



Faculty of Engineering

**Development of 3D-printed Universal Adapter in Enhancing Retinal
Imaging Accessibility**

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Development of 3D-printed Universal Adapter in Enhancing Retinal Imaging Accessibility

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DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.



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ABSTRACT

The concept of smartphone-based retinal image acquisition has been around for years where images of the retina are acquired using a portable device together with a smartphone. Having a device that is portable, easy to use, and low-cost enables eye care to be more widely accessible especially in geographically remote areas and enables early diseases detection for those who are in low- and middle- income populations that have very limited access to eye care. However, professionals still find this method limited to screening purposes only and incapable of competing against reference standards in terms of image quality and sensitivity. Studies have also expressed difficulty in optimizing the concept. This study investigates on existing smartphone-based retinal image acquisition devices to determine the best parameters or features for optimum image acquisition. Besides this, this study aims to develop a universal adapter that allows an existing smartphone ophthalmoscope to be used with a variety of smartphones and evaluate the performance of developed adapter. Adapter development was performed using AutoCAD 3D and Ultimaker Cura. Evaluation of performance includes stress test, and statistical and survey analysis. Finite element analysis (FEA) method was performed for the stress test where the minimum and maximum Von Mises stress and 1st principal stress were calculated and compared with PLA's yield and ultimate tensile strength. Subjective Image Quality Assessment based on a 5-point scale involving a non-mydratic clinical testing was performed and an end-user survey was prepared for the statistical and survey analysis. For the clinical testing, fourteen patients of age range 20 to 80 years old with various medical conditions were recruited. Images were obtained and graded by experts based on the clarity and field of view in accordance with the 5-point scale. From 140 images, 37.83% (95% CI = 22.16% to 53.47%) were clinically

adequate (Grade 3 $\geq$) as graded by the examiners. Furthermore, median and frequency scores were calculated from the end-user survey.

Keywords: Smartphone-based retinal imaging, portable ophthalmoscope, universal adapter, ophthalmoscopy, finite element analysis

Pembangunan Penyesuai Universal Bercetak 3D dalam Meningkatkan Kebolehcapaian Pengimejan Retina

ABSTRAK

Konsep pemerolehan imej retina berasaskan telefon pintar telah lama wujud di mana imej retina diperoleh menggunakan peranti mudah alih dengan telefon pintar. Mempunyai peranti yang mudah alih, mudah digunakan dan kos rendah membolehkan penjagaan mata lebih mudah diakses terutamanya di kawasan terpencil secara geografi dan membolehkan pengesanan penyakit awal bagi mereka yang berada dalam populasi berpendapatan rendah dan sederhana yang mempunyai akses yang sangat terhad kepada penjagaan mata. Walau bagaimanapun, professional masih mendapati kaedah ini terhad kepada tujuan saringan Sahaja dan tidak mampu bersaing dengan piawaian rujukan dari segi kualiti dan sensitivity imej. Kajian juga telah menyatakan kesukaran dalam mengoptimumkan konsep tersebut. Kajian ini menyiasat peranti pemerolehan imej retina berasaskan telefon pintar sedia ada untuk menentukan parameter atau ciri terbaik untuk pemerolehan imej yang optimum. Selain itu, kajian ini bertujuan untuk membangunkan penyesuai sejagat yang membolehkan oftalmoskop telefon pintar sedia ada digunakan dengan pelbagai telefon pintar dan menilai prestasi penyesuai yang dibangunkan. Pembangunan penyesuai dilakukan menggunakan “AutoCAD 3D” dan “Ultimaker Cura”. Penilaian prestasi termasuk ujian tekanan, dan analisis statistik dan tinjauan. Kaedah “Finite element analysis” (FEA) telah dilakukan untuk ujian tegasan di mana tegasan minimum and maksimum “Von Mises” dan “1st principal” dikira dan dibandingkan dengan hasil PLA dan kekuatan tegangan muktamad. Penilaian Kualiti Imej Subjektif berdasarkan “5-point scale” yang melibatkan ujian klinikal bukan mydriatik telah dilakukan dan tinjauan pengguna akhir telah disediakan untuk analisis statistik dan tinjauan. Untuk ujian klinikal, empat belas pesakit berumur 20 hingga

80 tahun dengan pelbagai penyakit telah direkrut. Imej diperolah dan digredkan oleh pakar berdasarkan kejelasan dan bidang pandangan mengikut skala. Daripada 140 imej, 37.83% (95% CI = 22.16% hingga 53.47%) didapati mencukupi secara klinikal seperti yang digredkan oleh pemeriksa (Gred $3 \geq$). Tambahan pula, skor median dan kekerapan dikira daripada tinjauan pengguna akhir.

Kata kunci: Pengimejan retina berasaskan telefon pintar, oftalmoskop mudah alih, adaptor universal, oftalmoskopi, finite element analysis

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LIST OF ABBREVIATIONS

2D	Two-dimensional
3D	Three-dimensional
ABS	Acrylonitrile butadiene styrene
API	Application programming interface
CA	Clinically adequate
CAD	Computer-aided design
CI	Confidence interval
CKD	Chronic kidney disease
CNS	Central nervous system
CPU	Central processing unit
D	Diopetre
DR	Diabetic retinopathy
ETDRS	Early Treatment of Diabetic Retinopathy Study
f	Focal length
FDM	Fused deposition modeling
FEA	Finite element analysis
FFF	Fused filament fabrication
FOTO-ED	Fundus photography versus Ophthalmoscopy Trial Outcomes in the Emergency Department
fps	Frame-per-second
GRIN	Gradient index of refraction
HPT	Hyperparathyroidism

IBM	International Business Machines Corporation
ICDR	International Clinical Diabetic Retinopathy
iOS	iPhone operating system
LED	Light emitting diode
MP	Megapixels
NPDR	Non-proliferative diabetic retinopathy
PDA	Personal digital assistant
PDR	Proliferative diabetic retinopathy
PETG	Polyethylene terephthalate glycol
PLA	Polylactic acid
RAM	Random access memory
n	Refractive index
SD	Secure Digital
SPSS	Statistical Package for the Social Sciences
TPU	Thermoplastic polyurethane
vCDR	Vertical cup-to-disc ratio

CHAPTER 1

INTRODUCTION

1.1 Study Background

Smartphones in general offer a variety of applications in the medical field, for example mobile access to patient relevant information, medical databases, patient and health care professional education, and act as a medical diagnostic tool (Ahn & Kim, 2024; Iqbal, 2021; Pujari, 2021). With the emerging ophthalmology technology in smartphones, eye care has become more accessible. Recent development in smartphone-based fundus photography has allowed a cost effective and efficient approach for screening purposes for a variety of diseases, for example diabetic retinopathy.

Current smartphone-based retinal image acquisition device is being developed with the intention of being able to provide early disease detection for those who are in low- and middle- income population or in general have limited access to ophthalmic examination (Jansen et al., 2021; Vilela et al., 2018). For instance, a study by Rajalakshmi et al. (2018) stated that developing an automated method involving a computer-based analysis of fundus images would significantly increase its efficiency and reduce the workload of the health systems for diabetes retinopathy screening. Fundus images obtained from the device can be shared among specialists for discussion and identification, hence reduces the need for direct referral of patient to tertiary care units for ‘in person’ examination purposes (Iqbal, 2021). In addition, smartphone-based retinal imaging also provides an early exposure for medical students and relevant health care trainees on the methods of smartphone-based fundus imaging which is relatively easier than conventional direct fundus imaging (Hakimi et al., 2019; Mamtara et al., 2018; Wintergerst et al., 2020a). Moreover, the operation of

smartphone-based ophthalmoscopy can be utilized not only to highly proficient healthcare professionals, but also to all healthcare workers (C. H. Tan et al., 2019). Examples of smartphone-based fundus imaging applications in ophthalmology includes diabetic retinopathy screening, optic nerve head evaluation, hypertensive retinopathy evaluation (Wintergerst et al., 2020a), and note progressions of a range of other retinal pathologies, age related macular degeneration, retinal tumors, and many more (Iqbal, 2021). Existing smartphone-based retinal image acquisition devices are available in two types, which are mydriatic and non-mydriatic with the majority being mydriatic. To put it simply, mydriatic refers to the dilation of pupils meanwhile non-mydriatic means no dilation is required. Devices that do not require dilation are generally integrated with much more advanced technology for their camera and illumination system. Most existing smartphone-based devices require dilation to acquire clinically adequate retina images due to the limitation of the smartphone itself as a smartphone has yet to be capable of replicating the illumination system of a conventional non-mydriatic fundus camera.

The reason why research on various retinal imaging methods especially ones that are affordable and portable are important is because of the positive impact it has on early diseases prevention. For example, according to Karakaya and Hacisoftoglu (2020), diabetic retinopathy (DR) is the most prevalent cause of blindness or vision loss, resulted by the bleeding of small blood vessels of the retina. As of now, there are 537 million adults worldwide have diabetes and is expected to rise to 643 million by 2030 and 783 million by 2045 which is a very alarming rate (International Diabetes Federation, 2021). The study by Karakaya and Hacisoftoglu (2020) further added that current studies have shown that in developed countries, access rate to medical care such as early diagnosis and accurate evaluation of diabetic retinopathy severity ranges from 60% to 90% whereas rates in

developing countries are much lower. In other words, patients in low- and middle- income populations are less likely to be exposed to early detection of diseases that would allow them to get effective treatment in a timely manner.

An ophthalmoscope utilizes light and refraction with lenses to allow the acquisition of retinal images. Light is defined as an electromagnetic wave that propagates through space. By nature, when light passes through an edge, it can become directionally polarized and curves slightly which allows it to be filtered or amplified. Light is also defined as a ray that travels in a straight line. Thus, lenses can be used to redirect its propagating wavefront along desired directions. In a vacuum, light has a speed of 3×10^8 meter per second. The speed of light depends on the refractive index, n whereby the higher the n , the lower the speed (Timberlake & Kennedy, 2005). Refraction is defined as the change in speed and direction of a light ray when it passes through two mediums of different refraction index. Similarly, the refraction index for both mediums determines the degree of refraction (change in direction) of the light ray. Besides this, the degree of refraction is also determined by curvature interface between two mediums; the lens and the cornea where the curvature of the cornea is constant, and the lens is variable (Fox & McGraw-Hill Companies., 2011).

Lens on the other hand is a transparent refracting medium (Wu & Ren, 2012) known as a popular optical device and is generally made of either glass, plastic, polycarbonate, or polymer. The most common types of lenses are spherical and cylindrical with the spherical lens being the most widely used for optical devices. Other examples of lens type are the gradient index of refraction (GRIN) lens, ball lens, and Fresnel lens (Wu & Ren, 2012). Spherical lens can be further grouped into two types, which are concave and convex. Figure 1.1 shows the different types of lens shapes adapted from Wu and Ren (2012) . Convex lens is defined as a converging lens. When a set of parallel light rays reaches this lens, the light

rays are refracted which causes the rays to converge. Similar to concave lens, convex lens comes in three forms which are bi-convex, plano-convex, and concavo-convex as shown in Figure 1.1. In contrast to concave lens, referring to Figure 1.1 (b), the spherical surfaces of a typical convex lens (bi-convex) bulge outward from the center where the structure is thick in the center but thin at the periphery. This results in the object seen through the convex lens appear magnified when the object is positioned close to the lens. Concave lens is defined as a diverging lens which means when a set of parallel light rays enters this lens, the light rays diverge outwards. Concave lenses come in three forms which are bi-concave, plano-concave, and convexo-concave. Referring to Figure 1.1 (d), a typical concave lens (bi-concave) comprises two surfaces that curve inward where its structure is thick at the periphery but thin at the center. This results in the object seen through the concave lens seems minified and image formed are virtual and erected (Khurana, 2007).

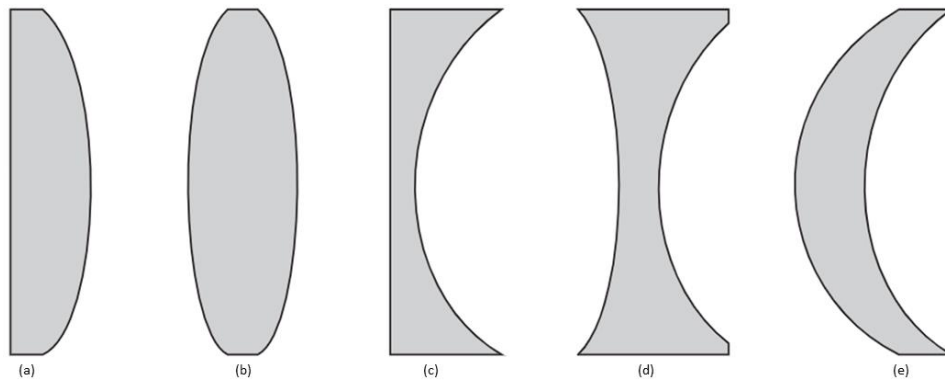


Figure 1.1: The different types of lens shape. (a) Plano-convex lens, (b) Bi-convex lens, (c) Plano-concave lens, (d) Bi-concave lens, (e) Convex-concave lens (Wu & Ren, 2012)

1.2 Problem Statement

Over the years, smartphone-based retinal image acquisition devices have shown its credibility in the medical field but only up to a certain extent. Despite being affordable, portable, and efficient data transfer with expanding internet technology and artificial

intelligence in smartphones, professionals still find this method limited to screening purposes only and beneficial only for non-ideal clinical settings (Pujari, 2021; Ryan et al., 2015; Wintergerst et al., 2020b). This is because the concept of smartphone-based fundus imaging itself is still incapable of competing against reference standards in terms of image quality and sensitivity. Furthermore, studies have also shown it is difficult to obtain the right adjustment of filming distance and alignment of these devices considering glares from the lenses in the devices and also external reflections. This suggests the need of further understanding on smartphone-based retinal image acquisition to identify the current patterns or system, factors affecting its efficiency and what can be improved.

Besides this, existing smartphone-based retinal image acquisition devices work best only when dilation is induced on pupils because dilated pupils provided much wider field of view. A study by Wintergerst et al. (2020b) have stated that most existing smartphone-based retinal imaging devices require pupil dilation in achieving retinal images of acceptable quality. For instance, the D-Eye and Peek Retina both require dilation for image acquisition (Karakaya & Hacisoftaoglu, 2020) mainly because of the small field of view on undilated pupils. There are devices that were built to accommodate non-mydratic retinal imaging such as the Pan Optic Ophthalmoscope and iNView according to their manufacturers. However, some studies have found that it without dilation, it was more difficult to conduct retinal imaging. For instance, a study by McComiskie Bsc et al. (2004) was conducted involving medical students trying the Pan Optic Ophthalmoscope on dilated and undilated pupils and have found that it was easier to use the device on dilated pupils. Another study has found that devices that provides smaller field of view have lower classification accuracy (Karakaya & Hacisoftaoglu, 2020). This shows that dilation has a significant role in improving retinal imaging. However, this is a disadvantage when conducting eye examination in

geographically remote areas where additional ophthalmic resources for dilation would be difficult to be brought along. Certain geographically remote areas would also have environments that would be unsuitable for conducting dilation. Furthermore, dilation may also generate the possibility of mydriatic-induced angle closure glaucoma in the absence of ophthalmic professionals (Rajalakshmi et al., 2021) and other risks as it causes pupils to be unresponsive to light for several hours. Hence, this shows more research is needed on conducting retinal imaging without dilation which helps to identify the measures that can be done for improvement.

Furthermore, certain existing smartphone-based retinal imaging devices do not come with a universal adapter. For instance, the Pan Optic Ophthalmoscope, D-Eye, iNView, and HEINCE-iC2 are only compatible with specific models of smartphone such as the iPhone 5 and iPhone 6 which is a disadvantage since the iPhone 5 and iPhone 6 are no longer iOS supported and are not easily obtained as of now. Among the existing devices in the market, only a few of them are universal such as the Peek Retina and the adapter Choroida Fundus Explorer. Hence, there is still a need to develop a universal version of the adapter that is compatible with various smartphone models, especially with currently available smartphone models in the market. Several studies have also developed their own smartphone-based 3D adapters where the adapters are utilized directly with a pair of lenses (Hong, 2015; A. Hu & Damji, 2019; Myung et al., 2014). However, there is a lack in describing the integrity and longevity of the adapters. Thus, a detailed experimentation is needed to be designed to ensure the universal adapter does not compromise the quality of image taken.

1.3 Objectives

The research aims to develop a 3D-printed universal adapter to enhance the accessibility of smartphone-based retinal imaging. This can be achieved through the following set of objectives:

- i. To identify the optimum setting for factors affecting the efficiency of retinal image acquisition.
- ii. To develop an improved prototype from an existing smartphone-based retinal image acquisition device.
- iii. To evaluate the overall performance of improved developed prototype through simulation.

1.4 Project Scope

In this project, the focus is on developing an adapter to be used with an existing smartphone-based retinal image acquisition device which is the Pan Optic ophthalmoscope by Welch Allyn. The Pan Optic ophthalmoscope has its own complex internal optical configuration that sets some limitation to the improvements that can be done onto the ophthalmoscope itself as the proposed adapter is to be used externally. Hence, this project focuses on external improvements/modifications specifically developing an adapter that is universal, easy-to-use, and efficient to be used together with the Pan Optic without compromising the quality of image. Finite element analysis (FEA) is applied as a stress test using the software Autodesk Inventor to analyse the physical stability of the developed adapter. For the second evaluation, Subjective Image Quality Assessment involving a non-mydratic clinical testing is conducted. The clinical testing involves five examiners with

optometry background, and fourteen patients of age range 20-80 years old with various medical conditions. The assessment on the images collected involves six examiners where the retinal images are graded using the 5-point scale which is based on the FOTO-ED (Fundus photography versus Ophthalmoscopy Trial Outcomes in the Emergency Department) studies. In addition, a user-end survey is prepared for the users to collect feedback of the developed adapter. The statistical analysis is performed using Microsoft Excel and IBM SPSS.

1.5 Chapter Summary

Chapter 1 introduces the concept of smartphone-based retinal imaging, the importance of early disease detection, and the concept of light, refraction, and lens. Chapter 2 describes the differences between direct and indirect ophthalmology, the different types of retinal imaging system, the internal anatomy and area of interest of the retina, challenges on smartphone-based retinal image acquisition, comparison of existing smartphone-based retinal image acquisition device/adapter, the optical configuration of retinal imaging, and configuration of the Pan Optic ophthalmoscope. In addition, the history on ophthalmoscopy technology is also discussed in this chapter. In Chapter 3, the proposed methodology is discussed which includes the project materials involved, the general workflow and timeline of project, and detailed procedures. Next, Chapter 4 describes the results and discussion of the study which includes the adapter prototypes developed, the results from the stress analysis, and subjective scores obtained from the survey. Last but not least, Chapter 5 summarizes the findings that have been achieved in this study.

CHAPTER 2

LITERATURE REVIEW

2.1 Overview

This chapter is mainly to provide an overview on the concept of smartphone-based retinal imaging which includes the system, functionality/features, techniques, and related methods in operating the devices, parameters such as field of view, illumination source, dilation requirement, working distance, image quality, overall efficiency, and the comparison of existing smartphone-based retinal imaging devices. Besides this, this chapter provides an overview of the Pan Optic ophthalmoscope which includes its compatibility, functions, other specifications and more. This chapter also describes the history on ophthalmoscope technology, general differences between direct and indirect ophthalmoscope technology, the other types of retinal imaging system besides smartphone-based retinal imaging, challenges using smartphone-based retinal acquisition devices, and the optical configuration of retinal imaging.

2.2 History on Ophthalmoscope Technology

In the 18th and 19th century, scientists have tried to understand the concept behind the inability of looking at a person's retina despite the eye having a transparent optical pathway between the cornea and the retina. A scientist named Gruithuisen had then discovered that in animals, there is a unique layer behind the retina known as the *tapetum lucidum* that reflects light which results in the bright glare we observe in animal eyes when light is directed towards them during night (Timberlake & Kennedy, 2005). On the other hand, a human's eye does not have that specific layer behind the retina, but the human's retina is still considerably reflective which raised the question on why it was not possible to observe

the retina with the naked eye. Two main hypotheses were then discovered. According to Timberlake & Kennedy (2005), a strong illumination source is required to ensure sufficient light gets reflected from the subject's retina to the observer to observe the retina. Secondly, the observer's eye somehow blocks some of the light rays that is supposed to illuminate the subject's retina. Later, in the mid-19th Century, it was found that the fundamental theory in developing an ophthalmoscope system is that the illumination axis and the observer's viewing axis are to be positioned as close as possible to efficiently illuminate the human eye. Figure 2.1 shows the concept illustrated by Timberlake and Kennedy (2005). Referring to Figure 2.1, a light source is placed adjacent to the observer's eye. Assuming the subject's eye is emmetropic, the path of light rays that are reflected is parallel. Most of the light rays that get reflected by the subject's eye will travel back towards the light source but only some of the light enter the observer's eye which allow the observer to observe the retina.

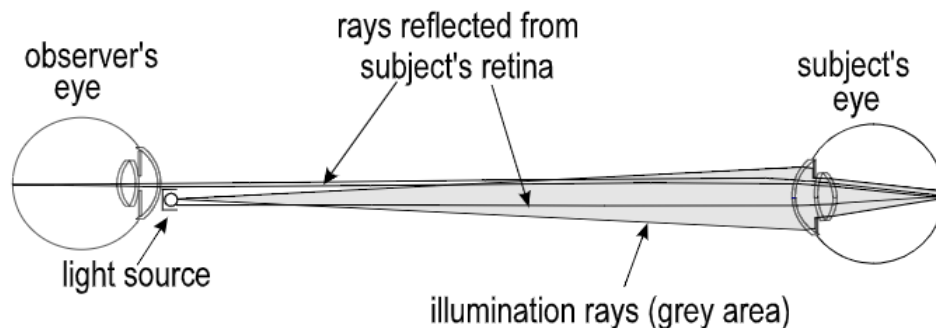


Figure 2.1: Concept of illuminating the human eye for retina viewing (Timberlake & Kennedy, 2005)

The first ever ophthalmoscope created was by Charles Babbage back in 1849 which consist of two main components; a mirror that has a small circular hole, and a light source from a gas flame (Singh et al., 2011; Timberlake & Kennedy, 2005). The mirror holds a significant role in allowing the illumination and viewing axes to be coincident. The hole was

made by rubbing off a small section of the silver patch on the mirror which makes that section see-through. It applies a straightforward concept where the light source is reflected by the mirror to redirect the light towards the patient. With the mirror, some of the light gets reflected back into the illumination axis by the patient's retina while some goes through the hole towards the observer's eye. The image of retina formed is positioned directly on the observer's retina hence this concept is known as direct ophthalmoscopy. A few years later, in 1851, Hermann Von Helmholtz had designed a practical ophthalmoscope that is similar to the ones that are used in this modern day. Figure 2.2 shows the fundamental design of direct ophthalmoscope invented by Charles Babbage and Hermann Von Helmholtz. The dotted lines represent the light rays that are reflected by the subject's retina meanwhile the dark lines represent the illumination source.

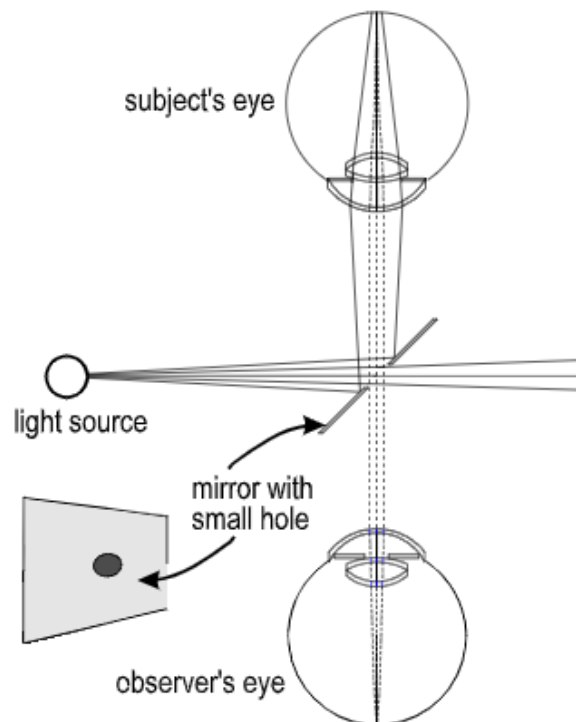


Figure 2.2: Fundamental design of direct ophthalmoscope invented by Charles Babbage and Hermann Von Helmholtz (Timberlake & Kennedy, 2005)

2.3 Internal Anatomy of Retina

For screening purposes in ophthalmology, acquiring images of the retina is sufficient to detect diseases. In a study by MacGillivray et al. (2014), it was stated that the observation of blood vessels through the retina does not necessarily require a complicated procedure where a simple non-invasive instrument is sufficient for retina viewing. Several studies have also stated that it is possible to identify early indicators of various long-term diseases for example stroke (Baker et al., 2008), diabetes melitus (Cheung et al., 2010), and hypertension (Wong & Mitchell, 2007). Another study by London et al. (2013) have stated that the retina is the only accessible part of the eye that allows research on the central nervous system (CNS) *in vivo*.

Figure 2.3 shows a sagittal view of the human eye and Table 2.1 summarizes the internal anatomy of the eye. Retina is made up of layers of tissues consisting of photoreceptor neurons called rods and cones, and other neurons. These photoreceptor neurons dissociate in response to light and this photochemical reaction leads to the production of action potentials in the optic nerve (Fox & McGraw-Hill Companies., 2011; MacGillivray et al., 2014). This is because the neural layers of the retina are a forward extension of the brain. The lens of the human eye consists of a thousand layers of cells that are tightly attached to one another which helps to prevent the formation of gaps whenever the lens changes its shape and provides roughly 20% of refracting power. The pupil is responsible for regulating the flow of light that enters the eye meanwhile the iris controls the diameter of the pupil by contraction of circular muscles. The vitreous humor is the chamber of the eye which is made up of thick fluid of gel texture that gives the ‘spherical’ shape of the eyeball. On the other hand, the aqueous humor that is located in the middle of the eyeball is responsible in maintaining a proper intraocular pressure, providing substrates, and lastly removing

metabolites from the avascular cornea and the crystalline lens. An emmetropic eye, which is referring to a normal eye has a power of +60D. In the compound lens of the human eye, approximately +40D is the corneal power which comes from the front surface and the crystalline lens has a power approximately +20D (Palanker & Blumenkranz, 2013).

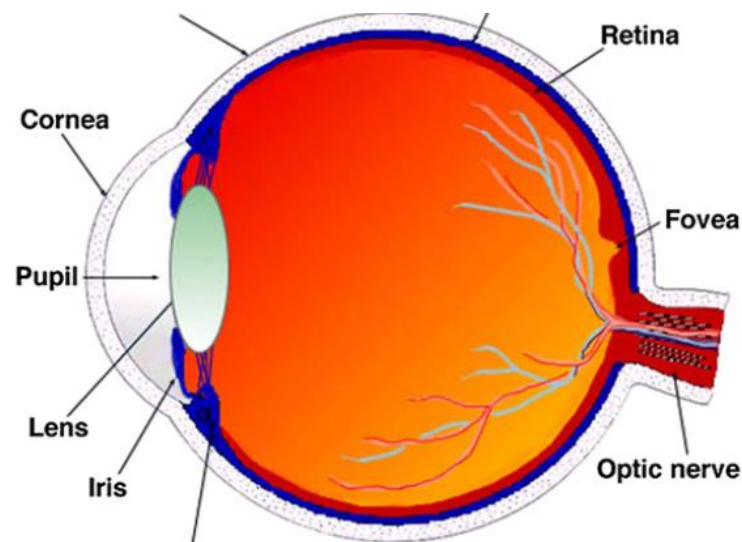


Figure 2.3: Sagittal view of the human eye (MacGillivray et al., 2014)

Table 2.1: Internal anatomy of the retina based on Figure 2.3

Structure	Location/Position	Function
Cornea	Anterior surface of eyeball	Transmits and refracts
Aqueous Humor	Middle layer of eyeball	Maintains a proper intraocular pressure, provides substrates, and remove metabolites from the avascular cornea and the crystalline lens

Iris	Anterior portion of vascular tunic; continuous with ciliary body	Regulates diameter of pupil (amount of light entering the vitreous chamber)
Pupil	Surrounded by the iris	Admits and regulates the flow of light to the retina
Crystalline Lens	Between posterior and vitreous chambers	Provides around 20% of refracting power, and able to change its shape (flexible) to allow accommodation for close focusing.
Vitreous Humor	Portion of the eye located behind the lens	Contains a thick fluid of gel texture named as vitreous humor/gel which helps to hold the 'spherical' shape of the eyeball
Retina	Principle portion of internal tunic	Photoreception; transmits impulses

Figure 2.4 shows a sample of a fundus image labelled with features of interest. The main features of interest that are generally observed or measured are the optic nerve, venule, arteriole, macula, and the diameter, vascular tortuosity, and bifurcation geometry of the vessels (MacGillivray et al., 2014). These measurements help to identify diseases such as diabetes mellitus or stroke. Besides this, other signs such as cotton-wool spots,

microaneurysms, hard exudates, and retinal hemorrhages are also observed as they are indications of diseases such as hypertensive retinopathy (Baker et al., 2008)..

