisitions” presents to the user the time-lapse IE which will display a suitable interphotographic interval that takes patient comfort and examination speed into consideration.

4.2 Implementation in Android

Following the design of all GUI interaction elements explained previously, the implementation was done using Android Studio. All IE were implemented in the EFS App already developed that was running in a Nexus 5X with Android 8.0 (API 26). The implementation of all vector assets followed the same principle. As an example, the implementation of the Pan IE follows.

The first step before implementing any of the components was to export them from Figma in a `.svg` file (Scalable Vector Graphic) which is a XML-based vector image format for two-dimensional graphics with support for interactivity and animation.

Then using Android Studio the `.svg` files were imported as "new">"Vector Asset" in the directory `app/src/main/res/drawable/`. Each vector asset already had the proper size, which was specified while on Figma, so after choosing an appropriate name a `.xml` file was added in the directory.



Before accessing all views (like *buttons* or *imageviews*) in the `activity_camera_screen_view.xml` (an activity is an application component providing views which users can interact with) each view should be "binded". In order to do so, the Android ButterKnife library, which is a view injection library that injects *views* into android activity using annotations (e.g. @BindView and @BindColor), was added to the project. The first step to add ButterKnife to the project was to add the dependency in the project's `app/build.gradle` file. Once the dependency was added, all the ButterKnife annotations were available for import.

`CameraScreenView.java`

```
...

import butterknife.BindColor;
import butterknife.BindView;
import butterknife.ButterKnife;
import butterknife.OnClick;

...

    // bind the SpaceShips (green, yellow left-side, yellow right-side,
red left-side and red right-side)

    @BindView(R.id.image_ic_horizontal_ship_green)
    protected ImageView mGreenSpaceShip;
    @BindView(R.id.image_ic_horizontal_ship_yellow_right)
    protected ImageView mYellowSpaceShipRight;
    @BindView(R.id.image_ic_horizontal_ship_yellow_left)
    protected ImageView mYellowSpaceShipLeft;
    @BindView(R.id.image_ic_horizontal_ship_red_right)
    protected ImageView mRedSpaceShipRight;
    @BindView(R.id.image_ic_horizontal_ship_red_left)
    protected ImageView mRedSpaceShipLeft;

    // bind the horizontal boxes (green, yellow and red)

    @BindView(R.id.image_ic_horizontal_box_green)
    protected ImageView mSpaceShipHorizontalBoxGreen;
    @BindView(R.id.image_ic_horizontal_box_yellow)
    protected ImageView mSpaceShipHorizontalBoxYellow;
    @BindView(R.id.image_ic_horizontal_box_red)
    protected ImageView mSpaceShipHorizontalBoxRed;

...

    // bind the view using butterknife

    protected void onCreate(Bundle savedInstanceState) {
        super.onCreate(savedInstanceState);
        setContentView(R.layout.activity_camera_screen_view);
         ButterKnife.bind(this); }
...
```

The previous excerpt of the `CameraScreenView.java` file shows exactly how the "binding" of the vector assets in the `drawable/` directory is performed. Note that for the yellow and red *SpaceShips* (pointers), there are two different "bindings", because these appear either on the right or left side of the horizontal box.

In the same `CameraScreenView.java` file we define the 5 positions that should appear in the layout according to the information of the sensors. Let's recall the 5 positions in the figure below.

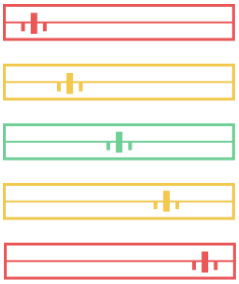


Figure 4.19 5 positions of the version C Pan IE

`CameraScreenView.java`

```
...
@Override
    public void inclinationY(@NonNull int position) {

        mGreenSpaceShip.setVisibility(View.GONE);
        mYellowSpaceShipRight.setVisibility(View.GONE);
        mYellowSpaceShipLeft.setVisibility(View.GONE);
        mRedSpaceShipLeft.setVisibility(View.GONE);
        mRedSpaceShipRight.setVisibility(View.GONE);
        mSpaceShipHorizontalBoxYellow.setVisibility(View.GONE);
        mSpaceShipHorizontalBoxRed.setVisibility(View.GONE);


        switch (position){
            case 1: {
                mGreenSpaceShip.setVisibility(View.VISIBLE);
                break;
            }
            case 2: {
                mSpaceShipHorizontalBoxYellow.setVisibility(View.VISIBLE);
                mYellowSpaceShipLeft.setVisibility(View.VISIBLE);
                break;
            }
            case 3: {
                mSpaceShipHorizontalBoxYellow.setVisibility(View.VISIBLE);
                mYellowSpaceShipRight.setVisibility(View.VISIBLE);
                break;
            }
            case 4:{
                mSpaceShipHorizontalBoxRed.setVisibility(View.VISIBLE);
                mRedSpaceShipLeft.setVisibility(View.VISIBLE);
                break;
            }
            case 5: {
                mSpaceShipHorizontalBoxRed.setVisibility(View.VISIBLE);
                mRedSpaceShipRight.setVisibility(View.VISIBLE);
                break;
            }
        }
    }

...
```

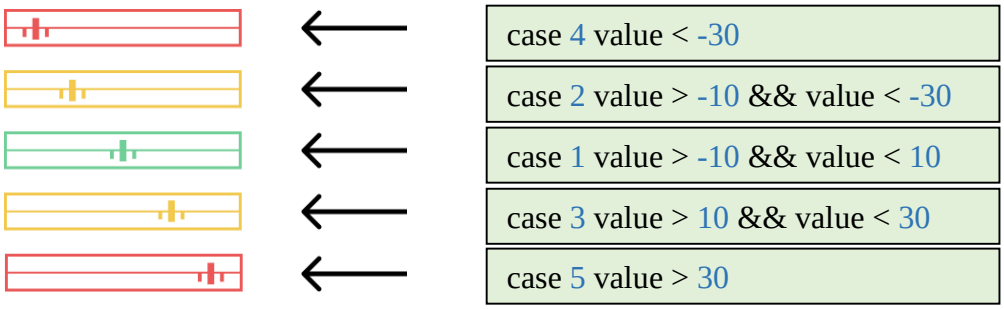
Once the “binding” is completed, all the *imageviews* are available in the `activity_camera_screen_view.xml`. Below is an excerpt of the layout of the Pan IE, where the *imageview* of the horizontal green and yellow boxes can be seen.

```
<RelativeLayout
        android:layout_width="match_parent"
        android:layout_height="wrap_content"
        android:layout_alignParentStart="true"
        android:layout_alignParentTop="true">

        <ImageView
            android:id="@+id/image_ic_horizontal_box_green"
            android:layout_width="wrap_content"
            android:layout_height="wrap_content"
            android:layout_above="@+id/control"
            android:layout_centerHorizontal="true"
            android:layout_weight="1"
            android:src="@drawable/ic_horizontal_box_green"
            android:gravity="center" />

        <ImageView
            android:id="@+id/image_ic_horizontal_box_yellow"
            android:layout_width="wrap_content"
            android:layout_height="wrap_content"
            android:layout_above="@+id/control"
            android:layout_centerHorizontal="true"
            android:layout_weight="1"
            android:src="@drawable/ic_horizontal_box_yellow"
            android:gravity="center"
            android:visibility="gone"/>
```

The final step was to establish the values for which each position should be visible. This was done in the `CameraScreenPresenter.java`. These values are relative to the rotation around the Y-axis of the smartphone, and the sensor readings of the accelerometer and gyroscope on the smartphone were used for this matter.



`CameraScreenPresenter.java`

The file `AutoSensorAnalysis.java` contained the code for the sensor readings of the accelerometer and gyroscope of the smartphone, and it was developed parallel to this project by another researcher at Fraunhofer. Since this type of sensors have a lot of uncertainties on their own, the file combined data of different sensors in a principle called “Sensor Fusion”, for a more certain outcome.

```
private void setUpSensorListenerStream() {
    mSensorManager = (SensorManager)
mContext.getSystemService(Context.SENSOR_SERVICE);
    mAutoSensorAnalysis = new AutoSensorAnalysis(mSensorManager,
mIsRightEye);
    mAccelerometer =
mSensorManager.getDefaultSensor(Sensor.TYPE_ACCELEROMETER);
    rxSensorListener =
mAutoSensorAnalysis.observeSensorChanged(mAccelerometer,
SENSOR_SAMPLE_RATE, AsyncEmitter.BackpressureMode.LATEST)
            .doOnNext(sensorEvent -> {
                mView.get().rotationAnimation((float)
mAutoSensorAnalysis.getRotation());

                if (mAutoSensorAnalysis.getRotation() > -10 &&
mAutoSensorAnalysis.getRotation() < 10) {
                    mView.get().inclinationY(1);
                } else if (mAutoSensorAnalysis.getRotation() > 30) {
                    mView.get().inclinationY(5);
                } else if (mAutoSensorAnalysis.getRotation() < -30) {
                    mView.get().inclinationY(4);
                } else if (mAutoSensorAnalysis.getRotation() > 10 &&
mAutoSensorAnalysis.getRotation() < 30) {
                    mView.get().inclinationY(3);
                } else if (mAutoSensorAnalysis.getRotation() < -10 &&
mAutoSensorAnalysis.getRotation() > -30) {
                    mView.get().inclinationY(2);
                }
...
```

Even though the gyroscope seemed to be the appropriate sensor to calculate the rotation around the X, Y and Z-axis based on the gravity vector, the fact that the smartphone is moving, means that acceleration will affect the gravity vector in a similar way as the gravity vector affects the acceleration vector for the accelerometer. Therefore, the acceleration vector is used to correct the gravity vector by subtracting it from the gyroscope data.

4.3 Interaction Elements Testing

Throughout all stages of design and implementation of the interaction elements on the EFS-App, several tests were executed using an ophthalmoscope trainer. This allowed for readjustments and modifications of the conceptual design of each interaction element, approaching the GUI to its specific requirements.

The model eye used was the Heine model eye ophthalmoscope trainer, which is an adjustable model that mimics the human eye. Regarding the refractive errors, these can be set in 1 dp, and they step from -10 to +10 dp. The diameter of pupil is also variable, and can be adjusted as 2, 3, 4, 5, 6 and 8 mm. It contains an aspheric optical glass lens with a focal length of 18 mm, and the lens curvature matches that of the retina. Lastly, the angle of examination is variable, mimicking when the patient is standing in front of the user, sitting, or lying down. [48]

For the purpose of the IEs testing alone, it was enough to have no refractive error, and 8 mm of pupil aperture. This made it easier to find the focus distance (app. 3 cm) and fill the entire viewing area of the retina, while testing the GUI interaction elements. Concerning the angle, the ophthalmoscope trainer was placed considering the use scenario in which the user is standing and the patient is sited (approximately 45º).

