Design of a Mobile Application for Eye Signs Screening

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"Who does not feel eagerness to be more, do not come to anything."
Miguel Unamuno

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Abstract

Advances in technology make mobile phones very attractive to everyone, specially smartphones, with a large number of applications, being the medical ones a growing market.

In the field of ophthalmology, some diseases or other health problems are being detected very frequently just by looking to a photograph, specially in social networks. This fact encouraged us to create a mobile application that may detect some eye pathologies and that could be used almost by everybody, even in low income countries.

In this master thesis the necessary features of a mobile application for eye signs screening are described, portraying some ocular pathologies (amblyopia and retinoblastoma e.g.) that can be detected with a photograph using solely a smartphone with flash. Also the data collection protocol necessary to obtain this data and later process it with the use of algorithms are depicted.

A beta version of the developed application is presented, with the set of instructions to the user. This application, to apply the defined protocol, was designed keeping in mind the target user, the parents, who can use it at home as a tool to trace the visual health of their children, given that an ophthalmologist follow-up is scarce or nonexistent in many places.

Finally, some results of a Hospital field study are portrayed with complementary medical opinions about the application and also about the protocol designed, which is assessed as a necessary complement to an early diagnosis for important diseases like amblyopia or strabismus that have large incidence in children.

Contents

List of Figures

List of Tables

Abbreviations

ADT	Android Developer Tools
AN	Acquired Nystagmus
DRP	Digital Retinal Photography
EOG	Electrooculogram
ERG	Electroretinogram
GUI	Graphical User Interface
FDT	Frequency Doubling Perimetry
HFA	Humphrey Field Analyzer
IDE	Integrated/Interactive Development Environment
IN	Infantile Nystagmus
IR	Infrared
IOP	IntraOcular Pressure
MEMS	Micro-Electro-Mechanical System
OCT	Optical Coherence Tomography
OOPL	Object-Oriented Programming Language
PD	Prism Diopters
PERRLA	Pupils Equal and Round, Reactive to Light and Accomodation
RAPD	Relative Afferent Pupil Defect
RRT	Red Reflex Test
SDK	Software Development Kit
UC	Use Case
UI	User Interface
UML	Unified Modeling Language
XML	eXtensible Markup Language
WHO	World Health Organization

Chapter 1

Introduction

Ophthalmology is the field of medicine that studies the anatomy, physiology and diseases of the eye. An ophthalmologist is the professional who specializes in this area and can diagnose and treat eye disorders [42].

Ophthalmic and optometric organizations recommend a visit to an eye care professional every $1-2$ years to have a comprehensive eye exam [43]. People with special clinical needs, like diabetes patients, should visit an eye care professional every year. Table 1.1 [44] presents the recommended frequency of an eye evaluation according to the age of the person, [45].

For the newborns the examination of the eyes is a routine part of the periodic pediatric assessment for detecting both obvious and insidious asymptomatic eye diseases. Because an early detection is a major concern, the American Academy of Ophthalmology recommends preschool vision screening as a means of reducing preventable visual loss [46].

Tab. 1.1: Recommended frequency of evaluation according to age.

Age (years)	Frequency of Evaluation
65 or older	Every 1 - 2 years
55 - 64	Every 1 -3 years
40 - 54	Every 2 - 4 years
Under 40	5 - 10 years

For a better understanding of the ocular anatomy the subsequent sections focus on some of its components, as well as the basic functioning.

1.1   Anatomy of the Eye

The eye is a special sense organ made up of three coats/tunics [2]:

1. The outer fibrous layer of connective tissue forms the cornea and sclera.

2. The middle vascular layer is composed of the iris, ciliary body and choroid.

3. The inner layers the retina.

Figure 1.1 presents an illustration of some components of the eye, including: iris, pupil, lens, cornea, posterior chamber, choroid, sclera, retina, macula, fovea, optic disk, optic nerve and retinal vessels, which will be described later [47].
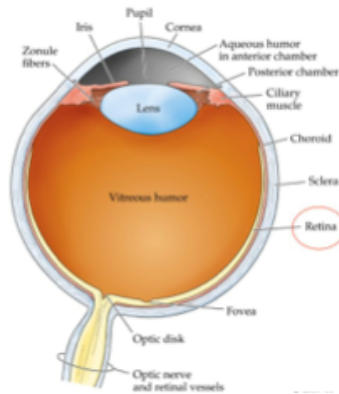
Fig. 1.1: Ilustration of components of the anatomy eye [1].

1.1.1   Sclera

The sclera is a membrane of tendon in the eye, also known as the opaque white of the eye. It is covered by the transparent conjunctiva and is composed by two main layers: the lamina fusca, and the episcleral layer anteriorly (which consists of dense vascular connective tissue) [48].

Because of its resistance and its robustness, the main task of the sclera is the protection of the inner and consequently, more sensitive parts of the eye, like the retina and choroidea. Its thickness is about $7,62 \times 10^{-4}$ m, but in the local where the eye muscles append has a depth more or less of $2,54 \times 10^{-4}$ m.

Sclera also contains an elastic tissue denominated of episclera, in its top. This is the blood vessels that nourish the sclera with oxygen and nutrients are located. These vessels are thus visible on the surface of the white of the eye [47].

1.1.2 Choroidea/Choroid

The choroidea is also an association of vessels that nourish the retina with oxygen and nutrients, that its located within the sclera. The choroid supplies the overlying retina to a depth of about 130 micrometers which includes the pigment epithelium layer, the layer of rods and cones, the outer nuclear and plexiform layers, and the whole thickness of the foveal retina [49].

Proliferative macular degeneration is an eye condition that is directly caused by malfunctioning of blood vessels within this layer.

In Figure 1.2, besides the representation of the choroidea, also the ciliary muscle-/body is represented where the aqueous humor is produced, which provides the nourishment of the surrounding structures, particularly the cornea and lens, and carries their wastes [2]. It also maintains the shape of the anterior portion of the eyeball. It is produced at a rate that replaces it every 90 minutes.

Aqueous humor leaves the anterior cavity through the scleral venous sinus (canal de Schlemm). Blockage of the scleral venous sinus results in the buildup of excess aqueous humor. This increases the pressure for the disease glaucoma [50].
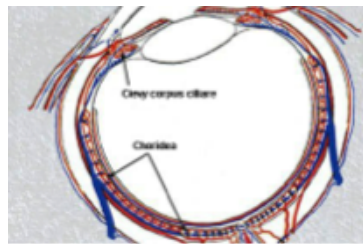
Fig. 1.2: Representation of the choroid and the ciliary muscle [2].

1.1.3 Cornea

The cornea is the transparent structure located in the front of the eye, covering the iris, pupil, and anterior chamber. Its transparency allows the refraction of the light rays entering the globe and helps bring light into focus on the retina. The region in which the transition from cornea to sclera and conjunctiva occurs is the limbus [2]. Although the cornea is clear and seems to lack substance, it is actually a highly organized group of cells and proteins. But, unlike other tissues it does not contain blood vessels (which will interfere in the process of refraction of light), so it is nourished with oxygen and nutrients through eye fluid and not through blood vessels (that also explains why the cornea is so clear).

The corneal tissue is arranged in five basic layers: epithelium, bowman's layer, stroma, Descemete's membrane and endothelium [47], [51].

1.1.4   Retina

The retina refers to the light sensitive tissue in the back of the eyeball. This neural tissue by complex biochemical processes can change light energy into a signal that is transmitted along a neural pathway. The signal passes through the retina, exits the eye through the optic nerve, and is transmitted to various parts of the brain for processing.

The retina contains two kinds of light receptors (photoreceptors): the cones and the rods. There are approximately 5 million cones and 100 million rods in each eye. The cones, which are color sensitive, are located in the center of the retina and mainly absorb stronger light. The rods are located peripheral to the fovea and are very sensitive light detectors, absorbing softer light in black and white with the capacity to generate a detectable photocurrent response when they absorb a single photon of light [47].

The positions of these two types of photoreceptors differ in many ways across the retina. Figure 1.3 b) shows how the relative densities of cone and rod photoreceptors vary across the retina. The rods initiate vision under low illumination levels, called scotopic light levels, while the cones initiate vision under higher, photopic light levels. The range of intensities in which both rods and cones can initiate vision is called mesopic intensity levels [3].
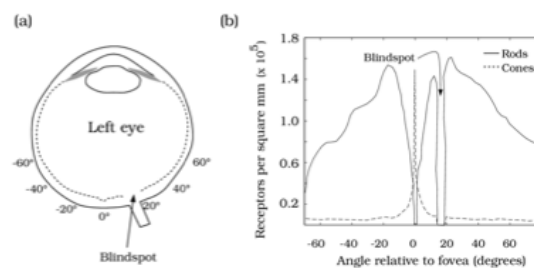
Fig. 1.3: Photoreceptors in the retina and localization of the blindspot [3].

1.1.5   Lens

The crystalline lens is a multilayered structure located in the area of the posterior chamber and provides additional refractive power for accurately focusing images onto the retina. That is to say, that it is the lens that enables the change of focus

according to different distances, so that the individual can perceive the object clearly and sharply.

The lens is attached to a mass called zonula which is attached to the ciliary body. When a person wants to focus on a near object, a muscle in the ciliary body retracts, allowing the change of shape by the lens, a process called "accommodation". This way the zonula "threads" can loosen up, allowing the lens to contract in diameter and thicken, thus increasing its acuity [52].

As a person becomes older, the flexibility of the lens decreases and vision can become blurry, resulting in a condition named cataracts. It can result in complete removal and replacement of the lens by an artificial one (not capable of accommodation) [47].

1.1.6   Vitreous Body/Humor

The vitreous body is a transparent gel-like substance, made up of small fibers and water in the posterior segment of the eye, behind the lens, that fills the space in front of the lens.

The main functions of the vitreous are to transmit light to the retina, and to exercise enough pressure to keep the retinal layers tightly pressed together. This pressure helps maintain the round shape of the eye so the lens can focus sharp images on the retina [53]. Beyond the formation of vitreous at birth, when a person is aging the vitreous body shrinks in volume. When the vitreous body decreases in size it can detach from the retina (named vitreous detachment).

After passing through the cornea, aqueous humor and lens (anterior segment of the eye), light finally enters in the vitreous. This fluid is not replaced but remains throughout life. A thinner fluid, much like aqueous humor, is added to it and leaves by diffusing through the retina [50].

1.1.7   Macula

Macula is an oval-shaped highly pigmented yellow spot near the center of the retina of the human eye (Figure 1.4). It has a diameter of around 6 mm, and has near its center the fovea, a small hole that contains the largest concentration of cone cells (photoreceptors with high acuity) in the eye that are responsible for central, high resolution vision. Because of macula's yellow color it absorbs excess blue and ultraviolet light that enter the eye, and acts as a natural sunblock for this area of the retina [5].
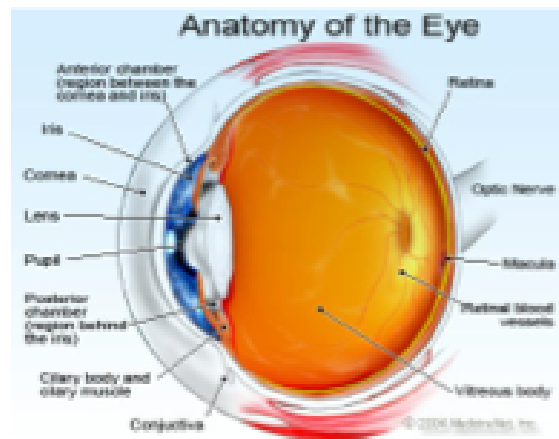
Fig. 1.4: Ilustration of the anatomy of the eye with the location of the macula [4].

A common eye disease, relative to the macula, amongst the elderly, is macular degeneration. The Figure 1.5) shows the optic disc as a bright area on the right (nasal side) where blood vessels converge. The spot to the left (temporal side) of the centre is the macula. The grey, more diffuse spot in the centre is a shadow artifact.
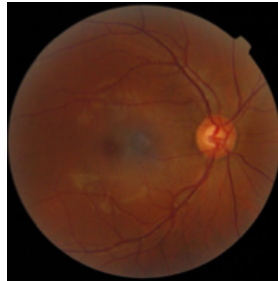
Fig. 1.5: Image of an ophtalmogram of the retina of the right eye with macula degeneration [5].

1.1.8   Fovea

The fovea, as said before, is the most central part of the macula. The visual cells located in the fovea are packed tightest, resulting in a region with optimal sharpness of vision.

The fovea contains no rods, but it does contain a high concentration of cones, approximately $50,000$ [3].

1.1.9 Optic Disc

Also known as the optic nerve head or the blind spot, the optic disc has an oval shape with approximately 1.5 mm diameter and is where the optic nerve attaches to the eye (Figure 1.6). It is the entry point into the eye for major blood vessels that serve the retina. Only can be seen in the back of the eye with an ophthalmoscope [54].

The absence of visual cells (photoreceptors, i.e., rods or cones) in the optic disc causes the appearance of a blind spot in the field of vision, not existing any image detection in this area.

The blind spot of the right eye is located to the right of the centre of vision and vice versa in the left eye. Clinical evaluation of the optic nerve head is critical in the diagnosis and monitoring of glaucoma and other optic neuropathies that may lead to vision loss.
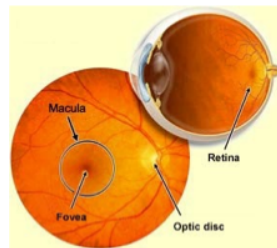
Fig. 1.6: Figure exemplifying the positioting of the optic disc [6].

1.1.10 Optic nerve

The optic nerve also known as cranial nerve II (Figure 1.6), transmits visual information from the retina to the brain, where the signals are interpreted into images. The optic nerve consists of about $1,000,000$ nerve threads. The optic nerves from both eyes are reconnected behind the eyes so that everything that is seen in the right field of vision is sent to the left cerebral hemisphere and vice versa [55].

1.1.11 Pupil

The pupil is considered a black hole in the iris, and it is black because the layer of pigment inside the eye absorbs major parts of the light, resulting in a darker shade. However, when pupils appear red in photos it is actually the color of the retina that is reflected.

During the visual process the eye must continuously compensate for changes from

light to dark and from near to far, so light-dark adaptation is achieved by dilation or contraction of the pupil, whereas near-far adaptation requires a change in the curvature of the lens (accommodation), a change in the lines of sight (convergence), and a change in pupillary width [56].

For example, for focusing on near objects, the pupil decreases in diameter, but it will expand when focusing on distant objects, because a smaller pupil enables better focal depth [47].

1.1.12   Iris

The iris (Figure 1.1) is the most anterior structure that regulates the amount of light that enters in the pupil, a hole through which the light enters the eye, as previously referred.

It has two muscles that control the shape and diameter of the pupil and that are controlled by the autonomous nervous system. In bright light, the iris constricts the pupil, effectively admitting less light. In dim light, the iris dilates the pupil to admit more of the available light. This is a reflex action [50].

1.2   Motivation

"Screening is a strategy used in a systematic approach to identify an unrecognized disease or risk factors in individuals in a population without signs or symptoms" [57].

The motivation for this work arose from several news around the world about parents who post photos of their children on social networks, with some friends noticing that something may be wrong with their vision. A correct diagnosis was made when parents went to an ophthalmologist, who actually detected an eye problem/disease, this led us to the development of a mobile application for eye signs screening in children [58], [59], [60], [61], [62].

As referred before, there is a need for regular evaluation of the eye health, especially in children, for early diagnosis and treatment. Knowing this, we propose to develop a tool on a smartphone, for parents to collect their childrens' eye images for continuous assessment and possible detection of eye pathologies.

This application may also be envisioned to be used in places where specialized medical doctors may not be available, such as is the case of low income countries were preventable blindness is still a major health problem [63].

Statistics show that five percent of worldwide blindness involves children younger

than 15 years of age; in developing countries 50% of the population is in this age group. By the World Health Organization criteria, there are 1.5 million blind children worldwide. There are accentuated differences in the causes of pediatric blindness in different regions, apparently based on socioeconomic factors that limit prevention and treatment schemes. In developing countries 30% to 72% of such blindness is avoidable, 9% to 58% is preventable, and 14% to 31% is treatable [63].

1.3   Objectives

The objectives settled for this thesis were:

- To design a data collection protocol capable of producing a set of images that allow detection of a series of eye pathologies;

- To assess the clinical needs for data collection in an observational study/interviews;

- To define the structure of a mobile application to cover the requirements settled in the protocol, and develop the design;

- To implement and test the beta version of the mobile application in the real clinical environment.

1.4   Organization of the Thesis

The present master thesis is organized as follows: In Chapter 2 some ophthalmology exams, specially non invasive, are represented to a better understanding of current medical procedures. Also a perspective of the actual market of applications in the field of ophthalmology for smartphones are reviewed.
The Chapter 3 presents some statistics about child blindness and the eye pathologies selected to approach in this master thesis: why they may be detected in a photograph, and how.
User stories, use cases, mockups and flow diagram developed when reflecting about the mobile application are described in the Chapter 4. The data collection protocol, the programming technologies applied and implementation of the application are portrayed as well.
In Chapter 5 the objectives and methods of the Hospital field study are depicted.

Finally, in the Chapter 6 an overview of the whole project is presented, showing the advantages of the development of the mobile application, with a discussion of its possible weaknesses.

Chapter 2

State of the Art

This chapter will address some of the most common eye exams, mostly noninvasive since is the focus of this mobile application. It will also be made an overview of the current market of mobile applications in the field of ophthalmology.

2.1 Non Invasive Ophthalmology Exams

Normally, the eye examination consists of an evaluation of the physiological function and the anatomical status of the eye, visual system, and its related structures. Some usual non invasive tests that can be executed by the specialist are: visual acuity, refraction, pupil function, ocular motility, visual field testing, external examination, slit-lamp, intraocular pressure and retinal examination. These tests will be described next.