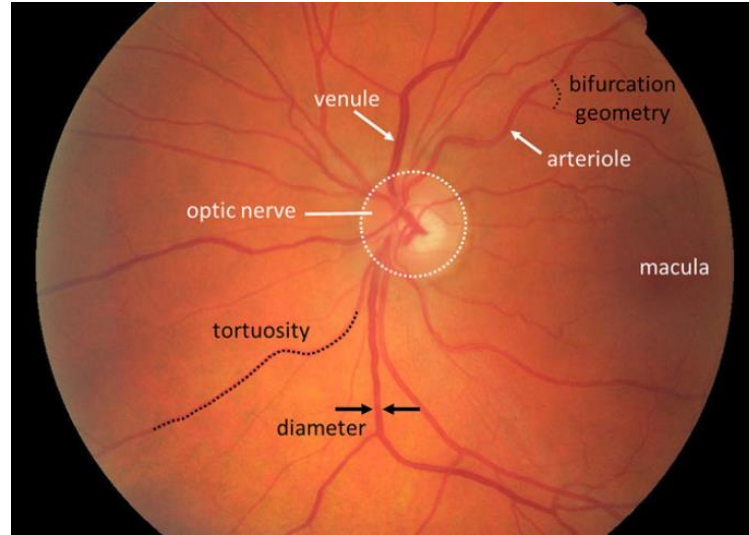


Figure 2.4: Sample of a fundus image labelled with features of interest (MacGillivray et al., 2014)

The different features and disease of interest also determine the methods of classification used to analyse the captured retinal images. For example, one of the earliest methods introduced for the analysis of diabetic retinopathy (DR) is the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system which was known as the gold standard (Solomon & Goldberg, 2019; Yang et al., 2022). The ETDRS grading system classifies the severity of DR by observing fundus lesions and characteristics for example microaneurysms, hard exudates, haemorrhages, and venous beading and loops individually into fourteen levels of severity. The grading system starts from Level 10 which represents the absence of DR to Level 85 which represents the highest severity of DR known as Proliferative Diabetic Retinopathy (PDR) (Yang et al., 2022). At present, the ETDRS grading system has been simplified into five severity levels instead, which is named as the International Clinical

Diabetic Retinopathy (ICDR) grading system (Atwany et al., 2022). The five severity levels are Level 0 representing no DR, Level 1 representing mild Non-Proliferative Diabetic Retinopathy (NDPR), Level 2 representing moderate NPDR, Level 3 representing severe NPDR, and lastly Level 4 which is PDR. Another example of grading system is the 5-point scale introduced in the FOTO-ED studies (Fundus photography versus Ophthalmoscopy Trial Outcomes in the Emergency Department) by Lamirel et al. (2012). This method was initially designed specifically for emergency departments where the main objective is to identify a few conditions in a non-mydriatic clinical setting, in contrast to disease-specific grading system such as the ETDRS and ICDR. The 5-point scale classifies non-mydriatic retinal images based on the general quality of ocular fundus images. Grade 1 represents images that do not contain any diagnostic values, Grade 2 represents a quality that is still not sufficient enough for experts to exclude all emergent findings, Grade 3 represent quality of images that allow graders to only exclude emergent findings, meanwhile Grade 4 are for images with quality that allow experts to exclude subtle conditions, and Grade 5 represents the best image quality (Bruce et al., 2011; Lamirel et al., 2012). A study by Day et al. (2016) has implemented the 5-point scale grading system which the study focused more towards the visibility of the optic disc and its surroundings.

2.4 Direct vs Indirect Ophthalmoscope Technology

The main purpose of indirect ophthalmology is to overcome the limitations of conventional direct ophthalmology. The concept of direct ophthalmoscope technology is that the image of the patient's retina is formed directly on the observer's retina as parallel light rays emanating from a point on the patient's fundus enter and focus on the observer's retina. However, this is only possible if the patient's fundus is sufficiently illuminated, which

requires the illumination source and the observer to be aligned optically (Colenbrander, 2006). Under normal circumstances, this occurrence is not possible due to the optics of the eye where any incident light that enters a pupil only reaches a part of the fundus onto which the image of the light source touches. Even with the current technology in direct ophthalmoscopy where a mirror is used as the main component to allow proper illumination, it still limits the visualization as the peripheral pencils of light gets cutoff progressively by the observer and patient's pupil. Hence, the field of view obtained from direct ophthalmoscopy is much smaller. In contrast, indirect ophthalmoscope technology refers to the process of changing the direction of light rays by inserting lens with zero vergence between the observer and the patient.

The main purpose of the lens is to bend the parallel light pencils towards the observer's pupil and bring them to a focus in the focal plane of the lens as demonstrated in Figure 2.5. Another characteristic that sets the two concepts apart is that in direct ophthalmoscopy, it is more advantageous to conduct it in close approximation meanwhile for indirect ophthalmoscopy, the observer is required to put some distance between them and the patient to accommodate for the aerial image plane as to focus the aerial image on the observer's retina. Besides this, a disadvantage of indirect ophthalmoscopy is that the retained image observed will always be inverted. In addition, it can provide a wider field of view with the expense of smaller magnification. Figure 2.6 demonstrates the concept of the aerial image magnification in indirect ophthalmoscopy adapted from Colenbrander (2006).

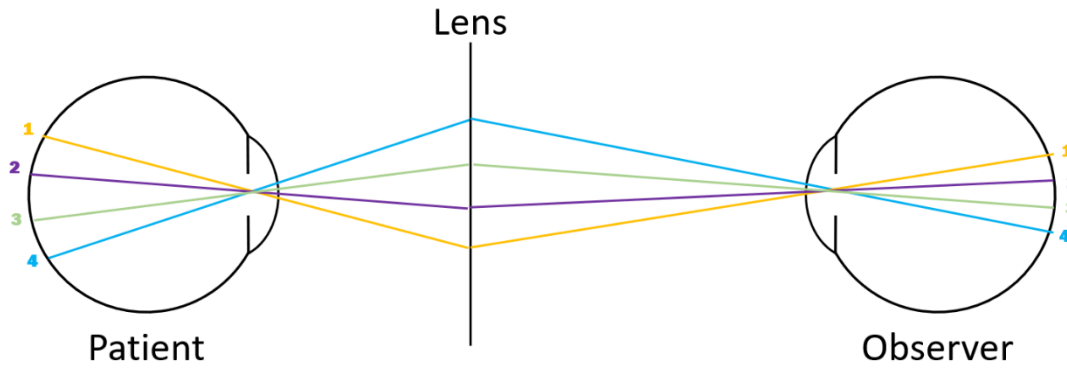


Figure 2.5: Concept of indirect ophthalmoscopy that shows the role of lens redrawn (Colenbrander, 2006)

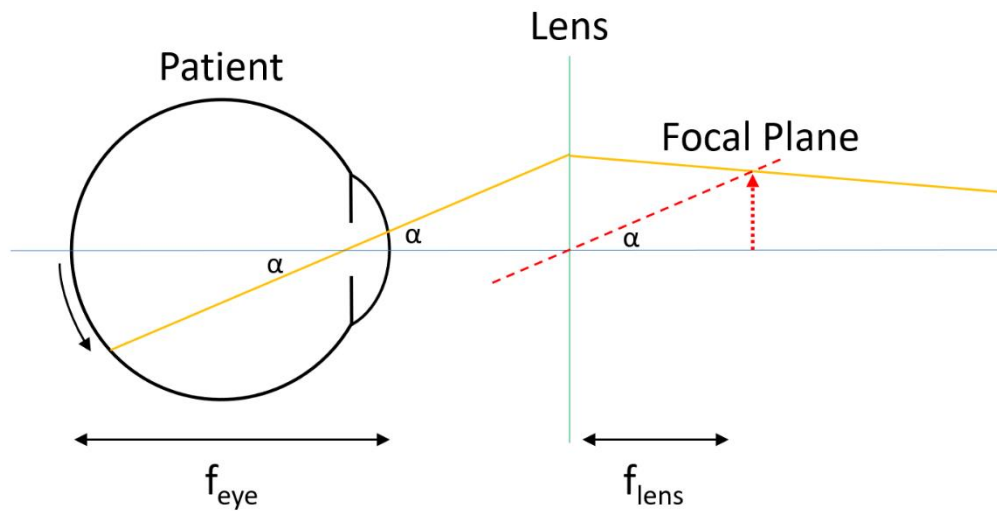


Figure 2.6: Concept of aerial image magnification in indirect ophthalmoscopy redrawn (Colenbrander, 2006)

Magnification is defined as the ratio of size of aerial image to that of patient's actual retina which can be calculated if the power of the ophthalmic lens is known as demonstrated from Equation 2.1 until Equation 2.4. In general, the magnification is calculated under the assumption that the patient's eye is emmetropic, which has +60D of power. For example, in the case of an emmetropic eye, and observation distance of 25cm which is the reference distance for magnification, the observed aerial image when a 20D ophthalmic lens is used

would appear three times larger than the patient's actual retina. When selecting which lens to use in indirect ophthalmoscopy, there are two elements involved which are dioptric power and diameter of the lens that directly determine the magnification level and field of view that the lens can provide. The power of the lens is determined by its focal length which is the distance between the centre of the lens and the focal point (Rowlands, 2020). The formulation of magnification (Gerhard, 2021) is expressed as;

$$\text{Magnification} = \frac{\text{Aerial Image}}{\text{Actual Retina}} \quad (2.1)$$

where,

$$\text{Dioptric Power (D)} = \frac{1}{\text{Focal Length, } f \text{ (m)}} \quad (2.2)$$

and,

$$\frac{\text{Aerial Image}}{\text{Actual Retina}} = \frac{f_{\text{lens}} \times \sin \alpha}{f_{\text{eye}} \times \sin \alpha} = \frac{f_{\text{lens}} \text{ (m)}}{f_{\text{eye}} \text{ (m)}} \quad (2.3)$$

hence, converting focal length (f) to Dioptric Power (D),

$$\text{Magnification} = \frac{f_{\text{lens}}}{f_{\text{eye}}} = \frac{D_{\text{eye}}}{D_{\text{lens}}} \quad (2.4)$$

While the main factor that affects the field of view observed in indirect ophthalmoscopy is the diameter and the power of the ophthalmic lens incorporated, the field of view for direct ophthalmoscopy is directly affected by the width of the illumination source beam. As mentioned previously; to achieve a wider field of view, the level of magnification must be sacrificed. According to Colenbrander (2006), the area of a patient's fundus that can be imaged increases quadratically when magnification is decreased. For instance, reducing

the linear magnification eight times hypothetically produces sixty-four times larger field of view. The field of view is determined by the ratio of the diameter and focal length of the lens used as shown in Equation 2.5. A wider field of view can be achieved using lenses with larger diameters. For instance, when comparing a 78D lens and a 90D lens, technically the 78D lens provides higher image magnification level but provides a smaller field of view. In contrast, the 90D lens provides a wider field of view but a smaller level of image magnification. However, if both lenses were to have the same diameter, the 78D lens would have the upper advantage of having a wider field of view while maintaining image magnification level (Colenbrander, 2006). The formulation is expressed as follows;

$$\frac{\text{Lens Diameter (m)}}{\text{Focal Length (m)}} = \text{Lens Diameter (m)} \times \text{Dioptric Power (D)} \quad (2.5)$$

2.5 Types of Retinal Imaging System

According to Kulkarni and Deshpande (2019), there are several types of retinal imaging systems. The standard method when it comes to retinal imaging is using a fundus camera which comes in two types, which are the mydriatic and non-mydriatic. Mydriatic cameras refer to conventional desktop fundus cameras that are bulky and big in size, expensive, and require trained and certified users, which concludes that the process is generally labor intensive and time consuming (Rajalakshmi et al., 2021). Besides this, Kulkarni and Deshpande (2019) stated that certain mydriatic cameras require an intense illumination source. The intense light would cause pupils to shrink, which is why dilation is required when mydriatic cameras are used to obtain decent retinal images. Despite mydriatic fundus imaging allows the sensitivity over 80%, issues on dilation were raised among

physicians due to their concerns towards the possibility of mydriasis-induced angle closure glaucoma incidents in the absence of ophthalmic professionals (Rajalakshmi et al., 2021).

On the other hand, non-mydriatic cameras are more advanced where the reflecting property of the retina is employed. Despite being a widely used method for DR screening, it has its own limitations. There have been contrasting findings on the efficiency and reliability of non-mydriatic cameras for retinal imaging. In the early days, a study by Hutchinson et al. (2000) had found that the performance of non-mydriatic cameras retinal imaging for diabetic retinopathy screening purposes was only notable when pupil dilation is applied. A study by Gosheva et al. (2017) had also stated that non-mydriatic cameras results in smaller field of view and lower image quality. A study was conducted in India by Gupta et al. (2014) and had also obtained similar results where a large quantity of the retinal images taken were of poor-quality and ungradable, specifically patients with dark irises. However, with the recent advancements for non-mydriatic cameras, most non-mydriatic cameras have much more advanced features such as auto-focus and auto-alignment, other task automations, and a wider field of view (Rajalakshmi et al., 2021). According to Kulkarni and Deshpande (2019); and Rajalakshmi et al. (2021), a low intensity of illumination source is sufficient for efficient retinal imaging where pupil dilation is not required. The performance of a new non-mydriatic camera was evaluated by Massin et al. (2003) by comparing the quality of fundus images taken with the camera against stereoscopic fundus images. According to Massin et al. (2003), the camera can acquire colored retinal images of the peripheral retina and posterior without any dilation. Although the study had shown the possibility of acquiring satisfactory retinal images without the need of pupillary dilation, the study concluded that more data was required to determine its efficiency. Examples of non-mydriatic fundus camera available in the market are the Canon CR02&AF, Center Vue DRS, and Forus Trinethra. Non-mydriatic

fundus cameras are mostly desktop-based which are similar to mydriatic cameras; bulky and large in size, and costly.

Besides this, there are handheld fundus cameras that are either a device on its own or it consists of a consumer camera with an attached optical system. These devices are portable, space-saving, less power required, and affordable. Handheld fundus cameras are also more user-friendly compared to conventional tabletop fundus cameras. In other words, this method requires less training and skills (Tran et al., 2012), hence non-professionals may find it easier to operate which makes these devices not limited to ophthalmologists only. Similar to previous retinal imaging methods mentioned, several studies have revealed contrasting findings on the validation of handheld fundus cameras. For instance, Quellec et al. (2016) have found that retinal imaging using handheld fundus camera is more time consuming and produces significantly lower retinal image quality when compared to using a conventional desktop fundus camera. The study did suggest that it may be used for screening purposes (Quellec et al., 2016). Similarly, another study by Yogesana et al. (2000) had compared the performance of a handheld camera named as Nidek NM-100 with Zeiss FF which is a desktop-based mydriatic fundus camera and concluded that the retinal images taken with the handheld camera were of poor quality. In contrast, Zhang et al. (2017) had conducted a study using Pictor, which is a handheld fundus camera for diabetic retinopathy screening purposes where the fundus images taken were for both with pupil dilation and was able to obtain retinal images of sufficient quality. A study by Tran et al. (2012) had constructed a handheld fundus camera system that combines the Panasonic Lumix G2 digital single-lens reflex (DSLR) camera and an optical configuration which provides an imaging path for retinal imaging. Figure 2.7 shows the general diagram of the prototype developed by Tran et al.

(2012) and Figure 2.8 shows the real-life developed handheld fundus camera prototype viewed in two different angles: front and rear.

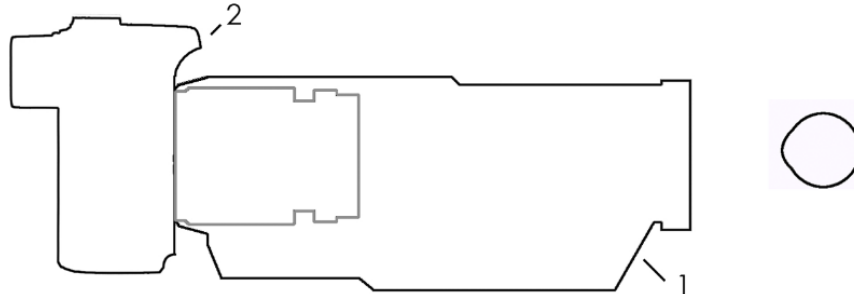


Figure 2.7: General diagram of handheld fundus camera prototype developed by Tran K. et al (1) an attachment housing optical components and (2) an off-the-shelf consumer digital camera (Tran et al., 2012)



Figure 2.8: Front and rear view of the developed handheld fundus camera prototype (Tran et al., 2012)

The prototype was able to acquire good quality retinal images; comparable to existing commercial handheld cameras (Tran et al., 2012). In addition, since the system uses the concept of attaching a separate optical configuration onto digital consumer cameras, it could be easy for non-ophthalmic medical users to use it. Hence, handheld fundus cameras still hold the potential of being a notable retinal imaging acquisition device since certain

studies were able to obtain good quality retinal images for screening purposes in addition to them being portable and are affordable compared to conventional desktop fundus cameras. However, several studies have also stated the limitations of the system (Cuadros & Bresnick, 2017; Quéllec et al., 2016; Rajalakshmi et al., 2021). Hence, more studies are required to validate the performance of handheld fundus cameras thoroughly.

Smartphone-based retinal imaging system on the other hand involves high-quality cameras and high-resolution video features from the smartphone itself that can be utilized to achieve portable and affordable retinal imaging (Iqbal, 2021). The role of smartphones for retinal imaging is becoming more significant with the deep integration of internet technology, expanding camera quality, and implementation of artificial intelligence in smartphones. In addition, smartphones-based retinal image acquisition devices have a prominent potential in becoming the first choice for direct ophthalmoscopy in non-ideal clinical settings for instance in geographically remote areas, or even emergency rooms (Lord et al., 2010; Micheletti et al., 2016). A study by DeBuc (2016) had stated the utility of smartphone-based retinal image acquisition devices has shown a steady increment with the recent advancements not only on the speed and coverage of wireless networks specifically in rural areas, but also on the power consumption efficiency of these devices that allows longer battery life. It was also stated in the study that in medical practice, 80% of doctors now utilize smartphones and mobile devices (DeBuc, 2016). Another study had also estimated that one out of two physicians incorporates either a smartphone or a personal digital assistant (PDA) in their work and this pattern is expected to increase (Lord et al., 2010). However, these devices are yet to be fully applicable as quality diagnostic tools, hence they are limited to screening purposes only as of now (Pujari, 2021).

Based on research conducted, smartphone-based retinal acquisition devices can be either be a full device or an adapter. There are several smartphone-based retinal image acquisition devices that are currently available in the market such as the D-Eye by S.r.l, Pan Optic by Welch Allyn, iNView by Volk, Peek Retina by Peek Vision, HEINE-iC2 by Heine Optotechnik, Paxos Scope by DigiSight Technologies, and Choroida Fundus Explorer by Choroida. The D-Eye, Pan Optic, iNView, Peek Retina, and HEINE-iC2 are full devices meanwhile the Paxos Scope and Choroida Fundus Explorer are adapters. Figure 2.9 shows the D-Eye attached on an iPhone that was developed by Russo et al. (2015a).



Figure 2.9: D-Eye prototype attached to an iPhone 5 and iPhone 5s from the left (Russo et al., 2015a)

Adapters are considered to be simpler to operate as it does not have an internal optical configuration, unlike full devices. Furthermore, adapters are more affordable as most of them are 3D-printed that are combined with off-shelf components such as bolts and nuts (Hong, 2015; A. Hu & Damji, 2019; Myung et al., 2014). Adapters typically comprise of two holders connected, one is the phone holder, and one is the lens holder. Figure 2.10 shows a 3D-

printed adapter developed by Hong (2015). The adapter was designed using a software named as SolidWorks Professional which is a computer-aided design (CAD) software. According to Hong (2015), the adapter is designed to accommodate different types of smartphones. and the lens holder has a specific dimension to hold a 20D condensing lens. In addition, the whole assembly involves bolts and nuts as shown in Figure 2.10. In contrast, the 3D-printed adapter designed by Myung et al. (2014) requires no off-shelf components where the assembly appears more straightforward as shown in Figure 2.11. However, the part of the adapter that holds the smartphone has as specific dimension for the iPhone 5. Besides this, the lens holder of this adapter is designed to hold the Panretinal 2.2 condensing lens by Volk.



Figure 2.10: 3D-printed retinal image acquisition adapter (Hong, 2015)

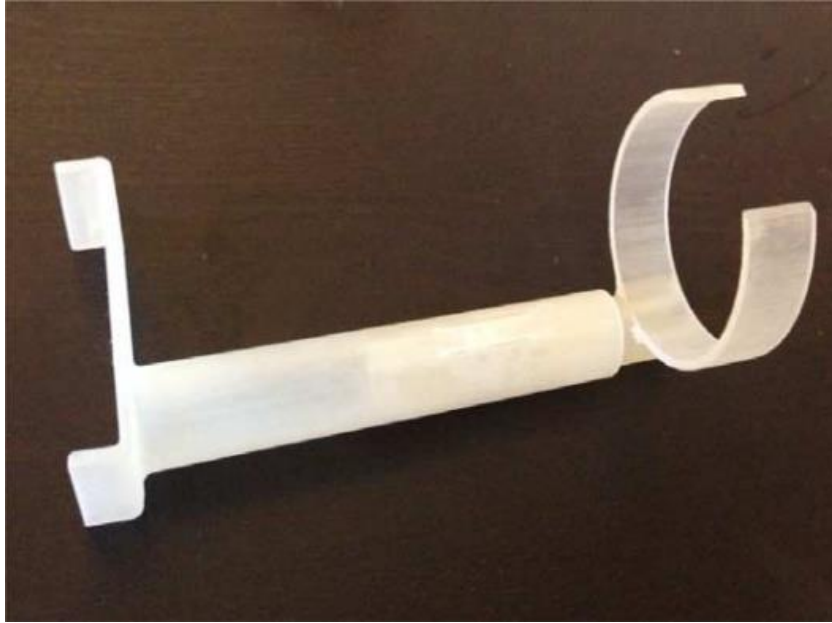


Figure 2.11: 3D-printed lens-to-smartphone mount-based adapter (Myung et al., 2014)

A typical retinal imaging in smartphone utilizes a 20D condensing lens which applies the same concept as indirect ophthalmoscopy. For the illumination, in general, this system uses the smartphone camera internal flashlight. However, since smartphone's camera illumination source is not able to replicate the co-axial illumination system precisely like the ones in indirect ophthalmoscopes, image quality can be improved by mounting an additional external illumination source near the smartphone's camera (Pujari, 2021). An example of a smartphone-based retinal image acquisition device that uses an external illumination source is the Paxos Scope developed by Digisight Technologies where the LED illumination source is mounted externally on the adapter (Mercado et al., 2017). In most cases, an illumination source is required for pupil dilation to acquire the retinal images. The 20D condensing lens are the component responsible for focusing the fundus while an image of the focused fundus starts to appear on the smartphone display screen. Figure 2.12 shows a comparison of optical principle for (a) indirect ophthalmoscopy and (b) smartphone-based retinal imaging (Iqbal,

2021) which demonstrates the placement of the 20D lenses and the pathway of both the light ray from light source and rays of light which forms a real inverted retinal image. For efficient acquisition of retinal images, sufficient training is required to be able to obtain the optimum filming distance to the point at which the fundus is focused (Iqbal, 2021). Once the desired fundus image is seen from the display screen, the image of the focused fundus is captured, and laterally inverted and upside down.

Moving the smartphone closer to the patient allows for a magnified glimpse of a retinal lesion. This is paired with the 20D lens' relative movement away from the patient. Similarly, the smartphone is positioned at a further distance from the patient in order to have a larger field of view. Different quadrants of the retina can be observed in the same way as in indirect ophthalmoscopy by shifting the patient's gaze (Iqbal, 2021). Stated in Iqbal, (2021), there are two main factors coming from the smartphone that could affect the efficiency of fundus focusing which are the position of camera lens of the smartphone and the location of illumination source.

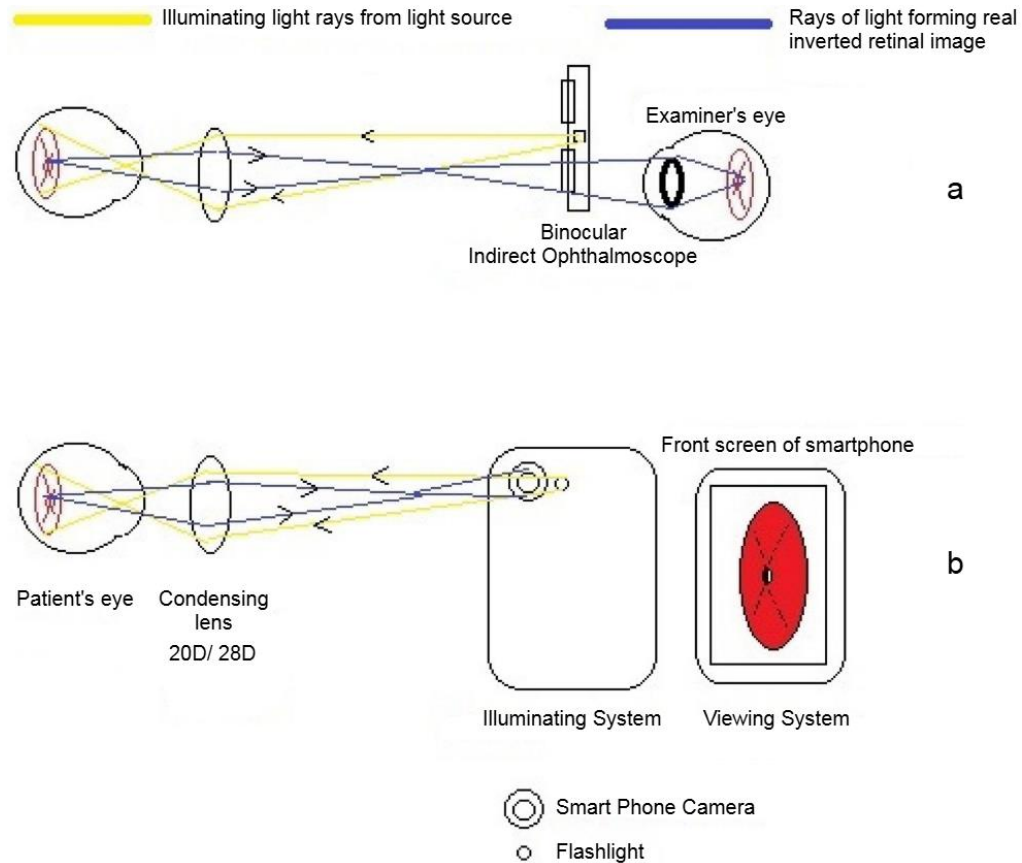


Figure 2.12: Optical principle of (a) indirect ophthalmoscopy and (b) smartphone fundus photography (Iqbal, 2021)

More advanced approaches of retinal imaging involve highly facilitated equipment and require professional manpower. For examples, ocular angiography, fundus autofluorescence, and optical coherence topography. The variety of retinal imaging methods have expanded the capability and accessibility of early detection and screening of diseases. This also applies to the development of improved portable and cost-effective acquisition devices.

2.6 Challenges on Smartphone-based Retinal Image Acquisition

Despite the astonishing advancement in smartphone-based retinal imaging, there are still limitations to the concept. As reported by Ryan et al. (2015), an evaluation of

smartphone-based fundus photography was conducted and have found that descriptions on the techniques of smartphone-based fundus photography are still limited which suggests further research is required. Smartphone-based retinal imaging still lacks validation in defining the extent of its applicability. In a study by Wintergerst et al. (2020b), there are studies that have shown that smartphone-based fundus imaging is still incapable of competing against reference standards in terms of image quality and sensitivity that have tested and reported on some retinal image acquisition devices only to find that most devices are still limited in terms of difficulty in obtaining images, alignment issues, and low accuracies of high rate of ungradable images obtained.