Figure 4.20 Fraunhofer-EFS interaction elements testing on the Heine model eye ophthalmoscope trainer

The most reviewed characteristics of each interaction element regarding the design process on Figma were the colors, shape and size. On the other hand, the most reviewed aspects regarding the Android implementation, were the correct placement on the fundus screen in addition to a precise behavior of the IEs to the different movements.

4.4 Usability Tests

According to the human factors engineering (HFE) and usability engineering (UE), all considerations in the development of medical devices involve the three major components of the device-user system: device users, device use environments and device user interfaces. The interactions of these three major components result in either safe and effective use or unsafe or ineffective use [47]. Hence, the final stage of this project was comprised of Usability Tests.

"The conditions under which simulated-use testing is conducted should be sufficiently realistic so that the results of the testing are generalizable to actual use. The need for realism is therefore driven by the analysis of risks related to the device's specific intended use, users, use environments, and the device user interface." - FDA [49]

4.4.1 Test Participants (Subjects)

The most important consideration for test participants in human factors validation testing is that they represent the population of intended users [50]. Since one of the Fraunhofer EFS-prototype main objectives is to encourage non-medical personnel to perform the retinal exam, several students/researchers were asked to participate in the usability tests Phase 1. In this phase, the researcher A performed the exam to the researcher B, and then researcher B performed the exam to the researcher A, and so on until 10 subjects have participated.

After Phase 1 was completed, and with the final assembly correctly modified, Phase 2 took place in a day care center (Senhor do Bonfim – A.S.S), so that nurses who provide care to the target audience for retinal exams (elderly people) can perform the usability tests and evaluate the behavior of the IEs in a simulated environment.

4.4.2 Tasks and Use Scenarios

According to the FDA Human Guidelines, the human factors validation testing should include all critical tasks identified in the preliminary analyses and evaluations. Also, tasks that logically occur in sequence when using the device can be grouped into use scenarios, which should be described in the test protocol. [49]

For the first phase of usability tests, there was three different versions of three different interaction elements. However, before testing any of the IEs, each user/researcher made at least one acquisition on both eyes using an App without any user guidance IE. Once the first phase was completed, the preferable design chosen by the researchers for the three IEs advanced to the second phase. The protocol for phase I follows.

4.4.2.1 Protocol for EFS Usability Tests

Use scenario: Evaluation of the three versions of the Roll IE

1 – During the exam procedure the "patient" should be sited and the user should be standing in front of him.

2 - The user should open the first App in order to test the first design of the Roll IE.

3 – Select "New Acquisition" and then choose which eye is going to be examined first by selecting "Right Eye" or "Left Eye"

4 – Once the Fundus examination screen appears the user may start the exam by approaching the EFS prototype closer to the "patient's" eye. Starting from approximately 15 cm until it reaches an appropriate focus distance of 3 cm.

5 –Once the exam begins the user should align the EFS prototype properly to keep the Roll IE green and approach the patients' eye while keeping a correct alignment.

6 – As soon as the retinal tissue appears, and the ideal alignment is met, the user should click a button on the handhold triggering an acquisition.

7- After the first acquisition, the time-lapse IE begins a countdown. The user can take another acquisition once the interphotographic interval ends.

8 – After one or two successful acquisitions, the user should leave the fundus examination screen and select the remaining eye.

After both eyes are examined the user opens the second and third App in sequence, in order to test the other two different versions of the Roll IE by repeating the same process.

Following this use scenario, the user should then evaluate the three versions of the Pan IE and the three versions of the Tilt IE. These should follow the same protocol as for the Roll IE. During the entirety of the exam the room should be kept under dim lighting.

4.4.3 Instructions for Use

The human factors validation testing can indirectly serve to assess the adequacy of the instructions for use of the device. The goal is to determine the extent to which the instructions for use support the users' safe and effective use of the device. If the device labelling is inadequate, it will be evidenced by participant performance or subjective feedback. [50]

For the first (researchers) and second (nurses) stages there was an initial explanation of how the EFS prototype works. For the first stage only, the focal point, as previously mentioned, was to isolate the movements that each IE translates and choosing one of the three versions according to the users' perspective. In order to help each user, understand what IEs are being tested in a given time, the tutorial developed was presented, showing some guide-lines for proper usage.

4.4.4 Participant Training

The extent of training that needs to be provided to users for them to adapt to a user interface in a handheld device can also be studied in these usability tests. Since the training provided to the human factors validation test participants should approximate the training that actual users would receive [50],

it would be expected that users had a couple hours to get used to the device and learn how to proper handle the EFS prototype. However, all the participants, including researches and nurses, only had a brief explanation (complemented by the tutorial) followed by approximately 5 minutes of training using the phantom eye.

4.4.5 Data Collection

The human factors validation testing should include observations of participants' performance of all use scenarios [50]. In this case, we have three scenarios in which three different IEs are evaluated through user performance and ability to interact with the GUI.

The observation of participant's test/task performance and assessment of their understanding of essential information was followed by a debriefing questionnaire (Appendix II). In this questionnaire, the participants gave a subjective assessment of any difficulties experienced during the test, and also their preferences between the three versions of each interaction element.

Chapter 5

Results and Discussion

In this chapter, several screenshots and images, taken during the design, implementation and testing of the GUI interaction elements, are presented. Furthermore, general problems encountered in each stage are discussed, as well as their consequences in the obtained results.

Finally, the results from the Usability Tests are shown, which include several retinal images taken from researchers and nurses as well as an analysis of the questionnaires that were performed during and after the tests.

5.1 Interaction Elements Designing, Implementation and Testing

The first full assembly (Figure 5.1) came together after several tests and trials of designing and implementing the interaction elements. All IEs were grouped in the most intuitive manner to the user so that it wouldn't impair the normal course of the retinal exam.

The Roll IE (outer green circle), was placed, as originally thought, along the perimeter of the retinal viewing area. Inside it's the time-lapse IE (dashed grey circle). As for the Pan and Tilt IEs, they were placed below the outer circle and in the top left corner, respectively. Lastly the left/right eye indicator appears above the outer circle at the top extremity.

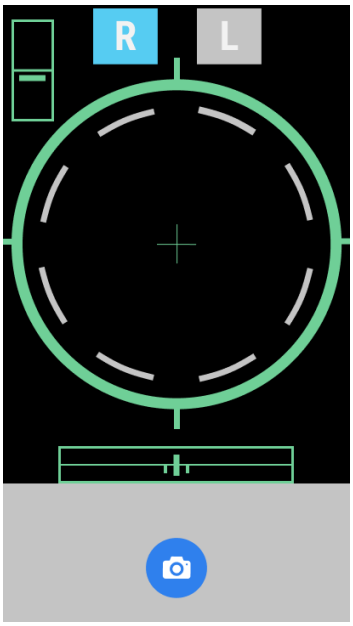


Figure 5.1 Full assembly scheme in Figma

For the purpose of the first Usability Tests stage, in which 10 researchers gave their preferences on the different alternatives for each rotational IEs, 3 different assemblies were implemented in the Nexus 5X.

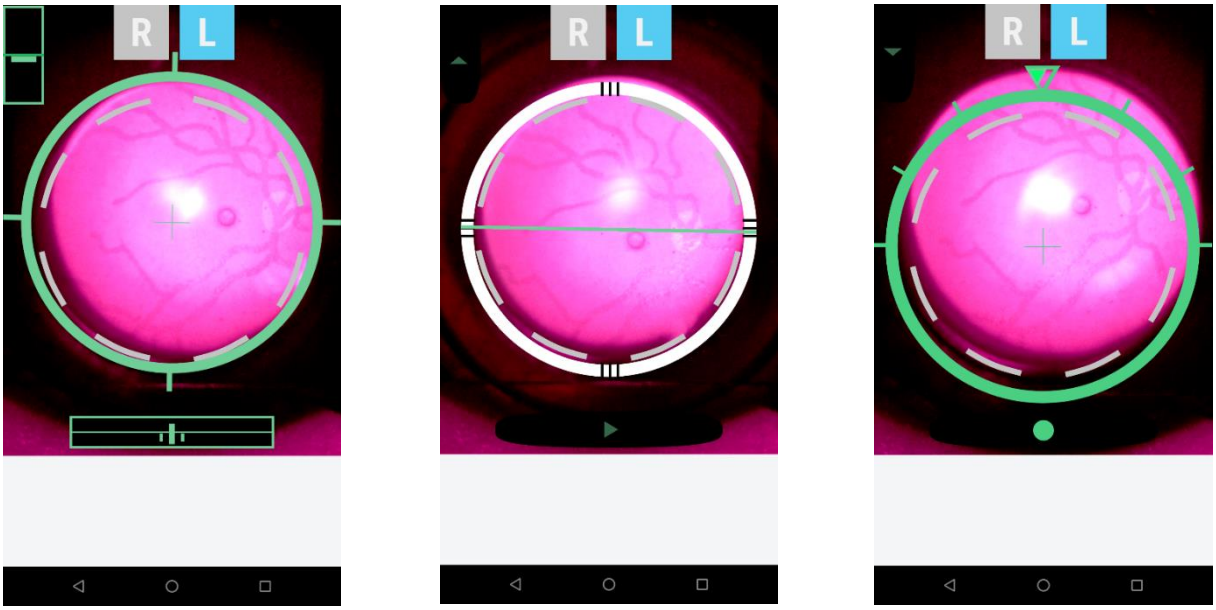


Figure 5.2 3 different assemblies implemented on the Nexus 5X for the first phase of usability tests

First assembly:	Second assembly:	Third assembly:
version A Roll IE	version C Roll IE	version B Roll IE
version C Pan IE	version A Pan IE	version A Pan IE (modified)
version B Tilt IE	version A Tilt IE	version A Tilt IE

As we can see, the first assembly, was identical to the assembly presented previously from Figma (Figure 5.1). The third assembly had a slight modification on the Pan IE in comparison to the second assembly (instead of a green arrow for the "middle" position, there was a green circle). The purpose is to analyze the users' response to the color versus the shape of the components. Besides, the use of an arrow (pointing right) for the "middle" position, may prove to be misleading.

After performing several tests with the ophthalmoscope trainer it was clear that some designs of the rotational IEs were more suitable for a certain motion. For instance, the design of the versions B Tilt and Pan IE doesn't have a "middle" position making it more suitable for the Tilt motion. This is explained by the fact that the height and head inclination of the patient may change what is considered a proper position of the EFS.