2.1.1 Visual Acuity

The visual function that is more frequently measured is visual acuity, the clinical testing for visual acuity that is based on letter recognition. This is used to determine the smallest letters a person can read on a standardized chart, which requires not only the optical ability to resolve the image but also the cognitive ability to recognize black and high-contrast optotypes on a white background and the motor ability to respond [64], [65]. Normally a Snellen Chart, as presented in Figure 2.1, is used, so the number of letters that the person can or cannot read can help to measure the progress of disease or vision improvement with treatment. Magnification is the factor on which Snellen's formula is based: if a subject needs letters that are twice as large or twice as close as those needed by a standard eye, the visual acuity is said

to be 1/2 (20/40, 0.5), if the magnification need is 5 times, the visual acuity is 1/5
(20/100, 0.2), and so forth.

In young children, in individuals with a developmental delay, and in elderly stroke
patients, it may be their inability to respond, rather than optical factors, that limits
their test application [66].
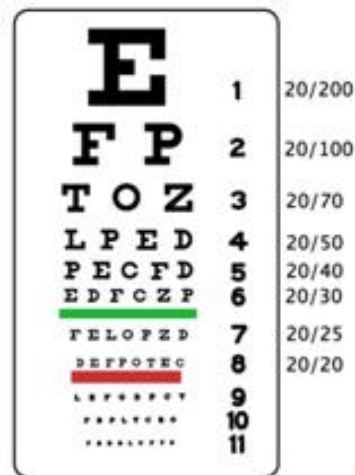
Fig. 2.1: Snellen Chart [7].

2.1.2   Refraction

Refraction can act as a diagnostic tool to differentiate decreased acuity caused by
uncorrected or incompletely corrected refractive error from blurred vision related to
eye disease, in other words, refraction is the procedure by which any refractive error
is characterized and qualified.

Refractive error is an optical abnormality of the eye in which a corrective lens is
needed for proper focusing, that is why the final determination of the refractive cor-
rection is based upon the patient's appreciation of the lens power that provides the
clearest vision at the desired viewing distance [67].

So, the specialist uses a lensmeter (also known as lensometer, focimeter or vertome-
ter) an instrument that can measure the power of a patient's spectacles. In general
two basic types of lensmeters are available: the standard lensmeters and the auto-
matic lensmeters (Figure 2.2). Sometimes this exam is performed using appropriated
eye drops, called cycloplegic eye drops, because of the name of this technique: "cy-
cloplegic refraction", used to determine the baseline refractive status of the eye.
The utilization of this eye drops is to inhibit any discomfort for the patient which

usually causes error in measurement especially in children. The general goal is to determine the maximum plus power correction that provides clear far vision and a near correction that provides clear vision at the desired distances [68].

Fig. 2.2: Model of a lensmeter [8].

2.1.3 Pupil Function

An examination of pupillary function includes inspecting the pupils for equal size (1 mm or less of difference may be normal), regular shape, reactivity to light, and direct and consensual accommodation. These steps can be easily remembered with the mnemonic PERRLA (D+C): Pupils Equal and Round; Reactive to Light and Accommodation (Direct and Consensual).

The pupil reactions to a direct torch light (light response) and to accommodation (near response) are important to exclude optic nerve and neurological disease. The direct exam tests gross retinal and optic nerve function, with the help of a pen torch light into one eye and assessing pupil constriction.

The use of a swinging flashlight detects the relative afferent pupil defect (RAPD, also referred as the Marcus Gunn pupil) which would be a sign of optic nerve anomaly [9]. It is done oscillating the light quickly back to the first eye, in a semidarkened room, with the patient still looking into distance. Both pupils constrict when one is exposed to light (Figure 2.3), if one pupil dilates instead of constricts, this is an afferent pupil defect indicating a serious retinal or optic nerve problem.

In other words, the normal pupil will constrict to the direct light as the light swings back and forth, and the normal pupil will also constrict to indirect light, having a consensual response. RAPD constricts to consensual light, and not to direct light [9].

At least, the near response is to test for neurological diseases. The ophthalmologist asks the patient to look from the distance fixation to a small accommodative target
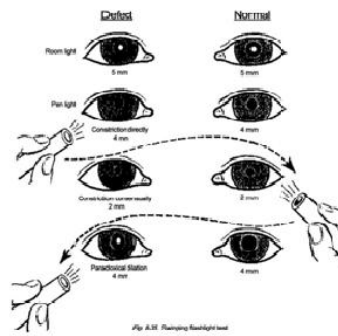
Fig. 2.3: Examination of the reaction to light [9].

that is brought towards her slowly, up to a distance of about 20 cm. Both pupils
should constrict equally [69].

2.1.4   Ocular Motility

This is something that should always be tested. The examination of the ocular
motor system generally consists of the evaluation of:

- Ocular Alignment: the ocular alignment may be tested subjectively or objec-
  tively, depending on the circumstances under which the examination is per-
  formed and the physical and mental state of the patient.
  The simplest subjective tests of ocular alignment use colored filters to disso-
  ciate the deviation and to emphasize and differentiate the images so that the
  patient and the observer can interpret them.
  Other kind of examination can be by analyzing pupillary light reflexes and
  then by performing alternate-cover tests (Figure 2.4) at distance and near.
  The alternate-cover test is used to measure both heterotropias (manifest stra-
  bismus) and heterophorias (latent strabismus) [70].
  If an abnormality is found, lateral gaze positions and upgaze and downgaze
  prism measurements are also recorded. If a vertical deviation is noted, head
  tilts are performed. The versions should correspond with the prism measure-
  ments. Ensure that the patient is not fixating with the palsied eye [71].

- Fixation and gaze-holding ability: in this test the ophthalmologist uses a hand
  light to cast a reflection on the corneal surfaces of both eyes in the cardinal
  positions of gaze. If the images from the two corneas appear centered, like in
  the Figure 2.5 a), then the visual axes are often correctly aligned. If the light
  reflexes are not centered an estimation of the amount of misalignment can be
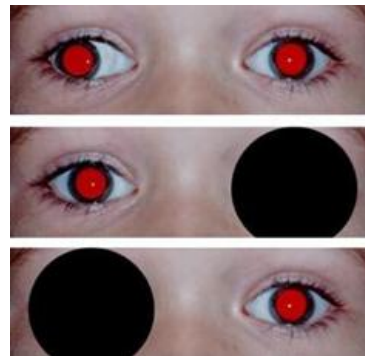
Fig. 2.4: Exemplification of the alternate-cover test [10].

calculated based on the apparent amount of deviation of the light reflex (with the fixation light held 33 cm from the patient, 1 mm of deviation equals 7 degrees of ocular deviation).

Other method is by placing prisms over either of the eyes until the light reflexes appear centered. In [71] the authors say that "Krimsky recommended that the prisms be placed over the non-fixing eye, but von Noorden considered this technique less precise and more difficult than placing prisms over the fixing eye", and they agree; however, if the non-fixing eye is so eccentric and limited in its excursion that centration of the light reflex is impossible or requires excessive prism over the fixing eye, holding the prism over the fixing eye results in a measurement of the deviation only in eccentric gaze.
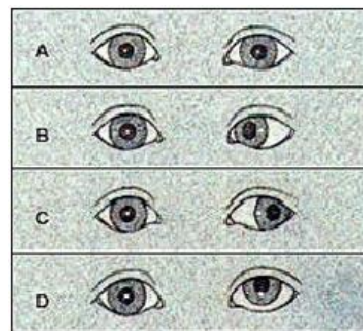
Fig. 2.5: Testing light reflexes [11].

- Range of monocular and binocular eye movements;

- Performance of Versions (saccades, pursuit): in this part of ocular examination the patient is asked to follow a target with both eyes as it is moved in each of the nine cardinal directions of gaze. The examiner notes the speed, smoothness, range and symmetry of movements and observes for unsteadiness of fixation.

These nine components of gaze test the extraocular muscles: inferior, superior, lateral and medial rectus muscles, as well as the superior and inferior oblique muscles.

The assessment for eyes deviations could result from strabismus, extraocular muscle dysfunction, or palsy of the cranial nerves innervating the extraocular muscles. Saccades are assessed by having the patient move his or her eye quickly to a target at the far right, left (Figure 2.6), top and bottom. This tests for saccadic dysfunction whereupon poor ability of the eyes to "jump" from one place to another may impinge on reading ability and other skills, whereby the eyes are required to fixate and follow a desired object.

In addition, depending upon the findings of the basic examination, it may be appropriate to test the vestibulo-ocular and optokinetic reflexes and to attempt mechanically to move the eyes using forced duction testing [72].
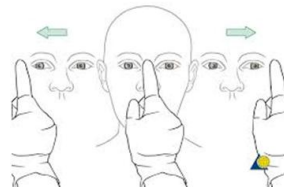
Fig. 2.6: Demonstration of eye deviations testing [12].

2.1.5   Visual Field Testing

Testing the visual fields consists of field testing in which each eye is tested separately to evaluate the extent of the peripheral field, testing the full horizontal and vertical range ("side vision").

To perform the test, the individual occludes one eye while fixated on a target object as the examiner's eye (which stands/sits in front of him) with the non-occluded eye. The patient is then, for example, asked to count the number of fingers that are briefly flashed in each of the four quadrants. There are other types of visual field tests, like an automated one, the Humphrey Field Analyzer (HFA) [73], which uses automated perimetry to measure responses to visual stimulation appearing in central and side vision (Figure 2.7).

This examination can highlight the presence of blind spots ("scotomas", areas of reduced vision), which, depending on the size and shape of the scotoma, could indicate a variety of eye diseases, such as hemianopia (half of visual field loss), homonymous hemianopsia and bitemporal hemianopia. But brain abnormalities

(like those caused by strokes or tumors) also can affect the visual field. In fact, the location of the stroke or tumor in the brain can frequently be determined by the size, shape and site of the visual field defect.

Fig. 2.7: Testing example using a Humphrey Field Analyzer [13].

If an eye disease is suspected formal types of visual field testing should be executed to evaluate the quality of central and peripheral vision of the patient [74]. Numerous tests for measuring visual field loss exist, and can include:

- Automated Perimetry: this tests can measure the patient responses to the presence of objects in different areas of your field of view and it is important in the diagnosis of many eye disorders, especially glaucoma [75]. The patient's head remain still on a chin support, while he stares at a source of light straight ahead. Random lights of different intensities are flashed in his peripheral field of vision and he has to press a button or use other means to indicate their response when perceive the computer-generated light suddenly appearing in his field of view. If this does not happen, it can be an indication for a blind spot which means he has a percentage of vision loss.

- Frequency Doubling Perimetry (FDT): frequency doubling is based on an optical illusion produced with vertical bars of contrasting colors (usually black and white) appearing on a screen. These bars appear to double in number when they alternately scintillate at higher frequencies, a phenomenon thought to be due to the unique response of specific light-sensitive cells (photoreceptors) in the retina. Inability to see vertical bars at certain frequencies could indicate optic nerve or other types of eye damage with accompanying loss of vision in certain areas of the visual field [76].

- Electroretinography: this test measures electrical activity generated by the photoreceptor cells in the retina when the eye is stimulated by a special strobe light or a reversing checkerboard pattern of light. The measurement is captured by an electrode placed on the front surface of the eye (cornea), and a graphic

record called an electroretinogram (ERG) is produced. Electroretinography is useful in diagnosing several hereditary and acquired disorders of the retina, including retinitis pigmentosa, a detached retina or functional changes in the retina caused by arteriosclerosis (hardening of the arteries) or diabetes [13].

2.1.6   External Examination

The external eye structures incorporates the eyelids and surrounding tissues, conjunctiva, lacrimal apparatus, cornea and anterior chamber. External examination of eyes includes the inspection of the eyelids, surrounding tissues and palpebral fissure. Palpation of the orbital rim (Figure 2.8) may also be done, depending on the presenting signs and symptoms.

The position of the eyelids are checked for abnormalities: the normal upper eyelid margin is located $1 - 1.5$ mm below the superior limbus. If the eyelid margin is too high, lid retraction occurs; if it is too low, blepharoptosis or ptosis (an asymmetry between eyelid positions) occurs. Whenever lid retraction is suspected, contralateral ptosis is excluded. The eyelids can also show too much movement (e.g., blepharospasm) or too little movement (e.g., Bell palsy). In addition, the ophthalmologist observes the margin of the eyelids for mucus or pus discharge, scales, or lumps, because the lids should fit smoothly against the eyeball [71].

Also a comparison between the two eyes is required. The conjunctiva on the eyeball should be equally white in both. The conjunctiva and sclera can be inspected by having the individual look up, and shining a light while retracting the upper or lower eyelid. The conjunctiva lining the inner eyelid of the lower lid can also be checked by gently pulling down the lid with a finger. The conjunctiva lining the upper lid can only be observed by everting the upper lid.

The lacrimal apparatus is checked by observing for excess dryness or tearing. Gently pressing the lacrimal sac at the medial corner of the lower lid and nose will normally not express any discharge.

Finally, the cornea and anterior chamber can best be examined by using a pocket flashlight. The cornea should have a lustrous surface and be crystal clear, allowing a crisp and lucid view of the iris. A scratch on the cornea can be readily demonstrated by applying a fluorescein strip and observing with a blue light [77].
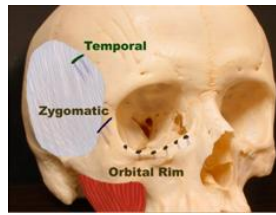
Fig. 2.8: Anatomic model indicating the location of orbital rim [14].

2.1.7 Slit-Lamp

Close inspection of the anterior eye structures and ocular adnexa are often done with a slit lamp which is a table mounted microscope with a special adjustable illumination source attached. A small beam of light that can be varied in width, height, incident angle, orientation and colour, is passed over the eye. Often, this light beam is narrowed into a vertical "slit", during slit-lamp examination. The examiner views the illuminated ocular structures, through an optical system that magnifies the image of the eye, the patient is seated while being examined, and the head stabilized by an adjustable chin rest (Figure 2.9).

The slit lamp exam uses an instrument that provides a magnified, three-dimensional (3D) view of the different parts of the eye. During the exam, the doctor can look at the front parts of the eye, including the clear, outer covering (cornea), the lens, the iris, and the front section of the vitreous gel that fills the large space in the middle of the eye.

Fluorescein staining before slit lamp examination may reveal corneal abrasions or herpes simplex infection, but it also can be used during the examination to make it easier to detect a foreign body, such as a metal fragment, or an infected or injured area on the cornea.

Special lenses can be placed between the slit lamp and the cornea (or directly on the cornea) to view deeper structures of the eye, such as the optic nerve, retina, and the area where fluid drains out of the eye (drainage angle). A camera may be attached to the slit lamp to take photographs of different parts of the eye.

Also ophthalmoscopy examination (a test to observe the back/fundus of the eye) can be performed through the slit lamp when combined with a diversity of special lenses. This exam can help to detect a variety of disorders such as infection or injury to the cornea, cataracts, conjunctivitis, or iritis, and also to identify eye problems that may be caused by other diseases, such as diabetes or rheumatoid arthritis. It can be performed with the purpose to monitor complications such as: bleeding after an eye injury, cataract formation that occur because of chemotherapy, radiation treatment,

after a bone marrow transplant or for glaucoma and macular degeneration [78].

Fig. 2.9: Demonstration of a Slit-Lamp examination [15].

2.1.8   Intraocular pressure (IOP)

Intraocular pressure is a function of aqueous humor drainage from the eye. The most accurate way to measure it is to cannulate the eye and directly measure it by water column or pressure gauge, however, this is not a practical approach. So, all the other methods of IOP measurements are indirect [79].

Tonometry is an indirect estimation of the constant circulation of fluid that maintains the shape and internal pressure of the eye, by measuring resistance of the eye to indentation by an applied force. Its normal range is $10 - 21$ mmHg, an elevated intraocular pressure produces blindness by its effect on the optic nerve at the point where the nerve bends to pass from the retina into the nerve head [80].

This measure is normally made on adults, unless there is a contraindication (e.g. trauma or corneal ulcer), but all children who have had cataract surgery should also have their IOP measured at every follow-up visit, if possible.

Many people with glaucoma have no symptoms and do not know they have the condition. Although elevated IOP is not the only sign of glaucoma, measuring it is simple and quick to do, what allows an early treatment, which will preserve the patient's sight. There are 3 different types of tonometers: indentation, applanation (Figure 2.10 (a)) and contour matching. The most common type of tonometry test is called "Goldmann Applanation tonometry" (Figure 2.10 (b)) which has been considered the international gold standard for measuring IOP for two decades, because of its presumed accuracy and ease of use [79].

There are other methods including alternative types of tonometry called "Pneumotonometry" as well as the Tono-Pen. Pneumotonometry is a procedure that involves contacting the eye with air pressure, using an instrument that resembles an air piston. The instrument blows a brief puff of air at the cornea, measuring the

(a)   (b)
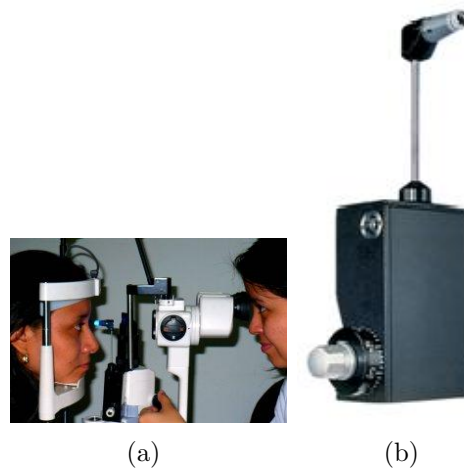
Fig. 2.10: Different tonometers: (a) One type of tonometer by applanation method [16]; (b) Model of a tonometer used for Goldmann Applanation tonometry testing [17].

pressure in the eye. This test is usually considered less accurate than Goldmann applanation tonometry.

The Tono-Pen is hand-held device that provides a digital readout of eye pressure. The doctor uses it to touch the eye and measure pressure. Though useful in many cases, the Tono-Pen is considered less accurate than the Goldmann tonometer in people with normal corneas [81], [17].