Besides this, despite being able to be utilized by all healthcare workers in general and not just skilled professionals, the use of smartphone-based retinal imaging devices still requires proper training. According to the study by Rajalakshmi et al. (2018), at present, retinal images measured from smartphone-based retinal imaging devices need to be graded by trained graders or ophthalmologists (retinal specialists). A study by Vilela et al. (2018) had also stated that its operation is still sparingly utilized by physicians who are not ophthalmologists due to certain technical difficulties and inadequate training. Furthermore, Jansen et al. (2021) have stated that till date it is uncertain whether non-expert operators can achieve sufficient results comparable to experts. Hence, it is important to identify the factors that affect the quality of images obtained.

From research conducted, there are several difficulties identified when operating a smartphone-based retinal image acquisition device. In the study by Iqbal (2021), difficulties faced include obtaining the right adjustment of filming distance and positioning the device considering the glare from the condensing lens of the device itself as well as external

reflections for example ceiling lights. Dilation also affects the quality of the retinal images. The study by Wintergerst et al. (2020b) have stated that the most available smartphone-based retinal imaging devices require pupil dilation to achieve high quality images but there also exist devices that do not require pupil dilation (Wintergerst et al., 2020b). Pupil dilation affects field of view considerably. For instance, some studies have found that retinal image acquisition conducted on dilated pupils can achieve up to 56-degrees or even more depending on the indirect ophthalmoscopy lens utilized meanwhile the retinal image acquisition in undilated pupils achieves only an estimated 20-degree field of view (Lord et al., 2010; Russo et al., 2015a; Wintergerst et al., 2020b).

2.7 Comparison of Existing Smartphone-based Retinal Image Acquisition Device/Adapter

Researchers and companies involved in clinical equipment manufacture have proposed and developed portable, easy-to-use, and affordable smartphone-based retinal image acquisition device/adapter with the objective of obtaining high-quality retinal images. This section discusses the comparison of existing smartphone-based retinal image acquisition device/adapter in terms of compatible smartphones, maximum field of view, illumination source, dilation dependency, working distance, weight, and mobile application optimization. Table 2.2 shows a summary of existing commercial and non-commercial smartphone-based retinal image acquisition adapter/device and its properties which is initially adapted from Karakaya and Hacisoftaoglu (2020). For research purposes, an unnamed device developed by Myung et al. (2014) that is listed in the comparison is labelled as Alpha.

2.7.1 Smartphone Compatibility

For most devices, selection of compatible smartphones is very limited which is a significant disadvantage. For example, the iNview by Volk are only compatible with iPhone 5, iPhone 6, and iPhone 6s, meanwhile the Pan Optic is only compatible with iPhone 6, and the D-Eye is only compatible with iPhone 6 and iPhone 7. The manufacturer of the Paxos Scope has stated that it functions as a universal mount (Business Wire, 2015) which has an adjustable arm where user can change the distance between the smartphone's camera and the lens as shown in Figure 2.13.



Figure 2.13: Side view of the Paxos Scope used with an iPhone (Mercado et al., 2017)

Among the listed commercial devices, only the Peek Retina, and Choroida Fundus Explorer adapter are universal. Both the Peek Retina and the Choroida Fundus Explorer use

the concept of ‘clip-on’ that allows it to be easily attached onto smartphones. This concept provides the flexibility in positioning the smartphone for camera alignment. As for the listed non-commercial devices, the Alpha adapter was designed following the dimensions of the iPhone 5, but the developers have stated that the adapter can be easily modified to make it universal (Myung et al., 2014). Meanwhile, the CellScope Retina has a fixed dimension for an iPhone 5s (Kim et al., 2018). Both used smartphone models in respective studies are no longer in production and not supported by the latest iOS due to the internal components of the models are unable to handle the iOS effectively. In addition, the camera quality of these models is much lower, considering the higher-quality cameras that latest smartphones models in the current market have. The camera system for latest smartphones provides broader functionality for instance more advanced lighting and magnification control. Furthermore, latest smartphones can be acquired easier compared to older models that are no longer being produced by manufacturers.

Furthermore, it is also observed that most of the listed smartphone-based retinal image devices listed in Table 2.2 are only used or tested with iPhones where no android smartphones were involved which further shows the limitation of existing devices. This may be due to iPhones are more popular among healthcare workers. Several studies on the usage of smartphone in clinical practices such as Franko and Tirrell (2012) and Wyatt and Krauskopf (2012) have found that there are more iPhone users over other smartphones in clinical practice.

2.7.2 Maximum Field of View

According to Pujari (2021), determining whether the maximum field of view provided by a smartphone-based retinal image acquisition device is sufficient or not can be

subjective. It correlates to the end-users' area of interest. For instance, if the area of interest sought by the user is an image of the optic disc, a small field of view is sufficient. Meanwhile, for retina images, they require a bigger field of view that can be further divided into two types which are regular field of view and a wide field, depending on the type, severity, or identifiers of diseases. In contrast, the study by Karakaya and Hacisoftaoglu (2020) have investigated the effect of field of view sizes on diabetic retinopathy detection using deep learning and have found that the efficiency of the detection increases with retinal images that have a larger field of view. This study has compared the field of view of four devices which are iNview, Peek Retina, D-Eye and Pan Optic. As shown in Figure 2.14, the iNview has the largest maximum field of view, which is approximately 50° , meanwhile the Pan Optic, Peek Retina, and D-Eye have significantly smaller maximum field of view that ranges between 20° to 30° . The Choroida Fundus Explorer adapter has several supported lenses which are the Volk 20D and 28D, Nikon 20D, Kashsurg 20D, Heine 20D, and Ocular 20D. 20D lens generally have an approximately field of view of 45° meanwhile 28D has a field of view of 69° . The Paxos Scope has a field of view of 56° (Business Wire, 2015) which is slightly larger when compared to the iNview meanwhile the HEINE-iC2 has a field of view of 34° . Among the commercial devices listed in Table 2.2, the Choroida Fundus Explorer can provide the widest field of view if used with the 28D lens.

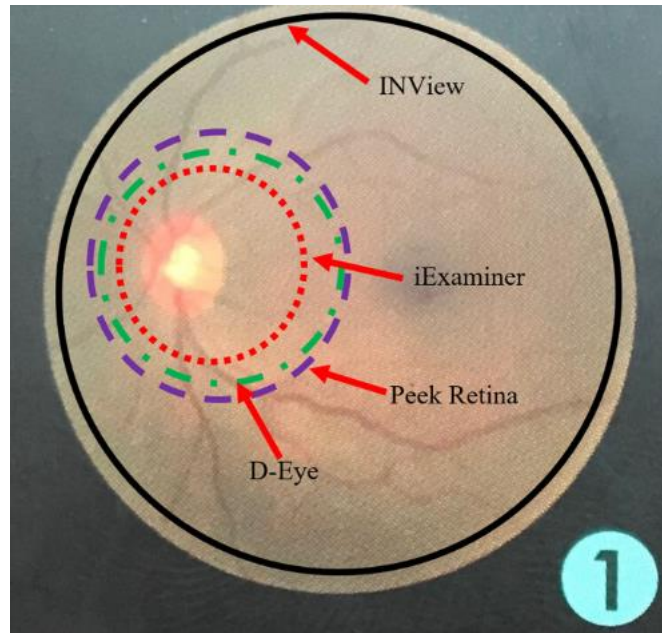


Figure 2.14: Field of view comparison for iNview, Pan Optic (iExaminer), Peek Retina, and D-Eye (Karakaya & Hacisoftaoglu, 2020)

Referring to Table 2.2, two non-commercial devices were listed which are the CellScope Retina and Alpha. The CellScope Retina provides the biggest maximum field of view by implementing automation and software intelligence to generate a retinal photomontage of 100° field of view from five overlapping images (each has a field of view of approximately 50°) that are taken in a rapid sequence. The device was clinically tested for referral warranted diabetic retinopathy and was able to achieve an average sensitivity of 93.3% and specificity of 56.8% which shows that wider field of view results in better performance. In the study by Myung et al. (2014), the lens holder for Alpha was sized to specifically hold a Volk Panretinal 2.2 lens. The lens used are able to provide a maximum field of view of 73° which is considered wide and sufficient for retina viewing. The adapter was initially designed specifically to hold the Volk Panretinal 2.2 lens. It was then modified be readily modified for holding other types of existing lenses. Despite the wide lens

compatibility, it does not determine the image quality taken. Other parameters (Section 2.7.3 until Section 2.7.6) are also evaluated to determine the overall performance.

2.7.3 Illumination Source

There are two types of illumination sources applied in smartphone-based retinal image acquisition device which are external and internal. Internal implies that the device has its own adjustable light source where a retinal image path has been designed specifically to redirect the light source accordingly between the lenses and the retina. External implies that there is a light source mounted on the outside surface of the device, or the device is dependent on the smartphone camera light itself. Based on Table 2.2, the Pan Optic, Peek Retina, HEINE-iC2, and CellScope Retina has an internal illumination source meanwhile the D-Eye, Volk iNview, Paxos Scope, Choroida Fundus Explorer and Alpha requires an external illumination source.

A device's illumination source correlates to the device's dilation dependency. Having its own adjustable light source that redirects the light into the pupil suggests that no dilation is required for some devices as the fundus are illuminated sufficiently. Furthermore, it is beneficial for the illumination source to have different brightness level because this allows less stress on the patient's eyes. A constant level of bright white illumination source may be uncomfortable or constraining for patients which leads to frequent gaze shifts and motions (Kim et al., 2018). The Pan Optic internal adjustable illumination source directly converges to a point at the cornea and diverges around the retina upon turning the device on. To control the level of illumination, the Pan Optic integrates a variation of filter options such as the cobalt-blue filter and red-free filter (Karakaya & Hacisoftaoglu, 2020). The red-free light filter enables a large amount of light meanwhile the cobalt-blue filter enables a small

amount of light. Similarly, the CellScope Retina implements red and white LED illumination system where the white LED has higher intensity compared to the red LED. The red LED is set to be a continuous source where it is used during the process of optimizing the focus on the retina. The white LED is set to be a pulsed source where it is used when capturing the retinal images once the desired camera position has been obtained and the focus on the retina has been optimized (Kim et al., 2018). This helps in reducing discomfort and constraint on the patients' eyes. Similarly, both the Peek Retina and the HEINE-iC2 provides three different levels of intensity which enables the users to use low intensity first during the focus fixation process and the highest intensity when acquiring the retinal images.

In contrast, the D-Eye, Volk iNview, and Choroida Fundus Explorer requires an external illumination source, which would be from the smartphones camera flash to illuminate the retina. One of the disadvantages of relying on the smartphone's camera flash is the position of the camera flash may not be compatible with the ophthalmoscope to provide a retinal imaging path due to the fixed position of the smartphone's illumination source. For example, the Volk iNview has an opening for the illumination source with fixed dimensions that is only compatible with the iPhone 5s, 6, and 6s. This indicates that other smartphones that have their camera flash positioned differently are not usable with the Volk iNview. In contrast, the Choroida Fundus Explorer is designed to work simply as a universal adapter. Unlike the Volk iNview, it does not have a fixed opening for the smartphone's camera flash. Another disadvantage is the brightness of the smartphone camera's flash may not be sufficient to illuminate the retina. Besides this, the brightness of a smartphone's camera flash is uncontrollable which should not be confused with the smartphone's flash. A smartphone's flash brightness level can be adjusted through its settings but is it not possible for the smartphone's camera default application.

2.7.4 Dilation Dependency

Dilation dependency is referring to whether the device requires the patients' pupil to be dilated or not. Referring to Table 2.2, according to respective manufactures, the Peek Retina, D-Eye, HEINE-iC2, Paxos Scope, CellScope, and Alpha require pupil to be dilated before image acquisition meanwhile no dilation is required when using the Pan Optic and Volk iNview. An advantage that non-mydriatic ophthalmoscopes (dilation not required) have over mydriatic ophthalmoscope (dilation required) is removing the possibility of mydriatic-induced angle closure glaucoma in the absence of ophthalmic professionals based on past incidences (Rajalakshmi et al., 2021). The safety of patients who have dilated pupils are exposed to certain risks as it causes pupils to remain unresponsive to light for several hours (Petrushkin et al., 2012). Furthermore, devices that requires no dilation simplifies the application of smartphone-based retinal image acquisition in terms of time taken and reducing the load or equipment to be brought for screening purposes in geographically remote areas. Dilation takes between 15 to 30 minutes which is not practical in emergency situations. Moreover, dilating drops are not always available and there is also a risk of doctors in emergency situations are not familiar with dilating drops (Petrushkin et al., 2012).

However, undilated pupils limits the field of view that can be captured using smartphone-based ophthalmoscopes. Among the devices listed in Table 2.2, the Pan Optic Pro, Peek Retina, and D-Eye have considerably small field of view when compared to other devices. For example, the manufacturer of the Pan Optic has stated that no dilation is required for retinal imaging, but some studies such as the study by Day et al. (2016) have found that it is difficult to obtain retina images that are clinically adequate without dilation. A study by Mecomiskie Bsc et al. (2004) which involved a group of first year medical students trying out both conventional ophthalmoscope and the Pan Optic ophthalmoscope,

have found that it was easier to use the Pan Optic ophthalmoscope on dilated pupils than undilated pupils. Another example is the D-Eye is only able to capture up to a 6° field of view from an undilated pupil but up to 20° field of view from dilated pupils at a distance of 1 cm (Russo et al., 2015b). In addition, the study by Karakaya and Hacisoftoglu (2020) have found that devices that have smaller field of view have lower classification accuracy. A study was conducted by Wintergerst et al., (2018) to analyze how pupil dilation affects the efficiency of smartphone-based fundus photography in terms of image quality for optic nerve head (ONH) imaging and vertical cup-to-disc ratio (vCDR) evaluation using the D-Eye. The study found that the efficiency of smartphone-based retinal image acquisition is significantly higher following dilation when compared to without dilation. Hence, based on the results obtained, the study concluded that dilation is best performed for smartphone-based fundus photography. However, it further stated that in cases where dilation is not possible for example in geographically remote areas where additional ophthalmic resources are not possible to be brought along, smartphone-based retinal image acquisition without dilation can be an alternative.

2.7.5 Working Distance and Weight

There are two main factors that affects the working distance of retinal image acquisition devices which are the weight and length of the lens used (Chalam et al., 2008). Generally, wider field of view enables a longer working distance. The working distance of a device depends mainly on the lenses used in its optical configuration. Longer working distance enables easier composition where users can have more flexibility in terms of positioning the device towards patients. Furthermore, longer working distance may be more comfortable for both users and patients. Besides this, it also ensures the surface of the lenses do not touch the patients' eyelashes hence minimal cleaning is required for each testing.

However, lens that provide wide field of view are heavier, hence it requires proper support to hold the lens which leads to another factor which is the stabilization requirement of the device. For example, the iNview ophthalmoscope uses the 25D lens for its optical configuration which is considerably large in size. To hold the 25D lens, the device uses a large end tube to hold the lens in place. This results in the device to be heavy which requires users to rely on patient's forehead as support for further stabilization. The wide field of view of the iNview compensates the weight of the iNview, which is known to be the heaviest smartphone-based ophthalmoscope in the market (Karakaya & Hacisoftaoglu, 2020). Referring to Table 2.2, the Peek Retina, Pan Optic, and D-Eye have a small field of view of 30°, 25°, and 20° respectively but all three devices have a working distance of 22 mm. Meanwhile, devices such as the iNview, HEINE-iC2, and Alpha that have wider field of view (>30°) has a longer working distance which are 65 mm, 30 mm, and 144 mm respectively. The Paxos Scope has an adjustable lens-to-smartphone sliding shaft of 146 mm that allows the working distance to be adjusted accordingly. From this observation, it is concluded that devices that have wider field of view allows longer working distance.

2.7.6 Mobile Application

The main advantage of a device having its own mobile application is it allows advanced control on the device and efficient data transfer over the internet. Most of the devices listed in Table 2.2 has their own mobile application except the Alpha which uses an existing application known as Filmic Pro that allows user to control the level of brightness and focus alignment. The iExaminer application developed by Welch Allyn has a simple GUI that requires user to sign up for an account. An individual profile can be created for each profile, allowing a systematic data collection and storage. Besides this, the iExaminer also allows direct data transfer over the internet. One disadvantage of the iExaminer is that

it only has a capture mode in video where images can only be obtained by stills from the video recorded which lowers the quality of the retina images taken. Furthermore, only five images can be saved for each eye in each session.

In contrast, the application for the Peek Retina and D-Eye has an advantage of having two capture modes, which are recording videos, or capture multiple retinal images. The image capture mode allows user to take an image of the retina directly so it will provide higher image quality when compared to the quality of images taken as still images from a recorded video. Hence, despite devices have their own mobile application, its efficiency in retinal imaging also depends on the features that are provided.

2.7.7 Summary on Existing Smartphone-Based Retinal Image Acquisition Device

From research conducted, most existing devices have restricted usability. For instance, the Pan Optic, D-Eye, iNview, and HEINE-iC2 are only compatible with Apple's smartphones, which are also from older generations for instance the iPhone 5, 6, 7, and 8 which are no longer in production and the current iOS operating system is also not supported on these models. This suggests that future smartphone-based retina image acquisition devices should be made universal, where the adapter to hold the smartphones is compatible to most smartphone models which helps to broaden its usability. Besides this, earlier smartphone-based retinal image acquisition devices such as the D-Eye (2015), Pan Optic (2016), and Peek Retina (2017) provides a small field of view (less than 30°). Studies such as the study by Karakaya and Hacisoftaoglu (2020) have shown that size of field of view affects the efficiency of the disease detection. Devices such as the iNview, Paxos Scope, and CellScope Retina have shown that a wide field of view provides higher quality of retinal images. As for dilation dependency, most of existing smartphone-based retinal image

acquisition device requires pupils to be dilated. Despite some manufactures stated that their device can be used without pupil dilation, studies have shown that dilated pupils evidently make it easier to use their device and allows a wider field of view (Day et al., 2016; McComiskie Bsc et al., 2004; Wintergerst et al., 2018). However, the safety risk of pupil dilation remains as a concern and the convenience of not having to involve pupil dilation (Petrushkin et al., 2012; Rajalakshmi et al., 2021). Furthermore, having an internal illumination source have shown to be a common characteristic among existing smartphone-based retinal image acquisition devices. An internal illumination sources provides general advantages over an external illumination source for example a smartphone's camera flash is not adjustable through the camera application that it comes with, but an internal illumination has its own control system. Secondly, a smartphone's camera flash may not be sufficient to provide a retinal imaging path. A similar case for the working distance and weight of a device, a longer working distances provide general benefits such as flexibility and comfortability, however, a longer working distance typically involves lenses of higher dioptric power, which are on the heavier side, hence requires more stability. Last but not least, among existing smartphone-based retinal image acquisition devices listed in the study, only the Alpha does not have its own mobile application. In general, devices that have their own mobile application allows efficient data transfer between platforms and have certain advanced control. However, the application used by the Alpha, which is the Filmic Pro was able to allow user to control the focus alignment and brightness of flash.

Table 2.2: Comparison of existing smartphone-based retinal image acquisition adapter/device properties

	Device Name	Main Specifications								Main Disadvantages
		Type	Smartphone Compatibility	Max. Field of View	Illumination Source	Dilation Dependency	Working Distance (mm)	Weight (grams)	Mobile Application	
Commercial	Peek Retina by Peek Vision	Full device	Universal	30°	Internal	Required	22	30	Own mobile application	• Small FOV • Requires dilation
	Pan Optic by Welch Allyn	Full device	iPhone 6/6s/6 plus only	25°	Internal	Not required	22	390	Own mobile application	• Limited smartphone compatibility • Small FOV • Works better with dilation
	D-Eye by S.r.l	Full device	iPhone 5/5s/6/6s/6 plus/6s plus/SE/7 only	20°	External (from smartphone)	Required	22	25	Own mobile application	• Limited smartphone compatibility • Small FOV • Requires dilation
	iNview by Volk	Full device	iPhone 5/6/6s only	50°	External (from smartphone)	Not required	65	332	Own mobile application	• Heavy due to large end tube to hold lens which affects stability

Non-commercial										Limited smartphone compatibility
	HEINE-iC2 by Heine Optotechnik	Full device	iPhone 5/5s/SE/6/6s/7/8 only	34°	Internal	Required	30	300	Own mobile application	- Limited smartphone compatibility - Requires dilation
	Paxos Scope by Digisight Technologies	Adapter	Universal	56°	External (built in adapter)	Required	146 (adjustable, max 146 mm)	Not stated	Own mobile application	Limited smartphone compatibility
	Choroida Fundus Explorer by Choroida	Adapter	Universal	69° (interchangeable lens)	External (from smartphone)	Not stated	Depends on lens used	60	None	Null studies conducted on device
	CellScope Retina by Kim et al., (2018)	Full device	iPhone 5s only	100°	Internal	Required	Not stated	310	Own mobile application	- Limited smartphone compatibility - Requires dilation
	Alpha by Myung et al. (2014)	Adapter	iPhone 5 only	73° (specific lens)	External (from smartphone)	Required	144	Not stated	Used Filmic Pro	- Limited smartphone compatibility - Requires dilation

2.8 Optical Configuration of Retinal Imaging

Retinal image acquisition devices involve an optical configuration that provides the retinal imaging path between the capturing device and the retina. Understanding the positioning of the lenses and other components inside the configuration is important in ensuring images of the retina can be formed. A study by (Russo et al., 2015a) explained on the optical configuration of smartphone-based direct ophthalmoscopy using the D-Eye device developed by D-Eye S.r.l. Figure 2.15 shows a collapsed view of the D-Eye module which was designed using Rhino 3D software. In order, the device components are glass platelet (A), with imprinted negative lens (A'), photo-absorbing wall (B), beam splitter (C), mirror (D), plastic case (E), diaphragm (F), polarized filters (G,H), flash a camera class (J,I respectively), and magnetic external ring (K). Referring to Figure 2.15, retinal images are acquired using coaxial illumination and imaging paths by utilizing a beam splitter (C). A glass plate with a front negative lens engraved on it acts as the top cover which is positioned closest to the eye. The front negative lens is responsible for shifting the smartphone's focus from infinity to around -8cm, allowing it to utilize the smartphone's autofocus range of about 18 diopters. This acts as a compensation system for refractive error adjustment ranging from -12 to +6 diopters. The blue arrow located near the outermost layer represents the path of light meanwhile the red arrow represents the path of fundus imaging.

The illumination source is first conveyed into the eye by a mirror (D) and the beam splitter (C) which is similar to the principle used in direct ophthalmoscope. The mechanical components responsible for removing reflections and flares are the photo-absorbing wall (B), diaphragm (F), and the polarizing filters (G and H). This structure represents a cross-polarization design (Russo et al., 2015a). The quality of the retinal images taken with the D-Eye have a small field of view and blurry as shown in Figure 2.16.

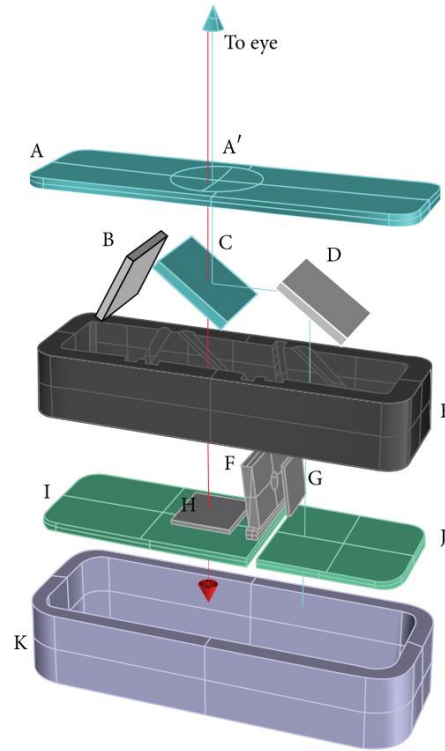
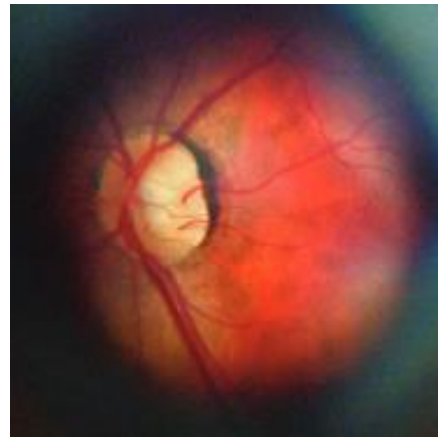


Figure 2.15: A collapsed view of the D-Eye module (Russo et al., 2015a)



(a)



(b)

Figure 2.16: Retinal images taken with the D-Eye (Russo et al., 2015a)

Another example of a smartphone-based retinal acquisition device optical configuration is the CellScope Retina by Kim et al. (2018). This device is an improved version of the Ocular CellScope developed by Maamari et al. (2014). Referring to Figure 2.17, the main components used for the optical configuration in the CellScope Retina are ophthalmic lens, wire grid beamsplitter, relay lens, polarizers, condenser lens, mask, diffusers, and collector. The illumination source used for the device is a multi-colour LED array, which is powered by a custom printed circuit board, consisting of a rechargeable battery and Bluetooth relay. The polarizing wire grid beam splitter is responsible in illuminating the retina using the polarized light and reduce any unwanted reflections. Without the polarizers, the nature of the illumination light that gets scattered inside the configuration would cause unwanted reflections. In other words, the polarizers have a significant role in ensuring clear retinal images can be taken. The light reflected by the beam splitter is passed through a 54D ophthalmic lens that allows the formation of an annulus at the surface of the cornea. An aspheric condenser lens is positioned in the configuration that allows it to transmit light from the multi-colour LED array to the diffuser through several layers of components; a polarizer, an annular mask of 8 mm and 15 mm inner and outer diameter respectively, and a condenser lens of focal length 50 mm.

In the study Kim et al. (2018), the CellScope Retina was used for diabetic retinopathy (DR) screening for performance evaluation. Figure 2.18 shows an example of the retina images taken with the CellScope Retina. The device was able to acquire high-quality retinal images. However, it is important to take into consideration that the CellScope Retina system incorporates automation and software intelligence tools that have significant roles in improving the quality of image taken. The automated system and algorithm integrated in the device allows five overlapping images to be taken in sequence rapidly where each image has

a field of view of approximately 50° and merged, producing a wide overall image (approximately 100° field of view).