On the other hand, the feedback regarding the Pan IE is more certain to help the user keep the lenses in line with the patients' pupil. This happens since the only constraint is the User being right in front of the patient. Thus, the "middle" position as seen in the version A and C of the Tilt and Pan IEs makes these more convenient for the Pan movement.

The feedback given by the Roll IE, as exemplified in the Figure 5.3, was deemed of great importance, given that by standardizing the orientation of all acquired images, it allows for easier detection of the quadrant (Figure 5.4) on which the lesions are found.

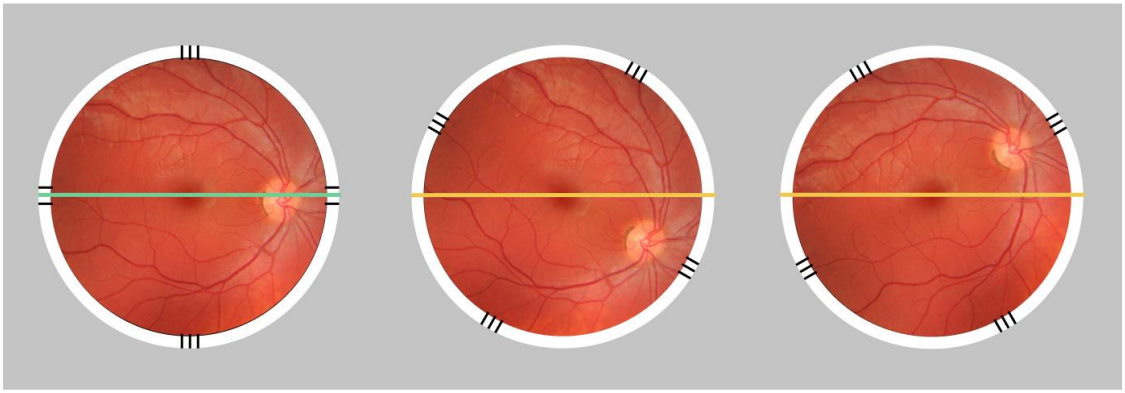


Figure 5.3 Illustration of the importance of the Roll IE in standardizing the orientation of acquired images

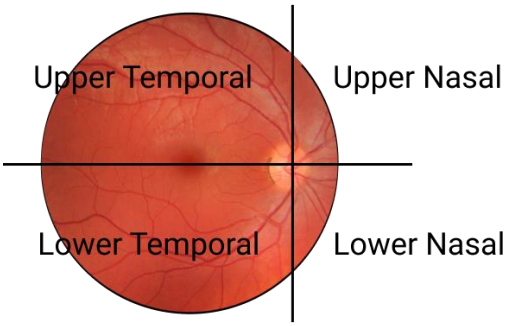


Figure 5.4 Schematic image of the 4 quadrants of the retina

5.1.1 Misalignment feedback and resulting image artifacts

The most common user errors that occur during a retinal exam are related to misalignments and improper camera-to-eye distance. These errors were depicted in Figures 2.15 and 2.16, and follow the descriptions of several user manuals.

One of the key points of interest, during the interaction elements tests with the ophthalmoscope trainer, was to evaluate the relation between the artifacts that appeared on the retinal images and the respective feedback given by the rotational IEs.

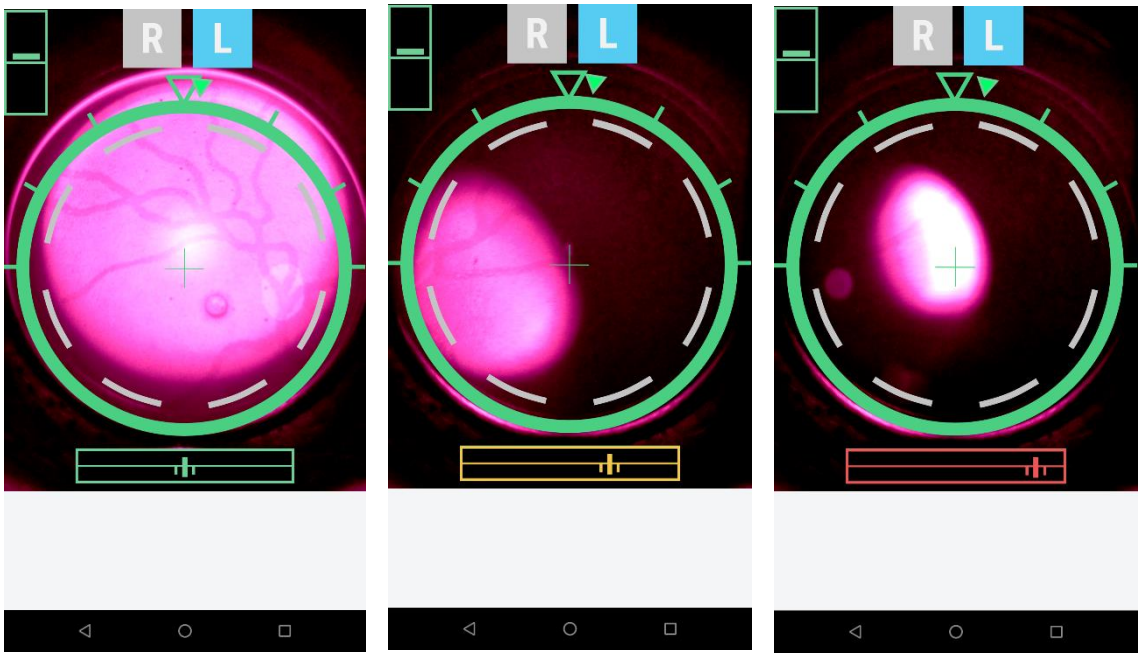


Figure 5.5 Panning IE feedback after deviating the EFS to the right. Left side: correct alignment. Middle: mild deviation. Right-side: severe deviation

As we can verify, in the previous figure (while using NIR light), once we start rotating the EFS to the right along the Y-axis, the Pan IE immediately changes, giving the user knowledge on the deviation level. In this particular deviation, the retinal area only appears on the left side of the fundus screen. The greater the deviation the bigger the shadow on the sides of the image, consequently giving a smaller retinal FOV.

If in turn we compare the resulting retinal images taken while deviating the EFS (Figure 5.6), we can confirm exactly that when the camera is deviated to the right the shadow appears on the right side of the image. On the contrary if the EFS is deviated to the left the shadow appears on the left side of the image.

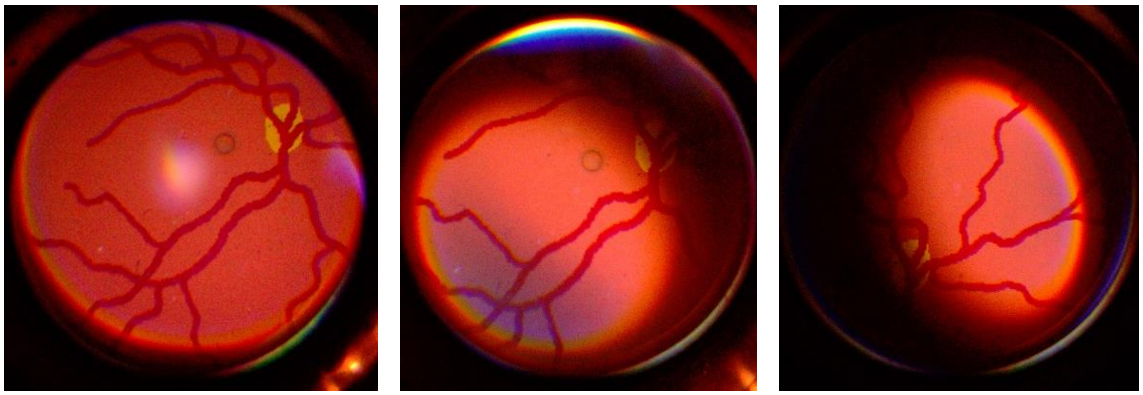


Figure 5.6 Retinal images taken while testing the EFS rotational IEs on the ophthalmoscope trainer. Left: good alignment and positioning. Middle: misalignment to the right side. Right: misalignment to the left side.

5.2 Usability Tests

5.2.1 Phase I

In regard to the first phase of the Usability Tests, where 10 researchers had the opportunity to experiment the three different assemblies, the feedback from the new GUI was very important to validate the usefulness of each interaction element apart from the preferences in design.

All researchers followed the guidelines from the protocol for the three rotational IEs. Each session of two researchers, in which researcher A performed the exam to the researcher B, and then researcher B performed the exam to the researcher A, took about 40 minutes to complete. For each researcher it took about 5 minutes of training with the ophthalmoscope trainer, around 10 minutes to examine the other researcher, and 5 minutes to fill the questionnaire and the SUS questionnaire. This time limitation proved harmful, as expected, to the quality of the images acquired.

From the 10 researchers, only one wasn't capable of capturing a retinal image in which the optic disc appeared. The retinal images were taken, after experimenting all assemblies and being more comfortable with the GUI. Capturing the optic disc while keeping the rotational IEs stabilized (green), was the focus of each researcher, since the optic disc is the structure from the retina that is more easily observable.