2.1.9 Ophthalmoscopy

Examination of retina (fundus examination) is an important part of the general eye examination, using eye drops to dilate the pupil, and enhance the view and extensive examination of the peripheral retina. If the pupil is undilated the doctor will have a limited view and will not be able to detect tears, holes, hemorrhages, or abnormalities that occur in the periphery of the retina. For best results in this case, he will make the room darker and ask the patient to look towards the far corner. In [82] the authors refer some side effects for this procedure, like light sensitivity for $4-6$ hours and blurred vision specially at near distances, because of mydriasis effect. But side effects from the drops rarely occur.

Retinal examination is highly recommended for people with diabetes, high blood pressure and cholesterol, people aged over 40 years old with family history, and for people with frequent or severe headaches, light sensitivity, loss of side vision, and others.

The appearance of the optic disc and retinal vasculature are also assessed during fundus examination. The optic disc should appear slightly oval, with a pink colour. A red reflex can be seen when looking at a patient's pupil through a direct ophthalmoscope (Figure 2.11). This part of the examination is done from a distance of about 50 cm and is usually symmetrical between the two eyes. An opacity may indicate a cataract.

Nowadays there are other exams like Digital Retinal Photography (DRP), a quick and high resolution (approximately less than 5 minutes) screening photograph, which does not require eye drops and with no side effects associated. DRP is not a replacement for dilation of the eyes but it is an effective screening tool for eye disease [82].

Fig. 2.11: Red reflex examination using a direct ophthalmoscope [18].

Based on the patient's history and findings, additional tests or evaluations might be indicated to evaluate further a particular structure or function. These are not routinely part of the comprehensive medical eye clinical evaluation described before. Specialized clinical evaluation may include the following [83]:

- Monocular near-vision testing

- Potential acuity testing

- Color-vision testing

- Testing of stereoacuity and fusion

- Testing of accommodation and convergence amplitudes

- Central visual field testing (Amsler grid)

- Pupillometry

- Corneal sensation, among others.

Additional diagnostic testing may include the following [83]:

- Analysis of the corneal shape (e.g. keratometry and/or corneal topography)

- Ocular wavefront analysis (aberrometry)

- Measurement of corneal thickness (pachymetry)

- Anterior and posterior segment imaging (e.g., optical coherence tomography, Scheimpflug photography, high-frequency ultrasound, or confocal microscopy)

- Stereophotography or computer-based image analysis of the optic disc and retinal nerve fiber layer or macula

- Ophthalmic ultrasonography

- Fluorescein or indocyanine green angiography

- Electrophysiological testing

- Microbiology and cytology

- In-office point-of-care testing (i.e., immunochromatography)

- Radiologic testing

- Laboratory tests for systemic disease, and others.

2.2   Smartphones and their Applications

Currently, utilization of mobile applications has experienced a substantial growth, becoming part of day-to-day life of many people [84]. With the increasing use of smartphones several applications in several areas are being developed, including the medical field. These can help people to keep informed of the latest updates in the world of medicine, but also help in the diagnosis or monitoring of disease.
More ophthalmologists than ever carry a smartphone with them on a daily basis. There are many ophthalmic applications and reference texts available on a variety of platforms [22], [85]. Remotely or with lack of experts this may become crucial for early diagnosis and, consequently, a higher probability that the disease does not progress to an advanced stage.
Following some mobile applications and devices that may be found in the market in the ophthalmology field will be presented.

2.2.1   Applications for ophthalmology tests

- **Eye2phone** - is a portable tool that may help ophthalmology practitioners, physicians and students in their daily routine. It includes the most usual tests: Near Visual Acuity, Distance E, Ishihara (Color Test), Amsler grid, Target for fixation tests and Pupil Gauge Check (Figure 2.12). This software is provided by Renato A. Neves, MD, director of the Eye Care Hospital [19].

Fig. 2.12: Main menu of the mobile application "Eye2phone" [19].

- **OPSM** - a free application proposing to help people to get a better understanding of their vision, and inform them of where they may benefit from an eye test and book an appointment.
  The OPSM Eye Check application uses different tests to screen the eyes (Figure 2.13) and can give the results in an easy to understand way but, of course, does not replace a full eye exam with an ophthalmologist [20], [86].

- **Teste de Visão** - This application has 6 different types of ophthalmologic exams, such as visual acuity tests (with a Snellen table, numbers and text, with black or white fund), Ishihara (Daltonism) test, Amsler grid or AMD test for macula degeneration (Figure 2.14). Has a "pro" version that includes additional tests [21].

- **Macula Tester** - Diseases that affect the macula (the center of the retina), including macular degeneration and diabetic retinopathy, are the main causes of blindness worldwide. Up to 80% of patients with diabetes lose vision due to retinopathy and up to 20% of patients with age related macular degeneration (AMD) go blind. The best way to prevent these conditions to happen is an early detection [87].
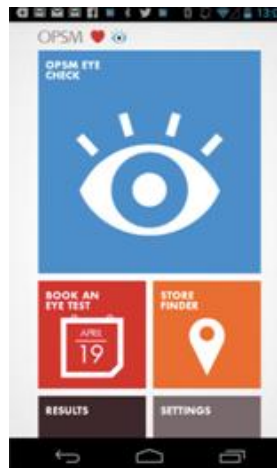
Fig. 2.13: Screenshot of the application "OPSM" [20].
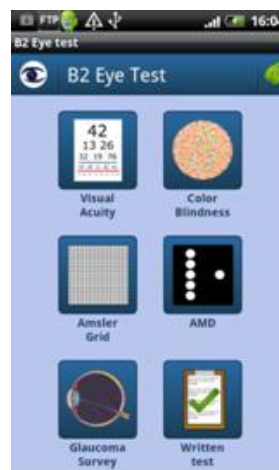
Fig. 2.14: Example of some tests that "Teste de Visão" provides [21].

The MaculaTester is a mobile application (only available for iPhone) with an interactive version of the Amsler Grid (Figure 2.15) - the standard test used by ophthalmologists to check macular function for over 50 years. Because image distortion is often the first visual change of patients in this condition, this test can alert for the condition. Since the distortion can be subtle and difficult to notice at first, the Amsler grid is used to help detect AMD as early as possible while it is still treatable.

Most doctors give their patients a card with an Amsler grid on it to test themselves at home between eye exams. Unfortunately many patients lose it, or forget to use it. Using this electronic format of the test they can have the advantages shown below:

1. It is interactive, allowing to record the area of distortion by touching the screen. The recorded image is saved with date and time so the patient can show it to the doctor, as well as compare to previous images to look for any changes (Figure 2.16).

2. It resides on patient mobile phone, so he does not lose it

3. It has a free "push notification" feature reminding the person to perform the test at regular intervals - so he does not forget to use it [22].

Fig. 2.15: "Macula Tester" mobile application [22].
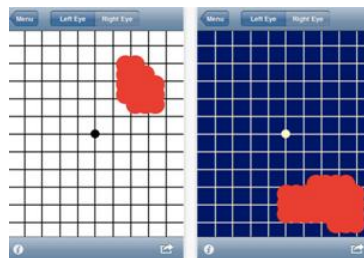
Fig. 2.16: Interactive test present in "Macula Tester" application [22].

- **SightBook** - allows the user to test his vision frequently and share the results with their designated physician in real time. In Figure 2.17 b) some of the various vision tests that the application are shown. In "My Test Sequence" the user can turn on or off different ones such as: Acuity, Amsler Grid, DigiGrid, Low Light Acuity, Acuity and Contrast, Red-Blue Acuity, Inverse Acuity, Contrast, Inverse Contrast and Low Light Contrast [23], depending on the doctor's advice.

- **Eye Handbook** - this application has a collaboration with the American Academy of Ophthalmology. It has different features, such as [24]: Calculators

Fig. 2.17: Main menu of "SightBook" application and its settings [23].

(Figure 2.18) - Age to Bifocal Add, Diopter to Radius Conversion, Glaucoma Risk Factor Calculator, Vertex Conversion, Visual Acuity Conversion, etc; Atlas of ophthalmic images; Testing - Duochrome Test, Amsler Grid, Color Vision Test, Contrast Acuity, Pupil Gauge, Pediatric Optotypes, Worth 4 dot, etc; Vision Symptoms Menu: can be used to help patients understand a common disease process that they had not fully understood before; Ophthalmic Medications; Treatment and others.
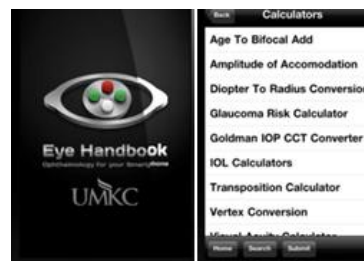
Fig. 2.18: Eye Handbook logo and "Calculators" feature [24].

- **myVisionTrack** - is an user-friendly system available only by prescription, that enables patients with retinal diseases, like diabetic retinopathy (DR) or Age Related Macular Degeneration (AMD), to quickly and efficiently monitor their own vision function at home not using the standard test (Amsler Grid), which sometimes cannot properly help a self-detect activity in an effective way [88].

  This application uses a VAS (Vital Art and Science) software that can store the tests results and automatically compare it with prior test results [25]. In the event that a significant change is detected (Figure 2.19), the physician would be notified to review the data to determine if the patient needs to come in earlier for a check-up. This feature can help to obtain timely care and treatments, something very important for these diseases, as approached before in the "Macula Tester" application description.

Fig. 2.19: Example of "myVisionTrack" testing [25].

2.2.2   Applications using an external camera

- **NETRA** - this mobile application, developed by scientist from the Massachusetts Institute of Technology (MIT), is a portable and inexpensive solution for estimating refractive errors in the human eye [89]. While expensive optical devices for automatic estimation of refractive correction exist, the goal of this application is to simplify these mechanisms. They based their work in the traditional Shack-Hartmann wavefront sensor that uses lasers and highly sensitive digital sensor which makes those solutions expensive, voluminous and requiring trained professionals.

  This solution creates an inverse Shack-Hartmann sensor (Figure 2.20), that is based on a high-resolution programmable display, combining inexpensive optical elements, interactive GUI, and computational reconstruction [26]. The key idea is to interface a lenticular view-dependent display with the human eye at close range, a few millimeters apart. Via this platform, they created a new range of interactivity that is extremely sensitive to parameters of the human eye, such as the refractive errors, focal range, focusing speed, lens opacity, etc. They propose several simple optical setups, verification of their accuracy, precision, and their validation in a user study.

Fig. 2.20: Netra hardware [26].

- **Handyscope/Dermatoscope** - Handyscope is an alternative to conventional handheld dermatoscopes: it has the ability to convert a iPhone into a digital

dermatoscope (Figure 2.21), allowing the user to take brilliant polarized and non-polarized pictures with up to 20 times magnification, and save them in the password protected application. With its twin light mode, great optics and ergonomic use, this handyscope offers a degree of handiness that is unmatched in digital dermoscopy. This way the doctor can keep a distance during the skin exam and easily evaluate moles on-screen or show the result to the patient [27]. The company FotoFinder has also proposed the eDermoscopy, that combines handyscope with the FotoFinder Hub web database (like a "cloud") with extended features for image management and analysis. FotoFinder Hub also provides a second opinion service.

Fig. 2.21: Handyscope hardware in a mobile phone [27].

These mobile applications are just a few examples within the wide variety that currently exists in the market.

2.2.3 Applications for detecting eye pathologies

- **Peek** - Is another example of a mobile application that uses the camera to scan the lens of the eye for cataracts, and also can be applied to look at the retina at the back of the eye by using the camera's flash light to illuminate it, checking this way the health of the optic nerve. It can also be used to do a basic vision test by observation of a shrinking letter on screen. The patient's records are stored on the phone with their exact location using GPS, and the results can be emailed to doctors [90].

  The developers are still testing and comparing the images obtained with the application with the ones taken with a conventional eye examination gear, but the results are satisfactory [91]. Their idea with this tool is to take it to low-income countries where trained health staff is scarce, enabling relatively untrained people to use it. This way, they can go to patients' homes, examine and diagnose them there and at the exact moment.

2.2.4   Devices

The first device presented in this subchapter, was developed by the researchers from the Massachusetts Institute of Technology (MIT) in collaboration with the University of Erlangen and Praevium/Thorlabs. These researchers developed a portable instrument that can scan a patient's entire retina in seconds, and that could aid in the early detection of a variety of retinal diseases including diabetic retinopathy, glaucoma and macular degeneration.

This is a really good improvement in ophthalmologic instruments because, normally, to diagnose retinal diseases, the specialists must examine the patient in his office due to the use of table-top instruments. This new tool would improve public access to eye care since it can be used outside the office.

Although other research groups and companies have created hand-held devices using similar technology, this new design is the first to combine leading edge technologies such as ultrahigh-speed 3D imaging, a tiny micro-electro-mechanical system (MEMS) mirror for scanning, and a technique to correct the unintentional movement by the patient [92], [28].
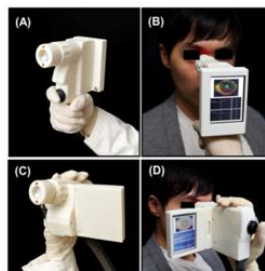
Fig. 2.22: Hand-held device using Optical Coherence Tomography (OCT) [28].

Several devices for retinal/fundus imaging are available commercially [29], [30], but because this is not the focus of this work, we will not go into further detail. The following images show other devices built for this propose.
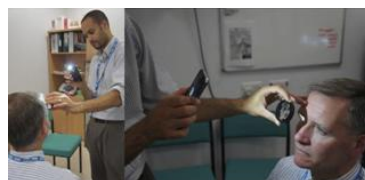
Fig. 2.23: Smartphone with 20 diopter indirect lens used to capture a fundus image [29].

Fig. 2.24: Image of a fundus [29], [30].

2.3 Summary

In recent years smartphones have changed the way the information gets to the people. It became a way of living and with the installation of additional applications, the list of potential uses of smartphones grows exponentially every day, both for professional and personal life activities. The number of professional applications of smartphones is constantly increasing in all domains (medicine, engineering, sports, etc).

Regardless the innumerable potential uses and versatility of smartphones applications, the risk produced by, or associated with, smartphones is also increasing and alarming [93]. That is why the users should be very careful about the use that they will give to a mobile application and the purposes of it. Therefore, the application developed here has a warning information to the user at its opening. It is important to refer that this mobile application does not replace a medical appointment, and the report associated to the data collection can lead to false positives or even false negatives, being necessary a further specialist evaluation.

However, nowadays, applications are going far beyond the role of providing information and basic education. For instance, for dermatology, in [94] the authors argue that use an evidence-based approaches and sophisticated programming to facilitate the promotion, inhibition, and self-monitoring of behaviors, symptoms, and other important outcomes. Even provide content that is customized (i.e., incorporating user-selected features or content), interactive or dynamic, which may facilitate user experiences and engagement. Applications can take advantage of diverse functions of smartphones including taking photographs, text and multimedia messaging, instant messaging or GPS. Based on these ideas we propose to develop an application for ophthalmology.

Chapter 3

Eye Pathologies

In this chapter we will describe some ocular pathologies that may be detectable through photographs, and how this process may be carried out in order to obtain the photos taken with a smartphone for that purpose. Also statistics about child blindness and eye disease are presented to depict the global status of eye health around the world.

3.1 Child Blindness

It is estimated that in the world there are approximately 1.5 million blind children, and this is one of the five priorities of the World Health Organization (WHO). The congenital cataract is the second priority and the most important cause of treatable childhood blindness in Latin America: responsible for approximately 40% of cases, representing a leading cause of low vision [31].

Global estimates of the prevalence and incidence of blindness highlight the importance and need of developing preventive measures and strategies to promote eye health. It is known that blindness in children is related to the socio-economic development, and statistics infer that 75% of those live in developing countries, with a prevalence in these countries of 15/10000 (five times more than that in developed countries) [95].

In a manifest published in 2006 by the WHO, it was demonstrated that there are about 161 million of people with visual disorders, of which 37 million were blind, and that around 75% of these cases of blindness could have been prevented or cured. It is recognized that there is a direct relation between poverty and blindness, and that this provides significant economic burden on families, communities and countries,

particularly in the developing countries [96].

One study was performed in [96] highlighting the importance of the application of the "Red Reflex Test" (RRT) as an effective form of blindness prevention and early diagnosis of serious diseases such as retinoblastoma, a malignant tumor that occurs more often in the childhood (more detail on this subject will be provided later). The RRT is a screening exam for detecting ocular abnormalities using an ophthalmoscope, that emits light with the appropriate intensity over the pupil of the newborn, even without the use of previous drops. The reflection of the incident light produces a reddish and continuous color on healthy eyes (Figure 3.1 a)), meaning that the main internal structures of the eye (like cornea, iris, pupil, lens and retina) are transparent, allowing the light normally to reach the retina.

In the presence of an abnormality that obstructs the arrival of light to the retina and its reflection, the light reflex undergoes changes that interfere with their coloration, homogeneity and binocular symmetry (Figure 3.1 b)).

(a)   (b)

Fig. 3.1: Difference between red reflexes in photos [31]: (a) Normal red reflex with bilateral presence; (b) Abnormal red reflex dubious in one case and absent in another.

This painless and non invasive test is a mandatory routine, by law, in delivery rooms in Rio de Janeiro and São Paulo, in Brazil, such as in Portugal, and should be done by the neonatologist in the first 6 hours of life of the newborn. However there are cases of pediatricians who do not examine the eyes of newborns and the result of this neglect is alarming: more than 50% of the cases have only been detected when the child is blind or nearly blind [97].

The test should be done early in a child's development, given that it is when the vision progresses, and if the diagnosis is late, the likelihood of full recovery is small. To perform the test there are some conditions to consider such as:

1. Environment with adequate lighting (dark or dim light) that benefits physiological pupil dilation and the visualization of the red reflex, therefore the

unnecessary use of proper solutions to the dilation of the eye, as previously mentioned;

2. Direct the ophthalmoscope near the face of the examiner and place the focus light to illuminate both child's eyes simultaneously, at a distance of 30 to 50 cm;

3. Interaction with the newborn so that he/she directs his/her gaze to the examiner;

4. When the light is directed towards the eye, the background (vascularized choroid) acts as a mirror reflecting the light back through the pupil, changing the color and giving the red reflex (shades of orange to red), which fill the entire pupil [95].