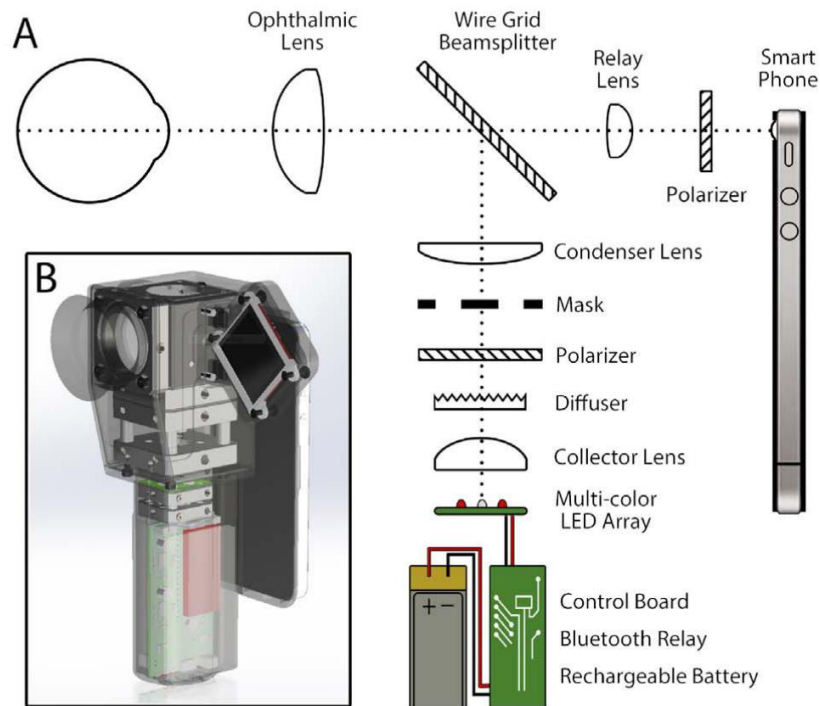


Figure 2.17: Schematic diagram of the optical configuration of CellScope Retina (Kim et al., 2018)

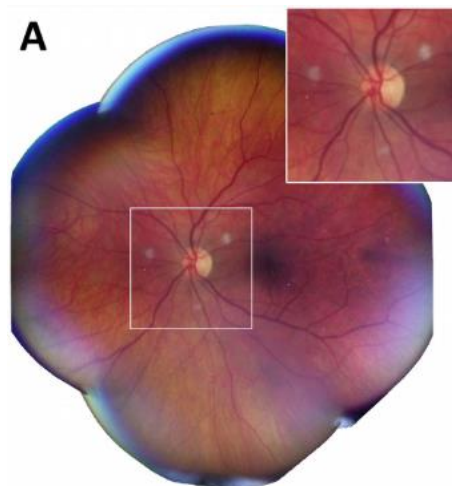


Figure 2.18: An example of a retinal image taken with the CellScope Retina (Kim et al., 2018)

An example of optical configuration that had allowed good quality fundus images is the optical configuration developed by Tran et al. (2012) for their handheld fundus camera prototype. Figure 2.19 shows the optical configuration of the prototype that is labelled with respective modules and Table 2.3 summarizes the description of each module. The housing for the optical configuration in Tran et al. (2012) was designed using a software named Rhino3D. The fundus camera's front objective lens used is the 22D indirect ophthalmic lens which features several advantageous characteristics. Besides having a field of view of 60° and a large and clear aperture of 52 mm which allows better light transmission, the lens is also layered with advanced anti reflection coatings. With reference to Figure 2.19, with a working distance of 39 mm, the front objective lens is mounted co-axially with the consumer camera's front lens meanwhile the distance between the objective lens and the consumer camera is 125 mm. Macro-lenses were implemented in ensuring the retinal image formed by the front objective lens is able to fill the whole camera sensor and to increase the camera's up-close focusing ability. In the study, the mechanism of the optical configuration was separated into three sections, which are fundus imaging, fundus illumination, and image artifact reduction. When compared to the retinal images taken with the D-Eye, the quality of the retinal images taken with the prototype were much better as shown in Figure 2.20. (Tran et al., 2012).

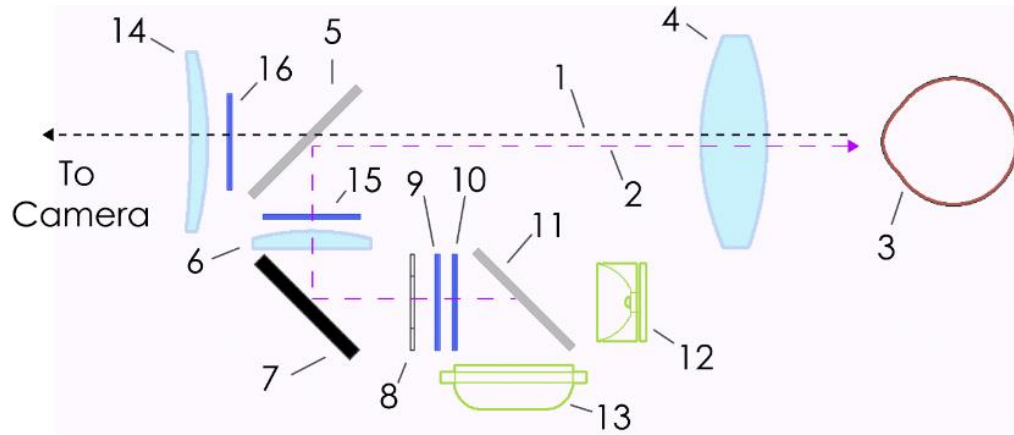


Figure 2.19: Optical configuration of handheld fundus camera prototype (Tran et al., 2012)

Table 2.3: Description of each module in the optical configuration

Module	Description	Module	Description
1	Co-axial imaging	9	Holographic diffuser
2	Illumination path	10	UV filter
3	Human eye	11	Beam splitter
4	Front objective lens	12	Visible LED unit
5	Beam splitter	13	Xenon flash tube
6	Condensing lens	14	Macro lens
7	Mirror	15	Linear polarizer
8	Image mask	16	Analyzer polarizer

The three optical configurations had several components in common such as a beam splitter to create a co-axial illumination system, and a set of polarizers and diffusers to remove any unwanted reflection and to focus the illumination source onto the retina, specific selection of lens. Furthermore, specific types of lenses were used as each type of lens has a significant role in terms of field of view, aperture size, and the coatings applied. Besides this, it was also observed that multiple lenses are used together in their optical configurations in creating the retinal imaging path such as the macro lens, ophthalmic lens, condenser lens, and relay lens.

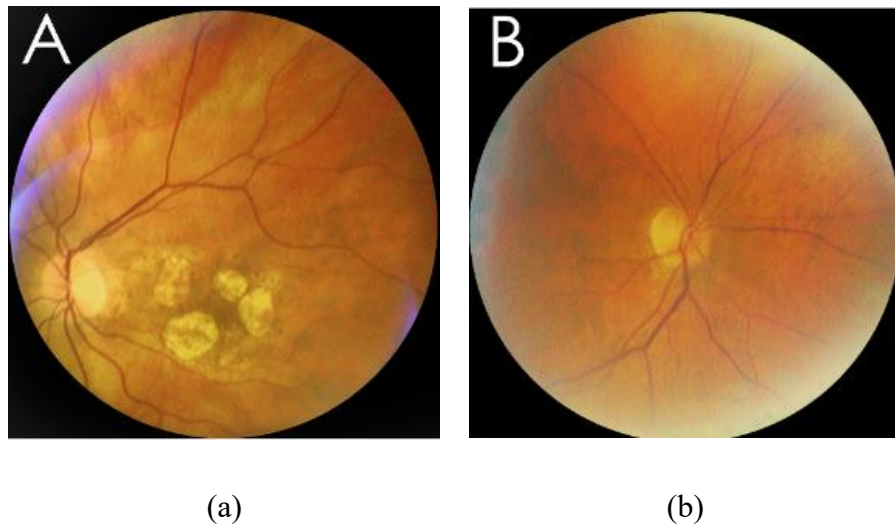


Figure 2.20: Unilateral retinal images taken with the prototype (a) geographic atrophy and (b) a healthy fundus (Tran et al., 2012)

Hence, optical configurations for smartphone-based retinal image acquisition devices can be complex, especially devices that have their own illumination source that require specific components to ensure the retinal imaging path is established as required. However, for adapters, modifications affecting the optical configuration that can be done are limited. For instance, the Paxos Scope, Choroida Fundus Explorer, and Alpha are adapters that mainly function to hold a smartphone and a single piece of lens. Adapters have a much

simpler optical configuration where no components such as beam splitters, mirrors, or polarizers are in their overall system. Despite that, adapters are still considered as smartphone-based retinal image acquisition devices and have shown their great potential (Collon et al., 2020; Mercado et al., 2017; Myung et al., 2014).

2.9 PanOptic Ophthalmoscope

Several studies on the Pan Optic were conducted that discusses on its current state and efficiency in acquiring retina images (Day et al., 2016; H. Hu et al., 2020; McComiskie Bsc et al., 2004; Patel et al., 2019; Petrushkin et al., 2012; A. Tan et al., 2010) and have obtained different findings. The Pan Optic provides approximately a field of view of 25° which is considered small due to its optical configuration as shown in Figure 2.21. The field of view is small because the high-power Plano convex lens used in the device diverges the illumination source widely hence only a small amount of light can enter the pupil resulting in a poor red reflex (A. Tan et al., 2010).

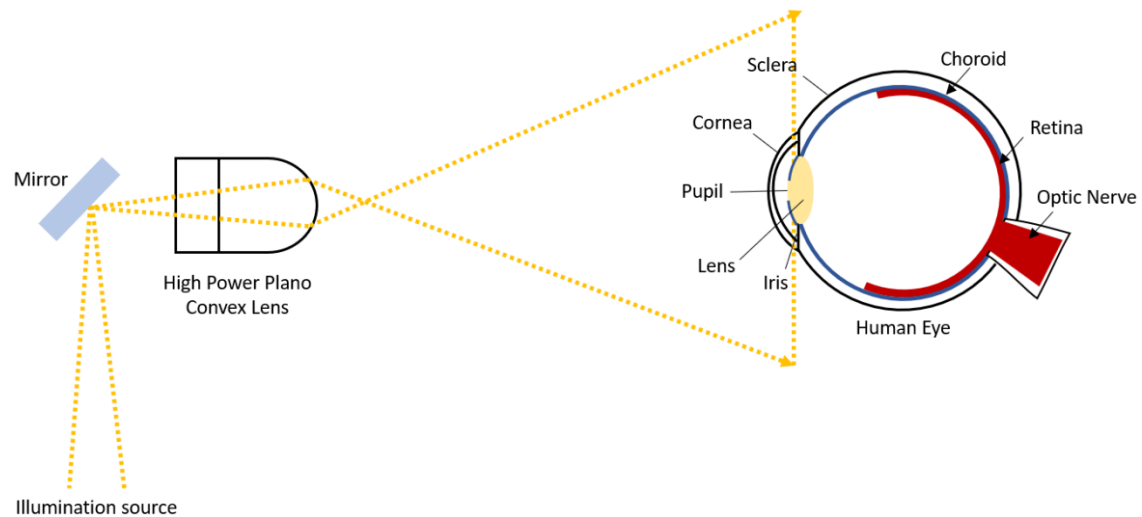


Figure 2.21: Redrawn schematic ray diagram of Pan Optic ophthalmoscope (A. Tan et al., 2010)

The developer of the Pan Optic Ophthalmoscope has stated that the device allows retinal imaging without dilation. However, the study by Day et al. (2016) have found that field of view provided by the ophthalmoscope was not large enough, where even the optic disc and macula was not seen in any of the images taken and suggested further testing to determine the best way to utilize the Pan Optic Ophthalmoscope optimally. The study by Karakaya and Hacisoftoglu (2020) have also found that the Pan Optic Ophthalmoscope has the lowest classification accuracy of 61% when compared to other existing commercial smartphone-based retinal image acquisition devices such as the iNview, Peek Retina, and D-Eye. However, the study by McComiskie Bsc et al. (2004) involving eight medical students have provided statistical analysis that shows the Pan Optic Ophthalmoscope is preferred over the conventional ophthalmoscope for the ‘ease-of-use’ despite the quality of image acquired were much poorer. The study by H. Hu et al. (2020) have used the Pan Optic Ophthalmoscope together with a slip-lamp translator and a rest system for patient’s chin and head which greatly improves stability but caused increment in the cost overall. In addition, the study by H. Hu et al. (2020) have also stated that the software in the iExaminer

application caused the resolution of fundus images acquired is low. The iExaminer application also captures images by selecting stills from video recorded which also lowers the quality image taken. This suggests the possibility of better image quality taken if the image is taken directly and using the smartphone's default camera application. Furthermore, the study by Petrushkin et al. (2012) have also compared the performance of Pan Optic Ophthalmoscope and a direct ophthalmoscope and have found that the Pan Optic Ophthalmoscope has higher sensitivity and specificity. Hence, the Pan Optic Ophthalmoscope still shows its potential as a portable and low-cost smartphone-based retinal image acquisition device which suggest that there is still room for improvement. Table 2.4 summarizes the optical and mechanical parameters of the Pan Optic ophthalmoscope according to its manufacturer and Karakaya & Hacisoftaoglu (2020).

Table 2.4: Main specification of Pan Optic ophthalmoscope

Properties	Description
Field of view	25°
Working distance (mm)	22
Dilation dependency	Not required (according to its manufacturer)
Smartphone compatibility	iPhone 6/6s/6 plus only
Application	Has own application named as iExaminer
Type of data collected	Image stills from recorded video

Cost	Considered to be much affordable when compared with conventional retinal imaging devices
Other features	• Has a focusing wheel to adjust focus level • Has an aperture/filter dial to control aperture level or type of filter

Based on the specifications listed in Table 2.4, the development procedure and experimental design proposed are constructed with the objective to determine the measures that could be done to optimally utilize the Pan Ophthalmoscope and improve mainly on the smartphone compatibility, and type of data collected while maintaining its primary features such as its practically, portability, and low-cost.

As for the imaging system, the Pan Optic Ophthalmoscope comprises of three main lenses which are objective lens, the imaging lens, and eye piece lens (Goldfain et al., 2001). The objective lens is responsible in focusing the parallel light beam reflected from the patient's eye to the retina image focal plane. The objective lens has a focal length of 25 mm and a diameter of approximately 25 mm. The eye piece is mainly for user viewing and can be replaced with image sensors for direct data collection (Goldfain et al., 2001). The imaging lens helps in projecting an internal image from the objective lens focal plane to eye piece focal plane at a magnification of 0.6x. The imaging system has an aperture stop which functions to allow light needed to form a retinal image to pass through while blocking unwanted light that does not form the retinal image. This helps to reduce the amount of glare and improve the quality of image. Working distance of an ophthalmoscope is defined as the distance between the front end of objective lens and patient. The Pan Optic ophthalmoscope

has a working distance of 22 mm and a maximum field of view of 25° (Karakaya & Hacisoftaoglu, 2020). Figure 2.22 shows how the Pan Optic ophthalmoscope is typically used with its adapter that has a fixed dimension to only fit the iPhone 6, iPhone 6s, and iPhone 6 plus models only. In addition, an eyecup is also provided by the manufacturer where it was suggested that the eyecup is compressed halfway against the patient's brow to provide the largest view.



Figure 2.22: Assembly of PanOptic with its original adapter (Baxter, n.d.)

2.10 Chapter Summary

In this chapter, firstly, the history of ophthalmoscope, internal anatomy and area of interest of the retina, and the differences between direct and indirect ophthalmoscopy was described. This chapter specifically focuses on the different retinal imaging systems, the concept of smartphone-based retinal imaging system, comparison of existing smartphone-

based retinal image acquisition device in identifying the ideal and optimum internal and external parameters of a smartphone-based retinal image acquisition device, and optical configurations used in existing devices in creating a retinal imaging path. Last but not least, this section also discussed the theoretical analysis of the optical configuration of Pan Optic ophthalmoscope and its overall system.

CHAPTER 3

METHODOLOGY

3.1 Overview

In this chapter, the proposed methodology of the project and the relevant materials are described. An overview of the process flow is detailed in this section. The focus will be on development of proposed adapter and method used to conduct the performance evaluation of developed adapter.

3.2 Project Materials and Software

For this project, the Pan Optic ophthalmoscope developed by Welch Allyn was selected to be experimented and improved based on research conducted. A personal computer with the specifications of Intel(R) Core™ i5 12400F processor for CPU, 16GB for Random Access Memory (RAM) and 64-bit operating system powered by Windows 10 is utilized for this project. Besides this, five software have been selected to perform this project which are AutoCAD 3D, Autodesk Inventor, Ultimaker Cura, Microsoft Excel and IBM SPSS. Furthermore, a few tools and materials are used for this project. For 3D-printing, Ender 3 V2 3D-printer by Creality is used along with polylactic acid (PLA) as the filament. For measurement purposes, a pair of Vernier Caliper is used.

3.2.1 Software

AutoCAD 3D has been selected to perform the adapter designing because of its easy user interface and broad utilities. AutoCAD 3D by Autodesk is a three-dimensional (3D) computed-aided design (CAD) software specialized for design and technical documentation for engineers, architects, construction professionals. It allows users to create 2D geometries

and 3D models in different forms such as solids, surfaces or mesh, with precision and flexibility, besides allowing a clear visualization and representation of modelled objects. The software consists of seven industry-specific tools which are 3D-mapping, electrical design, mechanical design, plant design, raster images conversion, architecture layout drawings, and scanned images addition. Besides this, it also provides automation features such as blocks addition, counting objects, drawing comparisons, and more that increases workflow efficiency. The software itself is customizable with add-on applications and application programming interface (API).

The Ultimaker Cura is an open-source software used to convert 2D or 3D drawings files or any similar proprietary (closed-source) files into a readable format for the 3D printer. This process is more known as slicing. The software provides users a range of controls and settings to optimize the slicing and printing processes. In addition, there are plug ins available that can be used with the software that gives the software have additional functions such as calculating the optimal orientation for an object, and calibrate dimensions such as the layer height, wall thickness, and infill density. This allows maximum optimization for production. The Ultimaker Cura supports a variety of 3D formats namely G-Code (.gcode), object file (.obj), stereolithography (.stl), 3D manufacturing format (.3mf), and more.

To perform the stress test, the AutoDesk Inventor has been selected. Similarly, Autodesk Inventor is also a CAD engineering software specialized for 3D mechanical drawings, assemblies, visualization, simulations, and documentation that is developed by Autodesk. However, unlike the AutoCAD 3D software, the Autodesk Inventor is a parametric, feature-based system where everything is governed by parameters, dimensions, or relationships. The Autodesk Inventor provides users with more flexibility as a parametric

modeler where users have control over their design intent by setting determining the parameters, dimensions, and relationships. Furthermore, users can test the associativity between different parts or assemblies. This is useful for builders to simulate their product before production.

Last but not least, Microsoft Excel and IBM SPSS are used to conduct statistical analysis. Microsoft Excel is a software designed to organize, format, and analyze data in the form of spreadsheets. It provides various tools to calculate, compute, and visualize data. For example, Visual Basic for Application (VBA) is a programming tool in Microsoft Excel that applies various numerical method. Meanwhile, IBM SPSS is a software used for statistical analysis. Similar to Microsoft Excel, IBM SPS provides a wide variety of tools to conduct data management and analysis, data visualization, data validation, and many more.

3.2.2 Tool and Materials

To print the adapter, the Ender 3 V2 3D-printer by Creality will be used together with polylactic acid (PLA) as the filament. The Ender 3 V2 3D-printer uses fused filament fabrication (FFF) and fused deposition modelling (FDM) technology. The 3D-printer supports three types of materials which are polylactic acid (PLA), thermoplastic polyurethane (TPU), and polyethylene terephthalate glycol (PETG). It uses an SD card to transfer files and has a 4.3-inch LCD display for user navigation. Other tools such as a pair of Vernier callipers were used to obtain accurate measurements.

3.3 Project Workflow

This section discusses on the proposed general workflow for this project. The first step of this project is reviewing existing smartphone-based retinal image acquisition devices that are either on the market or non-commercial to identify the specifications, advantages,

and disadvantages. This acts as a guidance or benchmark during the selection of properties of proposed device. The second step is preparing the project development procedures and experimental design. The procedure will include four main processes which are Adapter Designing and Printing, Stress Simulation, User-End Survey, and Eye Examination which will be discussed in the next section. Following that, the project will commence with the actual development and testing of proposed device, followed by simulations and data collection. Then, the project proceeds with analysing the data and results collected where all critical findings will be discussed. Finally, the device is finalized, and the project is concluded. Figure 3.1 shows a flowchart representing the workflow of the project.

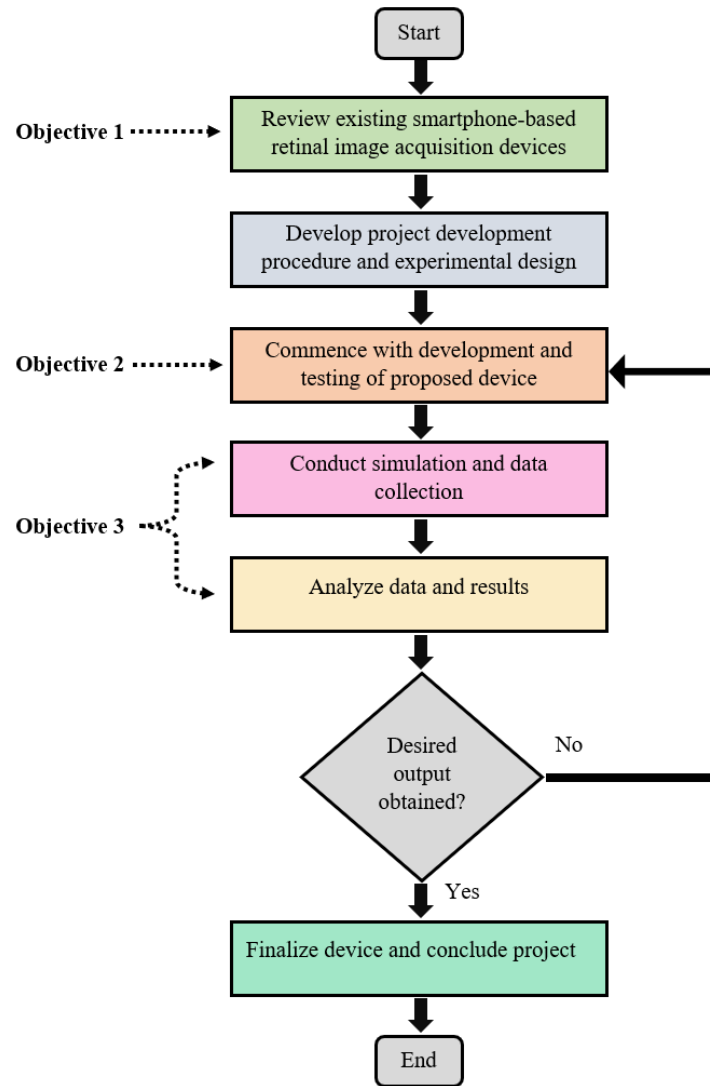


Figure 3.1: Thesis workflow

3.4 Requirements of the Proposed Adapter

This section describes the requirements for the proposed adapter which includes its purpose and functionality. The most important feature that the proposed adapter must include is universal smartphone compatibility since the original adapter is only usable with the iPhone 6 series. This would allow users to employ the PanOptic with any smartphones that they already own. Besides this, the general ergonomic aspect of proposed adapter is also considered to ensure that the developed adapter with minimal to no discomfort. The

comfortability level that will be experienced by the users of the proposed developer also determines the suitability of the proposed developed and overall stability. In addition, the ease-ness of assembly and usage which directly affects the usability and repeatability of the proposed adapter is also considered. Furthermore, ideally, the assembly for the proposed adapter should be easy for experts and workers in the clinical field. In addition, as the PanOptic is intended to be used in non-ideal clinical setting, for instance, in geographically remote areas, the proposed adapter should also be portable and practical for easy transportation.

3.5 Development of the Adapter

This section discusses on the methods used to develop the adapter which also discusses on the existing smartphone-based retinal image acquisition device, the Pan Optic Ophthalmoscope. The development of the adapter consists of three main processes which begins with reverse engineering, followed by adapter designing, and lastly adapter printing. Figure 3.2 shows the flowchart that summarizes the process of adapter development. The development procedure and experimental design proposed are constructed with the objective to determine the measures that could be done to optimally utilize the PanOptic ophthalmoscope and improve mainly on the smartphone compatibility, and type of data collected while maintaining its primary features such as its practically, portability, and low-cost. Since the placement of the lenses inside the configuration of the Pan Optic ophthalmoscope are considered as the fixed variable, the project is limited to external modification only on the Pan Optic such as the adapter itself.

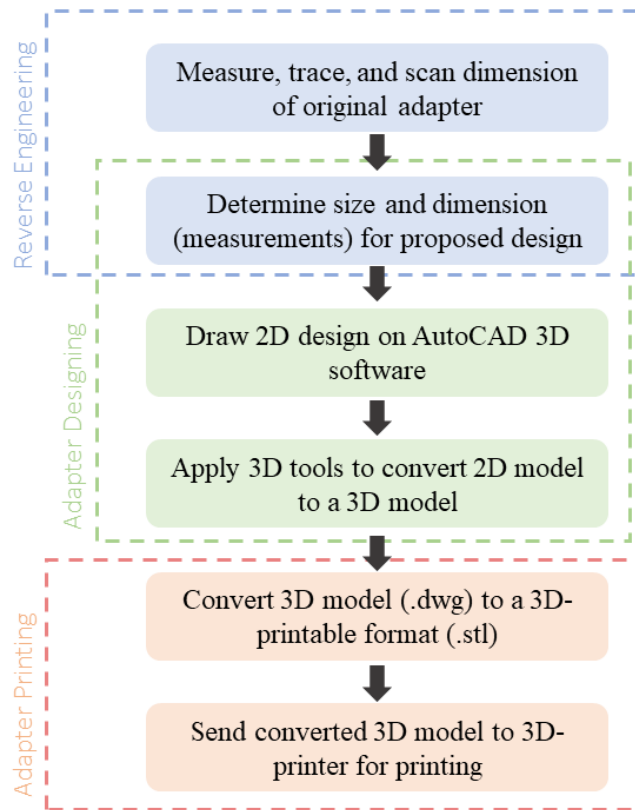


Figure 3.2: Adapter development workflow

3.5.1 Reverse Engineering and Adapter Designing

The main criterion of the proposed adapter is to have a universal smartphone compatibility. As stated previously, the original adapter provided by the manufacturer of the Pan Optic ophthalmoscope could only be used with the iPhone 6 series. The iPhone 6 series have been long discontinued and can no longer be obtained. Without a universal smartphone adapter, it would not be possible to use the Pan Optic. Hence, the first step in developing the universal adapter is reverse engineering to understand the mechanism of the original adapter and identify the required changes. In general, reverse engineering refers to the process of extracting significant information from an existing object and hence the information is utilized to create a new model (Saiga et al., 2021). According to Helle & Lemu (2021),

reverse engineering is employed for a variety of reasons for instance when a product documentation is lost, or the product is no longer in production, the product needs a digital computer-aided design (CAD) model for future modifications or improvements, and more. Thus, this method is useful in developing the proposed universal adapter. In addition, this helps to determine the mechanism of the ophthalmoscope and how the adapter is attached to the ophthalmoscope.

For this purpose, the adapter is divided into two main parts which are the lens cap and the body as shown in Figure 3.3 and Figure 3.4. Referring to Figure 3.3, the existing adapter provided by the developer of the Pan Optic Ophthalmoscope consists of two parts, which is the main phone holder labelled as A and the connector labelled as B. The connector provides extra support and grip between the phone and the device. The main holder comprises of the lens cap and the main body. Figure 3.3(b) shows how the adapter is assembled onto the ophthalmoscope. Figure 3.4 shows the front view and side view of the adapter that shows that the phone holder has a fixed dimension for an iPhone 6 which is 131.1 mm in height, 67.0 mm in width, and 6.9 mm in depth. Besides this, the distance between the surface of the eye piece lens and camera opening of the original adapter was measured to be approximately 12.4 mm.



Figure 3.3: Original adapter of Pan Optic ophthalmoscope. (a) Main phone holder labelled as X and connector labelled as Y, (b) Assembly of the adapter with the ophthalmoscope



Figure 3.4: Different viewing of the original adapter. (a) Front view, (b) Side view

Initially, manual measurements were conducted in determining the dimension of the lens cap using tools such as the Vernier Callipers. However, upon measuring, the lens cap has a specific shape and have different thickness in certain parts of the lens cap. Hence, tracing was employed. The measurement obtained from tracing is then scanned into the AutoCAD 3D software to generate a CAD model. However, the values measured manually using the Vernier callipers was kept obtaining approximate values for measurement changes if necessary. Once the CAD model of the lens cap is obtained in 2D, it is converted into a 3D model using the 3D tools available in AutoCAD 3D. The completed 3D model which will be in *.dwg* format is then converted to a printable format known as *.stl* for the 3D-printer to recognize. This conversion process is known as ‘slicing’. The process of drawing the 2D and 3D models, and format conversion is repeated until the desired dimension of lens cap is achieved to proceed with proposing designs for the body of the adapter. Figure 3.5 shows a representation of the traced lens cap dimension which was developed into a CAD model meanwhile Figure 3.6 shows the technical drawing of the finalized lens cap.

The completed 3D-model of the lens cap was printed to test with the PanOptic which involved several adjustments and printed prototypes. Only once the right dimension of the lens cap was obtained, the main body of the adapter was designed. The finalized lens cap has different thickness and diameter at the top and bottom. The top has a thickness of 3.13 mm meanwhile the bottom has a thickness of 4.83 mm. The top vertical and horizontal inner diameter is 36.50 mm and 34.74 mm respectively meanwhile the bottom vertical and horizontal inner diameter is 35.58 mm and 33.90 mm.