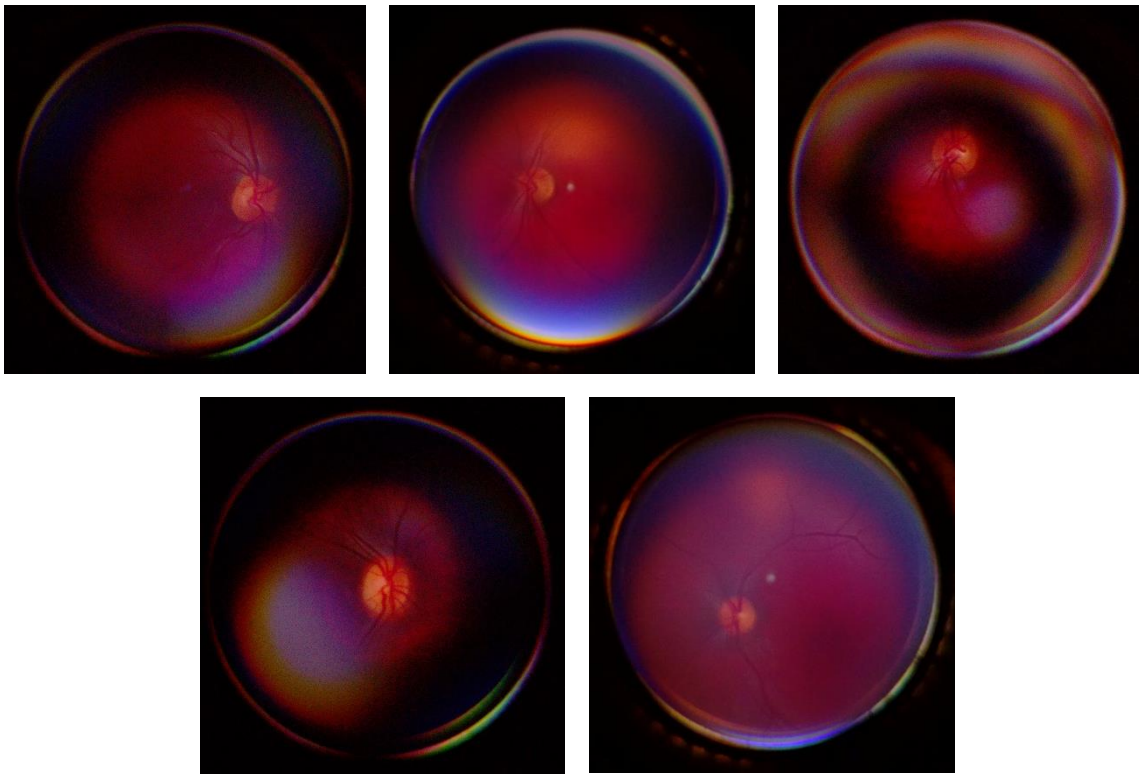


Figure 5.7 Retinal images taken by researchers while testing the EFS rotational IEs (Phase I of Usability Tests)

The results from the first questionnaire (Appendix II) are reflected in the table below. From its analysis it's pretty clear that all the participants had experience using a smartphone, and 4 of them had already used the EFS previously in any context (only one participant had some experience of capturing retinal images).

The EFS system and apparatus was considered simple to use from 7 out of 10 participants, and 9 participants considered that the interaction elements facilititated the acquisition process. Participant 6

showed many difficulties in working with the EFS and wasn't able to capture a satisfactory retinal image.

Table 2 Questionnaire Results from Phase I

	Q 1	Q 2	Q 3	Q 4	Q 5	Q 6	Q 7	Q 8
Participant 1	Yes	Yes	No	Yes			Yes	Yes
Participant 2	Yes	Yes	Yes	Yes			No	Yes
Participant 3	Yes	No	Yes	Yes			Yes	Yes
Participant 4	Yes	No	Yes	Yes			Yes	Yes
Participant 5	Yes	No	No	Yes			Yes	Yes
Participant 6	Yes	No	No	No			Yes	No
Participant 7	Yes	Yes	Yes	Yes			Yes	Yes
Participant 8	Yes	Yes	Yes	Yes			Yes	Yes
Participant 9	Yes	No	Yes	Yes			No	Yes
Participant 10	Yes	No	Yes	Yes			No	Yes

5.2.1.1 Rotational Interaction Elements

One of the objectives of this first phase was to understand how users reacted to different designs of the three movements that were being tested. They chose which of them were more suitable, according to their preference. The votes for each IE are listed in the Figure below.

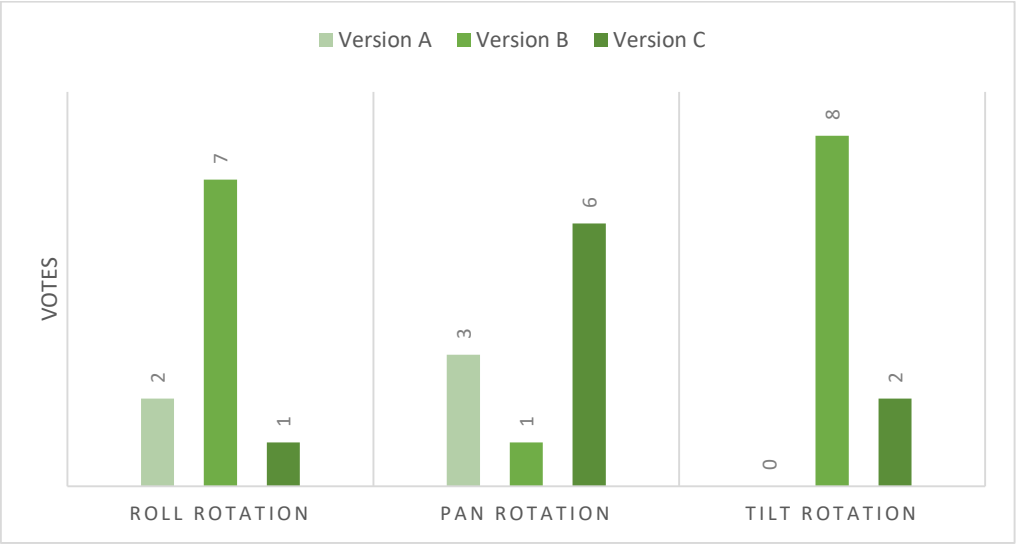


Figure 5.8 Votes for the three versions of the three rotational interaction elements presented in Phase I.

As seen from the image, the version B of the Roll IE was chosen among the three. On the other hand, the version C of the Pan IE gathered more votes, and lastly the preference for the Tilt IE fell on the version B.

The other purpose was to discover how difficult it was for users to stabilize (green) each IE while searching for the retina. For this matter, the users chose from 1 to 7 (1 being *very hard* and 7 being *very easy*) how dificult it was to stabilize each IE while trying to get a good retinal image. The results are shown in the Figure below.

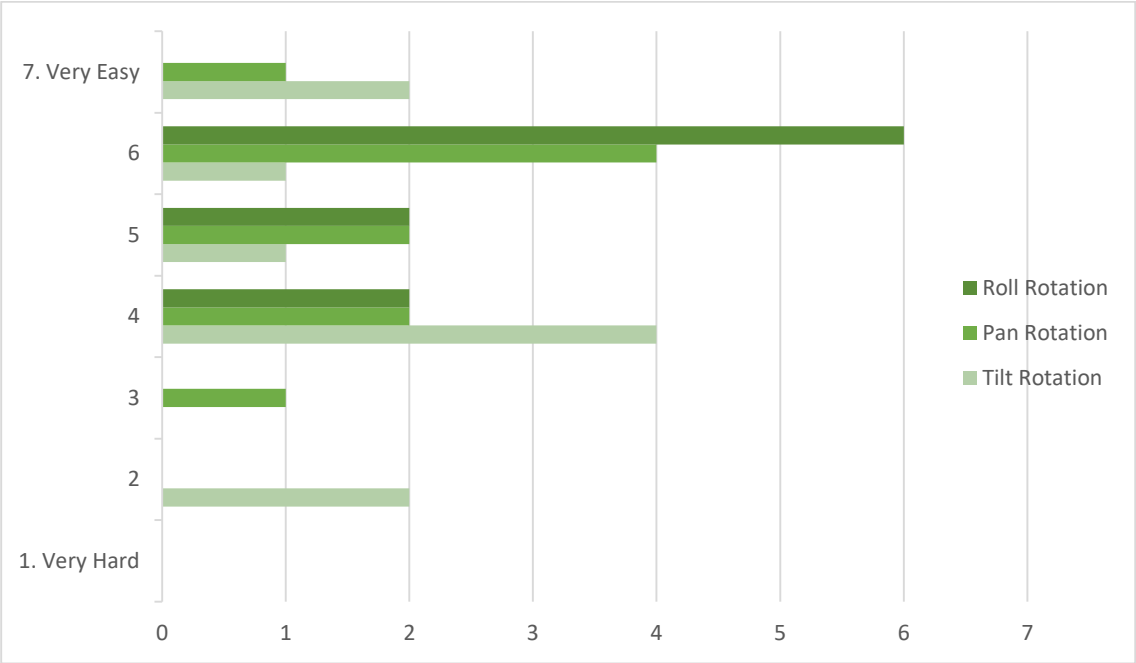


Figure 5.9 Evaluation of the difficulty Users felt while using the three rotational interaction elements (Phase I)

The figure above tells us that the Roll IE was the easiest for the majority of users, in comparison to the other two. In fact, the feedback received from users was that it was the most noticeable IE out of the three, and they felt it was easier to keep the IE green.

In its turn, the Pan IE also received positive feedback from the majority of users. It was somewhat consensual that it was important to maintain the IE green, since it kept the users in line with the "patients" pupil.

On the other hand, the Tilt IE showed a greater dispersion of results, with 2 users that said it was very easy, and other two said that it was by far the hardest. This was considered by the majority as a medium difficulty task. However these results may be related to the fact that the Tilt IE was the smallest of the three besides being in the periphery view of the users (far from the central point of the retinal viewing area). In fact, three users said they mostly ignored the feedback that was given by the Tilt IE because it was hard enough to find the retina while keeping the other two (Roll and Pan IEs) stabilized.

5.2.1.2 Tutorial and time-lapse

Concerning the Tutorial that was presented to the users right at the beginning, a great majority said that it made it easier to understand the correct positioning they should take during a retinal exam, and without it, they woldn't have noticed the time-lapse IE. When asked to choose from 1 to 7 (1 being *made it worse* and 7 being *made it easier*) about how the positioning and movement knowledge they had changed from seing the tutorial, 6/10 users chose the highest score. Moreover, the mean value for

this question was 6.3, which seems quite conclusive that the tutorial is of great value from the user's perspective.

However, when asked if they would add or change anything from the tutorial, 7/10 users said they would. The most noticeable comments were the lack of representation of the Pan and Tilt IEs in slides 4 and 5. Also, some users proposed the implementation of an animated `.gif` file, instead of a static image, to better illustrate some of the movements and IEs feedback.

Regarding the time-lapse IE, as seen from the table 1 (Question 8), 9 out of the 10 users said the timelapse IE was a great addition to the fundus screen, since it allowed the users to control the time during acquisitions on the same eye. Yet, many users said the colors that were being used weren't "bright" enough and some blinking effect could help making it more noticeable.

5.2.1.3 System Usability Scale Questionnaire

After the first questionnaire, all users where asked to fill the SUS questionnaire (Appendix II). This is composed of ten statements, each having a five-point scale that ranges from *Strongly Disagree* to *Strongly Agree*. There are five positive statements and five negative statements, which alternate.

In order to find the SUS Final Score, these 5 steps were followed:

1. for every odd-numbered question, subtract 1 from the score (X-1)
2. for every even-numbered question, subtract the score from 5 (5-X)
3. sum the resulting values of odd and even-numbered questions (SUS Raw Score)
4. multiply the SUS Raw Score of each participant by 2.5 (SUS Final Score)
5. find the average of the SUS Final Score

These calculations were done using an Excel spreadsheet found below.