RRT can be useful to identify several visual diseases like:

- Congenital Cataract (it is defined as an opacification of the lens [98], and it can look like leukocoria, with the white pupil, and that is why it is necessary to conduct a differential diagnosis) [99];

- Prematurity Retinopathy (a vascular disease of the retina that affects premature infants with very low birthweight. It is responsible for $40 - 60\%$ of blindness in the developing countries [99]);

- Retinoblastoma;

- Congenital glaucoma;

- Retinal detachment;

- Coats' disease;

- PHPV: Persistent Hyperplastic Primary Vitreous;

- Leucomas (corneal opacity);

- Uveitis (inflammation of the uvea);

- Vitreous Hemorrhage [96].

In summary, several different diseases may be detected with a mobile application. The following section is focused on the description of these diseases in detail.

3.2   Eye Pathologies and Proposals for Smartphone Screening

There are many eye disorders but not all of them are detectable looking at a photograph and examining it, so this section focuses only on those that through a photograph taken with a smartphone equipped with camera with flash, will be liable to be evaluated.

3.2.1   Retinoblastoma

Retinoblastoma is a tumor that originates from immature retinoblasts in the neural retina and it is the most frequent intraocular tumor in children, being responsible for 11% of cancer cases in the first year of life. The incidence ranges from $1/14,000$ to $1/20,000$ live births, depending on the country, and over 90% of cases are diagnosed before 5 years old.

The treatment of retinoblastoma is complex and requires a trained multidisciplinary team at all stages of therapy, so early diagnosis of retinoblastoma is essential to reduce disease morbidity and mortality. Initial lesions are more easily treated and result in a higher cure rate and conservation of the eye and vision [100].

The most common signs of retinoblastoma are: leukocoria $(50 - 60\%)$, strabismus $(20 - 25\%)$ and inflammatory signs $(6 - 10\%)$ [101]. In other cases children may develop: secondary glaucoma, pseudoveitis and proptosis [102].

3.2.2   Leukocoria

Leukocoria is an abnormal (white) reflex when a direct light source reaches the eye, but it is not a eye pathology, it is a sign. Because retina is highly vascularized and has red-orange color the light reflected toward the eye must have a reddish appearance, but in this disease there is a change in some internal structure of the eyeball so this reflex is absent, and there is usually a whitish reflection.

The authors in [103] recommend parents to take photos once a month (according to the eye pathology, a monthly photograph can become excessive), in a room with soft light and without red-eye reduction, to check for a normal red-eye reflex in children under six years of age. The idea is to also have an alert in the application that monthly advises parents to take a series of photos with the application.

So, the purpose is to develop an algorithm in the application to detect the white spot in the eye of the children, by taking a serie of photos. The application will provide the using of flash (if the smartphone has this feature), independently of the lights in the room, and the camera in the application will not make a red eye reduction, in any occasion. Ensuring that the reflex of the light from the flash is present to allow an evaluation.

3.2.3 Coats' disease

Coats' as well as leukocoria, can be seen in photographs taken with flash too, but the eye presents a yellowish color like in the Figure 3.2. Coats' disease affects the retina and is often mistaken with retinoblastoma, because common modes of presentation include reduced vision, strabismus, and leukocoria, but it is not a cancer, it is a progressive disease that can cause partial or even complete blindness [104].
It is usually sporadic and unilateral, affecting predominantly males in the first decade of life, and there is no established genetic basis. The mean age for diagnosis is 10 years [105].

Fig. 3.2: Photograph of a children presenting coats' disease [32].

To detect this disease it is only necessary to photograph the face or child's eye, then the algorithm instead of searching a white spot in the eye (like in leukocoria), will seek for a yellow one.

3.2.4 Amblyopia

Amblyopia is commonly referred as "lazy eye" and, as consequence, an unilateral or, more rarely, bilateral reduction in visual acuit appears. Amblyopia is being considered the most common cause of vision loss in children. This eye condition occurs during the critical period of brain development, and its primary causes are strabismus, anisometropia (significant difference in refractive error between the 2 eyes) or

bilateral high refractive errors, and stimulus deprivation.

The Table 3.1 display the major types of amblyopia and its identifying characteristics.

Tab. 3.1: Major Types of Amblyopia and Detection Characteristics [33].

Types of Amblyopia	Characteristics
Commom	
Strabismic	Eye misalignment leads to visual cortex suppression
Anisometropic (refractive)	Difference in refraction (from prescription lenses) between eyes leads to the vision in the eye with a higher prescription being chronically blurred
Combined strabismic and refractive	Eye misalignment with refractive error leads to visual cortex suppression and chronic image blur
Less Common	
Ametropic	Bilateral high, symmetric refractive error leads to chronic image blur in both eyes, and subsequent subnormal visual cortex development
Deprivation (rare)	Obstruction of visual axis leads to visual cortex suppression

Early detection of amblyopia is crucial in obtaining the best response to treatment, because the younger the child, more effective will be the treatment [106].

If amblyopia goes unnoticed or is not treated early in life, often can not be successfully treated and vision can not be fully restored in the amblyopic eye (because amblyopia responses to treatment are best in the first few years of life). The majority of the ophthalmologists consider the age of visual maturity to be about $8-9$ years old, although there are exceptions to the rule. Beyond visual maturity, most cases of amblyopia respond poorly to any form of treatment [107].

Parental cooperation is essential during the treatment to achieve a more effectiveness one, and it is based on occlusion or penalization of the healthy eye, allowing the amblyopic eye to develop a better vision. Maintenance therapy must be performed until the end of the critical period to avoid recidivism [106].

The examination for this kind of pathology, as the others referred in this chapter, go through red reflex testing (Figure 3.3). But also fixation preference of one eye can

signify amblyopia: in infants and children up to two and a half years of age, using a toy or other near fixation target to hold the child's attention, one eye is occluded with an occluder or adhesive patch, and fixation behavior is observed. When the other eye is then occluded, a similar fixation behavior is expected. If a child consistently appears uncooperative when patching one eye, amblyopia is suspected. In children with straight eyes, fixation preference can be determined by using a prism over one eye to induce separate visual images (induced tropia test). In a child with strabismus, fixation preference is often easily determined in the non-deviating eye [33].

Fig. 3.3: Child with asymmetric red reflexes and left exotropia (the patient was found to have retinoblastoma of the left eye) [33].

Four randomized clinical trials were performed to evaluate the effect of age on response to amblyopia treatment and concluded that children seven years and older were less responsive to treatment than children three to six years of age [33], confirming what have been said.

The diagnosis of amblyopia must be confirmed prior to treatment. Confirmation is based on cycloplegic refraction, visual acuity measurement and orthoptic assessment.

3.2.5 Strabismus

Strabismus is an ocular misalignment [108], where one eye is either constantly or intermittently not directed towards the same point as the other eye when the patient attempts to fixate an object. As a result, an image of the fixated object is not formed on the fovea of the strabismic eye.

Depending on the eye direction when it tries to fixate the object, the strabismus has different denominations such as: "esotropia" - convergent (inward, towards the nose) misalignment of one eye; "exotropia" - divergent (outward, away from the middle) misalignment; "hypertropia" - an upward misalignment and finally, "hypotropia", a downward misalignment. It usually develops during childhood but can occur at any age. Most cases begin before 6 years of age, being the peak age of onset around 3 years [109].

The American Academy of Pediatrics and the American Association for Pediatric Ophthalmology and Strabismus recommend vision screening in children three years

and older with an eye-chart based test [33]. The standard exams that are made by ophthalmologist to detect strabismus are: the "Hirschberg test", the "Cross-over" and the "Cover-uncover" test which reveal latent strabismus. The tests are generally performed in that order [110].

The Hirschberg test can be used to determine the type and degree of strabismus using a small penlight and directing it towards the eyes. When the patient is looking at the light, a reflection can be seen on the front surface of the pupil (Figure 3.4). The reflected point of light will reveal the type and degree of strabismus: if the eyes are properly aligned with one another, then the reflection will be in the same spot of each eye. Therefore, if the reflection is not in the same place in each eye, then the eyes are not properly aligned [111].

In general, for every mm that the light is decentered, the eye is turned about 15 diopters (7 degrees from center) [34], in other words, if the reflection of the light is at the margin of the pupil, there is approximately 15° deviation and, if it lies at the edge of the cornea, there is 45° deviation [112].
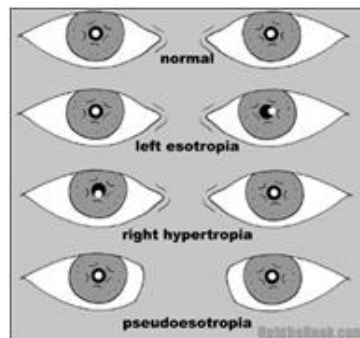
Fig. 3.4: Scheme of the possible results of "Hirschberg Test" [34].

The cover-uncover test (Figure 3.5) can reveal latent strabismus, "heterophoria". To discover the latent deviation a cover (occluder) is placed briefly before the eye that appears to fixate while the patient looks at a small object [35]. If it is present, the eye will normally be kept straight by fusion. If there is movement of the eye when the occluder is removed then there is latent strabismus. The latent deviation will be revealed with either eye covered.

At least, the Cross-over test can reveal latent as well as manifest strabismus. As the name suggests in this test, an occluder is transferred from one eye to the other without interval (Figure 3.6).

The longer the occluder is left over one eye before transferring it without an interval to the other eye, the more disruptive it is to fusion, tending to reveal the full extent
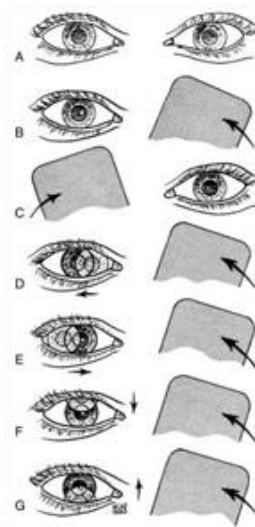
Fig. 3.5: Diagram of the performance of "Cover-uncover test" [35].

of any strabismus [35]. That being said, the idea is to develop features in the application that can be helpful in the diagnosis of strabismus. Such as the other disorders referred before, the application will take a photograph with flash, and then, with an algorithm, evaluate the local of the reflex in the pupil, like in the Hirschberg test.

To simulate the other two tests the application will provide a transfer to video recording. After the tests are done in this mode, an algorithm may read and calculate the deviation of the eye relatively to the center of the image.
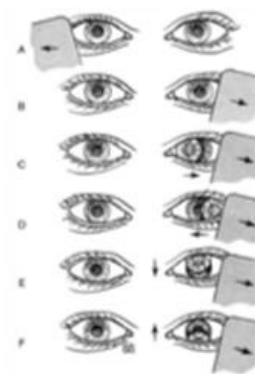
Fig. 3.6: Diagram of the performance of "Cross-over test" [35].

It should be noted that pseudostrabismus can also be noticed in photos (is where it is more obvious), so the photos taken with the application can also help diagnose it, when seen by a specialist.

Pseudostrabismus is a fake appearance of strabismus due to a skin fold a slightly wider in the inner corner of the eyelid, combined with a nasal base more flared, like in the Figure 3.7.

Fig. 3.7: Eyes photo of a children with pseudostrabismus [36].

This leads to the children look like having strabismus, since the space between the iris and the inner corner of the eyelid becomes reduced, with less sclera (white part of the eye) appearing.

This condition does not requires treatment like strabismus, which should be treated as soon as possible, to not affect vision development [36].

3.2.6   Saccades and Nystagmus

The human visual system is characterized by binocular visual fields and a high-resolution fovea that offers considerable advantages for a detailed exploration of visual objects. Two forms of eye movements (saccades and smooth pursuit) enable us to make use of this specialization. Saccades are high-velocity eye movements (up to 1000 deg.s) [113], that are used to redirect the line of sight from one target of interest to another [114], allowing us to bring the image of an object of interest onto the fovea, that are followed by visual fixation [115].

Normally the eye movements are measured in degrees. One example how this can be recorded with a help of an EOG, is described in [114]. The subject has to sit $0,17$ m from the monitor and the "target" option is chosen. Then the target will go with, different degrees, leftward and rightward.

But there are other devices that can measure eye movements, just like the ones that are shown in the Table 3.2 [116].

In this scope, the methodology that interests is video recording, because the application will provide video mode and then send the obtained images to a server. In Table 3.2 the methodology of video image is combined with computer software to calculate the position of the pupil and its centre. This allows vertical and horizontal eye movements to be measured. However, image based methods tend to have

Tab. 3.2: Saccades Measurement Devices.

Methodology of the eye movement recording	Measures	Does not measure
EOG (Electrooculogram)	Horizontal well, vertical poorly	Torsion
IR (Infrared)	Small horizontal very well, vertically poorly	Torsion
Video	Horizontal and vertical moderately well	Torsion only by inspection or by using unusual, non-commercially available equipment
Scleral eye coil	Horizontal and vertical very well	With special measures can measure torsion moderately well

temporal and spatial resolutions lower than that achieved with IR techniques. As technology improves, the resolutions these systems can deliver will also improve.

According to [117] the examiner can test saccades by holding two widely spaced targets in front of the patient (such as the examiner's thumb on one hand and index finger on the other) and asking the patient to look back and forth between the targets. To test saccades in the application the user will have to perform something like described before while video recording is functioning.

Saccadic testing is sometimes useful as cerebellar disorders and degenerative disorders of the central nervous system can sometimes be revealed through saccadic testing. While the clinical examination by an experienced examiner is the more efficient method of making these diagnosis, such expertise is not always available. The idea to make this application available to be used in low income/developing countries is supported by this. The three saccadic parameters most relevant to clinicians are peak velocity, latency, and accuracy [118].

There are three types of disorders of saccadic velocity: saccades may be too slow, too fast, or have substantially different velocities in one eye or direction than the other. When saccadic slowing is observed, drug ingestion should be the first consideration. Others causes can be: drowsiness or fatigue (common), basal ganglia syndromes, cerebellar syndromes, peripheral oculomotor weakness (cranial nerve palsies, myopathy), white matter diseases or miscellaneous disorders.

Patients with strabismus may alternate the eye that they view from, depending on the direction of gaze, and allow one eye to drift out away from the target. In these instances, measured saccadic velocities are wrong, because the calibration is

inappropriate. Monocular recording and single eye viewing are essential to avoid error in these patients. In patients without problems of ocular alignment, evidence that the calibration is stable over several trials must be available before diagnosing abnormalities of saccades.

Nystagmus is an involuntary rhythmic oscillation of the eyes, leading to a reduced visual acuity due to the excessive motion of images on the retina. It can be divided into: infantile nystagmus (IN) (which usually appears in the first $3-6$ months of life) and acquired nystagmus (AN) (which appears later) [119].
Typical symptoms of nystagmus are: reduction of visual acuity (and amblyopia in IN), abnormal head posture and oscillopsia (often connected with vertigo and disorders of gait and orientation). Treatment strategies include pharmacological treatment, surgical therapy and optical devices. Choice of treatment depends on the type of nystagmus and its characteristics [120].

Table 3.3 summarizes some of the pathologies approached before and a brief explanation of the proposed processes involved in its detection.
For amblyopia and nystagmus some of the procedures would be similar.
The feature of video mode in a smartphone, to detect with the necessary kind of detail for this pathologies, does not have the required temporal resolution. For this and with the advice of specialists (the collaboration of the children during strabismus tests is low, even worse at home), we drop the idea to develop this feature. We left available the video recording, for future work, but without instructions for the user.

3.3   Summary

In order to develop the mobile application that we propose in this master thesis it was necessary, at an early stage, consider the eye diseases able to be detected using a smartphone and which are the suitable procedures.
The RRT is a crucial ophthalmology exam to detect various eye diseases like retinoblastoma, Coats', amblyopia and strabismus (also being detected through the Hirschberg test), diseases with high incidence in childhood with a very important early detection, reducing the possibilities of an irreversible development.
Through the reflection of the phone flash in the pupil of the subject was thought to reproduce this important test trying, this way, to reduce the number of cases

Tab. 3.3: Some eye pathologies and its technological detection proposal.

Leukocoria	Coats' Disease	Strabismus *Hirschberg Test*	Strabismus *Cover-Uncover Test*	Strabismus *Cross-Over Test*	Saccades
1. Photo	1. Photo	1. Photo	1. Video Mode	1. Video Mode	1. Video Mode
2. Face Detection Algorithm	2. Face Detection Algorithm	2. Face Detection Algorithm	2. Face Detection Algorithm	2. Face Detection Algorithm	2. Face Detection Algorithm
3. Eye Detection Algorithm	3. Eye Detection Algorithm	3. Eye Detection Algorithm	3. Eye Detection Algorithm	3. Eye Detection Algorithm	3. Eye Detection Algorithm
4. Pupil Detection Algorithm	4. Pupil Detection Algorithm	4. Pupil Detection Algorithm + Localization	4. "Cover" Placement	4. "Cover" Placement	4. Pupil Detection Algorithm + Localization
5. Server	5. Server	5. "White/Red Spot (flash)" Detection Algorithm + Localization	5. Repeat "Cover" 3 times	5. Repeat "Cross" 3 times	5. Server
6. White Spot Detection Algorithm	6. White/Yellowish Spot Detection Algorithm	6. Server	6. Server	6. Server	6. Difference calculation between eye center and deviations
7. Counseling Report	7. Counseling Report	7. Difference calculation between 2 locations	7. Difference calculation between eye center and deviation	7. Difference calculation between eye center and deviation	7. Counseling Report
		8. Counseling Report	8. Counseling Report	8. Counseling Report	

detected late since parents would be able to monitor the eye health of their children through photos taken with their smartphone.

As strabismus can be detected through other two tests ("Cross-over" and "Cover-uncover"), we also study the possibility of video, since it is not possible to be performed statically. Opening this new possibility, we also studied other diseases capable of being detected with this feature: saccades and nystagmus.

Chapter 4

Software Engineering

In this chapter the user stories, including the use cases and the protocol designed for the development of the mobile application are presented.

4.1 User Stories

The first task when designing a software is to envision how it is going to work, the requirements and needs of the software. So, initially, and to understand it, the user story was written.