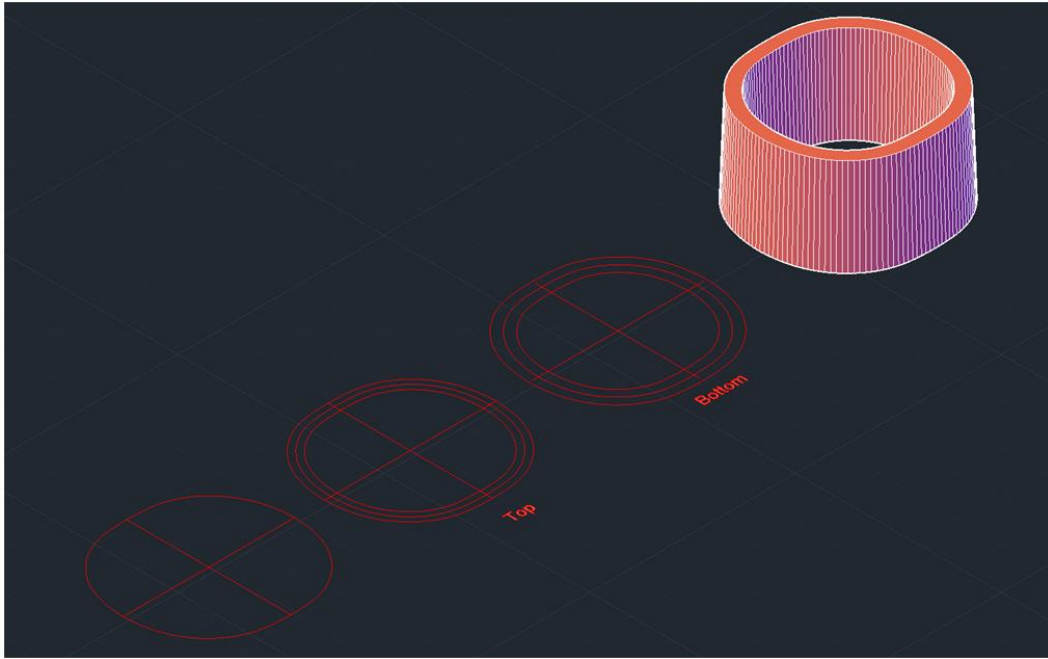


Figure 3.5: Southwest view of lens cap traced and developed into a CAD model

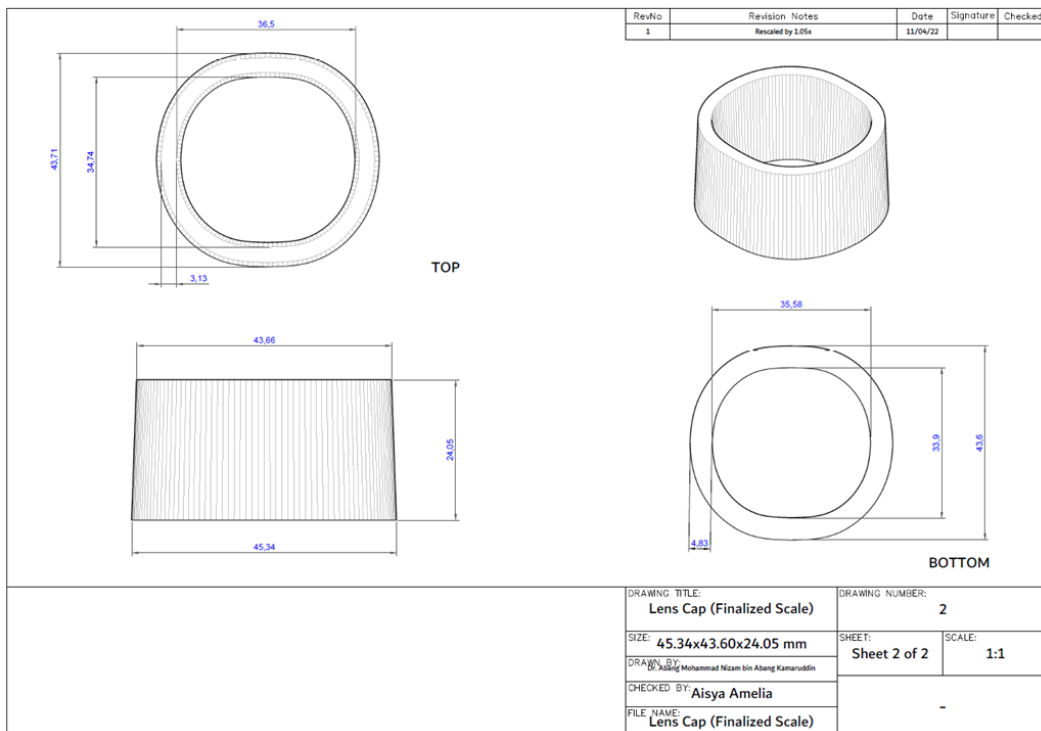


Figure 3.6: Technical drawing of finalized lens cap

Designing the body of the adapter involves the same steps except the tracing and measuring using the Vernier callipers. The size and dimension of the adapter's body is measured with reference to the average dimension of a smartphone. The designing process of the body had resulted in four prototypes produced where preliminary tests were conducted to test the stability and usability of each prototype when assembled with the PanOptic and a smartphone. For this purpose, several smartphones were employed and compared which were an iPhone 11, Huawei Y9 and Google Pixel 6. From the testing, the position of the main camera for all smartphones had no issues in camera alignment with the PanOptic ophthalmoscope. In terms of camera specifications, when compared to the iPhone 6 which only provides a camera resolution of 8MP, all tested smartphones outperform it. The Google Pixel 6 is able to provide the highest image quality as it features a camera resolution of 50MP (megapixels) meanwhile the iPhone 11 and Huawei Y9 only provides 12MP and 13MP respectively. Besides this, for video recording, the iPhone 6 and Huawei Y9 are capable in providing a standard resolution of 1080 pixels, with the iPhone 6 have a higher rate of frame-per-second (fps) at 60fps, meanwhile the Huawei Y9 at only 30fps. However, both the iPhone 11 and Google Pixel 6 are able to provide the highest resolution of 4000 pixels at 60fps, and 1080 pixels at 240fps. A higher rate of frame-per-second provides a smoother motion and higher resolution enables more details captured which are both beneficial during retinal imaging. From the comparison, the Google Pixel 6 is selected to be used in proposed clinical testing. Table 3.1 summarizes the camera specifications between the iPhone 6 and the tested smartphone models according to respective manufacturers.

Table 3.1: Comparison of camera specifications between iPhone 6 and selected smartphones

Specifications	Original	Tested Smartphones		
	iPhone 6	Huawei Y9	iPhone 11	Google Pixel 6
Main camera (MP)	8	13	12	50
Video recording (pixels/fps)	1080/60, 720/240	1080/30	4000/60, 1080/240	4000/60, 1080/240

3.5.2 3D-Printing of Adapter

The method for 3D-printing used in this project is fused deposition (FDM) which is a technology involving melt extrusion for the deposition of filaments made of thermal plastics to form assigned pattern (Walker & Santoro, 2017). According to a study by Kumar et al. (2012), the FDM method distributes the 3D-printing into two materials. The first material is to build the main part of the 3D model meanwhile the second material is to produce a disposable structure that acts as support for the 3D model. The layer thickness is set to 0.2mm which is an ideal height for optimized printing (Bintara et al., 2021). Table 3.2 summarizes the properties used for 3D-printing in this project. To start 3D-printing, there are important steps need to be taken to prepare the 3D-printer which is the Ender 3 V2. First, the printing bed and filament should always be heated for a few minutes before begin printing. The second important method is to level the printing bed. To level the printing bed, simply use a piece of paper, place it under the printing nozzle, and gently move the paper underneath and feel the grip. The grip should not be too tight, or too loose. If the grip on the paper appears to be tight, the printing bed should be lowered. Vice versa, if the paper appears

to be loose, the printing bed should be raised. Once this process is completed, the 3D-printing can begin.

Table 3.2: 3D-printing settings of Creality Ender 3 V2

Process	FDM
Nozzle Size (mm)	0.4
Layer Thickness (mm)	0.2
Infill (%)	20
Material	PLA
Filament Size (mm)	1.75

3.6 Performance Evaluation

This section discusses on the methods including simulations that are used to evaluate the performance of developed adapter. The first evaluation would be a stress test on the designed adapter using Autodesk Inventor software to analyse the physical stability of the device. The method used for the second evaluation is Subjective Image Quality Assessment involving a non-mydratic clinical testing. The assessment on the images collected is evaluated using the 5-point scale which is based on FOTO-ED (Fundus photography versus Ophthalmoscopy Trial Outcomes in the Emergency Department) studies (Bruce, Lamirel, Biousse, et al., 2011; Day et al., 2016; Lamirel et al., 2012). In addition, a user-end survey is prepared for the users to collect feedback of the device in terms of compatibility, stability, usability and repeatability, and suitability of the device in real clinical settings.

3.6.1 Stress Simulation

For the stress analysis, the finite element analysis (FEA) method is applied using the Autodesk Inventor software. Finite element analysis is known as a numerical method used to calculate strains and stress in describing the behaviour of elastic solids (Dues, 2006). The main purpose of performing stress analysis is to observe and evaluate the possible forms of deformation of proposed adapter in terms of stress, displacement, and strain. This helps to identify which areas are subject to excessive stress when force is applied. Each part was evaluated individually but focus is on the main body and the movable handle as the handle cover is only to cover the movable handle. Figure 3.7 shows the flowchart that summarizes the process of stress simulation.

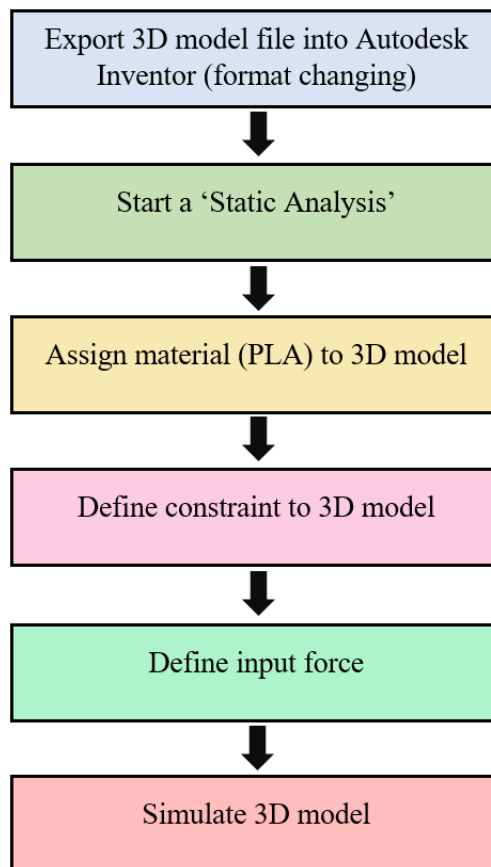


Figure 3.7: Process of stress simulation using Autodesk Inventor

To begin the simulation, the 3D model file is first exported into the Autodesk Inventor which converts the *.dwg* format to a format that allows the software to recognize the 3D model. The export process involved several steps in ensuring the CAD model is converted correctly into the Autodesk Inventor. Next, a static analysis is selected where the main input force is not affected by time, temperature, or atmosphere pressure. The next step is assigning a material to the 3D model. The filament used to print the adapter is polylactic acid (PLA). PLA is a type of biodegradable thermoplastic that is derived from renewable resources and has mechanical properties suitable for 3D-printing such as high strength and high stiffness (Mirkhalaf & Fagerström, 2021). In the materials library of the software, PLA is not listed, thus, a new material is created where the mechanical and thermal properties of the PLA is set with reference to the average values of PLA provided in MatWeb which is an online service that provides database of engineering materials such as thermoplastic, metals, ceramics and more based on existing products in the market where data and specification sheets are supplied by manufacturers and distributors. Table 3.3 summarizes the properties of the PLA material.

Table 3.3: Properties of PLA material

Name		PLA
General	Mass Density	1.280 g/cm ³
	Yield Strength	40.100 MPa/ 5.816 ksi
	Ultimate Tensile Strength	62.900 MPa/ 9.122 ksi
Stress	Young's Modulus	2.270 GPa

	Poisson's Ratio	0.3
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Next step is defining the constraints of the 3D model by identifying the location of the adapter that will be restrained from any movement, displacement, or rotations (Dues, 2006). This is to establish relationships between components in an assembly that helps to control its position and behaviour, thus, creating boundary conditions. Figure 3.8 and Figure 3.9 show the location of constraint for each part. Arrow in blue represents the constraint placement meanwhile arrow in yellow represents the load placement. The following step is defining the external force that is going to be exerted on the adapter. In this experiment, a singular force of 5 lbf will be applied. After that, the stress simulation is started.

FEA is a method that converts a structure into a mesh by cutting the structure into a set of finite cells called as the elements which are interconnected through nodes. Each node has a set of degrees of freedom (DOFs) which defines the displacement vector of each element (Bhavikatti, 2015). By using the assigned properties of PLA, applied force of 5lb, the boundary condition, FEA creates a system of equation defined by:

$$[k]_e \cdot \{\delta\}_e = \{F\}_e \quad (3.1)$$

where k_e is the element matrix stiffness matrix representing the relating forces to displacement, δ_e is the nodal displacement vector of the element, which is the unknown variable, and F is the nodal vector that represents the applied load (Bhavikatti, 2015). Thus, the displacement at each node is calculated. Next, FEA calculates the stress at each element until the stress distribution is obtained for the entire structure by relating the displacements

to the deformation formed from Hooke's law (Bhavikatti, 2015; Unnikrishnan Nair & Somanath, 2023) which is defined by:

$$\text{Stress}, \sigma = E \cdot \varepsilon \quad (3.2)$$

where E represents the Young's modulus of PLA, and ε is the strain computed from calculating the displacements. The state of stress of a 3D body are generally defined in terms of the stress values due to the normal and shear loads acting on the body (Javidinejad, 2023) which the 3D body is bounded by three mutually perpendicular planes where each plane is perpendicular to the x , y , and z -axis (Bhattacharjee, 2021). Normal stresses are defined as σ_x , σ_y , and σ_z meanwhile the shear stresses are defined as τ_{xy} , τ_{yx} , and τ_{yz} .

For this experimentation, the stress evaluation on proposed adapter will be conducted based on von Mises stress and 1st principal stress (Bhattacharjee, 2021). Von Mises stress is also known as equivalent stress. The criterion of von Mises states that if the von Mises stress of a material under a load is equal or greater than its yield limit under a simple tension, then the material will yield (Popescu, 2019). As for the 1st principal stress, it is to observe the areas experiencing the maximum tensile stress induced on the adapter under applied load. The formulation for von Mises stress and 1st principal stress are expressed as follows;

$$\text{Von Mises stress}, \bar{\sigma} = \sqrt{\frac{(\sigma_x - \sigma_y)^2 + (\sigma_y - \sigma_z)^2 + (\sigma_z - \sigma_x)^2}{2}} \quad (3.3)$$

$$\text{1st principal stress}, \sigma_1 = \frac{\sigma_x + \sigma_y}{2} + \sqrt{\left(\frac{\sigma_x - \sigma_y}{2}\right)^2 + \tau_{xy}^2} \quad (3.4)$$

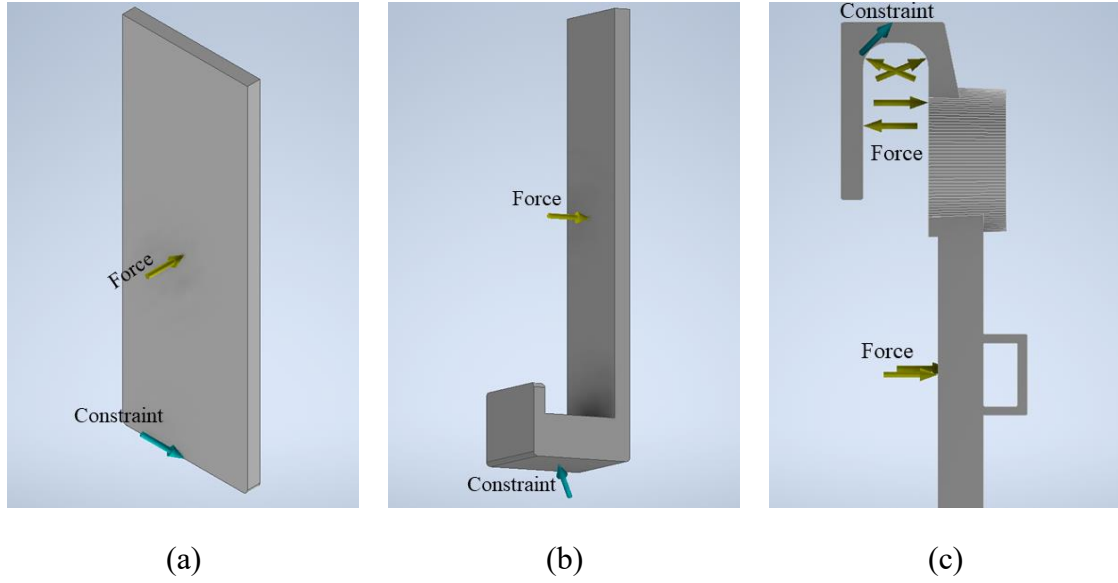


Figure 3.8: Location of constraint and force displaced. (a) Handle cover, (b) Movable handle, and (c) Main body

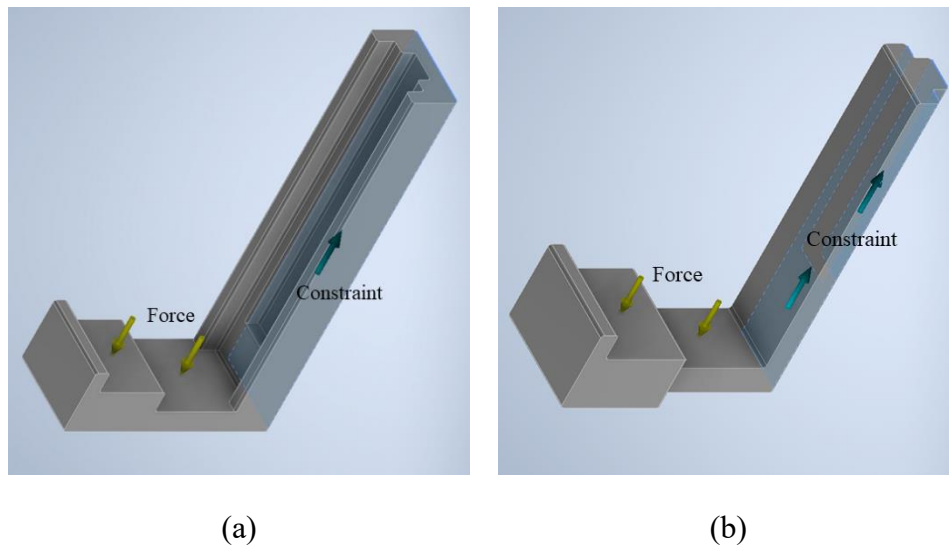


Figure 3.9: Location of constraint and force displaced. (a) Right holder, (b) Left holder

3.6.2 Statistical and Survey Analysis

A non-mydratic clinical testing will be conducted to collect retinal images from real patients. The PanOptic ophthalmoscope together with the developed universal adapter and

Google Pixel 6 smartphone will be utilized. For this purpose, a collaboration with Eye Specialist Centre (ESC) Kuching is conducted for the recruitment of patients and examiners (Approval number: FME/22/43). Based on availability, three ophthalmologists and two optometrists are recruited as examiners meanwhile for the review and grading of images, six examiners are selected which includes the same examiners from the clinical testing, one postgraduate medical student from UNIMAS, and one associate professor doctor from the Faculty of Medicine and Health Sciences, UNIMAS. Table 3.4 lists the examiners and their availability for the clinical testing, and review and grading of the images collected.

Table 3.4: Lists of examiners

Examiner No.	Position	Clinical Testing (Y/N)	Review and Grading (Y/N)
1	Ophthalmologist (UNIMAS)	Y	N
2	Optometrist (ESC)	Y	Y
3	Ophthalmologist (UNIMAS)	Y	Y
4	Optometrist (Focus Point, Aeon Mall)	Y	Y
5	Ophthalmologist (ESC)	Y	Y
6	Postgraduate medical student (UNIMAS)	N	Y
7	Associate Professor Doctor (UNIMAS)	N	Y

From the patient recruitment process, fourteen patients between the ages of 20 and 80 are recruited as subjects based on availability and medical background. The aim is to obtain as much patients as possible with various medical conditions. Among the patients, some of the medical conditions identified are Diabetic Mellitus (DM), hyperparathyroidism (HPT), and chronic kidney disease (CKD) with DM being the most common medical condition. Full written informed consent will be obtained on both the examiners and patients. Table 3.5 lists the details on the patients which includes gender, age, and medical condition.

Table 3.5: Details of patients

Patient No.	Gender	Age	Medical Conditions
1	Male	72	DM, HPT, dyslipidemia, gout, prostate enlargement
2	Male	77	DM, HPT, dyslipidemia
3	Male	46	DM, HPT, CKD
4	Male	41	DM, dyslipidemia
5	Male	23	Healthy
6	Female	38	Healthy
7	Male	63	DM, dyslipidemia
8	Male	42	History of brain tumour
9	Male	23	Healthy
10	Female	55	DM, HPT, polycythemia
11	Female	49	DM

12	Male	46	DM
13	Male	42	DM
14	Male	38	DM, dyslipidemia

A manual along with instructional videos are first provided to all examiners on how to assemble and conduct retinal imaging using the device a week before the scheduled clinical testing. During the clinical testing, an hour-long session is held in which the examiners first practiced with the device before proceeding with retinal imaging on the patients. The duration allocated for each patient is 30 minutes. A total of 28 eyes are imaged (left and right) and recorded in video format where the best images from each eye were selected (by frame) by the examiners for review and grading. After each session, each examiner is required to complete the user-end survey which was prepared to obtain feedback from the examiners on the developed universal adapter and overall device assembly based on the clinical testing. The user-end survey is structured using a Likert scale (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent) where basic statistical values such as mean, median, and frequency of rating are calculated from the survey. A Likert scale is defined as a type of psychological measurement tool comprising various options for respondents to express their opinions or viewpoints regarding a specific issue or topic in a scientifically accepted and validated method (Joshi et al., 2015; Nemoto & Beglar, 2014).

Next, the scores on the difficulty level of acquiring the image of the retina on the first try and after several tries is compared using Wilcoxon Signed-Rank Test (Mccomiskie Bsc et al., 2004) where the sample size, n is set to 5 (three ophthalmologists and two optometrists) and scores are reported in median, Mdn . The Wilcoxon Signed-Rank Test is

defined as a non-parametric test that is used for the analysis of matched-pair data or a one-sample problem (Woolson, 2008). In this analysis, the matched-pair Wilcoxon Signed-Rank Test is applied as the objective is to observe the median differences between the difficulty level of acquiring the image of the retina on the first try and after several tries. Meanwhile, the frequency scores on the compatibility, stability, usability and repeatability, and suitability of the device are calculated using Microsoft Excel based on the scores obtained from the clinical testing survey. The statistical values (mean, median, and frequency of ratings) are as equated from Equation 3.5 until Equation 3.7.

$$\text{Mean}, \bar{x} = \frac{1}{n} \sum_{i=1}^n x_i \quad (3.5)$$

$$\text{Median}, \text{Mdn} = \left(\frac{n+1}{2} \right)^{th} \quad (3.6)$$

$$\text{Frequency of rating}, f_k = \sum_{i=1}^n 1(x_i = k) \quad (3.7)$$

where n refers to the number of respondents, x_i refers to the numerical value of the response for respondent i , and lastly k is referring to respective rating in the Likert scale.

The method applied to review the images collected is the method used in the study by Day et al. (2016) where a 5-point scale was used to grade the quality of images taken. This method was based on the FOTO-ED studies (Bruce, Lamirel, Biousse, et al., 2011; Bruce, Lamirel, Wright, et al., 2011). Table 3.6 shows the 5-point scale with its description where Grade 3 and above is considered as clinically adequate (CA). Grade 1 is given for images where the fundus is not visualized at all. Grade 2 is given for images where the fundus is visualized, but the optic disc is not clear. Grade 3 is given for images that have a

clear view of the optic disc. Grade 4 is given for images where the optic disc and its surrounding structures are clearly visible and lastly Grade 5 is for images that has a clear view of both the optic disc and the macula. The percentage of patients with at least one CA image obtained using the device is calculated using Microsoft Excel (Day et al., 2016). The formulation is as follows;

$$A = \frac{N_{CA}}{P} \times 100\% \quad (3.8)$$

where A refers to the percentage of patients with at least one CA image, meanwhile N_{CA} refers to the number of patients with at least one CA image and P represents the total number of patients. Besides this, the overall number of CA images is also calculated:

$$B = \frac{\sum_{i=1}^n Q_i}{R} \times 100\% \quad (3.9)$$

where R refers to the overall number of CA images, Q_i refers to the numerical value (number of CA images) graded by examiner i , n refers to the number of examiners, and R represents the total number of images.

Table 3.6: Grading level with its description

Scale	Grade Description
Grade 1	Fundus is not visualized at all
Grade 2	Fundus visualized but the optic disc is not clear
Grade 3	Optic disc is clearly visualized
Grade 4	Optic disc and its surrounding structures are clearly visualized
Grade 5	Clear view of both the optic disc and macula

3.7 Chapter Summary

In this chapter, the proposed methodology for this project was explained. Three software were selected to conduct the project which are AutoCAD 3D, Autodesk Inventor, and Ultimaker Cura. The development of the universal adapter begins with reverse engineering which is then proceeded with the designing of the main body. The development of the adapter also includes 3D-printing the prepared prototypes. As for performance evaluation, it was divided into three experimentations, with the first being stress simulation, followed by statistical and survey analysis, and last but not least, the optical configuration of the adapter and the Pan Optic.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 Overview

This section describes the adapter prototypes developed, the results from the stress analysis, and subjective scores obtained from the survey. The von Mises stress and 1st principal stress were computed and compared with the material maximum yield strength and ultimate tensile strength. The quality of images taken using the finalized adapter together with the PanOptic and Google Pixel 6 were also compared with existing studies that have conducted non-mydratic retinal imaging using the PanOptic.

4.2 Developed Adapter

A total of four prototypes were developed in the study where each had undergone preliminary tests with the PanOptic and three different smartphones to determine the compatibility and alignment.

4.2.1 First Prototype

Figure 4.1 shows the concept design of the first prototype viewed in AutoCAD 3D. The first prototype was concluded to be unusable as defects were found on the design upon testing. Figure 4.2 shows a closed-up of the first prototype that has been printed and undergone tests. Due to the nature of how 3D-printer works, during the printing of the adapter, a part of the adapter had no support underneath. This resulted in a defect to appear at the upper part of the adapter, at the connector between the handle and the lens cap, as shown in Figure 4.2.

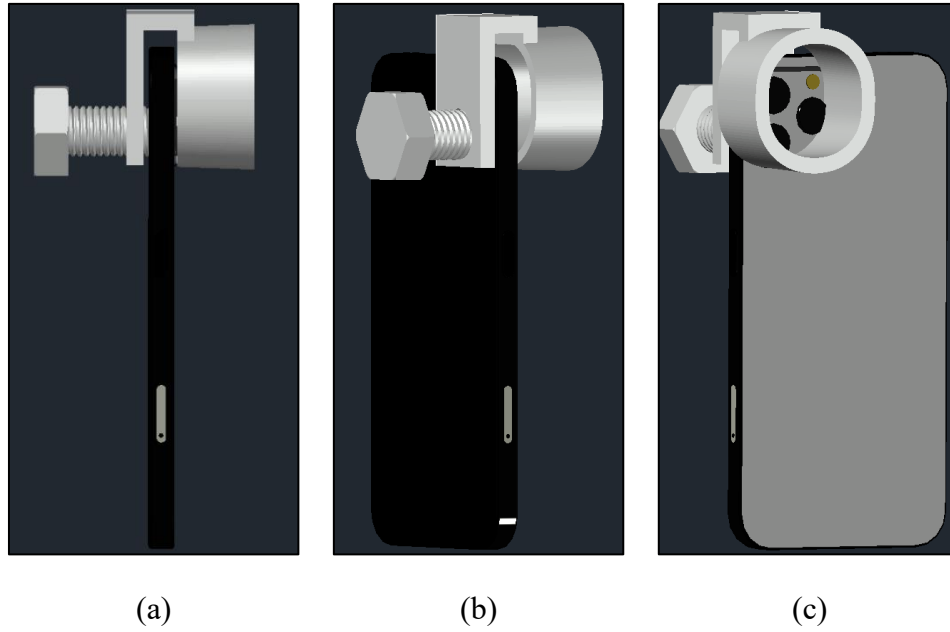


Figure 4.1: Diagram of first prototype designed in AutoCAD 3D. (a) Side view, (d) Angled view, (c) View at back camera of smartphone.