Table 3 Results from SUS Questionnaire (Phase I)

	Q1	*Q2*	*Q3*	*Q4*	*Q5*	*Q6*	*Q7*	*Q8*	*Q9*	*Q10*	*SUS Raw Score*	*SUS Final Score*
Participant 1	5	3	2	4	3	4	4	1	2	3	21	52.5
Participant 2	5	1	3	2	4	2	5	1	3	3	31	77.5
Participant 3	3	2	4	2	5	1	4	2	3	2	30	75
Participant 4	4	1	5	1	4	2	5	2	3	1	34	85
Participant 5	4	1	4	1	4	1	5	4	3	1	32	80
Participant 6	2	3	3	5	4	2	2	3	3	3	18	45
Participant 7	4	2	4	3	4	1	5	1	5	1	34	85
Participant 8	5	1	4	1	5	2	5	1	4	2	36	90
Participant 9	5	1	4	1	4	1	5	1	4	1	37	92.5
Participant 10	4	1	3	2	4	2	5	1	4	2	32	80

The average of the SUS Final Score is 76.25. According to several studies there are at least 3 different scale systems to interpret the SUS Score which are the adjective ratings, the school

grading scale and the acceptability ranges. These three scales are an adaptation from the work of Bangor et. al. [51]. The Figure below shows how these three different scales compare to each other.

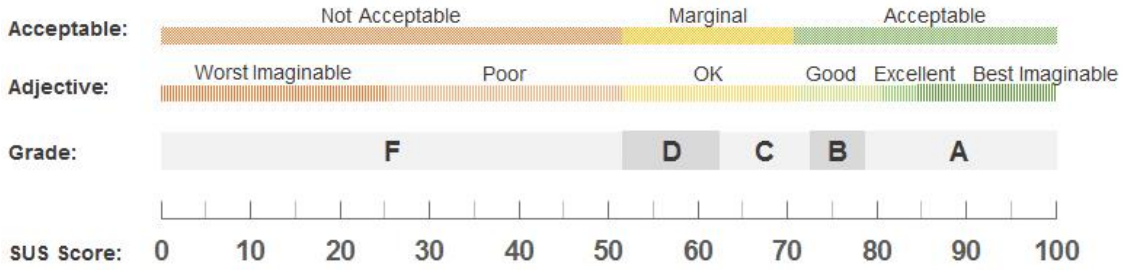


Figure 5.10 – A comparison of the acceptability scores, adjective ratings and school grading scales, in relation to the average SUS score [52]

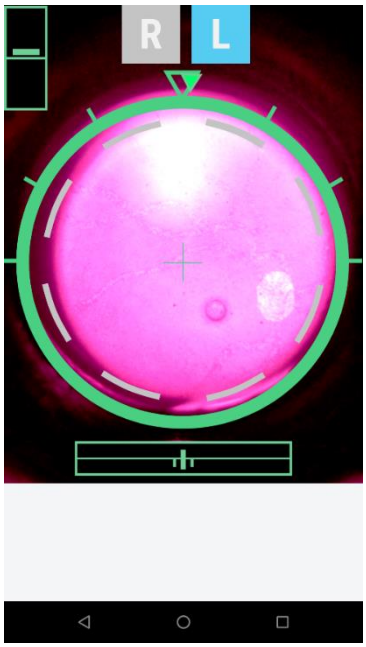
From this Figure we can see that the result from the SUS Final Score was in the acceptable interval. In addition, we can see that it's a B graded denoting a Good indicative of usability.

Besides, from the percentile rank analysis (Jeff Sauro et al. [52]) made from a database containing over ten thousand responses, we can say that a SUS Score in the interval 75 and 77.1 has a percentile range from 73 to 79. This means that it scored better than 73% to 79% of all the scores in the database.

5.2.2 Phase II

The second phase of the Usability Tests, was held in a day care center (Senhor do Bonfim – A.S.S). Two nurses who are used to provide care to elders (target audience for retinal exams) where able to perform some usability tests and evaluate the behavior of the interaction elements in a simulated environment.

The assembly that was used contained the versions of the IEs that gathered the most votes in the first phase.



Final assembly:

version B Roll IE

version C Pan IE

version B Tilt IE

Figure 5.11 Implemented assembly used for Phase II

Both nurses had never used the EFS, so they first practiced with the opthalmoscope trainer without any of the new GUI. After being familiarized with the EFS itself, the tutorial was shown together with an explanation of the protocol they would follow to evaluate the IEs.

The two nurses where asked to do several acquisitions in a volunteer from Fraunhofer and in the end they gave their feedback regarding the usability of the GUI. The two top images, of the Figure below, were acquisitions taken from the left eye, and the two bottom images were from the right eye.

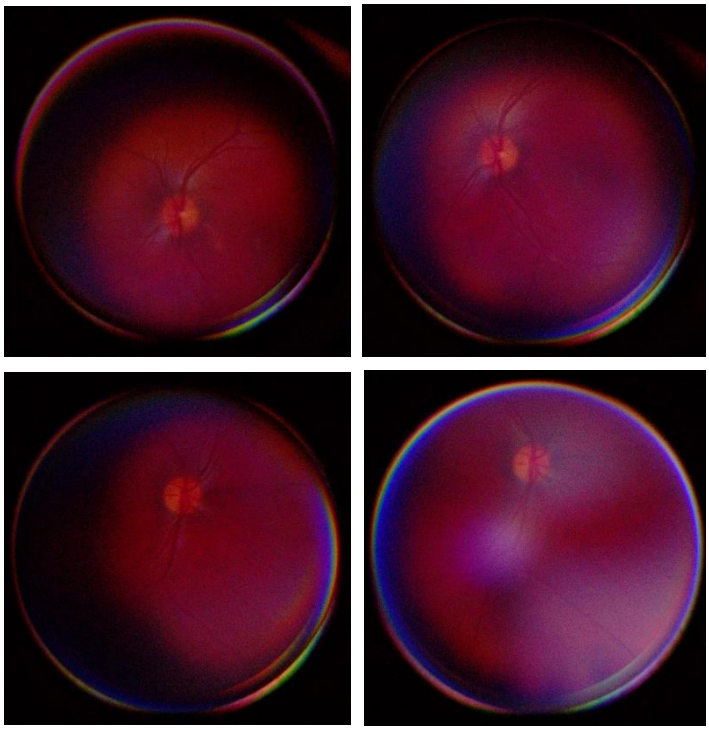


Figure 5.12 Retinal images taken by nurses while testing the EFS rotational interaction elements (Phase II of Usability Tests)

After having successfully captured images of the optic disc while keeping the rotational IEs stabilized, both answered some questions from the questionnaire (Appendix II) excluding the versions choices in question 5 and the SUS questionnaire. The two thought the EFS system and apparatus is a simple to use device, and also that the interaction elements facilititated the acquisition process.

When asked to categorize how difficult it was to stabilize (green) the Roll IE while searching for the retina (1 being *very hard* and 7 being *very easy*) one said it was very easy (7) and the other said it was slightly easy (5). In respect to the Pan IE both nurses said it was very easy (7). Regarding the Tilt IE one chose 6, but stated that the changes from the patients positioning and height difference between the user and the patient must be addressed. The other nurse said it was difficult to pay attention to this IE while trying to find the retina and considered the least important of the three.

Finally, regarding the tutorial, both said it was very helpful and in their opinion it didn't need any change. As for the time-lapse, they said it was of great value for the confort of both the patient and the user. Furthermore, the two nurses said they felt more confident in using the EFS with the new GUI, in comparison to not having any interaction element on the fundus observation screen.

Chapter 6

Future Work

The successful implementation of the rotational IEs, brought a new insight on several aspects of the handheld prototypes used for retinal exams. In this chapter I will present three innovative ideas that might be implemented to the EFS now that it has these new GUI interaction elements.

6.1 External fixation points

As we have seen in the sub-chapter of *Retinal Imaging Modalities, i*n order to create a panoramic view of the retina, multiple images are stitched together to create a greater FOV retinal image. For this matter, the existence of fixation points is paramount, since it allows an easier capture of the different quadrants of the retina. In fact, most of the solutions that already exist on the market, have 7 or 9 internal fixation points.

With the aid of the Roll IE, the idea of using external fixation points, to help fixate the patients eye, is more meaningful. The patient would use the eye that is not being examined as a guide to look to a certain position. The Roll IE would act as a leveler between both eyes, by keeping the EFS and the external target (which contains the fixation points) at the same level. Figure below illustrates this principle.

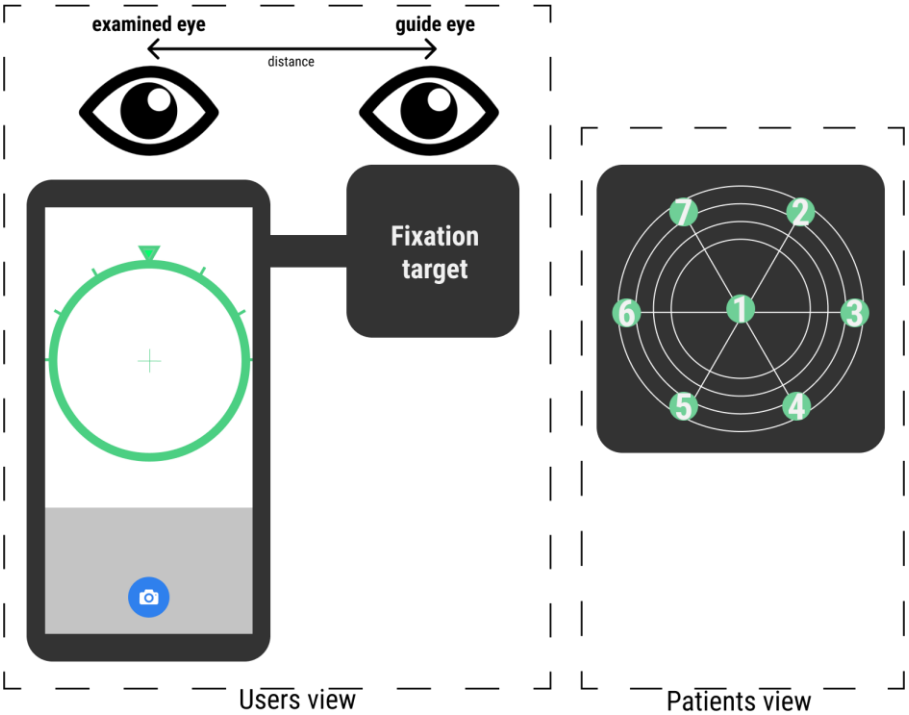


Figure 6.1 Illustration of the external fixation target in the EFS

The center of the fixation target would be placed at the same height as the center of the camera on the smartphone. Once the user sees the retina, which means the optical components of the EFS are aligned with the patients' pupil on the examined eye, the Roll IE would level the fixation target with the "guide" eye. Thus, during an exam with 7 fixation targets, where at least 7 acquisitions on the same eye must be made, to complete the panoramic retinal image (as shown in the Figure below), if the orientation of each picture remains the same it makes the stitching method a lot easier and effective.