It was established that the user of the mobile application is going to be a non medical person who wants to collect data and receive a report on the eye health status. Other situation that may occur is a doctor using the application when proper medical equipment for screening is not available, for example, in developing or low income countries. The procedures for both situations are the same, the only difference that may occur is the user, if he is a specialist in ophthalmology, he/she may make himself an evaluation, during the collection or after. This way the process from evaluation to medical appointment may be faster (the application does not replace an evaluation from a specialist). Thus, the moment of the evaluation may be the only difference between the two users, because the functionality of the application will be the same for both cases.

The user story starts with the non medical user, downloading the application for his smartphone from the android applications site, to check the visual health of someone. When opening the application the user will have to register someone to start using it. Clicking on "New" in the dropbox he will be forwarded to a new window where can write the name and the age of the child who wants to screen and

upload a photo for ID. After he saves it, the application returns to the initial menu and the button "Collect" will be now available (the other two buttons not yet), to initiate the collection with the respective person/child registered. After the first data collection made, the user may have access to the remaining buttons.

For the option "*Collect*" some instructions to this feature will pop-up to guide the user through data collection. After reading it he/she can start collecting. Five photos will be taken automatically, reaching to the next phase of the screening procedure: video recording. Instructions will appear on the screen indicating the procedures to collect, like step away or get closer to the subject, repeat 3 times for each eye or stay two seconds in each one, accomplishing in this way, the required procedure. After stopping it, the user is prompted to choose between sending the collection now or later to the server. If he chooses now, this data will be sent to a server by wifi or using a USB cable. Choosing to send it later, he returns to the start menu and can make this later in the "Records" feature.

For the option "*Alert*" he will have indications to set an alarm of thirty days between collections. After this, the calendar of his phone will appear, where he can see other events that have been scheduled. Clicking on the day that he wants, and setting the time, the alarm will be set. Then, in the set day he will receive a notification to remind him of the collection. Nonetheless the application is available for data collection whenever the user decides to use it, regardless of the alarm set.

Finally, when the user clicks on the button "*Records*" (History), the application will redirect him to the gallery where he can see the different folders of previous data collection sessions. The user will be able to delete or see the properties of something or send it to the server, if it has not been done before or if he wants to repeat it, receiving a new counseling.

4.2   Use Cases

After the user stories were written, the next step was to make a use case model, which consists of use case diagram and its description [121]. The use case diagram, in Figure 4.1, was made using UML (Unified Modeling Language) in Microsoft Visio 2010.

In this case, the system is the mobile application, and the actors are: non medical user, android, child and server (each one with a use case). To complete the use case model, its documentation has to be described: the description of the main flow of the use case, alternative flow, pre and postconditions, such as other aspects. Below,
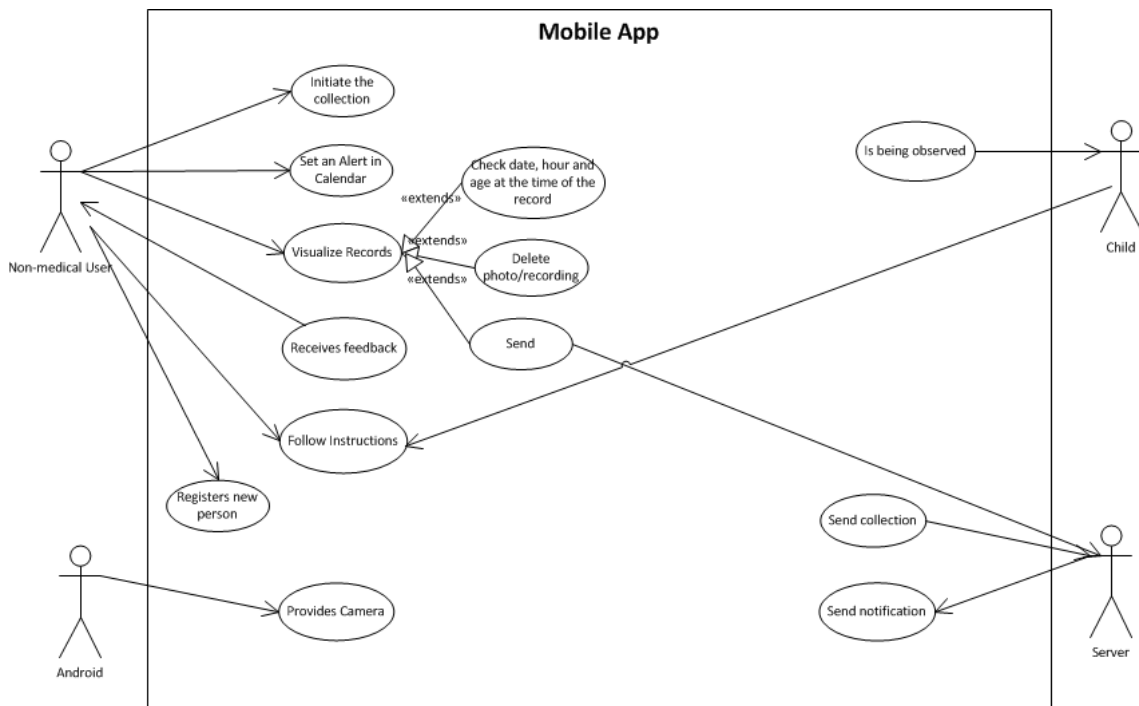
Fig. 4.1: General Use Case Diagram.

each use case and its corresponding description are presented.

The first use case portrayed, "Register new person" is presented in Table 4.1. There is only one alternative flow because only two options are available to the user: making a new login for someone or beginning the collection with an existent registered person. In the first option, the remaining buttons will be disabled, only "Collect" will be available after the login. Following collection, the user can access the other buttons ("Records" and "Alert").

The second one is "Initiate the Collection". In Table 4.2 all the descriptions about this use case are presented.

There are no exceptions or includes in this use case. Only the normal flow is referred, not existing an alternative one. There are two secondary actors, the child and the android, given that the child is the one who is going to be traced in the collection, and android provides the camera for the purpose, as it is depicted in the case described below.

The next use case is "Set an Alert in Calendar". Such as in the previous use case, there is no alternative flow, exceptions or includes (Table 4.3). The primary actor is the non medical user again.

The following use case, in Table 4.4, is "Visualize Records", an use case with

Tab. 4.1: Description table of the Use Case "Register New Person".

1st Use Case	
Use Case Identification	C1
Use Case Name	Registration of a new person
Primary Actors	Non medical user
Secondary Actors	None
Functionalities	This Use Case enables the user to register a new person or login with an existent one
Pre-Conditions	The user has to download the application
Postconditions	A new person is registered in the application
Trigger	The user clicks to register a new person (login)
Normal Flow	1. The user enters in the application and choose to register a new person in "New". 2. The user is forwarded to a window where he can register: name and age of the person, and a correspondent photo. 3. He saves this information. 4. Finally, he returns to the initial window, where he can begin the collection (the other options are not yet available).
Alternative Flow	1a. In step 1 of the normal flow, if the user already has a login: 1. The name registered before will appear. 2. The photo correspondent to the name will pop-up below the name. 3. All the buttons will be available.
Exceptions	—
Includes	—

Tab. 4.2: Table with the description of "Data Collection" Use Case.

2nd Use Case	
Use Case Identification	C2
Use Case Name	Data Collection
Primary Actors	Non medical user
Secondary Actors	Child and Android
Functionalities	This Use Case describes the process by which the non medical user makes the collection
Pre-Conditions	1. The user has to download the application 2. The registration of the child has to be made
Postconditions	The collection is stored on the memory card of the user mobile phone
Trigger	The users enters in the feature "Collect"
Normal Flow	1. The user enters in the application and chooses the option "Collect". 2. A serie of instructions are presented. 3. The user reads the instructions and clicks to start the collection. 4. The camera opens and the user initiates the collection.
Alternative Flow	—
Exceptions	—
Includes	—

Tab. 4.3: Detailed description of the Use Case "Setting an alert".

3rd Use Case	
Use Case Identification	C3
Use Case Name	Setting an alert
Primary Actors	Non medical user
Secondary Actors	Android
Functionalities	This Use Case allows the user to set an alarm in his calendar to remember to make a new collection
Pre-Conditions	1. The user has to download the application 2. One previous collection has to be made
Postconditions	The calendar has one (or more) alarm(s)
Trigger	The user enters in the feature "Alert"
Main Flow	1. The user enters in the application and chooses the option "Alert". 2. A series of instructions are presented. 3. The user reads the instructions and clicks to continue to calendar. 4. The calendar of his phone opens and he chooses a day. 5. Then he sets the time of the alarm.
Alternative Flow	—
Exceptions	—
Includes	—

alternative flows besides the normal one.

This use case has alternative flows because of the "extends" in the use case diagram. As such, the user can choose between 3 options: delete, send and properties, which are described more detailed in the anterior Table. But there are no exceptions or includes in this U.C.

The use case "Receives Feedback" has its description in Table 4.5.

There are no alternative flow, neither exceptions, but there are two includes in this use case. The first include (U.C "Initiation of the Collection") is basically the collection made by the user, because there cannot be a feedback of something that was not performed. So, the feedback is dependent on the collection, and also from sending it to the server, the other include of this use case.

The subsequent use case is "Follow Instructions". This use case has two actors: the child and the non medical user. Both follows the instructions from the mobile application to perform the collection in the best way.

In the Table 4.6 there is one include: the use case "Initiation of the Collection". Such as in Table 4.5 there is no alternative flow or exceptions.

"Provides Camera" it is the name of the next use case in Table 4.7 which illustrates the description of this use case, which does not have any alternative flow, exceptions or includes. The primary actor is android, it is the one who has the capability to provide the camera in the phone, and the secondary actor is the non medical user, the person who needs the camera to start the collection.

The following use case is "Send Collection", presented in Table 4.8.

Like in the Table 4.6, Table 4.8 has the use case "Initiation of the Collection" as an include, but there is no alternative flow or exceptions. The primary actor is, once again, the non medical user, and in this U.C. the server is the secondary one. He receives the collection from the user to analysis and then sends a notification (use case that will be detailed ahead). The penultimate use case is "Send Notification". Table 4.9 represents the description of this use case from the server.

Although the server is the primary actor in this use case, the non medical user is the secondary one, because he is the one who receives the notification and decides, depending on the advise, what to do next. This use case is related to the "receives feedback" described previously: the user receives feedback about the collection when the server sends a notification to the application.

The last use case presented has the name "Observation of the child" and the actor involved is only the child, which is observed during the collection, because he/she is the person who the user wants to receive a notification about the eye health. The

Tab. 4.4: Portrait of the Use Case "Visualizing records".

4th Use Case	
Use Case Identification	C4
Use Case Name	Visualizing records
Primary Actors	Non medical user
Secondary Actors	Android
Functionalities	This Use Case enables the user to enter in gallery to see the records: the photos and the videos recorded, as well as the age of the person/child when they were collected
Pre-Conditions	1. The user has to download the application 2. At least one previous collection has to be made
Postconditions	1. The user comes back to the application main menu 2. OR photo(s)/video(s) were deleted from the gallery 3. OR some photo(s)/video(s) were sent to the server
Trigger	The user enters in the feature "Records"
Normal Flow	1. The user enters in the application and choose the option "Records". 2. The folders corresponding to each collection are presented. 3. The user selects the folder which he/she wants to open. 4. In the chosen folder, the user can see the photos collected and the video recorded. 5. The user can delete, send ou see the properties of each record.
Alternative Flow	5a. In step 5 of the normal flow, if the user selects to delete something: 1. The user chooses the item or items he wants to delete 2. The application asks the user if he is sure he wants to delete the item 3. If he is sure, the item is deleted and he comes back to the items in the folder 4. If he is not: application returns to folder, and no item is deleted 5b. In step 5 of the normal flow, if the user selects the option "Send": 1. The user chooses the item or items he wants to send to the server 2. The user clicks on "send" 5c. In step 5 of the normal flow, if the user selects to see the properties of a photo: 1. The user chooses the item which he/she wants to see 2. The date and hour of the item are shown, as well as the age in months of the child/person when the photo was taken
Exceptions	—
Includes	—

Tab. 4.5: Overview of the Use Case "Receiving feedback".

5th Use Case	
Use Case Identification	C5
Use Case Name	Receiving feedback
Primary Actors	Non medical user
Secondary Actors	Server
Functionalities	This Use Case allows the user to receive feedback about the collection made
Pre-Conditions	1. The user has to download the application 2. At least one previous collection has to be made
Postconditions	1. The user is advised to go to a ophthalmologist 2. The user is advised to repeat the collection within a month
Trigger	The application receives one notification from the server
Main Flow	1. <<Include>> Use Case "Initiation of the Collection". 2. The server sends a notification to the user. 3. The user receives the notification with the feedback of the collection.
Alternative Flow	—
Exceptions	—
Includes	U.C "Initiation of the Collection" and U.C. "View Gallery: <<extends>> send.

Tab. 4.6: Description Table of the Use Case "Following instructions".

6th Use Case	
Use Case Identification	C6
Use Case Name	Following instructions
Primary Actors	Non medical user and child
Secondary Actors	None
Functionalities	This Use Case describes how the actors follow the instructions provided by the application
Pre-Conditions	1. The user has to download the application 2. The user has to start the collection
Postconditions	1. The collection is made 2. The collection is stored on the memory card of the user mobile phone
Trigger	The user enters in the feature "Collect" and starts the collection
Main Flow	1. <<Include>> Use Case "Initiation of the Collection". 2. The user and the child follow the instructions on the screen to do the collection correctly.
Alternative Flow	—
Exceptions	—
Includes	U.C. "Initiation of the Collection"

Tab. 4.7: Depiction of the Use Case "Providing Camera".

7th Use Case	
Use Case Identification	C7
Use Case Name	Providing camera
Primary Actors	Android
Secondary Actors	Non medical user
Functionalities	This Use Case shows how the android provides the camera for the collection
Pre-Conditions	1. The user has to download the application 2. The user has to start the collection
Postconditions	1. The collection is made 2. The collection is stored on the memory card of the user mobile phone
Trigger	The user enters in the feature "Collect"
Main Flow	1. The user clicks to start the collection 2. The Android provides the camera and opens it
Alternative Flow	—
Exceptions	—
Includes	—

Tab. 4.8: Table representative of the Use Case "Sending Collection".

8th Use Case	
Use Case Identification	C8
Use Case Name	Sending collection
Primary Actors	Non medical user
Secondary Actors	Server
Functionalities	This Use Case describes the process by which the non medical user send the collection that his had been made, to the server
Pre-Conditions	1. The user has to download the application 2. At least one previous collection had to be made
Postconditions	Receiving a counseling report
Trigger	The user opts for sending the collection made, to the server
Main Flow	1. <<Include>> Use Case "Initiation of the Collection". 2. After the collection is done the user sends it to the server.
Alternative Flow	—
Exceptions	—
Includes	U.C. "Initiation of the Collection"

Tab. 4.9: Representation of the Use Case "Send Notification".

9th Use Case	
Use Case Identification	C9
Use Case Name	Sending notification
Primary Actors	Server
Secondary Actors	Non medical user
Functionalities	This Use Case shows how the server sends the notification to the non medical user
Pre-Conditions	1. The user has to download the application 2. At least one previous collection has to be made and sent to server
Postconditions	The user sees the notification
Trigger	The algorithms finish running on the server
Main Flow	1. The server sends a notification to the user 2. The user receives it in the application
Alternative Flow	—
Exceptions	—
Includes	—

Tab. 4.10: Table describing the Use Case "Observation of the child".

10th Use Case	
Use Case Identification	C10
Use Case Name	Observation of the child
Primary Actors	Child
Secondary Actors	None
Functionalities	This Use Case represents the observation of the child who is being traced
Pre-Conditions	1. The user has to download the application 2. The user has to initiate the collection
Postconditions	The collection is made
Trigger	The users enters in the feature "Collect" and starts the collection
Main Flow	1. <<Include>> Use Case "Initiation of the Collection" 2. The child is observed during the collection
Alternative Flow	—
Exceptions	—
Includes	U.C. "Initiation of the Collection"

final Table 4.10 describing this use case has one include, the use case "Initiation of the Collection". Once again, if there is no collection from the user, the other use cases will be useless.

4.3   Protocol for Data Collection

After reviewing the most common pathologies and the clinical tests, determining which clinical signs may be detected using technology available in a smartphone, a protocol for data collection needs to be defined within the application. The protocol is a guideline which encompass all the steps that are made by the user, when handling the mobile application for data collection.

Procedures:

If the person who is going to be traced is a child, the best approach is to ask another person to help you by playing with your child while you take the photos so

her eyes do not follow the camera and he/she can replicate what is necessary.

- **STAGE 1/4:**

  Ocular Spot (Leukocoria, Coats' disease and Amblyopia) Hirschberg test (Strabismus)

  1. Create a soft light environment: turning the lights down (Figure 4.2) and ensuring that any light sources - such as table lamps or television - are behind the person (so they don not reflect in the eyes).
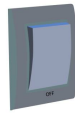

Fig. 4.2: Illustration allusive to a switch turned off.

  2. Position yourself about 3 meters (more or less 4 steps) from the child/person (Figure 4.3) and use the zoom to capture the subject's entire head.
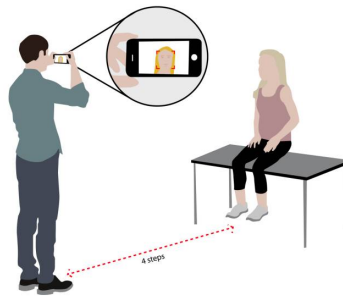

Fig. 4.3: Sketch illustrating the positioning of the person.

  3. Press the button when ready to initiate the collection.
  4. The head, eyes and pupil will be detected on the screen.
  5. When all is properly aligned the first of 5 photos will be taken automatically.
  6. Follow the arrows to incline your phone to where they indicate: 1st upwards (Figure 4.4).
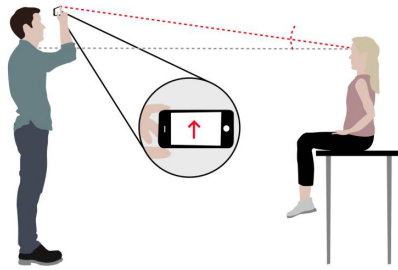
Fig. 4.4: Drawing exemplifying the indications on the phone.