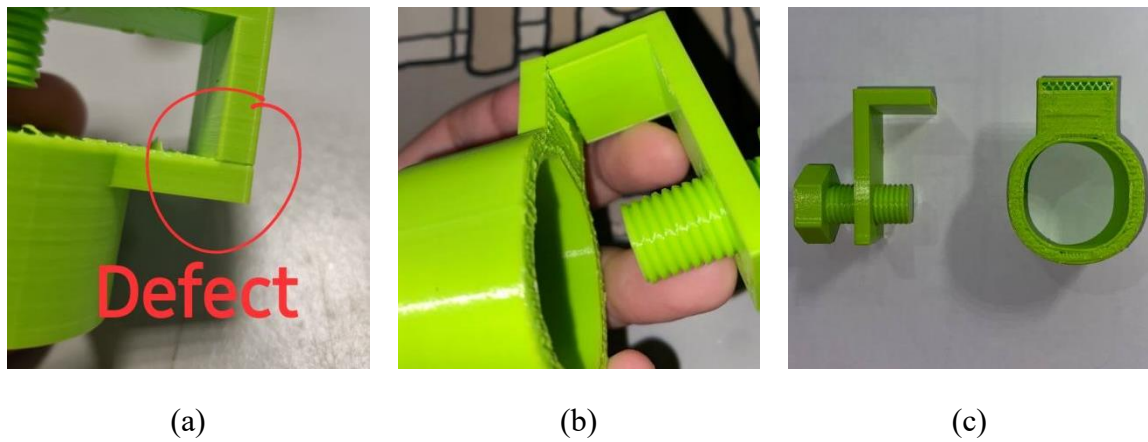


Figure 4.2: Defects found on first prototype. (a) Closed up view of the defect, (b) Connector detaching, (c) Adapter had broken after testing with the Pan Optic.

4.2.2 Second Prototype

Issues on the first prototype was identified and hence, a second prototype was developed that solves major of the issues that were previously found from the first prototype.

Figure 4.3 shows the concept design of the second prototype viewed in AutoCAD 3D. For the second prototype, one of the main changes that were made was the increased thickness of the adapter overall, which directly affects the connector strength. Besides this, the inner surface was also curved which increases the surface area of the connection and improves the 3D-printing process. Furthermore, a ramp was added on top of the lens cap that connects to the connector which also serves to provide better bond between those two parts. Figure 4.4 shows the printed second prototype when used with the Pan Optic ophthalmoscope. From the testing, it was found that the design of the second prototype was not enough to support the weight of the smartphones, hence making it impractical when used with the Pan Optic. Thus, the second prototype was further analysed and re-designed, developing a third prototype that has improved support system.

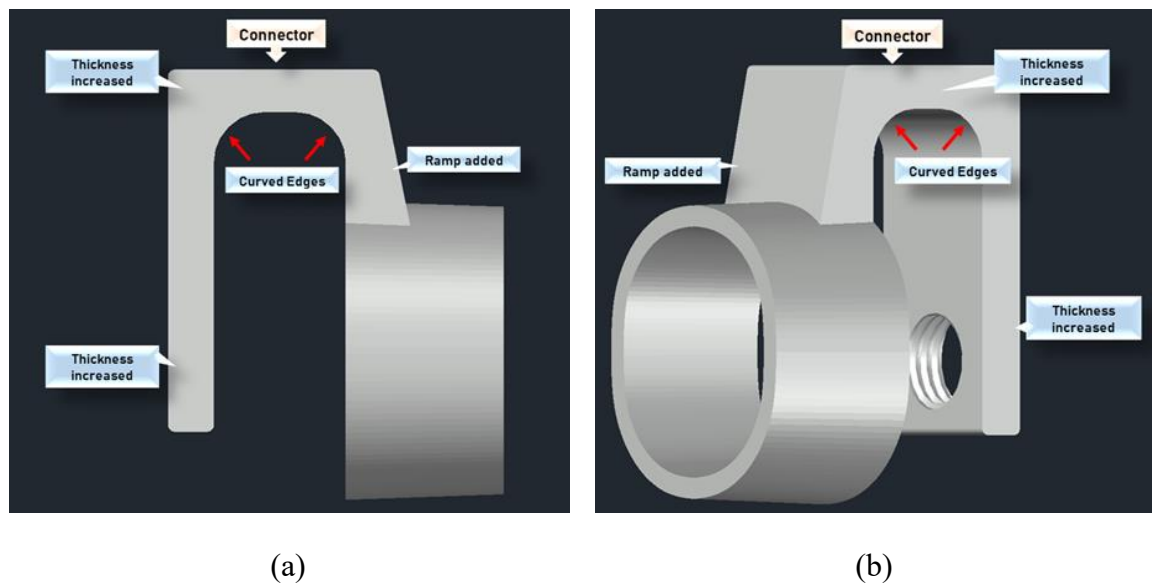


Figure 4.3: Diagram of second prototype designed in AutoCAD 3D

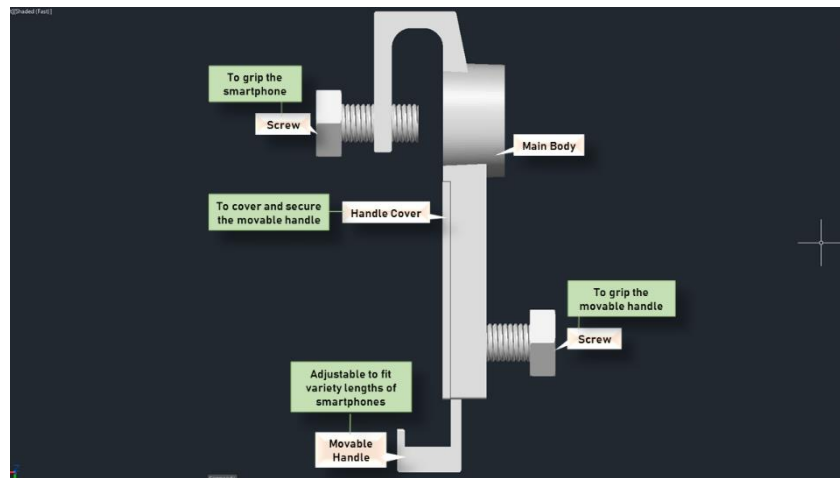


Figure 4.4: Printed second prototype when used with Pan Optic

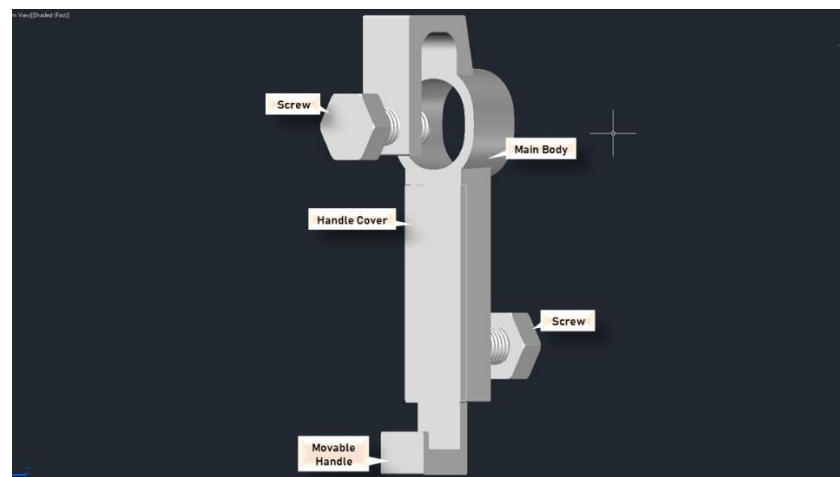
4.2.3 Third Prototype

From the first two prototypes, a third prototype was designed to overcome the issues obtained as shown in Figure 4.5. All three prototypes apply a screw system to secure the alignment of the smartphone's camera onto the Pan Optic ophthalmoscope. Technical drawings of the third prototype (all parts) and screw are attached in Appendix B. The third prototype is divided into three main parts (excluding the 3D-printed screws that holds the system altogether); the main body, the movable handle, and the handle cover. Figure 4.6 shows the third adapter prototype when used with an iPhone 11 and the Pan Optic. The adapter was also tested with an iPhone 14, Huawei Y9, and Google Pixel 6 and showed no issues in the alignment and compatibility. Referring to Figure 4.5, the main body has been extended to house the movable handle. The length and width of the main body of the adapter is 150.00 mm and 43.60 mm respectively. The width of the main body is measured as the overall measurement following the dimension of the lens cap. The height of the main body is 51.05 mm. The inner centre of the main body is designed to provide a gap of 4.00 mm to

fit the movable handle. The movable handle is made adjustable to fit a variety length of smartphones while providing sufficient support to hold the smartphones where its length, width, and total height is 105.00 mm, 23.00 mm, and 25.0 mm respectively. The handle cover is simply to cover and secure the movable handle where its length, width, and height is 85.00 mm, 30.00 mm, and 3.00 mm respectively. The technical drawings of each part of the third prototype are attached in Appendix B.



(a)



(b)

Figure 4.5: Diagram of third prototype designed in AutoCAD. (a) Sideview, (b) Angled view

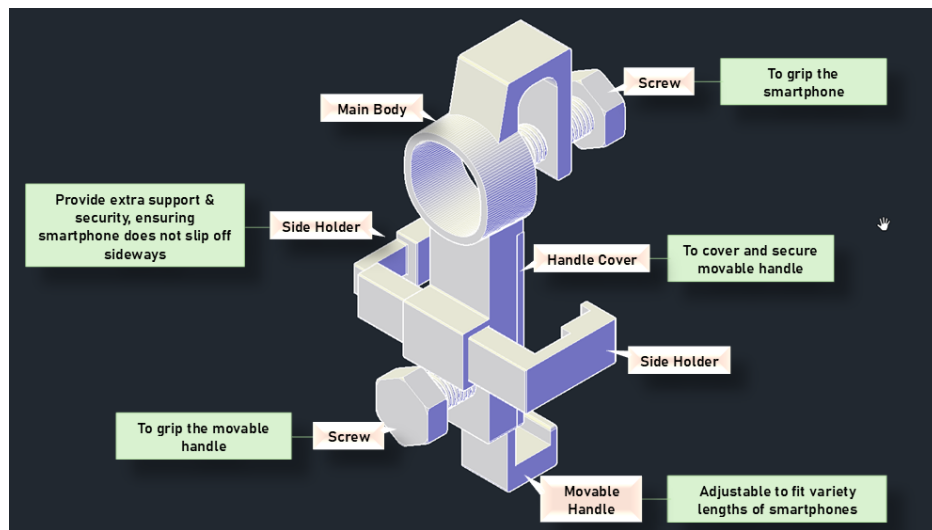


Figure 4.6: Printed third prototype when used with Pan Optic and smartphone

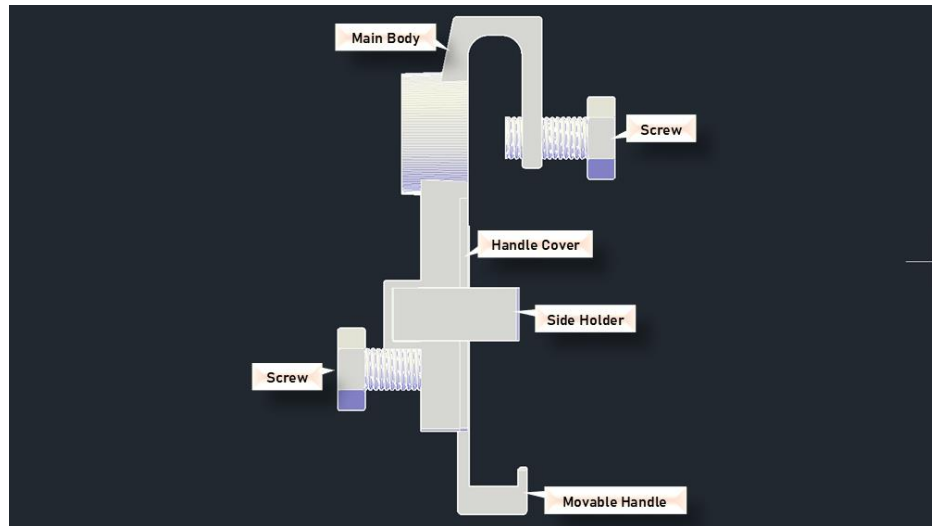
During the preliminary test for the third prototype, it was found that the adapter was able to provide sufficient support to hold the smartphone when attached onto the Pan Optic. From the test, the four smartphones that have different dimensions and camera lenses positions were found usable with the third prototype. With the lens cap designed to have a large opening, it provides the flexibility to position a smartphone accordingly regardless of the location of the camera lens. The movable handle has also shown its compatibility with the different heights of the four smartphones. In a case where a user has a smartphone with a shorter height, the movable handle can be easily adjusted in AutoCAD 3D to accommodate the required height. However, the stability and security of the whole assembly raised a concern as there is no support at the sides. Thus, this suggests the risk of the smartphone slip-away during retinal imaging.

4.2.4 Fourth Prototype

A fourth prototype was developed with the objective to improve the stability and overall support system to improve the repeatability of the adapter when attached to the PanOptic and smartphone. The technical drawing for the fourth prototype is attached in Appendix B. Figure 4.7 shows the overall assembly concept (without screws) of the fourth prototype. The main change of the final prototype is the main body, where a slot is added at the back of the body to insert the side holders which comes in a set of two. The measurement of the rest of the main body remains unchanged where only the overall width of the main body has increased approximately from 43.60 mm to 57.10 mm due to the addition of the slot at the back.



(a)



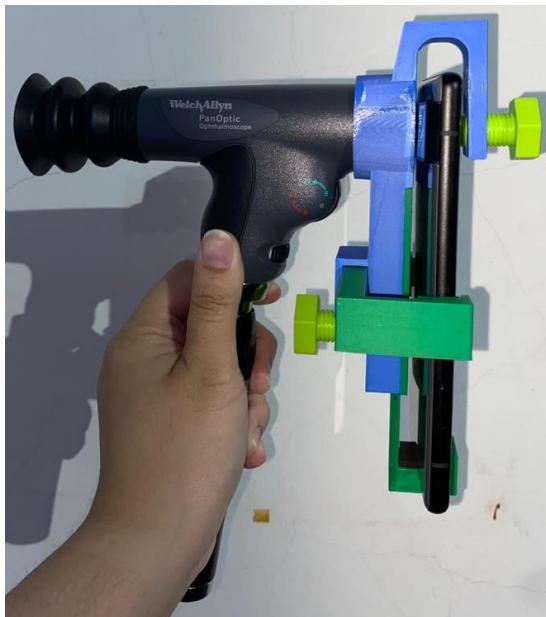
(b)

Figure 4.7: Assembly concept (without screws) of modified universal adapter in AutoCAD 3D. (a) Angled view, (b) Side view

Figure 4.8 shows the 3D-printed modified universal adapter (all parts) disassembled which includes the side holders and screws. As shown in Figure 4.8, grip tapes are added at specific areas which are (i) the inner bottom section of the movable handle, (ii) the inner side area of the two side holders, and (iii) bottom area of the screw that is used to secure the smartphone onto the adapter and PanOptic ophthalmoscope. The grip tape helps to prevent damage onto the smartphone's screen and for better friction so that the smartphone used would not slide easily. Figure 4.9 shows the assembly of the modified universal adapter with the PanOptic ophthalmoscope and smartphone of model Google Pixel 6.



Figure 4.8: Disassembled 3D-printed modified universal adapter



(a)



(b)

Figure 4.9: Assembly of modified universal adapter with PanOptic ophthalmoscope and Google Pixel. (a) Sideview, (d) Angled view

4.3 Stress Analysis

Starting with the movable handle, Figure 4.10 and Figure 4.11 show the von Mises and 1st principal stress results for the movable handle respectively. An outline of the original form of the movable handle before load is applied is represented with thin green lines meanwhile the coloured object is a representation of possible deformed appearance of the object. In Figure 4.10 and Figure 4.11, a concentrated red area is observed at the lower part near the base of the movable handle, which indicates the area that is the most vulnerable and the first area to deform if exceed the material's maximum yield strength. Based on Figure 4.10, the movable handle experiences a maximum von Mises stress of 2.294 ksi. However, the PLA material has a maximum yield strength of 5.816 ksi. Hence, this indicates that the movable handle can hold greater load before it begins to deform permanently as it has not reached the material's maximum yield strength. It is also noted that base and the top area of the movable handle experiences the least stress represented by the concentrated blue color. Referring to Figure 4.11, the movable handle experiences a maximum 1st principal stress of 2.290 ksi. The maximum stress value obtained is low, hence, it does not compromise the integrity of the model.

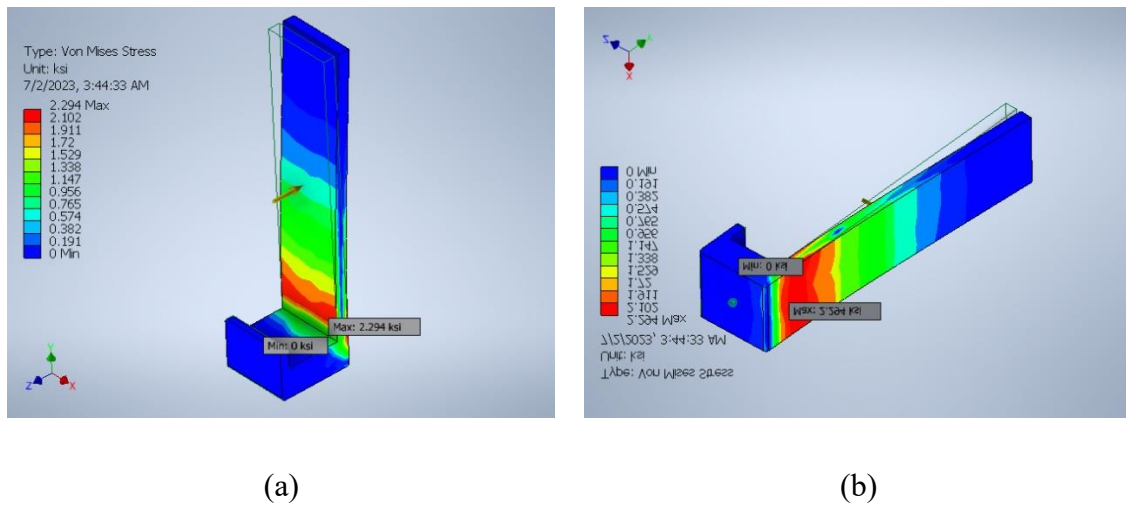


Figure 4.10: Von Mises stress result of movable handle observed from front (a), and back (b)

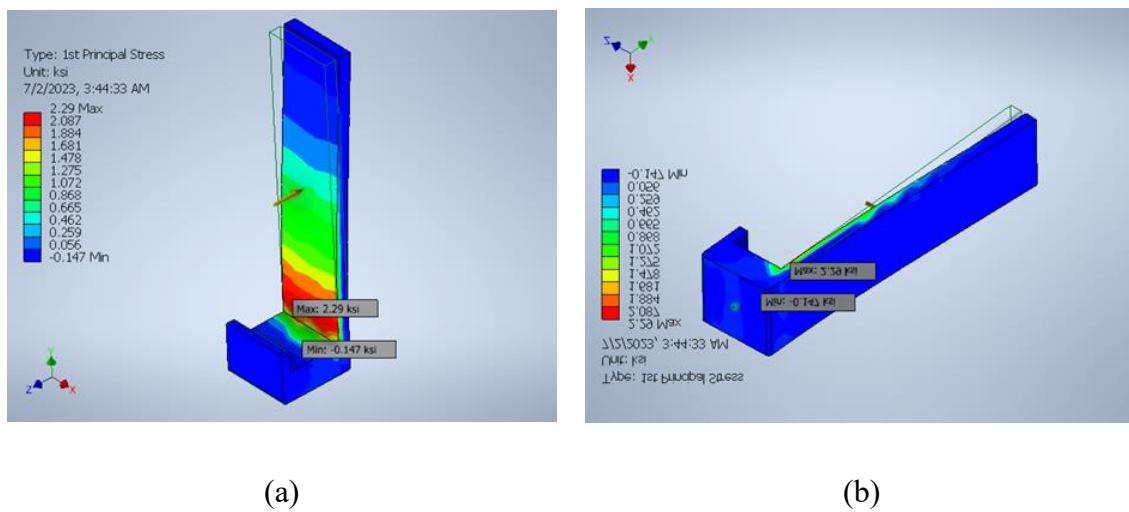


Figure 4.11: 1st principal stress result for the movable handle respectively from front (a), and back (b)

Similarly, the stress results obtained on the handle cover has shown a more positive output. Figure 4.12 and Figure 4.13 show the von Mises and 1st principal stress results for the handle cover respectively. It can be observed that there is minimum area concentrated

red colour on the handle cover. However, the calculated maximum von Mises stress for the handle cover is 3.676 ksi which is higher when compared to the movable handle previously. Referring to Figure 4.12 (b) and Figure 4.13 (a), it is observed that the handle cover experiences the most stress at the bottom nearing the edges represented by the concentrated red colour area. The maximum stress value that the handle cover is able to withstand is 3.457 ksi before it starts deforming. Both maximum values of von Mises stress and 1st principal stress calculated for the handle cover is below the maximum yield strength of the PLA material. Hence, the design is stable and can withstand more load.

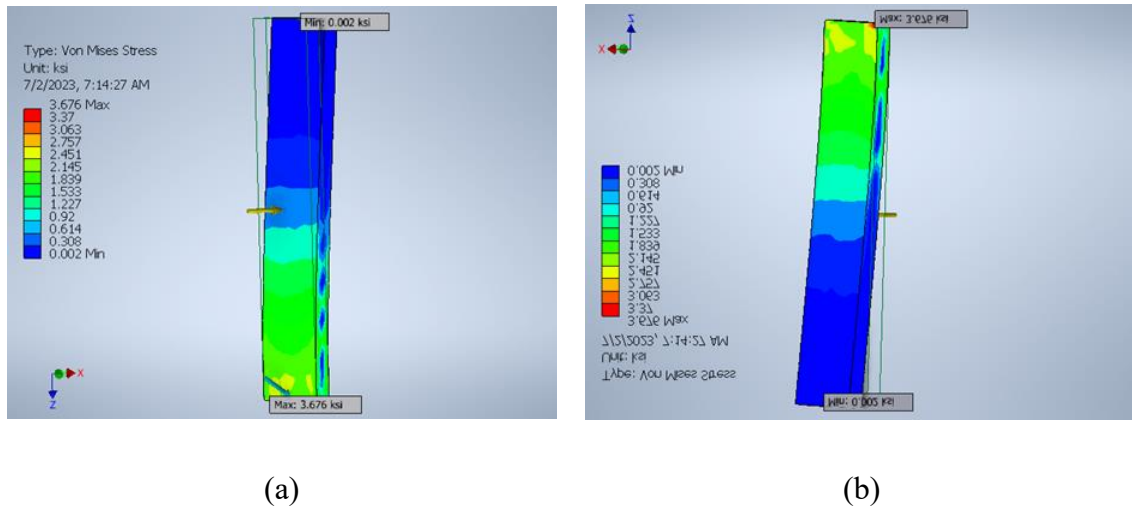


Figure 4.12: Von Mises stress result of handle cover observed from front (a), and back (b)

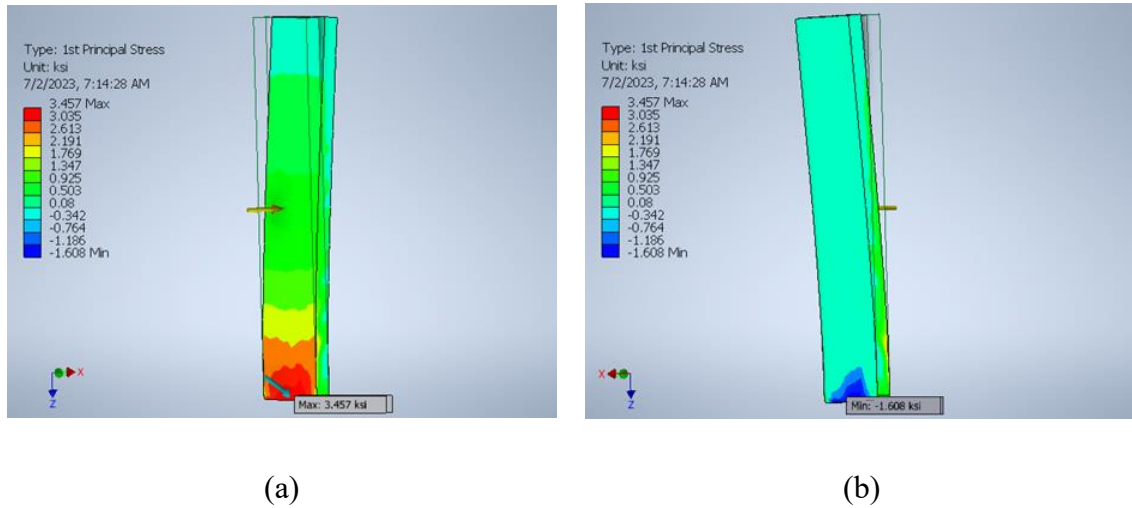


Figure 4.13: 1st principal stress result of handle cover observed from front (a), and back (b)

The main body have also shown positive output as observed from Figure 4.14 and Figure 4.15. Figure 4.14 shows that the modified main body is mostly concentrated in blue colour which means that overall, it experiences minimal stress even when force is applied. Referring to Figure 4.14 (b), a small concentrated red area is observed at the bottom edge area that is connecting the ramp and the lens cap. This shows that this area is the most vulnerable and the first area to deform if the force applied causes the main body to exceed its material's maximum yield strength. The maximum von Mises stress calculated for the main body is 3.869 ksi which is much lower than PLA's maximum yield strength of 5.816 ksi. Thus, this shows that the modified main body is sturdy and able to hold greater load before it begins to deform permanently as it has not reached the material's maximum yield strength. Referring to Figure 4.15, the calculated maximum 1st principal stress is 4.640 ksi where the area that experience the most stress is at the opposite side of the same area which is at the bottom edge area that is connecting the ramp and the lens cap. When comparing the 1st principal stress calculated and PLA's ultimate tensile strength which is 9.123 ksi, the 1st

principal stress is much lower which proves that the integrity of the modified main body will not be compromised under applied load.