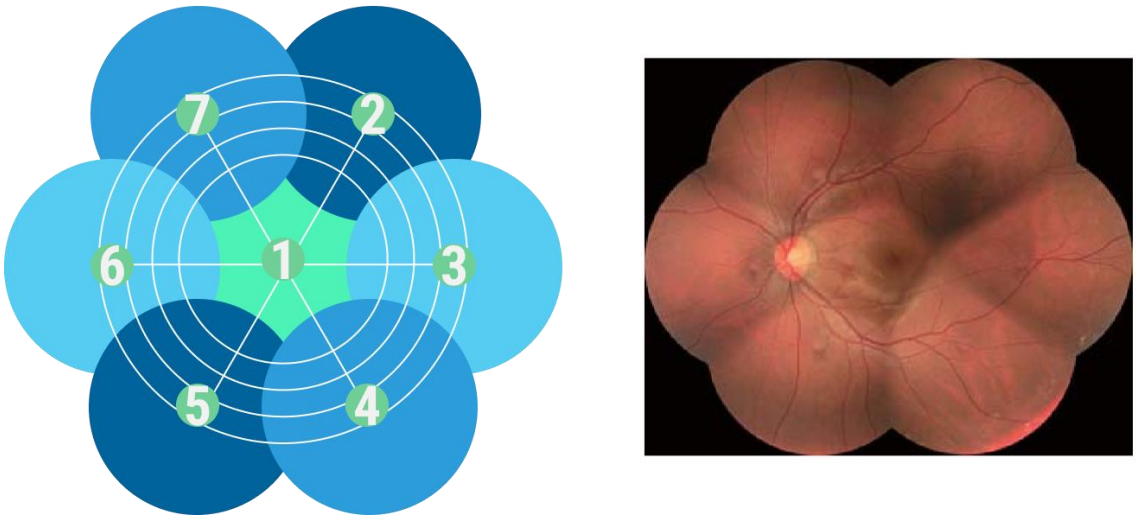


Figure 6.2 Illustration of the resulting retinal images creating a panoramic view of the retina. Left-side: image created using Figma. Right-side: Example of a panorama photograph [43]

The fixation points would be LEDs, turned on one at a time, either by user's choice (buttons on the fundus screen would pop-up) or in a pre-determined sequential fashion (e.g. starting in 1 and ending in 7).

6.2 App recognition of possible failures

As previously mentioned throughout several chapters, the user's ability to overcome possible failures, related to misalignments and improper camera-to-eye distance, was the main challenge in the creation of the new GUI that was implemented. Since the smartphone's greater computational power allows image recognition in real-time, the EFS Application could include the recognition of several failures, in order to complement or correct some of the feedback given by the smartphone's inertial sensors.

6.2.1 Improper camera-to-eye distance

One of the use scenarios would be to recognize the distance between the EFS and the patient's pupil, and giving real-time feedback so that the user could correct its distance. As we can see in the figure below, when the lens is too far away from the patient's eye we have a small fundus image. Once we start getting closer, the fundus image will start to increase proportionally.

This approximation must continue until the retina fully occupies the expected field-of-view. Once the appropriate focus distance is met the application should stop giving the user the "get closer" feedback. On the other, if the lens is too close to the patients' eye (excessive proximity), the user should see a white hot-spot on the top of the image, due to over-exposure.

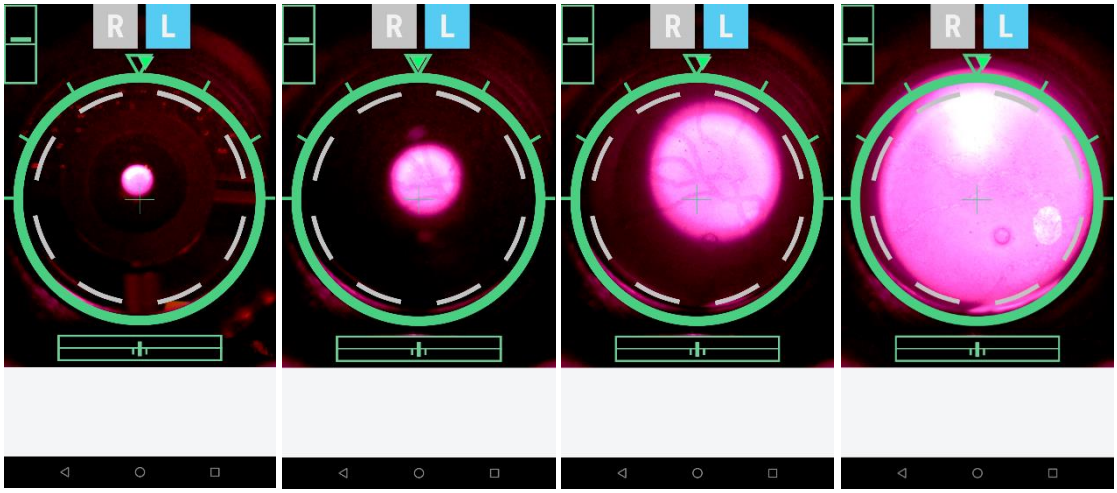


Figure 6.3 Distance vs retinal viewing area

For the feedback itself, the interaction element should be comprised of at least two components, like the ones proposed below, that would indicate the "moving closer" and the "moving farther" feedback.

Figure 6.4 Distance IEs

Concluding, if the EFS App is able to recognize both the hot-spot and the area occupied by the retina, it could give some unexperienced users valuable feedback.

6.2.2 Misalignment

The other use scenario would be to differentiate a misalignment caused from a rotational movement, like Panning or Tilting, from a misalignment caused by a horizontal or vertical planar movement.

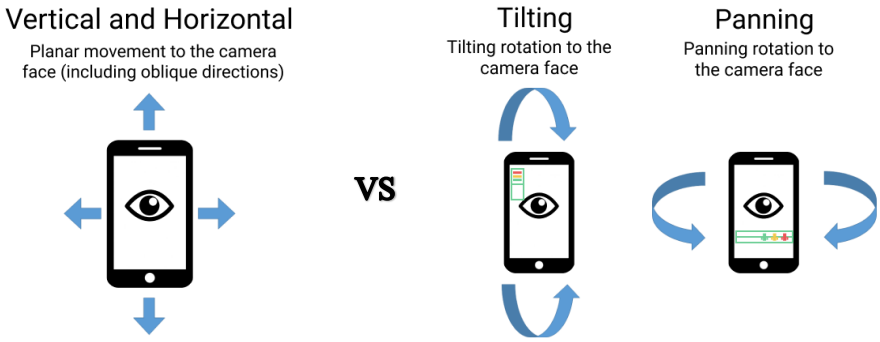


Figure 6.5 Difference from a horizontal or vertical planar movement versus a rotational movement, like Panning or Tilting.

As we have previously seen, when we rotate the EFS to the right along the Y-axis (Figure 5.5) the retinal area only appears on the left side of the fundus screen and the Pan IE changes according to the panning deviation level. However, if we move the EFS to the right, planar to the eye, we'll see the exact same failure in the fundus screen (retinal image only appears on the left, and a dark shadow occupies the right side of the fundus screen). Since the inertial sensors aren't capable by themselves of distinguishing these two failures, it is of great interest to use image recognition in order to complement the feedback given to the user.

The figure below explains how combining image recognition with inertial sensors readings may distinguish the cause of the misalignment. The EFS App correlates the information given by the Panning IE and the image recognition system and translates this into a command given to the user.

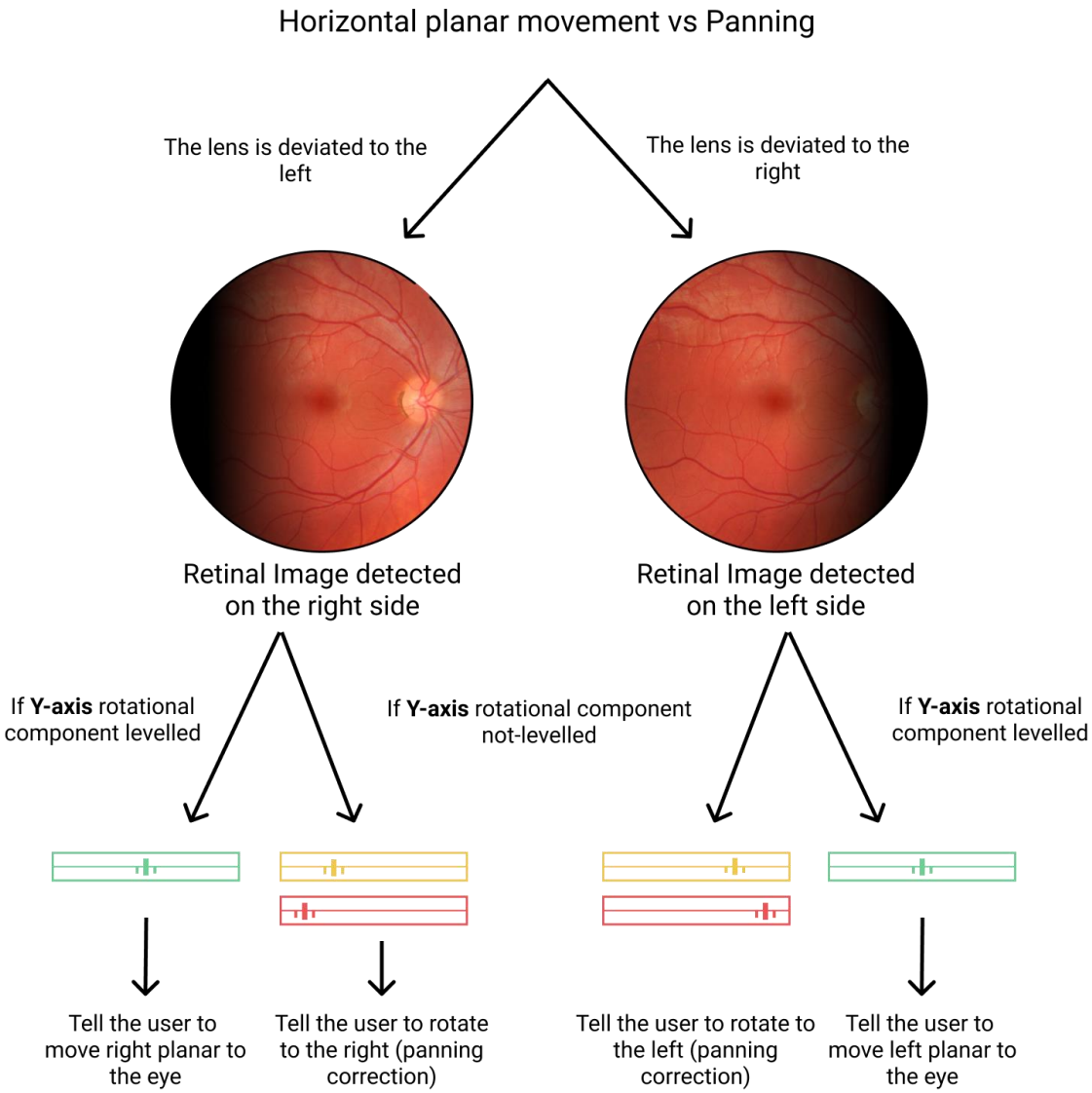


Figure 6.6 EFS recognition of misalignments using sensor data and image recognition data

This example illustrates that in order to distinguish the cause of failure, the EFS should in the first instance detect on which side the retinal image appears, and then given the Y-axis IE feedback,

choose between a horizontal planar movement versus a panning rotation. The same thought process applies for the tilting rotation versus vertical planar movement.