7. Repeat step 6 to down, left and right.

- **STAGE 2/4:** "Cover-uncover" (Unilateral cover) test

    1. A message to come 2 steps closer appears (Figure 4.5).
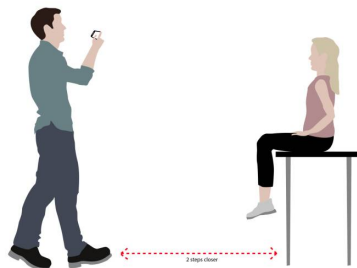
Fig. 4.5: Representative sketch of the person coming closer.

2. Make sure that in next steps the look of the child is directed to the camera.

3. When ready, press the button to initiate the second part of the collection: the recording will start.

4. Detection of face, eyes and pupil happens.

5. A hand on the screen appears with a message to click it (Figure 4.6).

6. Advise the person who is been traced to cover the same eye as the hand on the screen.

Fig. 4.6: Mobile indications to perform the test.

7. Click on the hand. The hand will appear again on the other eye.

8. Repeat steps 6 and 7 for 2 times.

- **STAGE 3/4:** "Cross-over" (Alternating cover) test

  1. Warning to start a new step: an animated hand will rapidly alternate between the 2 eyes to exemplify.

  2. Press the button when ready to start this stage.

  3. Another virtual hand appears on the screen with a clock on the right side (to count 2 seconds).

  4. Follow the movement of the hand, advising the person to repeat it.

  5. Pay attention to the clock: maintain the hand for 2 seconds in each eye (Figure 4.7).
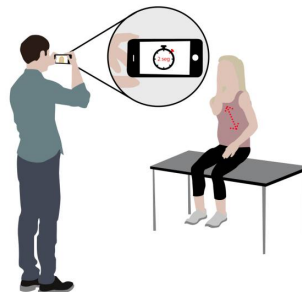

Fig. 4.7: Illustration of the clock appearing on the screen of the mobile phone.

6. Repeat the movement 3 times for each eye.

- **STAGE 4/4:** Saccades/Nystagmus test

    1. One message appears: "Stage 4/4".

    2. Position your arm with thumb up in front of the camera (without covering it), as the virtual one appearing on the screen.

    3. Advise the person to follow the movement of your hand with their eyes (not moving his/her head).

    4. Follow the arrows in the screen to move your arm, always with the thumb up, slowly to right (Figure 4.8).
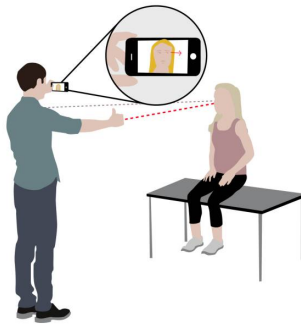
Fig. 4.8: Ilustrative draw of the person following the directions.

    5. Come back to the center of the image.

    6. Repeat steps 4 and 5 to left, up and down.

    7. Press stop button when collection finishes.

    8. A menu will show up asking to send the collection now or later.

        (a) Now: link your mobile phone to your computer by wifi.

        (b) Later: When you want, enter in "Records" - select the folder with the collection you want to send to analysis.

Subsequently a tutorial video was recorded to reproduce the anterior steps. So, the drawings presented before in different steps of the protocol are relative to it, to a better exemplification of how the protocol is followed.

4.4 Programming Technologies

Android is a mobile platform that allows the users to create mobile applications (such other features, like games) free of any charge. A platform is available with several features named "Android Developer Tools" where a Java IDE is accessible to create and debug Android applications in any device or creating a virtual one with the help of the emulator [122].

Smartphones are starting to be the latest technology tendency of the 21st century, as consequence, the number of Android applications has increased drastically in recent years [123], making Google's Android Operating System (OS) one of the leaders of the smartphone evolution [124].

Because of this and reinforcing the idea that medical applications for smartphones are growing exponentially and its used is increasing in healthcare [125], I develop the mobile application "EyePic" in android using Java, an object-oriented programming language (OOPL) [126], in the eclipse IDE plugin, Android Developer Tools (ADT), which provides, among other features, the capability to create an application UI, add packages based on the Android Framework API and debug the application using the Android SDK tools [127].

4.5 Mockups

Following the protocol portrayed in Section 4.3 we developed the mockups, designed in Balsamiq, an open-source interface with different tools designed for a simple use of sketching [128].

The first mockup, presented in Figure 4.9 represents the obligatory notification given the fact that this application does not replace a specialist appointment.

After agreeing the user can see the main menu like the one in the Figure 4.10. In the first use of the application, to have the privilege to access to all the available functions the user has to click on "New" in the dropbox, being directed to a login page to fill out the fields of Name and Date of Birth (of the children who he wants to trace), and as optional, download a photograph of him/her (Figure 4.11). By inserting the name, when returning to the menu of the application, the name will appear on the dropbox, saving this way the collection associated to this name. Thus, after the first collection, by accessing to the "Records" option, the user can see the folder belong to each name of the child and in "Properties" the age (at the moment of the collection) of him/her.

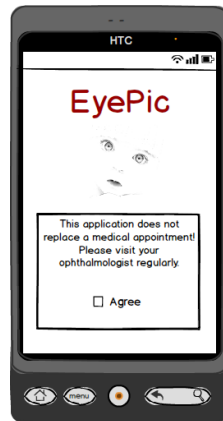**Fig. 4.9:** Design mockup of the first screen of the application: the notification for the user.

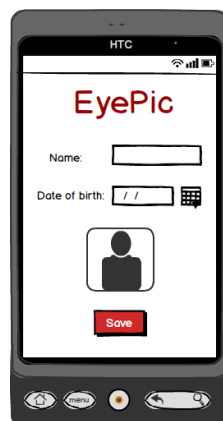**Fig. 4.10:** Main menu of the mobile application.

Fig. 4.11: Mockup of the login screen and its fields.

Clicking on "Save" he is directed to the main menu again, but with the difference that now he can start collecting, being this the only option available for now (Fig-

ure 4.12). Notice that if the download of the photograph was made in the previous step, it will appear here.
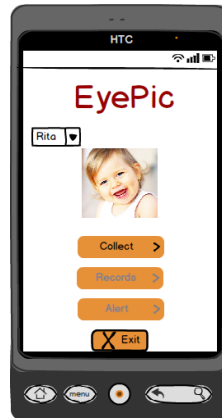
Fig. 4.12: Layout of the main menu after login.

Before starting the collection, the instructions to perform it in good conditions, are presented as exhibited in Figure 4.13. The instructions "Create a soft light environment", "Move away 4 steps from the subject" and "Use the zoom to capture the entire head" were defined based on the protocol for data collection. The light in the room is crucial for the contrast required in the eyes, to evaluate the incidence of the flash without any interference from other sources of light. The distance is important to not blind the subject with the intensity of the flash and to not close his eyes when it happens. By consequence, if necessary, the user can use the zoom to capture the entire head.

Fig. 4.13: Drawing of the instructions presented before/during collection.

Subsequently the camera opens and the algorithms to frame the pupil, eyes and face, act (Figure 4.14) ensuring that the photos will be taken in the best conditions.

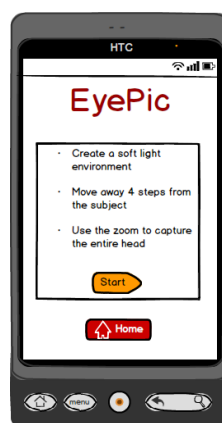The user has to turn the smartphone during the collection in order to make a more comfortable collection.
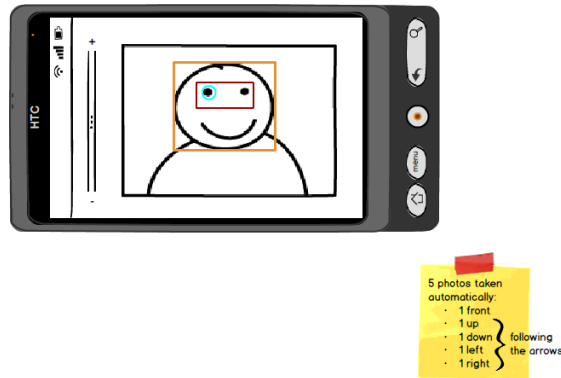
Fig. 4.14: Mockup of the camera with face, eye and pupil algorithmic detection.

After that, the first photo will be taken automatically as explained before in Section 4.1. Arrows will appear on the screen, indicating for each photo (left, right, up and down) where the user have to incline the phone (Figure 4.15).
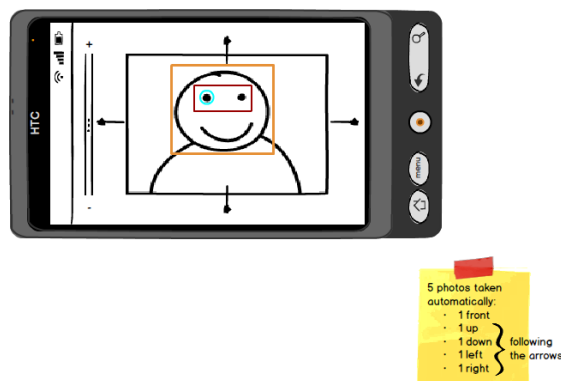
Fig. 4.15: Sketch mockup of the indication to angular movement.

Taken the five photos in four different angles, needed for ocular spot, amblyopia evaluation and Hirschberg test, the user as to come closer two steps from the subject, clicking in "Ready" to initiate the transition to video recording (necessary to other kinds of eye health evaluation), appearing again the algorithms for pupil, eye and face detection (Figure 4.16 and 4.17).

To reproduce the "Cover-uncover (Unilateral cover) test" instructions are required. An animated hand will appear on the right eye with a message to click it, simultaneously will pop-up another message in the top of the screen (Figure 4.18), advertising the user to request the subject to place the hand in front of the eye.

Fig. 4.16: Mockup with a instruction message before video recording.
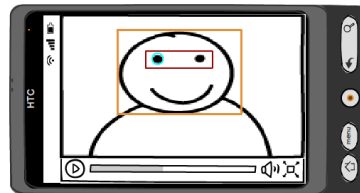
Fig. 4.17: Design of the first video recording screen.
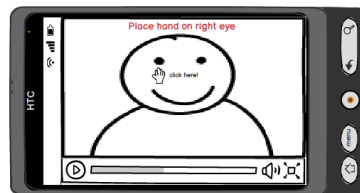
Fig. 4.18: Mockup picture with "Cover-uncover test" instructions.

After the subject place place the hand in the right eye and the user clicks on the animated hand, another one will show up in the left eye (Figure 4.19) again with a pop-up message. This action will happen two more times reproducing this way the test.

Fig. 4.19: Continuation of the "Cover-uncover test".

For the "Cross-over" (Alternating cover) test, a message emerges again on the top, but this time the animated hands alternate with each other (between the two eyes) exemplifying in this mode the test. A button "Ready" is on the bottom of the screen (Figure 4.20) so the user can click it after reading the instructions.

Afterwards the final collection begins with a clock on the right corner of the screen, counting two seconds (Figure 4.21 (a)). At the same time one hand will
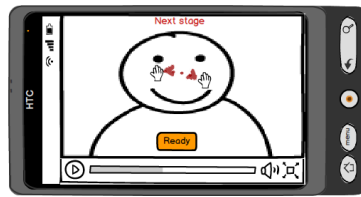
Fig. 4.20: Mockup with instructions to "Cross-over test".

be on one eye (starting in the right eye of the subject) to reproduce the action, alternating quickly three times (Figure 4.21 (b)).

(a)   (b)
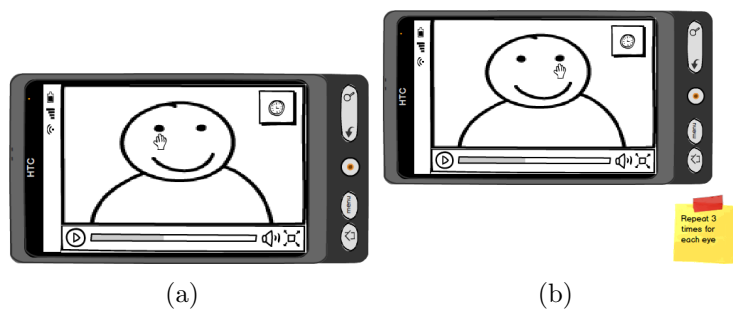
Fig. 4.21: "Cross-over test" recording: (a) Design of the first screen; (b) Continuation of the test.

The last test available is for saccades and nystagmus detection, showing up another text message: "Stage 4/4". This time the animated hand just has the thumb up and the user as to reproduce it, moving his arm in the direction of the arrow, like in the Figure 4.22 (a). The tracing subject/children only has to follow the arm with the view, without moving the head.

The arrow returns to the center of the image and then the user as to move it to the left. Also repeating to up and down (Figure 4.22 (b)). A "Stop" button appears after 20 seconds.

(a)   (b)
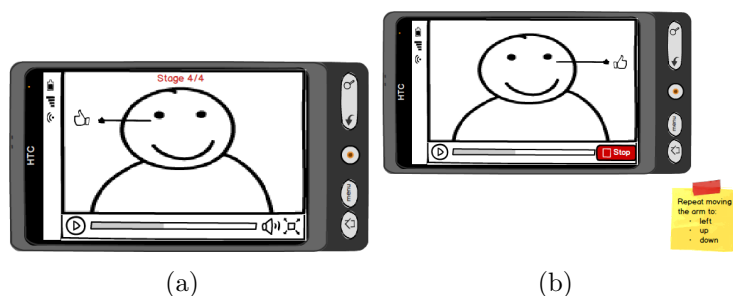
Fig. 4.22: Mockups of the final test: saccades/nystagmus: (a) Instructional mockup of the test; (b) Continuation of the test.

The collection has finished and the user can choose to load it to the server in that exact moment or later, such as in the Figure 4.23. If he clicks on "No", will be returned to the main menu (can send it later entering in "Records" and selecting the folder with the collection), but if he clicks "Yes" he has to link the mobile phone to one computer with wifi connection. In case of failed connection, has to try again (Figure 4.24 (a)), and in case of success (Figure 4.24 (b)), he just has to wait for the analysis, receiving a final report (Figure 4.25).
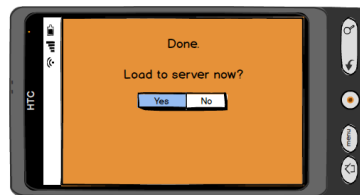
Fig. 4.23: Exemplifying mockup of the menu after the collection.
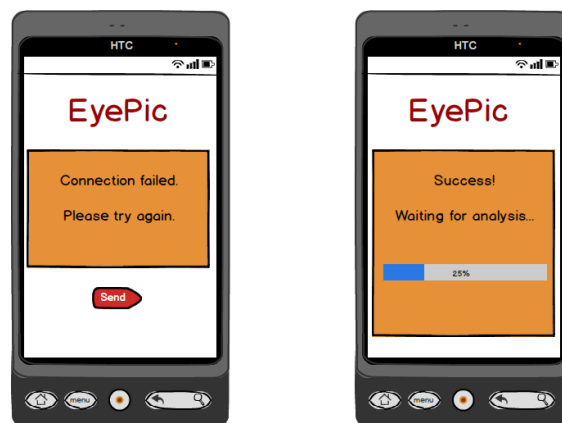
Fig. 4.24: Connection to the computer: (a) Failed attempt; (b) Successful attempt, waiting for analysis.

After the collection all the buttons will be available in the main menu like in the Figure 4.26 (a), because now the user has at least one collection that he can access, and a "follow-up" that can be achieved. If the user wants to schedule/create an alert to perform another collection can click on "Alert" button, seeing an advice before entering in the calendar (Figure 4.26 (b)). The advice is to schedule the next collection within 30 days because the follow-up/accompaniment to verify any ocular problem should be done in this period in case of any alteration. By clicking on "Continue" the user enters in his mobile calendar ((Figure 4.26 (c)), this way he can see his commitments and schedule according to that (Figure 4.26 (d).

Finally, another available button is "Records" that functions as the historical

Fig. 4.25: Illustrative mockup of the report.
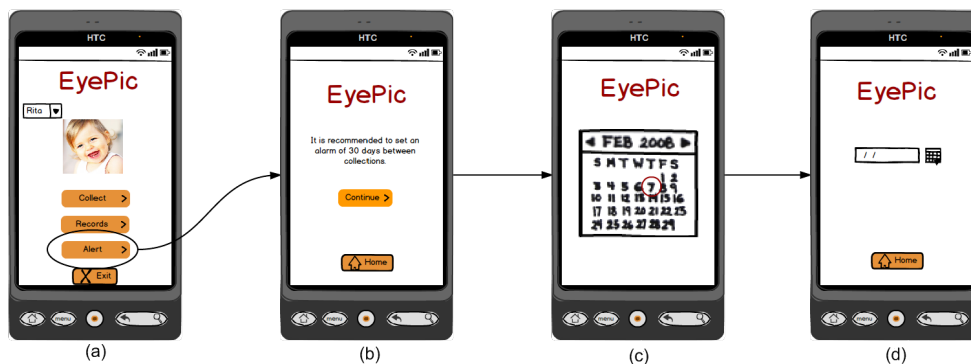
Fig. 4.26: Main menu after collection: (a) Mockup of the main menu after collection; (b) Instructions to alert; (c) Illustrative calendar; (d) and exemplifying scheduling.

data collection. This button directs to the gallery space in SD Card of the mobile phone (Figure 4.27 (a)), where the collection is stored. The user can select the folder that he wants (they are organized by name of login) and, in each one, see the photographs taken (Figure 4.27 (b)). Selecting one of them he can see its properties, delete it, send it to the server or come back to the folder (Figure 4.27 (c)). If he chooses "Properties", the information will look like the one in the Figure 4.27 (e), with the name of the photo which represents date and hour that collection occurred and with the calculation of the subject age when the photo was taken (by the date of birth set at login time).