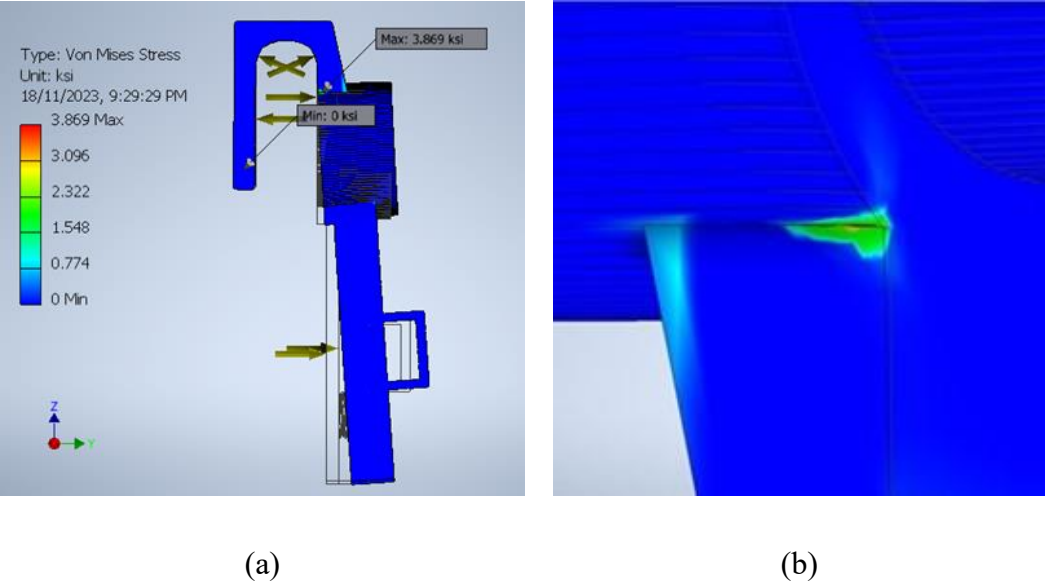


Figure 4.14: Von Mises result of main body observed from side (a), and closed-up view of the area that is the most vulnerable (b)

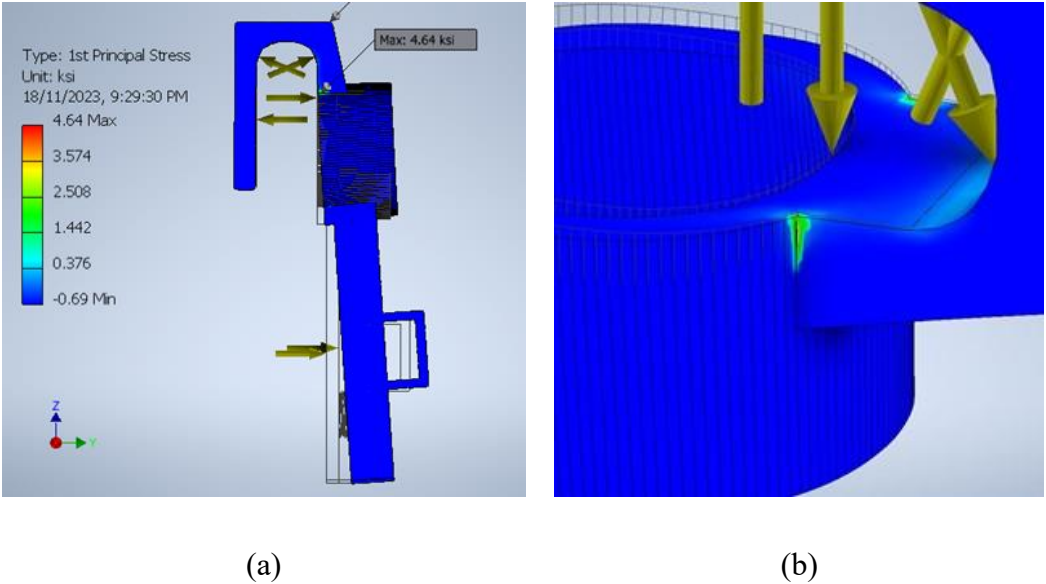


Figure 4.15: 1st principal stress result of main body observed from side (a), and closed-up view of the area that experiences the most stress (b)

Next, Figure 4.16 and Figure 4.17 show the von Mises and 1st principal stress of the right holder calculated respectively which also shows positive output. Referring to Figure 4.16, almost the whole area of the right holder is concentrated in blue which shows that the right holder is sturdy. The calculated maximum von Mises and 1st principal stress calculated are 1.302 ksi and 1.649 ksi respectively. Both values calculated are much lower than PLA's maximum yield strength and ultimate tensile strength respectively. Referring to Figure 4.16, the most vulnerable area for the right holder is represented by the concentrated blueish-green and yellow area near the middle at the inner side and the concentrated blueish-green area at the outer area. This indicates that this area is the area that will deform first if the von Mises stress exceeds the material maximum yield strength. Figure 4.17 shows that the area that experiences the most stress is mostly at the inner corner of the holder as represented by a small concentrated blueish-green, yellow, and red area.

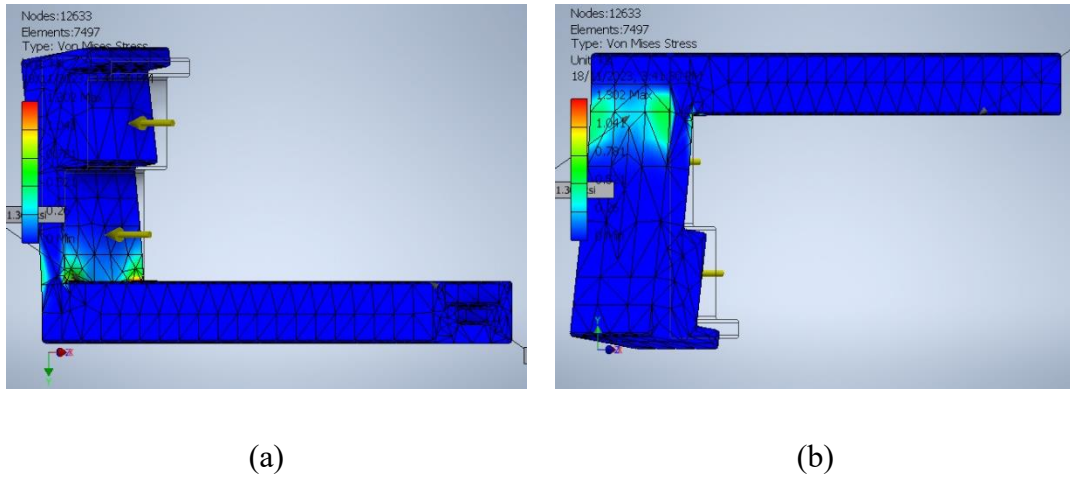


Figure 4.16: Von Mises stress result of right holder observed from front (a), and back (b)

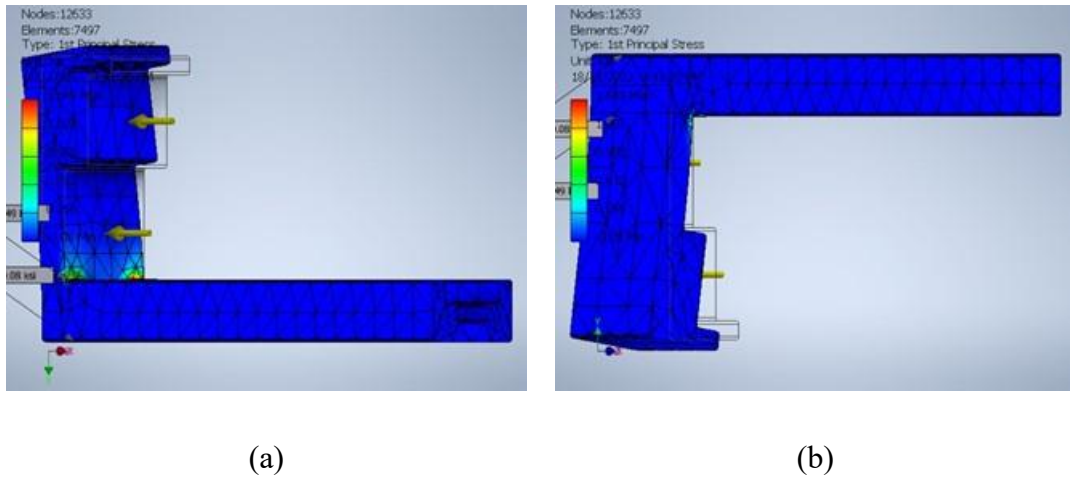


Figure 4.17: 1st principal stress result of right holder observed from front (a), and back (b)

Last but not least, the calculated von Mises and 1st principal stress for the left holder also show positive output, with the values being slightly higher than the values calculated for the right holder. Referring to Figure 4.18, the calculated maximum von Mises stress is 2.550 ksi which is much lower than 5.816 ksi. The most vulnerable area of the left holder can be observed at the area coloured in concentrated blueish-green and red spots at the inner corner meanwhile a small amount of concentrated blueish-green area can be observed at the outer part. Figure 4.19 shows that the area that experiences the most stress is also at the inner corner of the left holder where the maximum 1st principal stress calculated is 2.981 ksi which is much lower than the material ultimate tensile strength. Thus, the stress analysis on the left holder also proves that the left holder is sturdy even under load.

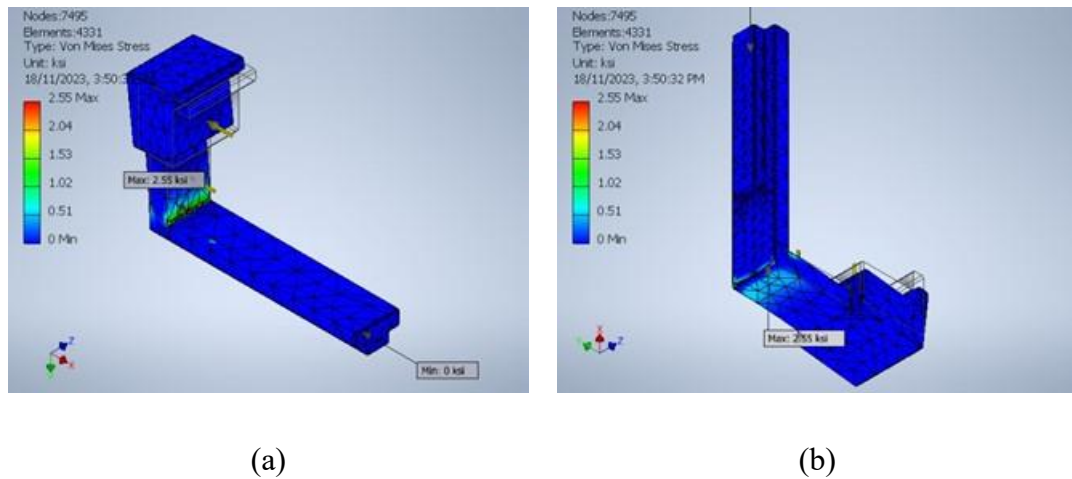


Figure 4.18: Von Mises stress result of left holder observed from top (a) and bottom (b)

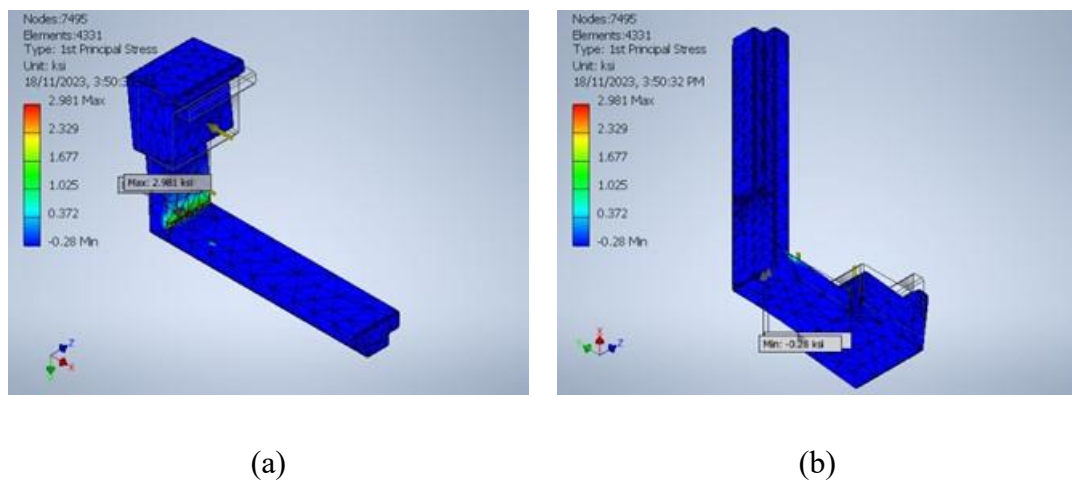


Figure 4.19: 1st principal stress result of left holder observed from top (a) and bottom (b)

Table 4.1 summarizes the minimum and maximum von Mises and 1st principal stress experienced by each part of the fourth prototype under applied load. Overall, the calculated von Mises stress and 1st principal stress shows that the design and material of all three parts are sturdy and is unlikely to deform under applied force. Thus, the integrity of developed adapter was proven. The FEA method applied calculates the stress values such as maximum

von Mises stress which allows direct comparison with the maximum yield strength of the PLA material. This method helps to determine the stress value for proposed adapter to begin deforming permanently. In addition, the finite element analysis determines which areas of proposed parts of the adapter experience the most stress, and areas that are the most sturdy and flexible. From the results obtained, the design and material of developed universal adapter is reliable and sturdy for experimentation and future reproduction based on the von Mises and 1st principal stress calculated using the finite element analysis (FEA) in Autodesk Inventor. Even under the load of 5 lb force (2.27 kg), it experiences minimum deformation as the maximum von mises and 1st principal are below PLA's yield and ultimate tensile strength.

Besides the performance of the 3D-printed adapters in retinal imaging, it is also important to conduct stress tests on the adapters that ensure replicability or reproducibility in case of high demand. Furthermore, understanding the physical and mechanical properties when developing a prototype helps to prevent any wastage especially when considering that one of the main purposes of the development of smartphone-based retinal image acquisition is to provide an affordable and portable method for patients in low- and middle- income populations that are less likely exposed to early detection of diseases, Hence, the FEA method presented allows direct comparison with the maximum yield strength of the PLA material. This method helps to determine the stress value for proposed adapter that would cause it to begin deforming permanently. In addition, the FEA method determines which areas of proposed parts of the adapter experience the most stress, and areas that are the most sturdy and flexible.

Table 4.1: Stress results of developed universal adapter using FEA method in Autodesk Inventor

Parameters	Movable Handle		Handle Cover		Main Body		Right Holder		Left Holder	
	Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
Von Mises Stress (ksi)	0.000 222	2.294	0.001 95	3.676	0.000 0947	3.869	0.000 00030 2	1.302	0.000 00022 0	2.550
1 st Principal Stress (ksi)	-0.147	2.290	-1.608	3.457	-0.690	4.640	-0.663	1.649	-0.289	2.981

Thus, the main difference between the original adapter and the developed adapter is smartphone compatibility. The developed universal adapter allows the PanOptic ophthalmoscope to be utilized with any smartphone models which further allow the ophthalmoscope to incorporate with the latest smartphone technology meanwhile the original adapter of the PanOptic has limited usage in the present as it is only usable with the iPhone 6 series. Furthermore, the developed universal adapter is highly modifiable to accommodate future standard dimensions of smartphones. Table 4.2 summarizes the advantages and disadvantages of both adapters.

Table 4.2: Advantages and disadvantages of the original adapter and developed adapter

Adapter	Original Adapter	Developed Adapter
Advantages	• Simple assembly • Lighter	• Universal (can fit variety of smartphone models) • Highly modifiable through AutoCAD for future standard smartphone dimensions
Disadvantages	• Only fit iPhone 6 series • Sold separately by manufacturer	• Slightly heavier • May be difficult to assemble for some

4.4 Preliminary Data Collection of Retinal Imaging

A preliminary data collection was conducted during the testing of the third prototype. Figure 4.20 shows example of images taken during the preliminary data collection using an iPhone 11. Based on Figure 4.20, the images obtained provided a relatively small field of view of the retina where the optic disc and blood vessels are observed. It was difficult to obtain good quality retina images and the duration taken to familiarize with the Pan Optic ophthalmoscope was quite long. Furthermore, glares and reflection were also visible on the images obtained. However, the process of viewing the retina was easier when the Google

Pixel 6 was used. The Google Pixel 6 was able to focus onto the optic disc notably faster when compared to the iPhone 11.

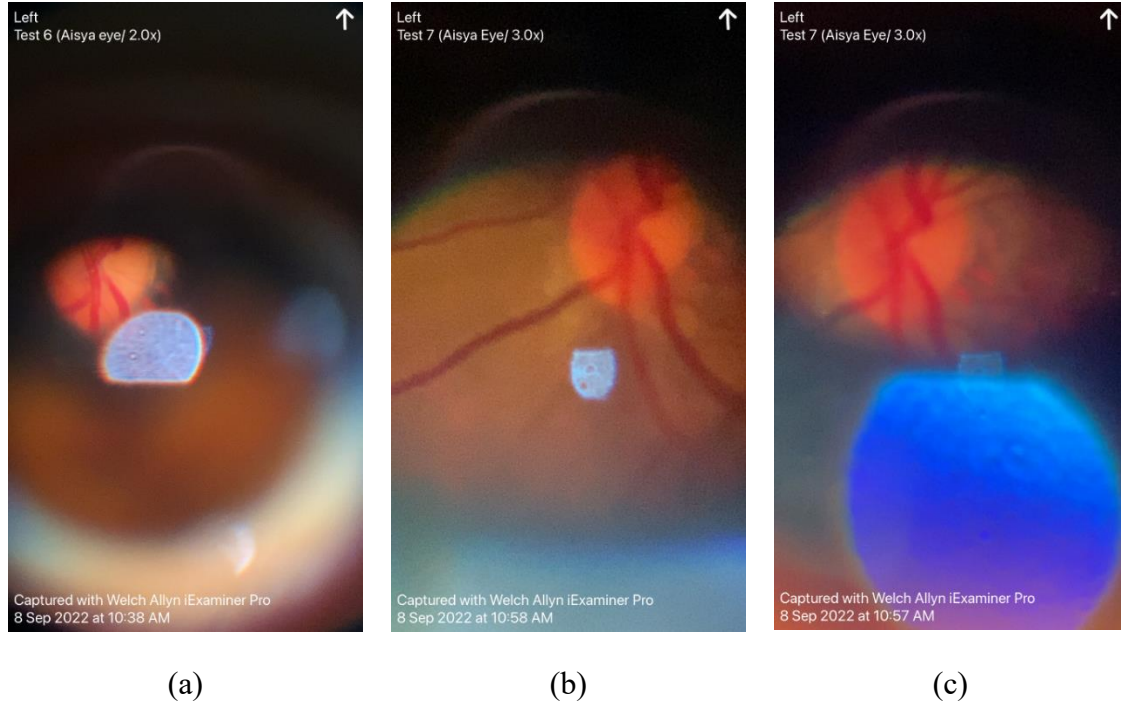


Figure 4.20: Samples of images taken during the preliminary data collection

4.5 Clinical Testing

A total of 53 videos were recorded by the examiners with an average of 4 videos per patient. Figure 4.21 shows two examples of best images obtained by one of the examiners which shows a clear view of the optic disc and its surroundings. Besides this, the images also contain minimal glares and reflections. When compared with the images collected during the preliminary data collection, the images collected from the clinical testing are of higher quality. As shown in Figure 4.21, it can be observed that the Google Pixel 6 captured more details of the optic disc when compared to the images captured using the iPhone 11 (refer to Figure 4.20). This is because the Google Pixel 6 features a camera resolution of 50

megapixels meanwhile the iPhone 11 only provides 12 megapixels. Meanwhile, the iPhone 6 and iPhone 6s/ 6s plus (the only smartphone series that is compatible with the PanOptic's original adapter) only provides 8 megapixels and 12 megapixels respectively. This further highlights the importance of developing this universal adapter that allows studies to utilize the latest smartphones technologies.

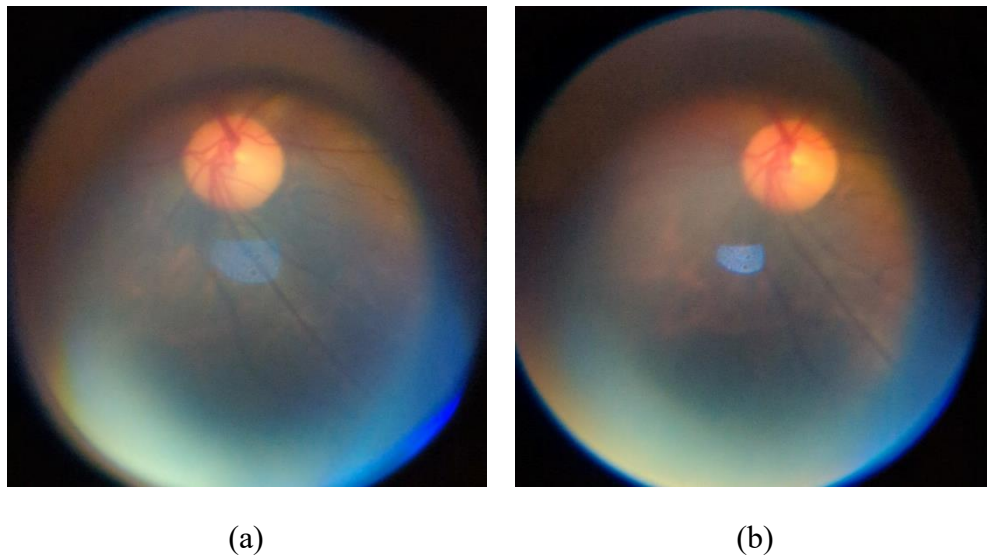


Figure 4.21: Samples of images acquired by one of the examiners

4.5.1 Subjective Image Quality Assessment using 5-Point Scale based on FOTO-ED Studies

A total of 140 images were graded by each expert and reviewed. From the review, 37.83% (95% CI = 22.16% to 53.47%) of the images were found to be CA (Grade $3 \geq$). Figure 4.22 shows a set of images that have been graded by one of the experts. Referring to Figure 4.22, Grade 1 was given to an image where no optic disc was visualized meanwhile Grade 2 was given to an image where the fundus was slightly visualized, and unclear view of the optic disc. Lastly, Grade 3 was given to an image where there was a clear view of the optic disc and Grade 4 was given to an image with a clear view of the optic disc and its

surrounding structures. Grade 5 images, which is referring to images that have a clear view of both the optic disc and the macula, were not obtained from the Clinical Testing as graded by the experts.

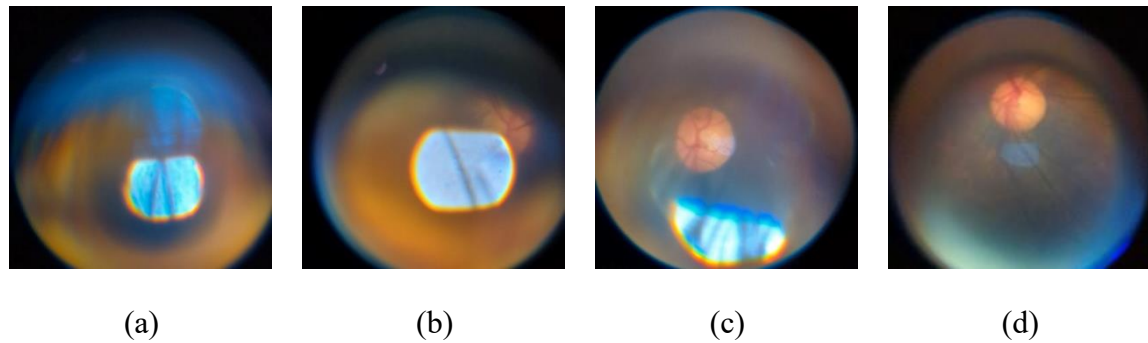


Figure 4.22: Example of images as graded by one of the experts. (a) Grade 1, (b) Grade 2, (c) Grade 3, and (d) Grade 4

Figure 4.23 shows the percentage of patients with at least one CA image according to each expert among the 14 patients with standard error bars. Based on Figure 4.23, the highest percentage of patients having at least one CA image (Grade $3 \geq$) was observed by Expert 1 which was 71.43% which indicates that most of the patients had at least one CA image according to Expert 1. However, there is a significant difference between the percentage of patients with at least one CA image as observed by Expert 1 and the rest of the experts where no overlapping in standard error bars is observed. Expert 3, Expert 4, and Expert 5 have shown small differences in percentage among each other which are 50%, 42.86%, and 50% respectively which indicates a high degree of agreement among the three. The standard error bars for these three experts also overlaps which indicates minimal to no difference. But when comparing the percentage of patients with at least one CA image observed by Expert 3, Expert 4, and Expert 5, with the other three experts, there is a significant difference. According to Expert 2 and Expert 6, there are 14.29% and 21.43% of

patients with at least one CA image respectively. Both Expert 2 And Expert 6 showed overlapping in standard error bars which also indicates minimal to no difference. However, there is a significant difference between the percentage of patients with at least one CA image as observed by Expert 2 and Expert 6 and the other three experts. Based on Figure 4.23, the percentage of patients with at least one CA image as observed by each expert can be further grouped into three groups. Group 1 consist of only Expert 1 where the percentage indicates that most patient had at least one CA image which also indicates that most of the images were good quality. Group 2 consists of three experts which are Expert 3, Expert 4, and Expert 5 with an average of 47.62%. This indicates that according to these three experts, a fair number of the images obtained during the clinical testing were clinically adequate. For Group 3, the lowest percentage of patients with at least one CA image was observed by Expert 2 and Expert 6 which were 14.29% and 21.43% respectively. This indicates that according to these two experts, the images obtained from the clinical testing were mostly not clinically adequate.

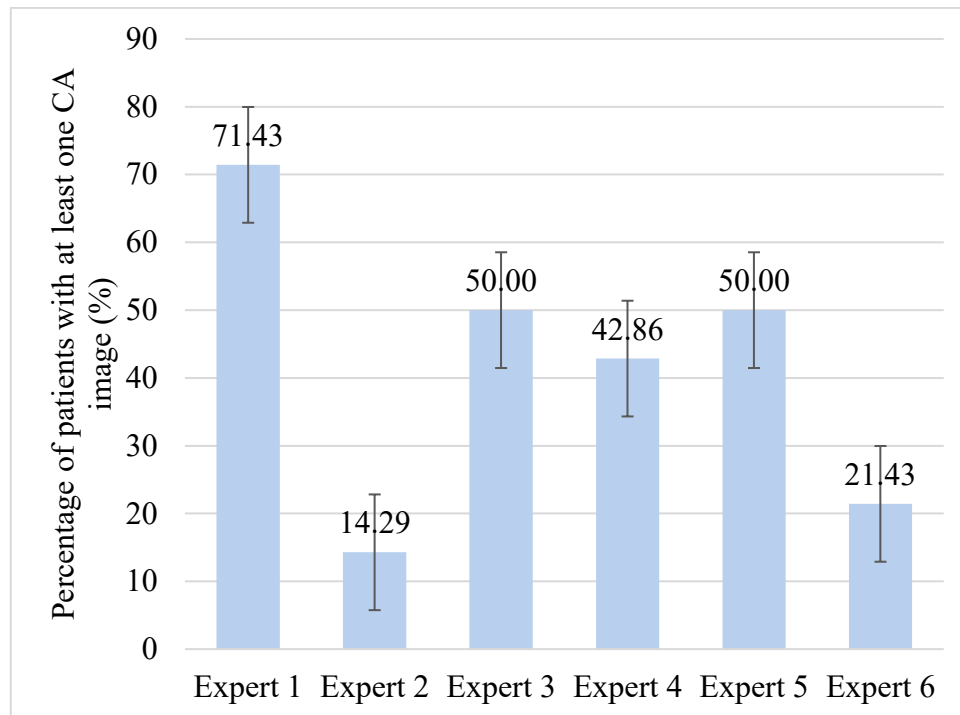


Figure 4.23: Percentage of patients with at least one CA image graded by each expert

The study by Day et al., (2016) had conducted non-mydratic testing in the Pediatric Emergency Department using the PanOptic ophthalmoscope which involved 184 patients between the age of 2 to 18 years old, and a total of 360 images were reviewed and another 45 images for secondary review. The study was able to obtain 58.70% (95% CI = 53.67% to 63.73%) of CA images (Day et al., 2016) which is considerable higher than the ratings obtained in this study but still comparable. With the patients in this study ranged between 20 and 80 years old, the difference in the ratings suggest the effect of patients' age in the quality of images. Beside this, A. Tan et al., (2010) had conducted a study to compare the sensitivity and specificity between the conventional direct ophthalmoscope and the PanOptic ophthalmoscope in detecting sight threatening retinopathy involving 200 patients above 20 years old and pupil dilation. The overall sensitivity and specificity of the PanOptic found by A. Tan et al., (2010) were 58.50% (95% CI = 42.10% to 73.70%) and 93.70% (95% CI =

88.70% to 96.9%) respectively. In contrast, a study by Pérez et al. (2014) which had conducted a mydriatic (dilation) retinal imaging in a rural hospital involving 16 HIV-infected patients, have found that the images obtained were not satisfactory for remote ophthalmologists to reach a diagnosis with confidence. According to Pérez et al. (2014), artifacts such as internal reflections and unwanted glares were also present in the images obtained. Despite the significantly lower ratings obtained in this study which was 37.83% (95% CI = 22.16% to 53.47%), it is still comparable with existing studies with and without dilation. Referring to Figure 4.23, it is also notable that there were also no overlapping standard error bars between certain experts which also indicates that the percentage is also dependent on one's learning curve with smartphone-based retinal imaging in general.