In a real scenario, both vertical and horizontal misalignments can occur while trying to find the suitable focus distance, so it would be a matter of aligning one position at a time.

6.3 Evaluate the performance and improvement

Lastly, the new GUI could provide the EFS with an application for educational purposes. The creation of an interactive tutorial using the GUI, would be of great value to teach new users the mechanics behind a handheld retinal exam procedure. For example, each movement (panning, tilting and rolling) could be explained separately and in an orderly fashion, so that the user gets used to control and stabilize each of them without compromising the others.

Furthermore, the establishment of certain performance evaluation metrics, like time of operation for each patient, or the number of attempts for each successful retinal photograph, could be a good indicative of the student's examination technique. Since the time-lapse helps to keep track of time, and the rotational IEs helps to align and position the EFS, it would allow an efficient monitoring, in real time, of the student's learning process.

Chapter 7
Conclusion

Throughout this project, new GUI interaction elements were designed and implemented on the EFS App. The intended approach was to make the EFS easier to use by non-ophthalmic trained personnel, both in non-clinical and clinical environments. Therefore, before facing the challenges of the retinal exam procedure, it was important to establish the concepts behind handheld acquisition.

The positioning and alignment of the ophthalmic camera with the patient's pupil can be a difficult and time-consuming task. Learning how inertial sensors data could improve the acquisition procedure was the first step to design IEs that were easy for the users to interact with and comprehend. The three axis, in which the accelerometer and gyroscope detect changes, were discretized into three different rotational IEs: Pan, Tilt and Roll IEs, that allowed to stabilize the EFS.

Besides the rotational IEs, a time-lapse and a left/right eye indicators were implemented on the EFS App, so that users keep track of the time between acquisitions on the same eye and avoid mistakes on which eye is being examined. These may prove quite effective under screening scenarios where one user examines multiple patients throughout the day.

The usability tests, that ensued the development phases of the GUI, gave a valuable insight on the interaction technique between users and the EFS during a retinal exam. Apart from the different designs that were tested, ultimately leading to the final assembly, it was important to analyze how some interaction elements were more impactful than others. Overall the feedback was very positive, and although changes in the GUI are inevitable, the final assembly tested by the two nurses shows promising results for future applications.

Certain aspects of the GUI can be further improved as soon as a dedicated study of user errors with the EFS is conducted. Narrowing the rotational IEs from 3 to 2 may prove more efficient once that several users showed difficulties in interacting with the 3 rotational IEs while searching for the retina. Besides, as seen in the previous chapter, the implementation of an image recognition algorithm for user failures, in real-time, can complement the rotational IEs feedback, as well as solving the problem for the distance feedback. Regarding the Tutorial, it would be of great value the implementation of a short video, illustrating the positioning and alignment of the EFS, with the guidance of the rotational IEs.

The main challenge of this project was to reconcile the android implementation of the rotational interaction elements with the sensor readings of the accelerometer and gyroscope of the smartphone that was being developed parallel to this project by another researcher. At the time the rotational IEs were first implemented, sensor readings only used the gyroscope, which by itself wasn't accurate enough to make the IEs feedback a reliable source. Besides, the gyroscope data becomes inaccurate over time as it starts to drift due to error accumulation. The EFS App that was later used for the usability tests had more stable and reliable data sensor readings, which proved to be of utmost importance for the correct performance of the rotational IEs. However, each time the user starts the exam, the EFS needs to be placed towards the patient with the lens pointing down. This temporary constraint ensures the smartphone sensors are correctly calibrated.

A setback to this project was the lack of time and availability of the nurses that tested the final assembly. If there was more time available, the final assembly would have been tested on an elderly population (target population for retinal exams). This would have made the conditions under which this simulated-use testing was conducted sufficiently realistic for a much meaningful feedback.

Overall, this project has shown the importance of creating a GUI that suits the device users and the use-case environments. In fact, with a specific GUI, the interaction technique performed in clinical practice can be greatly perfected, allowing for the human operator to contribute to the improvement of the acquisition task.

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Appendix I

The sketches that are presented in this Appendix were the starting point for the final versions that were later redesigned and implemented in the EFS Android App,

The version A sketch (Figure 1 Appendix 1) comprises a circle that revolved according to the rotation around the Z-axis. In the background there is a referential illustrative of the tilting rotation.

The version B sketch (Figure 2 Appendix 1) comprises an upper semicircle with angle indicators, like the final version, and a pointer that moves accordingly to the rotation around the Z-axis. In the background there is a referential just like the version A sketch for the tilting rotation.

Finally, the version C sketch (Figure 3 Appendix 1) comprises a double arrow pointer that spins inside a circle representing the angle for the Z-axis. In this sketch was firstly introduced the bar IEs that were redesigned and altered to provide the three versions that were tested regarding the Tilt and Pan IEs.