Choosing to delete something, another screen will appear asking if the user is sure he wants to delete that photo (Figure 4.27 (d)), because it can be important to show to the ophthalmologist all the collection, to obtain a specialized evaluation as

notified in the beginning.
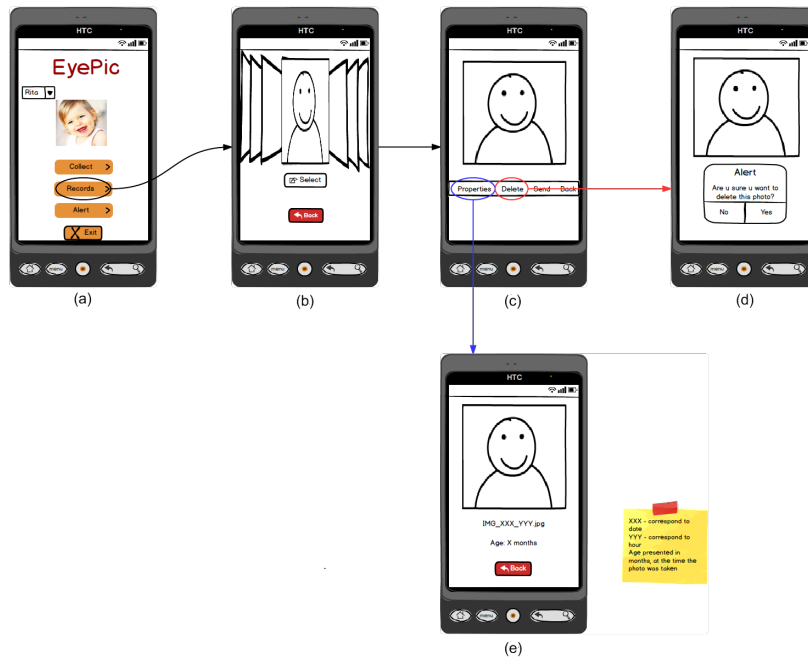
Fig. 4.27: Mockup of the "Records" feature: (a) Main menu after collection; (b) Phone gallery with the folders correspondents to the collections; (c) Selection of a photograph; (d) Mockup of the deleting action; (e) Properties of a photograph.

The following diagram in the Figure 4.28 summarizes the general functioning/flow of the mobile application.

4.6 Development

The following subsections explain some steps taken to the development of the mobile application "EyePic" (Figure 4.29) and early tests.

4.6.1 Building camera and its features

We want to control the camera of the mobile phone so it can be customized for our purpose. In that way we start with the right permissions in the XML Manifest file: for handling the camera device, for the use of camera features and the permission for external storage, saving the data collection in SD card (explanation in the next
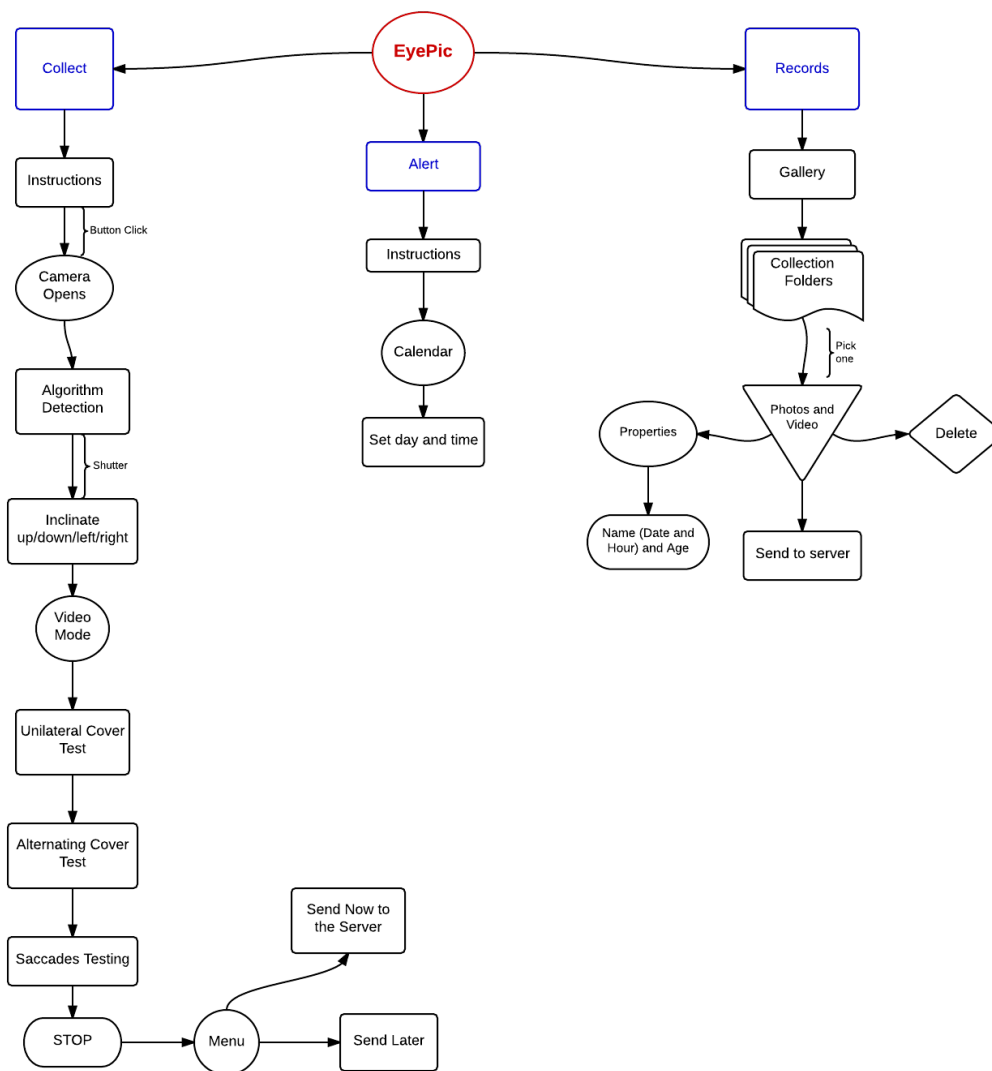
Fig. 4.28: General functioning and features of the mobile application.

subsection). Because we need to personalize our camera we can not use Camera Intent for taking a photograph, so we created an activity checking first the existence of cameras devices, and if that is true request its access. Then we need to create a camera preview class that extends *SurfaceView* (excerpt of code is described next) and implements the *SurfaceHolder* interface; this is necessary because we must be able to see what the device camera sees, the live images.
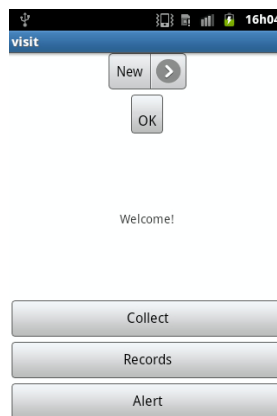
Fig. 4.29: Initial menu of the developed mobile application "EyePic".

```java
public void surfaceCreated(SurfaceHolder holder) {
    try {
        mCamera.setPreviewDisplay(holder);
        mCamera.startPreview();
    } catch (IOException e) {
        Log.d(TAG, "Error setting camera preview: " + e.getMessage());
    }
}
```

We also implemented *surfaceDestroyed* and *surfaceChanged*. The latter is where we get an instance of camera's parameters object (holder - the SurfaceHolder whose surface has changed; format - the new pixel format of the surface; width and height - new width and height of the surface) important to check the availability of camera features and with them use different methods to obtain the final outcome. For example, for the user be able to rotate the camera as he wish, we execute the following code:

```java
public void surfaceChanged(SurfaceHolder holder, int format, int w, int h) {
(.....)
        Parameters parameters = mCamera.getParameters();
Display display = ((WindowManager)
getContext().getSystemService(Context.WINDOW_SERVICE)).getDefaultDisplay();

        if(display.getRotation() == Surface.ROTATION_0)
        {
            parameters.setPreviewSize(h, w);
```

```
        mCamera.setDisplayOrientation(90); }
    if(display.getRotation() == Surface.ROTATION_90)
    {
        parameters.setPreviewSize(w, h); }
    if(display.getRotation() == Surface.ROTATION_180)
    {
        parameters.setPreviewSize(h, w); }
    if(display.getRotation() == Surface.ROTATION_270)
    {
        parameters.setPreviewSize(w, h);
        mCamera.setDisplayOrientation(180); }
    // start preview with new settings:
    try {
        mCamera.setParameters(parameters);
        mCamera.setPreviewDisplay(mHolder);
        mCamera.startPreview();
    } catch (Exception e){
        Log.d(TAG, "Error starting camera preview: " + e.getMessage()); }
  }
```

We must not forget to release the camera after using it to be available for other applications. We need to turn on the flash to be able to verify the red reflex in the photographs. Using the *Parameters parameters = mCamera.getParameters();* method aforesaid we can use the class *setFlashMode* with the value "FLASH_MODE_ON".

Another feature we start implementing in the mobile application was video recording. We built another button, with the same characteristics as the "Capture" button, in the layout, but allowing the user to start recording when clicking on it. We already have the preview, so when the user clicks on "Video" button the intent will be to initiate the *class MediaRecorder recorder = new MediaRecorder();*. Then we have to configure different methods, such as *recorder.setVideoSource(...);*, prepare and start the "MediaRecorder". Like in "Image Preview", we have to stop the camera, release it and save the file.

4.6.2   Interface for the user

After the preview class we need to build a view layout containing the camera preview and the user interface controls. So we develop a XML file using *FrameLayout* to

display it. In this file we also include other two XML files: one for the controls, like buttons, and another for text, the instructions for the user. The 3 layers (XML files) are overlapped, such as in Figure 4.30.
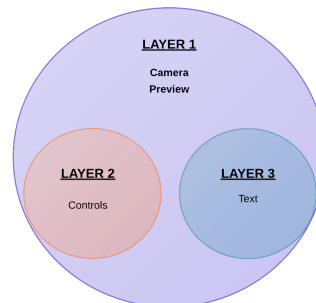
Fig. 4.30: Diagram of the three layers implemented.

The button for image capture is connected to a listener which is associated to the action of capturing images so, when the user clicks it, the listener connects with the controls interface and responds to the user action. "OnClick" a new intent begins, starting the correspondent button activity. If the capture button is pressed we need to be able to capture and save the correspondent image/photo. To receive the image data received in JPEG format and to write it in a file we must implement *Camera.PictureCallback* interface, shown as below:

```
PictureCallback mPicture = new PictureCallback() {
        @Override
        public void onPictureTaken(byte[] data, Camera camera) {
            File pictureFile = getOutputMediaFile(MEDIA_TYPE_IMAGE);
            if (pictureFile == null) {
                return; }
            try {
                FileOutputStream fos = new FileOutputStream(pictureFile);
                fos.write(data);
                fos.close();
(.....)
        camera.startPreview();
      }
   };
```

So when the user presses the "Capture" button to retrieve a picture we used the *OnClickListener*, as referred before, and the *camera.takePicture(null, null, mPic-*

ture) method. To the user has a feedback that the photograph was taken, we also add a text notification:

```
Toast.makeText(Activity1.this, ''Photo Taken'', Toast.LENGTH_SHORT).show();
```

Because the instructions for the user are photo after photo (to incline the phone, etc.), we call the correspondent RelativeLayout to appear here too.
The final aspect of the camera preview is the following one in the Figure 4.31.
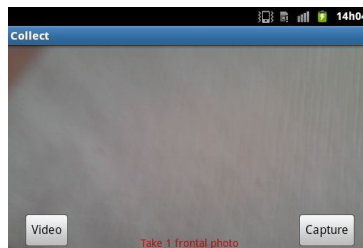
Fig. 4.31: Preview of the camera in "EyePic".

To save the media file obtained in the SD Card we employed the following method:

```
Environment.getExternalStoragePublicDirectory(Environment.
DIRECTORY_PICTURES),''MyCameraApp'');
```

If the user wants to uninstall the application, the files saved in this location will not be removed, and to avoid the interference of other users (because this directory is public), we create a sub-directory named "MyCameraApp", where the user can access to visualize the photographs taken with the application.
The media file is saved using a timeStamp (*SimpleDateFormat*) in its name:

```
mediaFile = new File(mediaStorageDir.getPath() + File.separator +
"IMG_"+ timeStamp + ".jpg");
```

4.6.3   Other features

Other features that application should have are:

- **Calendar API**: we want to allow the user to schedule another data collection, that is why in the main menu of the application there is a button named "Alert" and by clicking it the user receives a notification advising him to schedule preferentially within a month between the last one performed. The "Calendar Provider API" [129] provides the necessaries tools to access the calendar

of the mobile phone of the user, with its intents: inserting, visualizing and editing events. Using this intents the mobile application sends the user (after reading the notification) to the calendar application to make the requested operation in a pre-filled form. After this, he is returned to the main menu. We can also include reminders associated with events, notifying the user to the recommended monthly data collection.

- **Gallery API**: another feature that provides the possibility for the user to view the collection made through "EyePic" by clicking on initial menu in "Records". The simplest way of making it is using this piece of code [130]:

```
Intent intent = new Intent(Intent.ACTION_VIEW,
Uri.parse("content://media/internal/images/media"));
startActivity(intent);
```

The previous collections (especially when performed regularly) are important to assess whether or not there was some progression/modification during the ophthalmologist appointment.

- **Sensors**: there are three main categories of sensors [131]:

  - *Motion Sensors* - here we can access to accelerometers, gravity sensors, etc. Motion sensors can measure acceleration forces and rotational forces along three axes.

  - *Environmental Sensors* - these sensors measure various environmental parameters, such as ambient air temperature and pressure, illumination, and humidity; thereby includes barometers, photometers, and thermometers.

  - *Position Sensors* - in this category we can find orientation sensors and magnetometers, which are capable of measuring physical position of a device.

Not all the sensors are supported by the Android platform, but using Android sensor framework (belongs to android.hardware package and includes several classes and interfaces to manage sensors) we can access to many of sensors, as those previously mentioned.

The sensors useful for implementing in the mobile application are: accelerometer - to detect motion when the user needs to follow the instructions to perform

data collection; and light sensor - to measure the illumination of the room, giving the user a feedback.

4.7   Summary

The user stories and use cases initially written have led to the definition of the necessary requirements for the development of mobile application "Eyepic".

The data collection protocol was defined in line, because had to meet the requirements for eye diseases discussed before, and at the same time be easy to handle for the non-medical user.

After the designed mockups corresponding to the protocol, user stories and U.C., was developed in android the "Eyepic", involving the features to the established procedures.

A beta version of this application was needed to be tested in order to verify its applicability and usability required, being this the next step of this thesis (described in the following section).

Chapter 5

Hospital Field Study

To assess the usability of this type of technology with a smartphone, especially the viability of the red reflex/Brückner test, the main test that will be available in the application, a field study was conducted in a hospital environment. This test is vital in the early detection of some anomalies, such as cataracts, glaucoma, retinoblastoma, retinal abnormalities, systemic diseases with ocular manifestations, and large refractive errors [38].

The Brückner test also acts as a risk factors' screener to identify two of them, very common: anisometropia and strabismus [37]. A difference in refractive error between the two eyes (anisometropia) is a common cause of amblyopia (known as "lazy eye" [132]), the only identifiable amblyogenic factor in 37% of the cases. In situations where strabismus coexists there is a 24% increase in this identification [133]. The "Pimpolho" project, lead by Dra. Sandra Guimarães, aims to assess the vision of all children born since the year 2010 (between 3 and 4 years old) in Braga, in order to prevent amblyopia, a disease almost exclusive in childhood and that up to 5 years old is almost always treatable [134], [135]. From this age the results of the treatment will not be as effective, therefore the major importance of an early detection, preventing vision below normal (entailed by a delayed treatment outside the recommended age-group). Accordingly to Dra. Sandra Guimarães, in [132], "in Portugal there are no studies on the prevalence of amblyopia, but worldwide it is estimated that two to four percent of the population is affected by this problem".

Participate in this project is an excellent opportunity to acquire annotated images to automatic processing. Thus, it is possible to determine the importance that a simple photograph of the eyes of a child can have in his/her visual health, and whether this information can be used in a mobile application for early detection of this type of

pathology.

Thereby, the main objective of the realization of this study was to obtain a bank of photographs, anonymized, of patients who consult the ophthalmology service of Braga Hospital, within the scope of the "Pimpolho" project. So it is possible to verify the feasibility of the collection protocol defined for the use of the developed application. Also several experts opinions were collected regarding the use and applicability of such an application.

5.1   Methods

The material used in the study is only the smartphone with flash and with beta version of the mobile application as described in the previous sections.

The initial method to be followed is the subsequent one: in an environment with poor lighting a smartphone is used to photograph the eyes of different patients. These photographs will be framed to capture only the two eyes of the patient in such a way to not compromise the anonymity and confidentiality.

Sex and age, will also be recorded and if he/she suffers from any eye abnormality, the characteristics of the local where the patient was photographed (such as brightness, distance at which the researcher is from the children), as well as the features of the smartphone employed.

Through the photographs taken the initial idea is to evaluate different points, such as:

- Testing algorithms of iris/pupil detection;

- Algorithms for segmentation and comparison of ocular symmetry;

- Elaboration of some statistics data given the sex and age of the child, and the detection of some anomaly;

- Image processing of the collected photos, such as in Figure 5.1 and 5.2, verifying the existence of some visible ocular alteration in them, liable to be detected in photographs taken with a smartphone with flash, and performing the collection protocol predefined;

- Preparation of the final report with the results obtained.