4.5.2 Analysis on User-End Survey (Likert Scale)

Difficulty level on the viewing or image acquisition the retina on the first try and after several tries for each session are scored by the examiners. Figure 4.24 shows a boxplot of the difficulty level scores rated by the examiners. The Wilcoxon signed rank test revealed that the difficulty level scores showed minimal increment in the ratings. The median score was slightly higher after several tries ($Mdn = 4.00, n = 5$) compared to on the first try ($Mdn = 3.00, n = 5$) which suggests the possibility of practice over time affecting the efficiency of retinal imaging using the device. Furthermore, the rankings for the difference in the variables were also calculated. Table 4.3 shows the calculated mean rank, sum of ranks, and the number of positive ranks, a (difficulty level score after several tries < difficulty level score on first try), negative ranks, b (difficulty level score after several tries > difficulty level score on first try) and number of ties, c in IBM SPSS. According to Table 4.3, the positive ranks is of higher value (3) when compared to the negative rank (0) meanwhile the number of ties is 2. Besides this, the calculated mean of the positive ranks is greater (2.00) than the mean

of the negative ranks (6.00). Thus, this concludes that most of the examiners agree that there is an improvement in the efficiency of viewing or acquiring image of the retina after several tries.

Table 4.3: Wilcoxon Signed Ranks Test

	n	Mean Rank	Sum of Ranks
Negative Ranks	0	0.00	0.00
Positive Ranks	3 ^b	2.00	6.00
Ties	2 ^c		
Total	5		

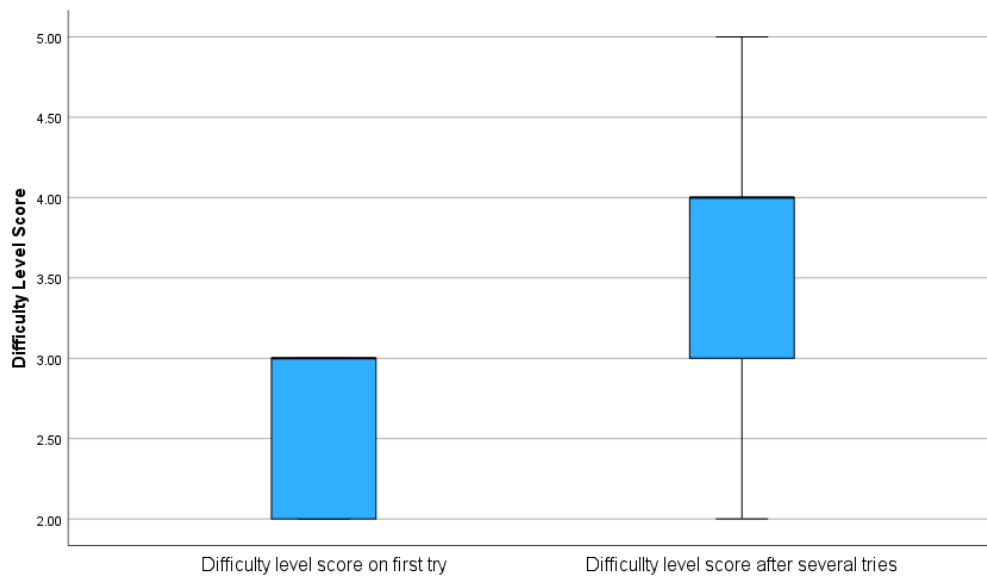


Figure 4.24: Comparison of median score for difficulty level in viewing or acquiring image of the retina between first try and after several tries

Next, the distribution of ratings from the examiners on the (i) consistency, (ii) stability, (iii) usability and repeatability, and (iv) suitability of the device are shown in Figure 4.25. The x-axis represents the five rating score levels, while the y-axis represents the frequency of examiners who selected that specific rating score level. For the consistency, a minimum rating score level of '3' was obtained, meanwhile two examiners provided a rating score level of '4' and the other two examiners provided a rating score of '5'. Based on the positive scores, all examiners agree that the developed adapter when used together with the PanOptic ophthalmoscope is able to produce image of similar quality over time. When it comes to the stability of the assembled device throughout the process, the results also show a similar positive output. A minimum rating score level of '3' was obtained from two examiners, two examiners presented a rating score level of '4', and one presented a rating score level of '5'. Based on the positive scores, it was concluded that there was no issue throughout the retinal imaging acquisition process in terms of stability. Furthermore, the positive score on the stability also suggests that the integrated side holders and grip tapes and overall design of developed adapter is capable to provide optimum stability to the examiners. As for the usability and repeatability, positive scores were also obtained. Two examiners gave a score of '5', another two examiners rated it at '4', and the last examiner gave a score of '3'. This concludes that the examiners find that the overall device is user-friendly, and capable of producing consistent results. Finally, positive ratings were obtained for the suitability of the developed adapter for the PanOptic where two examiners gave a score of '5' and the other three examiners gave a score of '4'. This concludes that all examiners agree that the develop adapter is compatible with the PanOptic ophthalmoscope. Overall, the examiners have given positive ratings on all four aspects. The minimum rating level score given by the examiners was '3' for all four aspects, with the exception on the

ratings on the suitability of the overall device which showed the best result where the minimum rating level score given by the examiners was '4'.

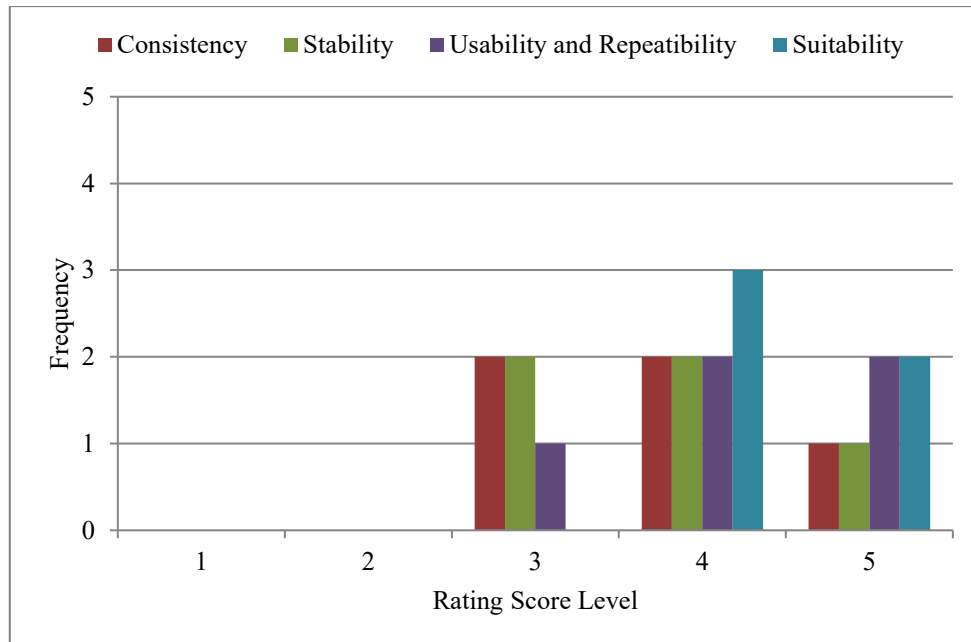


Figure 4.25: Histogram of the frequency of rating score for the consistency, stability, usability and repeatability, and suitability of the device

4.6 Chapter Summary

In this chapter, the designs of developed adapter were discussed and analysed which includes the improvements made on each prototype and the importance of the changes. Besides this, the results on the stress analysis of the finalized adapter were also discussed and analysed where the minimum and maximum Von Mises stress and 1st principal stress were calculated and compared with PLA's yield and ultimate tensile strength. Finally, the results obtained from the statistical and survey analysis based on the images collected from the clinical testing involving experts and feedback from the experts were also discussed.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

The concept of smartphone-based retinal imaging was introduced address the limitations of conventional methods of retinal imaging. An example of a conventional retinal imaging method is the desktop mydriatic and non-mydriatic fundus cameras which are known to be bulky, expensive, and highly dependent on trained professional users. Smartphone-based retinal imaging has a great potential in providing an accessible and low-cost diagnosis method that could improve the current healthcare systems especially in situations where patients are limited in getting proper disease screening and early treatment. However, smartphone-based retinal imaging still has significant limitations, thus, in-depth research is imperative to improve the current state of smartphone-based in realizing its full potential.

The first objective is to identify the optimum/best setting for factors affecting the efficiency of retinal image acquisition. This objective was achieved by comparing existing smartphone-based retinal image acquisition devices. Based on the research, a smartphone-based retinal device should have universal smartphone compatibility and sufficient field of view for retinal imaging. Despite there has been contradicting views on the best maximum field of view where some studies have stated its subjective to the area of interest, some studies have shown that size of field of view affects the efficiency of the disease detection. Besides this, an internal illumination sources provides general advantages over an external illumination source for example a smartphone's camera flash is not adjustable through the camera application that it comes with, but an internal illumination has its own control

system. Secondly, a smartphone's camera flash may not be sufficient to provide a retinal imaging path. When it comes to dilation dependency, it was proven that dilation enables easier retinal imaging process and better image quality. While dilation does improve significantly of the efficiency and quality of image taken for smartphone-based retinal imaging devices, the concern on the safety risk remains in the absence of ophthalmic professionals, as well as the preferred convenience of not needing to conduct pupil dilation especially in geographically remote areas or limited clinical settings. In addition, contradicting performance rate stated by the manufactures and the one from studies on devices that are not dilation dependent were also observed, which shows further research is needed. Moreover, it is also identified that devices that have higher dioptric power has longer working distance but are typically heavier and larger, which directly affects the overall stability of the device. Lastly, most of the existing smartphone-based devices comes with their own mobile application which provides users more control over the configuration. In a case where the device does not have its own mobile application, it uses an external mobile application.

Besides this, the second objective was achieved as a usable universal adapter was developed. Several prototypes were involved in developing the optimum version of the adapter. The main requirement of the adapter was for it to be a universal adapter that allows a variety of smartphones can be used with the PanOptic ophthalmoscope as the original adapter was only usable with the iPhone 6 series. This requirement was successfully achieved as the developed adapter was found usable with three different smartphones which were the iPhone 11, Huawei Y9 and Google Pixel 6. Furthermore, the adapter was designed based on the general ergonomic aspects which also leads to the compatibility, stability, usability and repeatability, and suitability of the device for the PanOptic ophthalmoscope. In

addition, the developed adapter allowed both preliminary data collection and clinical testing involving real experts to be conducted.

Finally, the third objective which is to simulate the reliability, validity, and performance overall of improved prototype was also achieved. Stress analysis was conducted by applying the FEA method using Autodesk Inventor. From the stress analysis, it was found that the designed adapter is sturdy since the calculated von Mises and 1st principal stress are far below PLA's yield and ultimate tensile strength. In addition, Subjective Image Quality Assessment was conducted through a non-mydratic clinical testing which involved real patients and experts. The assessment on the images collected was evaluated using the 5-point scale which is based on the FOTO-ED studies. From 140 images, 37.83% (95% CI = 22.16% to 53.47%) were clinically adequate (Grade 3 $\geq$) as graded by the experts. In addition, statistical analysis was conducted based on the experts' feedback obtained from the user-end survey. Scores on the difficulty level of acquiring the image of the retina on the first try and after several tries were compared using Wilcoxon Signed-Rank Test and reported cores are reported in median. The results revealed minimal increment in the ratings which suggests the possibility of practice over time affecting the efficiency of retinal imaging using the device. Besides this, all examiners have given positive ratings on all four aspects (compatibility, stability, usability and repeatability, suitability). The minimum rating level score given by the examiners was '3' for all four aspects, with the exception on the ratings on the suitability of the overall device which showed the best result where the minimum rating level score given by the examiners was '4'.

5.2 Future Work and Recommendations

For future work, the design of the universal adapter should be revised to provide better experience for the users. Retinal imaging can be a taxing process for experts especially if there is a large number of patients which also leads to longer duration. Thus, improvements should be done to improve its overall ergonomic properties. This includes adjusting the device's centre of weight or integrating additional features that could facilitate retinal imaging. Furthermore, the universal adapter could also be re-designed into a wearable tool such as a virtual-reality (VR) headset for ease-of-use.

Besides this, more non-mydratic smartphone-based retinal imaging device alternatives should be explored. For example, the iNview, and Paxos Scope both provide a wider field of view. A wider field of view helps in improving the process of retinal imaging and quality of images taken.

Another future work of this research is developing our own portable ophthalmoscope that uses cost-effective materials and catered for any smartphone model. As one of the main objectives of smartphone-based retinal imaging is to facilitate the healthcare system for those who are from low- and middle- income populations, having a cost-effective portable ophthalmoscope increases its rate of reproducibility. Thus, more people are able to access eye screening.

Next, other 3D filaments should also be considered for the adapter. For instance, polyethylene terephthalate glycol (PETG) or acrylonitrile butadiene styrene (ABS). In this project, the stress test simulation has shown positive output. However, in the real world, PETG is known for its higher durability, strength, and UV resistance, and resistance to heat

and chemicals. Meanwhile, ABS is also suitable great mechanical properties such as higher heat resistance and durability.

Last but not least, other methods of stress analysis such as experimental stress analysis or topology optimization could be applied to validate the performance of the proposed adapter. Experimental stress analysis method is a method that involves physically testing the proposed adapter with various loading conditions meanwhile the later method uses computer algorithms for the optimization of proposed adapter given a set of loading condition.

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APPENDICES

Appendix A: Journal Publications

1. **Latip, A. A. A.,** Kipli, K., Kamaruddin, A. M. N. A. et al. Development of 3D-printed universal adapter in enhancing retinal imaging accessibility. *3D Printing in Medicine*, 10(1), 23 (2024). <https://doi.org/10.1186/s41205-024-00231-0>

Appendix B: Technical Drawings

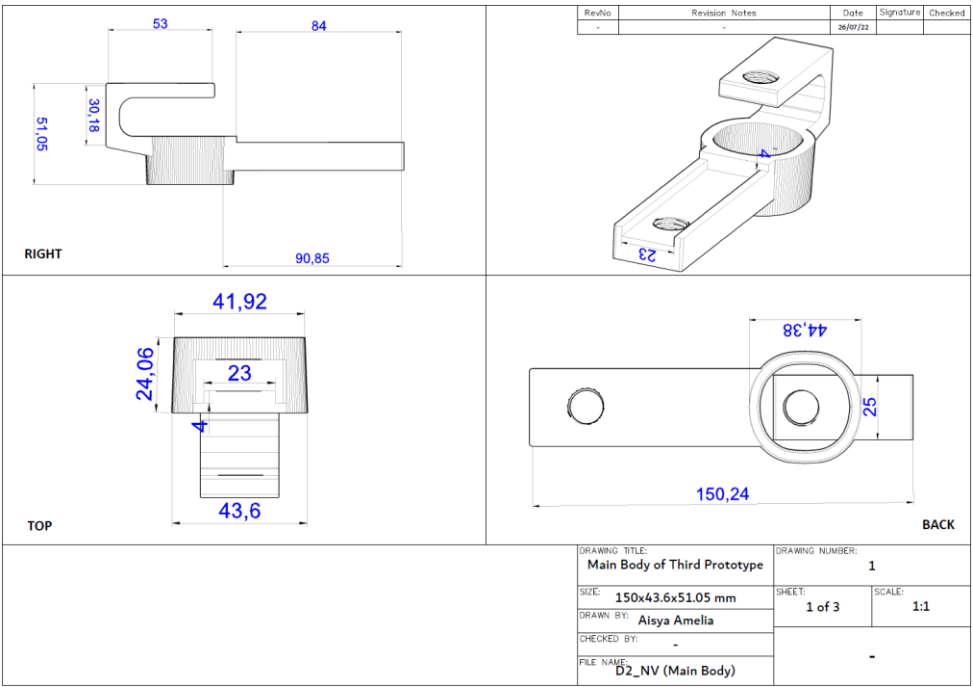


Figure 1: Third prototype

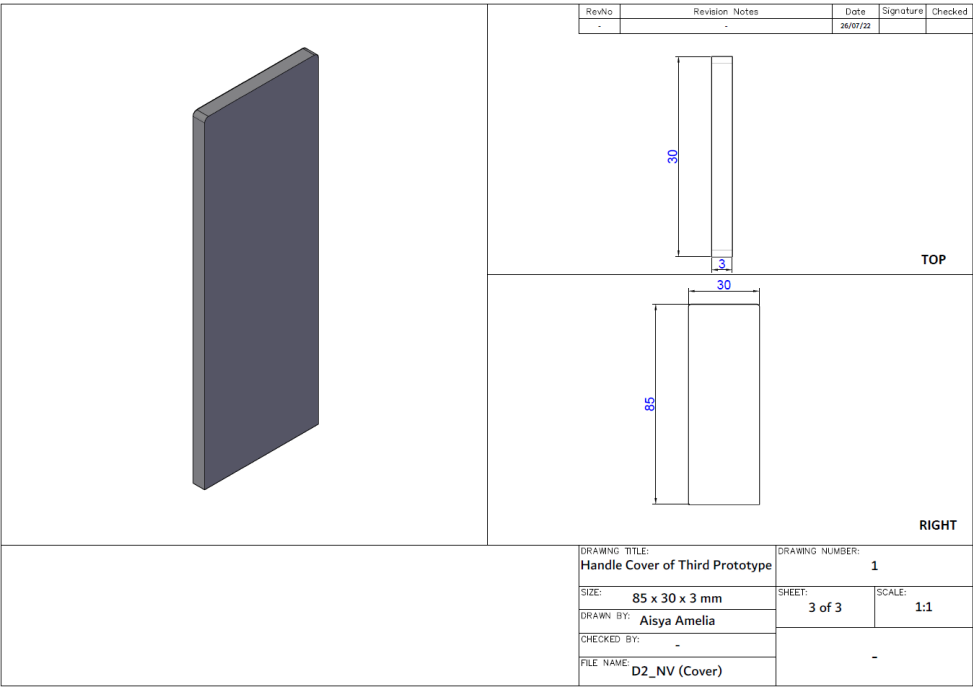


Figure 2: Handle cover

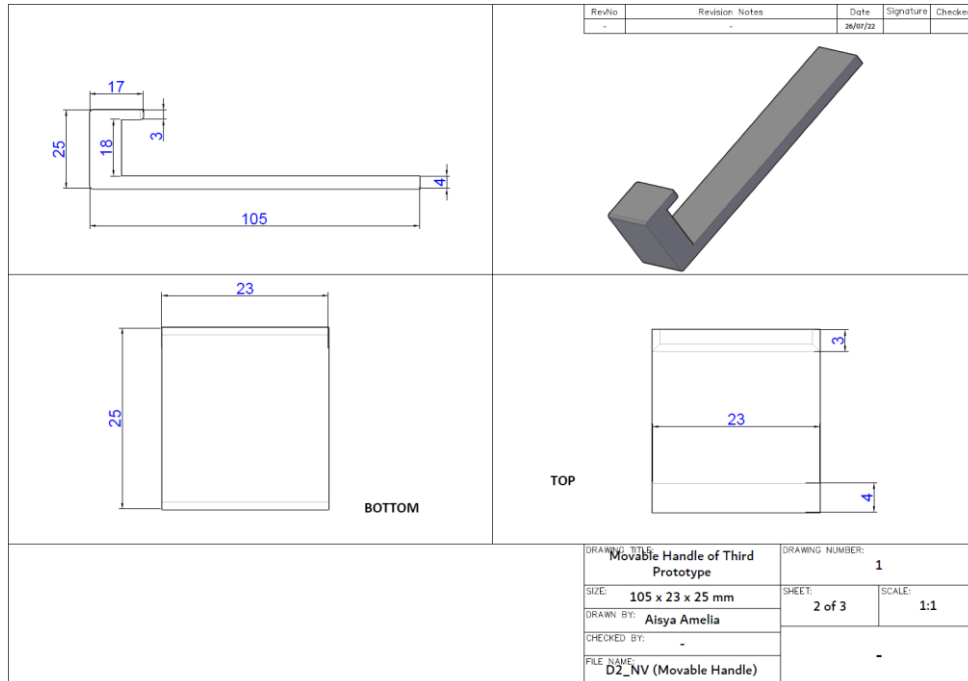


Figure 3: Movable handle

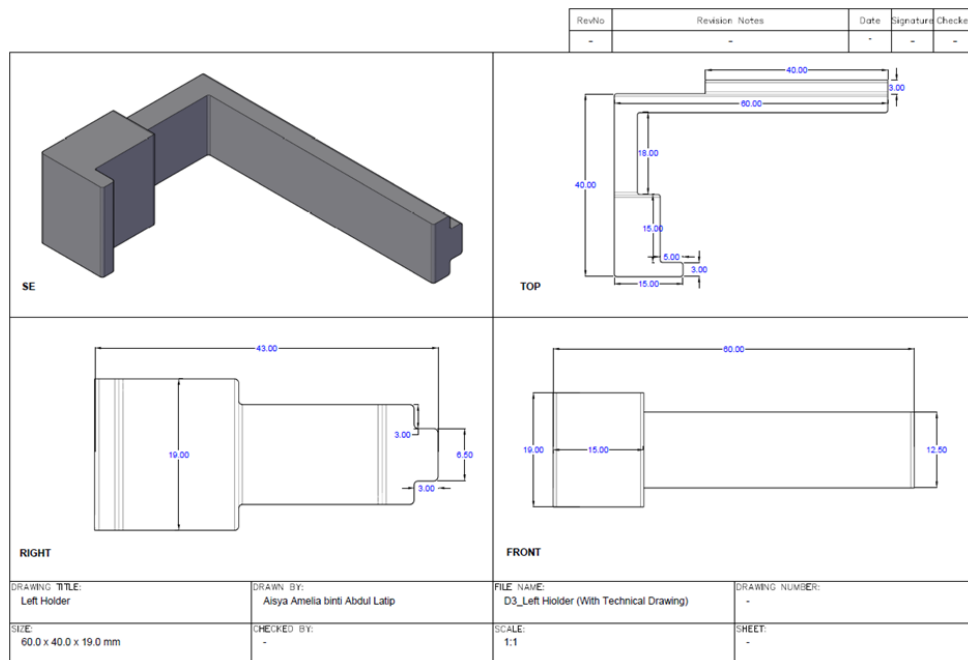


Figure 4: Left holder

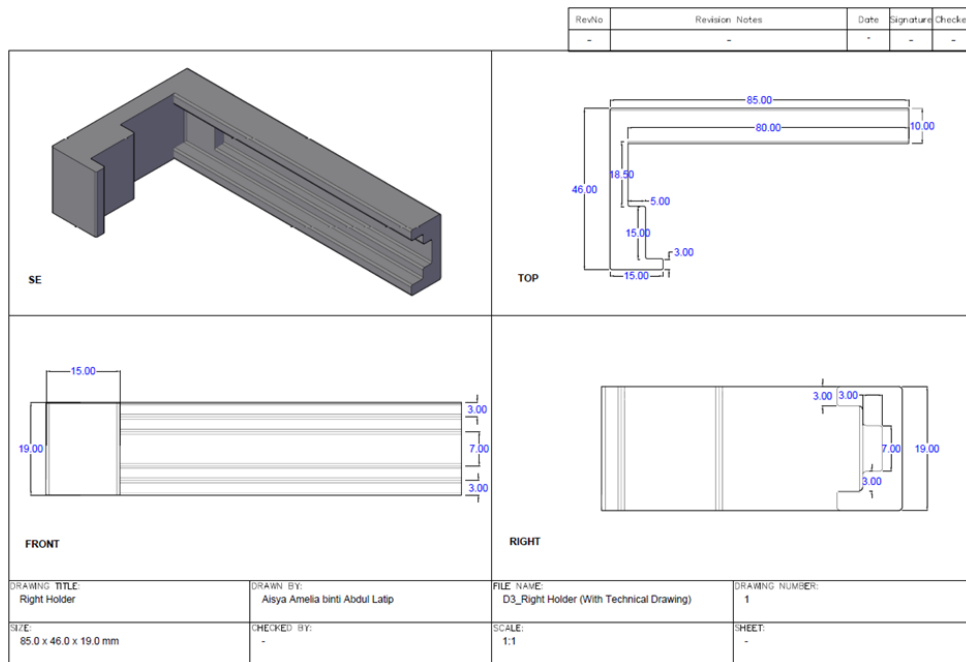


Figure 5: Right holder

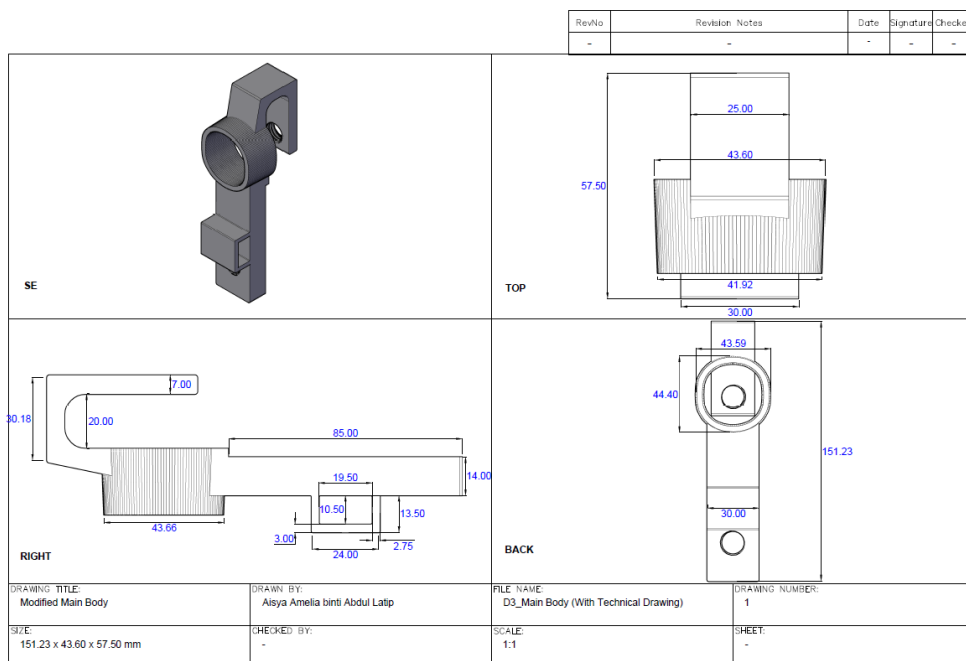


Figure 6: Finalized main body

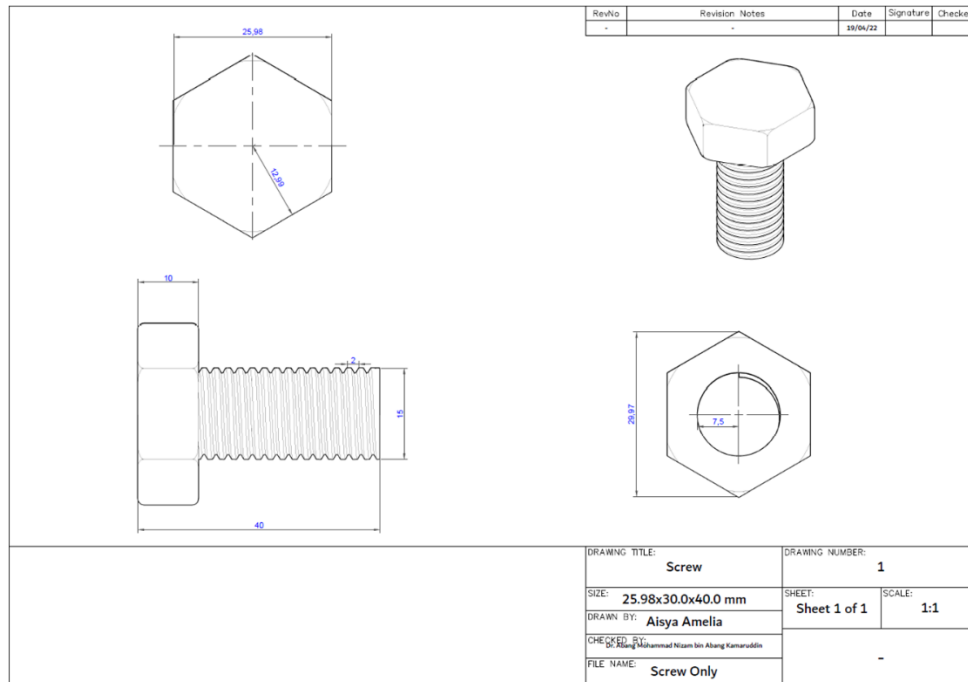


Figure 7: Screw