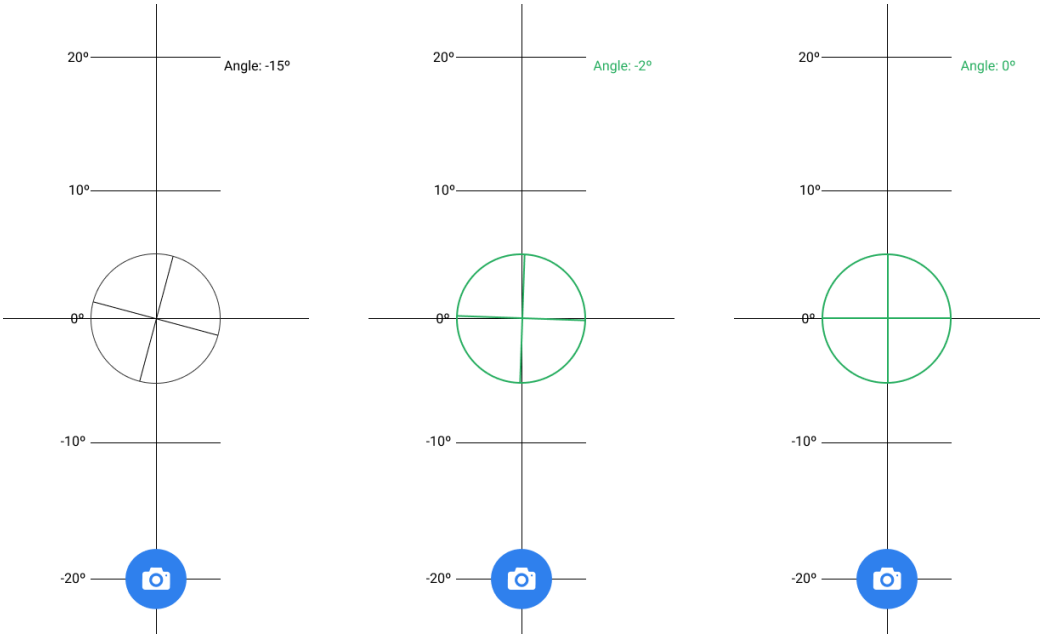


Figure 1 Appendix 1 – Version A sketch

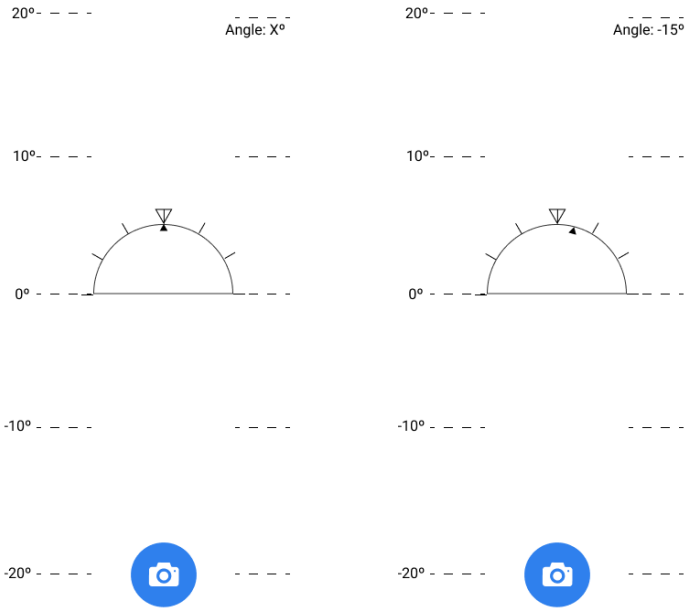


Figure 2 Appendix 1 – Version B sketch

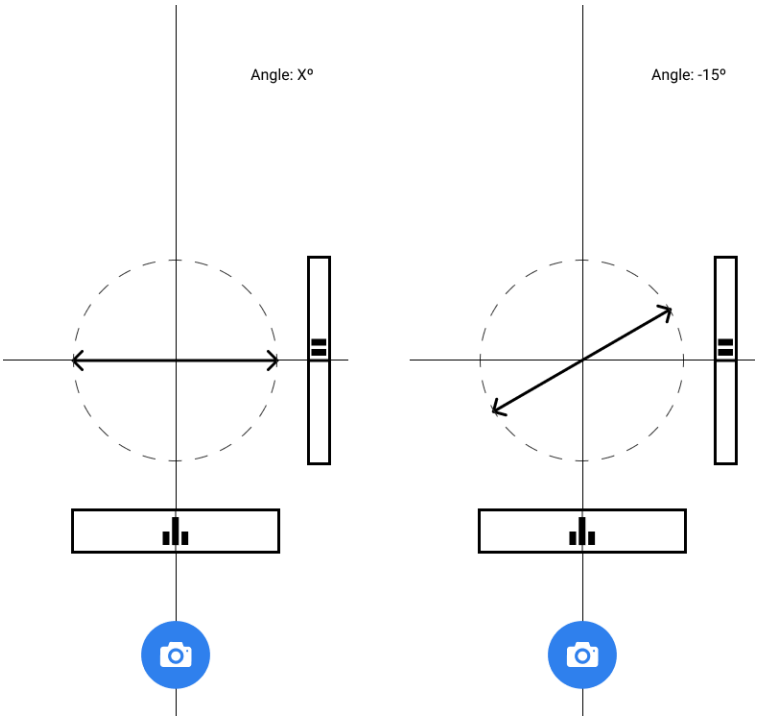


Figure 3 Appendix 1 – Version C sketch

Appendix II

Formulário de recolha de dados

1. Possui um *smartphone* ou tem experiência na utilização de *smartphones*?
   ☐ Sim ☐ Não

2. Anteriormente a este teste já tinha utilizado o protótipo do EyeFundusScope?
   ☐ Sim ☐ Não

3. Considera que a utilização do sistema é simples? ☐ Sim ☐ Não

4. Considera de forma geral que os elementos de interação (EI) facilitaram a aquisição?
   ☐ Sim ☐ Não

   Se acha que não, quais os aspetos que na sua opinião podem ser melhorados?

   _____

   _____

   _____

   _____

5. No que diz respeito aos vários elementos de interação, diga de que forma é que a sua utilização lhe pareceu intuitiva e qual a sua preferência.

Elemento de Interação Roll

De forma geral a tarefa foi?

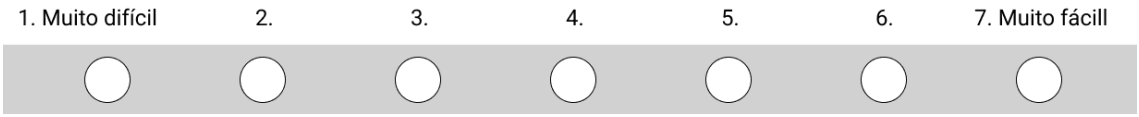
1. Muito difícil	2.	3.	4.	5.	6.	7. Muito fácill
○	○	○	○	○	○	○

Qual das versões que lhe foram apresentadas parece a mais apropriada?

Versão A ☐ Versão B ☐ Versão C ☐

Elemento de Interação Pan?

De forma geral a tarefa foi?

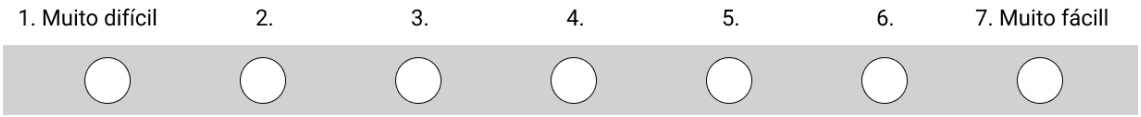


Qual das versões que lhe foram apresentadas parece a mais apropriada?

Versão A ☐ Versão B ☐ Versão C ☐

Elemento de Interação Tilt?

De forma geral a tarefa foi?

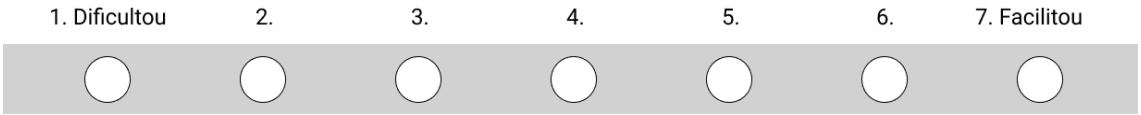


Qual das versões que lhe foram apresentadas parece a mais apropriada?

Versão A ☐ Versão B ☐ Versão C ☐

No que diz respeito ao **tutorial**:

6. Considera de forma geral que o tutorial facilitou a compreensão dos movimentos e posicionamento do protótipo durante a aquisição?



7. Na sua opinião há algo que deva ser acrescentado no tutorial?

   ☐ Sim ☐ Não

   Se acha que sim, o que deveria ser acrescentado?

   _____

   _____

   _____

   _____

No que diz respeito ao componente ***timelapse***:

8. Tendo em consideração o conforto do paciente e a rapidez do exame. Considera que este componente é uma mais-valia para o operador controlar o tempo entre aquisições no mesmo olho?

   ☐ Sim ☐ Não

SUS – System Usability Scale Questionnaire

Usando a escala abaixo, por favor coloque um círculo no número mais próximo da palavra que mais se aproxima aos seus sentimentos acerca do sistema/aplicação.

1. Penso que gostaria de usar este sistema frequentemente

Discordo fortemente	1	2	3	4	5	Concordo fortemente

2. Achei o sistema desnecessariamente complexo

Discordo fortemente	1	2	3	4	5	Concordo fortemente

3. Achei o sistema fácil de usar

Discordo fortemente	1	2	3	4	5	Concordo fortemente

4. Penso que precisaria do apoio técnico para conseguir usar o sistema

Discordo fortemente	1	2	3	4	5	Concordo fortemente

5. Achei que as várias funções do sistema estavam bem integradas

Discordo fortemente	1	2	3	4	5	Concordo fortemente

6. Achei que havia demasiadas inconsistências neste sistema

Discordo fortemente	1	2	3	4	5	Concordo fortemente

7. Imagino que a maioria das pessoas consegue aprender a usar este sistema muito rapidamente

Discordo fortemente	1	2	3	4	5	Concordo fortemente

8. Achei o sistema muito incómodo de usar

Discordo fortemente	1	2	3	4	5	Concordo fortemente

9. Senti-me muito confiante ao usar o sistema

Discordo fortemente	1	2	3	4	5	Concordo fortemente

10. Precisei de aprender muitas coisas antes de conseguir começar a usar o sistema

Discordo fortemente	1	2	3	4	5	Concordo fortemente

Appendix III

Consentimento informado para os profissionais de saúde

CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

de acordo com a Declaração de Helsínquia[1] e a Convenção de Oviedo[2]

Por favor, leia com atenção a seguinte informação. Se achar que algo está incorreto ou que não está claro, não hesite em solicitar mais informações. Se concorda com a proposta que lhe foi feita, queira assinar este documento.

Título do estudo: Aquisição de Imagem Portátil com Visualização em Tempo Real para Interação Homem-Computador em Aplicações Móveis (Handheld Image Acquisition with Real-Time Vision for Human-Computer Interaction on Mobile Applications)

Enquadramento: Este estudo de investigação está a ser realizado pela Associação Fraunhofer Portugal Research – Fraunhofer Portugal Research Center for Assistive Information and Communication Solutions (Fraunhofer Portugal AICOS) e constitui uma tese de mestrado do aluno Ricardo Meneses, no âmbito do Curso de Mestrado Integrado em Engenharia Biomédica e Biofísica (MIEBB) na Faculdade de Ciências da Universidade de Lisboa (FCUL). O trabalho conducente à tese de mestrado é feito sob orientação do Prof.ª Doutor Hugo Ferreira da FCUL e do Prof. Doutor Filipe Soares, do Fraunhofer Portugal AICOS.

Explicação do estudo: O estudo de investigação acima mencionado destina-se a validar a utilização de um sistema portátil para recolha de imagens da retina. O protótipo desenvolvido pelo centro de investigação Fraunhofer Portugal AICOS denomina-se EyeFundusScope (EFS) e no presente estudo está em avaliação novas formas de interação em tempo real dos utilizadores, operadores do protótipo, com o intuito de melhorar o manuseio do *smartphone* durante a aquisição. A sua participação consiste na recolha de imagens da retina usando o protótipo. O sistema não fornece qualquer resultado de análise das imagens e nada será comunicado quer ao profissional de saúde, quer ao doente participante. O teste tem uma duração de cerca de cinco minutos para cada olho. A sua participação consiste ainda na resposta a um questionário/entrevista que terá uma duração prevista de 10 minutos, com o objetivo de estudar a usabilidade e a aceitação da tecnologia em estudo. As respostas ao questionário/ entrevista serão registadas, guardadas e analisadas de forma anónima, isto é, não será registada ou guardada qualquer informação que permita a sua identificação enquanto participante.

Confidencialidade e anonimato: As informações recolhidas são confidenciais e a sua identificação não será revelada. Os dados recolhidos serão utilizados para o presente estudo. Os dados serão recolhidos e analisados pelo investigador ou por outro elemento com autorização delegada pelo investigador e serão apresentados em publicações científicas e conferências ou outro tipo de evento científico ou de divulgação do projeto, assim como nos diversos meios de comunicação social. A S/ identidade não será revelada em qualquer situação. Os dados pessoais, assim como as respostas aos questionários/entrevistas, serão mantidos numa base de dados, de forma anonimizada. Gostaríamos de contar com a S/ participação. Agradecemos muito o S/ contributo, fundamental para a nossa investigação!

[1] http://portal.arsnorte.min-saude.pt/portal/page/portal/ARSNorte/Comiss%C3%A3o%20de%20%C3%89tica/Ficheiros/Declaracao_Helsinquia_2008.pdf

[2] http://dre.pt/pdf1sdip/2001/01/002A00/00140036.pdf

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Assinatura: _____

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Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela/s pessoa/s que acima assina/m. Foi-me garantida a possibilidade de, em qualquer altura, recusar participar neste estudo sem qualquer tipo de consequências. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando em que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas pelo/a investigador/a.

Nome: _____

Assinatura: _____ Data: ____ /____ /_____

SE NÃO FOR O PRÓPRIO A ASSINAR POR IDADE OU INCAPACIDADE

(se o menor tiver discernimento deve também assinar em cima, se consentir)

NOME: _____

BI/CD Nº:_____ DATA OU VALIDADE _____ /_____ /_____

GRAU DE PARENTESCO OU TIPO DE REPRESENTAÇÃO:_____

ASSINATURA _____

ESTE DOCUMENTO É COMPOSTO DE 2 PÁGINAS E FEITO EM DUPLICADO:

UMA VIA PARA O/A INVESTIGADOR/A, OUTRA PARA A PESSOA QUE CONSENTE