Fig. 5.1: Photographs of 3 children exhibiting brückner reflex [37].
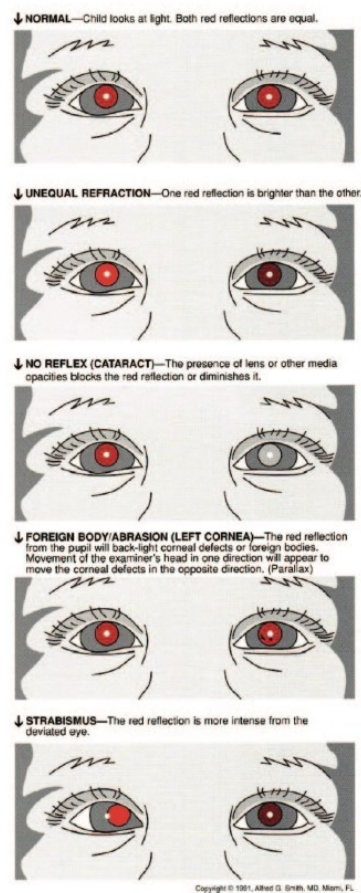

Fig. 5.2: Illustration allusive to the Red Reflex Test [38].

The proposed data collection method has taken into account the data collection protocol suggested in this master thesis, in order to verify its viability/usability, what detect points which should be revised.

5.2   Test Beds

The test beds were inserted in the "Pimpolho" project ongoing in Hospital de Braga, which will be described next.

5.2.1   "Pimpolho" Project

Every Thursday a group of approximately 25 children, with ages between 3 and 4 years old, comes to the Hospital de Braga with an assistant to do the screening tests under the "Pimpolho" project (Figure 5.3). The parents authorization has been signed before the visit and the responsible, bring them on the scheduled day.

The group of children is divided to start the exams in the specialist room with the ophthalmologist and the technician, normally an orthoptist. The routine exams made by them are quite different. The orthoptist measures the visual acuity without correction (with correction only when applicable), asking the child to reproduce the letter/symbol displayed with an exemplar, and uses the plusoptix to obtain different measures (value of refraction, pupil sizes, interpupillary distance and eye alignment [136]) with binocularity. If a child has eyeglasses he/she can not perform the plusoptix test.

The ophthalmologist doctor starts with biomicroscopy (to evaluate the anatomy of the eye) and fundoscopy. After that, he/she uses the "Lang Cube" to verify the oculomotor balance, also performing Cover and Hirschberg test (with an ophthalmoscope) and evaluation of ocular movements. Finally, the Randot test is performed to evaluate stereopsis.

After the standard exams an evaluation report is made by the doctor and the result can be: the child does not present amblyopia or other amblyogenic factor or, the child presents them and the parents should make an appointment. This report is sent by the responsible of the day care to be delivered to the parents.

Some of these medical methods are clarified in the Appendix A.

5.3   Results

We performed a field study in partnership with Hospital de Braga and "Pimpolho" project, so in our visits we gather different opinions relative to the development of the data collection protocol and respective mobile application, which are presented next. Also the results of the field study are presented.

Fig. 5.3: Slogan and logo of the "Pimpolho" project.

5.3.1 Medical Opinions

This application was shown to some professionals of the area (ophthalmologists and orthoptist) who expressed their opinion about the designed protocol, respective mobile application and early results.

Relatively to the defined protocol, the lighting in the room should be low (as we noted when starting the data collection) in order to allow scotopic vision (vision produced by the eye in low light conditions) and frontal photos will be the ideal, since taken from another perspective may mislead the diagnosis.

They agree that this kind of mobile application is very useful for various reasons, mainly because it is low-cost, but also because most parents are not informed or do not even have knowledge on the subject, the majority thinks they can not take a baby to an appointment, that he will not cooperate. So, because nowadays everybody adheres to mobile applications quite well, this new one, easy to access, allowing to perform a data collection at home and transmitting important information, becomes very usefull for an early ophthalmologist appointment. This is an important tool to battle with a delayed diagnosis, having, consequently, huge impact in the medical field. In fact, Brückner test plays an important role in detection of these eye pathologies, that must be detected as soon as possible.

Their main concern was the quality of the phone camera, which may not have the required conditions for a complete assessment of lunar reflections like in the Brückner test.

5.3.2 Data Collection

Using the developed mobile application, "EyePic" we collected several children photos during "Pimpolho" project, completing sometimes the protocol and in others not fulfilling it, in order to verify its viability and points which may be needed to reevaluate. For example, if taking the photograph closer to the children (only 2 steps of distance) is better than the 4 steps stipulated in the protocol defined.

Patient confidentiality was maintained, with no record of their identity, and the photographs were only taken with a frame for the eyes.

In the Figure 5.4 (a) we present the results of the protocol. The child presented white reflexes in the two pupils.

Figure 5.4 (b) illustrates the red reflex in both pupils in a different collection. Because they are present in both eyes we do not consider the possibility to have an eye problem (and the medical diagnosis does not reveal any problem conforming the application of this protocol for data collection) but if, for example, one eye had a red reflex and the other a white one, it would be suspicious (accordingly to the eye pathologies discussed) and maybe require a more detailed medical examination.

(a) (b) (c)

(d)
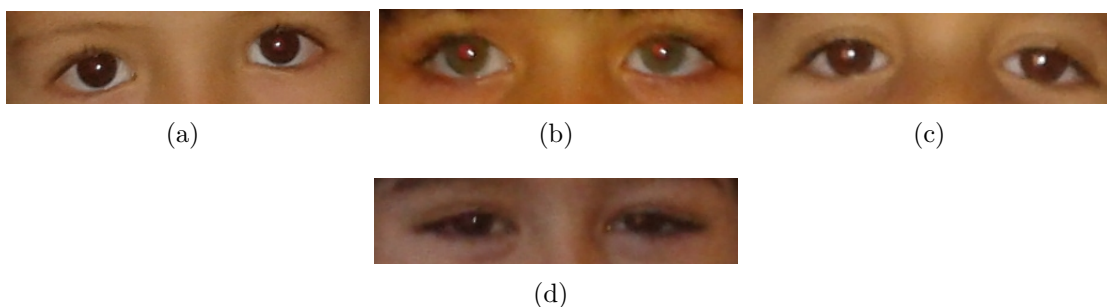
Fig. 5.4: Children photos taken with "EyePic" application: (a) Photograph of a child with white reflexes in both eyes; (b) Child apresenting red reflexes; (c) Infant with white reflexes; (d) Photo of a child with hyperopia and dubious reflections.

In Figure 5.4 (c) both white pupil reflexes, but we do not followed the protocol to take this picture: we take it close to the infant (one meter, more and less) and using a dual flash, which caused pupil closure, not allowing the appearance of a red reflex. This was performed to compare with a photograph taken following the proposed protocol.

The last result presented is in Figure 5.4 (d), where is noticeable a distinct reflex in the right eye (whitish reflex) comparing to the left (red reflex). The diagnosis of this child was hyperopia/hypermetropia and perphaps the difference between reflexes

is due to that, allowing, once more, to associate a dubious reflex detected in a photograph with an eye health problem.

5.4 Summary

The "Pimpolho" project was very important allowing to check the usability of the data collection protocol defined. Because we only took photographs to the children, we only spent about 1 or 2 minutes with each child to perform the protocol. If we added the video recording we estimate approximately 3 to 4 minutes to do all the steps of the data collection protocol.

The protocol and application developed, provided useful images for the detection of certain pathologies identifiable by the red reflex such as amblyopia, hyperopia, strabismus (Hirschberg test), among others. The assessment of red reflexes concern the evaluation of its quality and intensity, size of the pupil, position of the light reflex and quality of the corneal light reflexes [137]. The reflexes should be mirror images of each other in a normal situation, being this condition very dificult to detect in a photograph taken with a smartphone. In the future we intend to implement different algorithms to detect different colour reflexes in the photographs.

A pathological case was detected by the ophthalmologist through the exams and also in the photograph taken with the application developed, enhancing the viability of the same. The gathered medical opinions, as well as the results obtained, allowed us to infer that the protocol has the necessary characteristics for the detection of the defined ocular pathologies using only a smartphone equipped with flash.

The low light environment, the distance between the subject and the child and the power of the phone flash proved to be suitable for this type of evaluation. The medical opinions, despite its informality, highlighted the importance of the contribution of this kind of technology can have in reducing the number of cases detected late, enabling a timely treatment.

Chapter 6

Conclusion

The proposal in this thesis is a framework for eye pathology screening using a mobile application, with special emphasis in children and fast degrading eye pathologies. The most common diseases that benefit from early detection, and respective signs were described. This allowed for the design of a novel data collection protocol for a range of eye pathology screening, specially designed for non-medical users, and with only the technology available on a smartphone. In this application there is no need for external devices.

Given the importance of the eye diseases covered in this work, early detection is essential to a timely and effective treatment, making this mobile application quite advantageous, due to its practical and easy to use aspects for a regular monitoring, something extremely important for this diseases with high incidence during childhood.

A "beta" version of this mobile application was be tested at Hospital de Braga in a screening project named "Pimpolho", aiming to make an evaluation of the eye health of children aged 3 to 4 years, with special focus on amblyopia or some amblyogenic risk factors. In the different results obtained in this hospital field study, one photograph presented dubious reflexes, proven to be a pathological case when detected by the ophthalmologist through the exams, reinforcing the viability of the developed smartphone application.

In conclusion we can say that one of the strengths of this application is its accessibility: it can reach everyone, since low income countries where medical instruments are scarce this can become an alternative, and mainly because it allows a first screening, collecting usefull images to the detection of serious diseases and follow-up.

Another great advantage is the ability to store all collections made by date (record-

s/history), and thus can be viewed by a medical expert. As parents with young
children usually attend a pediatrician, and he only performs any non routine eye
exam in case of alarm, it will be a great asset to have a visual history of the de-
velopment of eye disease (if that manifest) for an accurate diagnosis. Also, a image
repository can be achieved with this collection, not only for doctor evaluation, but
for science research as well. Apart from that, this is a very innovative mobile appli-
cation, there are no currently similar applications, to our knowledge, including the
same features an without the use of additional hardware to obtain the imagens for
the analysis [138].

Besides the features presented before in the future we intend to make available a
video recording what could add more value to the application, covering more eye
pathologies, like nystagmus or other evaluations for strabismus. But there are some
important issues to be considered like the child's attention during the recording, and
the resolution required to implement it.

Lack of time was a major limitation, not allowing, for example, formal interviews
to various professionals and its documentation, being a future assignment. There is
also a chance to continue, in the future, the collaboration with Hospital de Braga.

Finally, with this work we published a short paper in BIOSTEC Conference, hap-
pening in Lisbon in 2015, approved on November 13th.

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Medical Methods

The following items describe some medical methods used in "Pimpolho" project.

- **PlusoptiX**: it is a hand-held autorefractor for pediatric use (Figure A.1 (a) and (b)) being appropriate for infants from 6 months of age and older [136]. Has several features such as: both eyes are measured simultaneously (binocularity) (Figure A.1 (c)), measurement distance is one meter, acquisition time is 0.8 seconds, and refraction can be measured through glasses [139] (the PlusoptiX model used in the hospital does not allow measurements with glasses as referred before, the model here is PlusoptiX A09).
  Refraction is measured through photo-retinoscopy: similar to retinoscopy, the difference is the employment of a low level infrared light (completely innocuous), instead of visible light to avoid brightness [136].

  There are other models/brands of photoscreeners in the market, like iScreen and the Pediavision SPOT, and the new ones promise to detect amblyopia risk factors early in such a way that pediatric monocular and binocular vision impairment is reduced.

  One observational screening study following AAPOS guidelines on pediatric patients with and without developmental delays compared the three available commercial photoscreeners. The results were: inconclusive rate ranged from 1-4% (iScreen) to 12% (PlusoptiX). Sensitivity ranged from 72% (iScreen) to 84% (PlusoptiX) and specificity ranged from 68% (SPOT) to 94% (PlusoptiX). The iScreen can provide results in 99% of high risk patients. The conclusions were that photoscreeners in 2011 had favorable validation that is expected to improve with further clinical study and pediatricians have, nowadays, practi-

cal technology with a recognized procedure code to assist in amblyopia reduction [140].

Other study enlight that Plusoptix should not be used exclusively to evaluate strabismus because its sensitivity decreases significantly specially in esotropic patients with less than 30 PD (Prism Diopters [141]) deviations [142]. They used PlusoptiX S08 photoscreener to examine eighty-three patients, between 6 months and 40 years, determining the type and amount of the deviation. The overall sensitivity of the device to detect strabismus was of 70%; 25% was for exophoria, 67% for esotropia, 73% for exotropia, and 89% in patients who had mixed strabismus. Regarding degree of deviation, sensitivity was 46% in deviations less than 30 PD, rising while the degree of deviation increases.
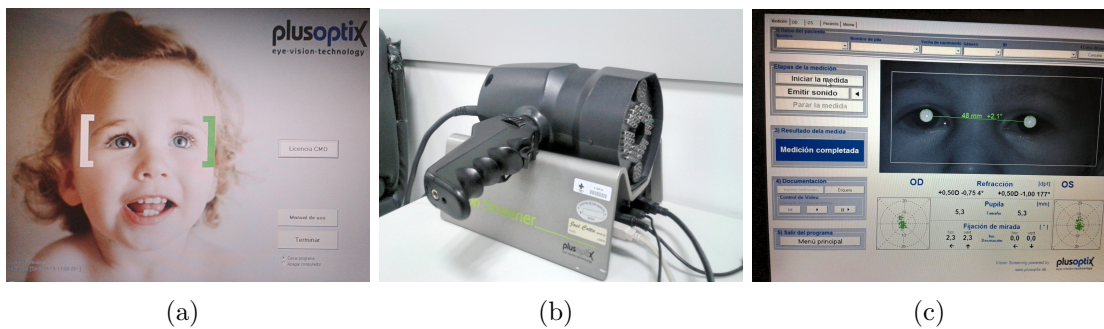

(a)   (b)   (c)

Fig. A.1: The PlusoptiX pediatric autorefractor: (a) Software; (b) Autorefractor; (c) Measurements in a patient.

- **Biomicroscopy**: the biomicroscope is an instrument that can be used to examine the lids and anterior segment of the eye to evaluate the fit of the lenses, to study the nature of any corneal defect resulting from the wearing of such lenses and even to inspect the lenses of the eye [143]. A slit-lamp biomicroscopy can provide a brilliant illumination and high magnification, helping in the observation of subtle pathological changes to the diagnosis of some eye pathologies [144].

  When using the slit light biomicroscope, the examinee's head is supported by a headrest having a chin rest and a forehead rest so that the examinee's head is not allowed to move, like the one in the Figure A.2. Once the eye is properly positioned, the main body of the biomicroscope is moved as necessary to observe a cross-sectional image of the cornea, anterior chamber, crystalline lens, vitreous body or other portions of the eye can be observed [145].

- **Stereopsis Tests**: Stereopsis is the perception of depth arising from binocular

Fig. A.2: Example of a biomicroscope [39].

horizontal retinal disparity and its presence or absence is an important indicator of the state of binocularity in patients with ocular motility disorders [146]. Therefore can be affected by strabismus, refractive blur and contrast sensitivity between the two eyes [147]. Consequently stereoacuity become very important in the role of detecting strabismus, amblyopia and anisometropia in children.

There are many tests of stereoacuity such as Lang, Randot, Random-Dot Estereotest (RDE), TNO, Titmus Stereotest and New stereo tests [148]. Brief description of some of them are presented next:

– **Randot Stereotest**: consists of RDS screening plates, together with modified animal and Wirt circle sections for near threshold measurements of stereoacuity (Figure A.3 (b)). The test uses the vectographic method to present disparity, so patients are required to wear polarising filters [147] (polarized glasses such as the ones in the Figure A.3 (a)).
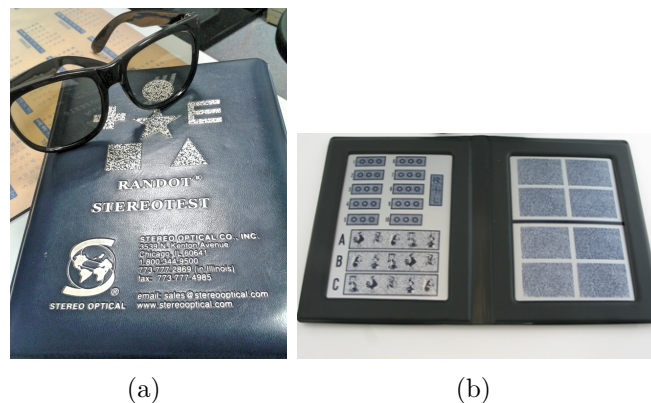

(a) (b)

Fig. A.3: Randot Stereotest: (a) Photograph of the polarized glasses to perform Randot Stereotest; (b) Stereograms of Randot [149].

– ***Lang Stereotest***: Accordingly to [148] Lang stereotest is a simple and useful screening test in the younger children, as is not requires the use of eyeglasses. There are two versions of this tests: Lang I and Lang II stereotest (a revised version of Lang I) which incorporates a monocularity visible shape. It is proven that children with normal binocular vision cannot pass the test monocularly and that children with strabismus cannot pass the test either. However, some children with anisometropic amblyopia can achieve stereoacuity levels within normal limits [147].

The Lang stereotest combines a random-dot pattern/stereograms and cylinder gratings that overlies the target providing a haploscopic (stereoscopic vision produced by the haploscope or mirror-type stereoscope [150]) testing device. This combination results in three familiar objects: a cat, a star and a car [151], [152].

Comparing Lang I with II, I can be performed in children starting from 6 months of age: if the baby stares for a few seconds at the card can infer the presence of stereopsis [146].

Fig. A.4: Stereograms presented in Lang Stereotest [40].

Stereotests that use random dots are an accurate and established method to measure stereoacuity, besides the proof that the results obtained with differents tests will vary widely [146].

- **Lang Fixation Cube**: in Figure A.5 is represented a picture of Lang Cube, a pencil with a fixation cube on the top with pictures recommended for near examination [153].

Also can be used for cover test as well as for holding the child's attention in Lang Stereotest I or II examination. Each turn of the cube shows a new object: for example, the star on the top side and the other prints can be used for testing convergence [154].
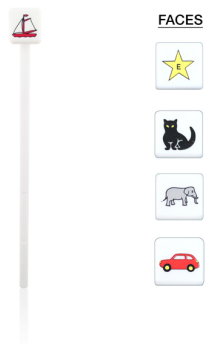
Fig. A.5: Lang Fixation Cube [41].