FACULTY OF HEALTH SCIENCES

DIVISION OF BIOMEDICAL ENGINEERING

Developing a mHealth-based portable ultrasound platform for breast cancer screening

A dissertation submitted in fulfillment of the requirements for the MSc in Biomedical Engineering

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Declaration

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Abstract

Background

Breast cancer is amongst the 10 most common cancers globally. The disease burden is increasing rapidly in Sub-Saharan African countries, where women living in rural and or remote areas are particularly prone to be diagnosed with late-stage breast cancer. This is due to the limited availability of advanced screening and diagnostic options. Ultrasound is a feasible screening tool for breast cancer, due to its portability, affordability and accuracy. The integration of mHealth with portable ultrasound enables the provision of screening services in rural and remote areas, through electronic consultation by a non-specialist with a specialist for interpretation and reporting of the ultrasound results. This project developed an application for a mHealth-based portable ultrasound platform that could be used by a non-specialist to provide breast cancer screening services with remote specialist support.

Methods

A systematic review of the literature was conducted for the period of 2004 to 2019 to gather evidence on the use of mHealth-based portable ultrasound platforms for improved access to ultrasound services like breast cancer screening. The evidence from the literature was used to design and develop a prototype of an application for a mHealth-based portable ultrasound platform suitable for breast cancer screening. The prototype application was integrated with a mobile-based portable ultrasound from Philips Lumify. Images generated by scanning a phantom breast using the portable ultrasound were uploaded onto the application and downloaded from the application to demonstrate the concept.

Results

The systematic review showed only two clinical conditions (obstetrics and cardiovascular disease) which used a mHealth-based portable ultrasound platform. The outcomes from the studies showed improved access to the respective ultrasound services in terms of patient management, early detection, improved quality of care and increased patient attendance, which resulted in access to other services. The integration of the prototype application with a mobile-based portable ultrasound resulted into a mHealth-based portable ultrasound platform prototype intended for breast cancer screening. The ability to upload images onto the platform and download images from the platform satisfied the design requirements for the platform.

Conclusion

A mHealth-based portable ultrasound prototype was developed, which has potential for improving access to breast cancer screening services. Further research including testing of the application with health professionals and patients is recommended to strengthen the feasibility of the concept.

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List of Abbreviations

2D	Two dimensions
apps	applications
BaaS	Backend as a service
BRAC1	Breast cancer 1
BRAC2	Breast cancer2
BSE	Breast self-examination
CBE	Clinical breast examination
CD	Compact disks
CSS	Cascading style sheet
DCIS	Ductal carcinoma in situ
DICOM	Digital Imaging and Communications in Medicine
DVD	Digital video disc
ECURIE	Ernest Cook Ultrasound Research and Education Institute
FDA	Food and Drug Administration
GE	General electrics
GPRS	General Packet radio services
GSH	Grooter Schuur Hospital
HICs	High-income countries
HTML	Hypertext markup language
HTTPS	Secure hypertext transfer protocol
IDC	Invasive ductal carcinoma
IDE	Integrated development environment
IEEE	Institute of Electrical and Electronics Engineers
ILS	Invasive lobular carcinoma
JPEG	Joint photographic expert group

LCIS	Lobular carcinoma in situ
LMICs	Low-and middle-income countries
MeSH	Medical subject heading
mHealth	Mobile health
MHz	Mega Hertz
MPEG	Moving Picture expert group
NCR	National Cancer Registry
NICD	National Institute for Communicable Diseases
PACS	Picture Archiving and Communications System
PNG	Portable network graphics
SFTP	Secure File Transfer Protocol
SMS	Short messages services
SSA	Sub-Saharan Africa
SSH	Secure Shell
UCT	University of Cape Town
UI	User interface
USB	Universal serial bus
USSD	Unstructured supplementary service data
UX	User experience

Chapter 1 Introduction

Breast cancer is among the 10 most common cancers globally and the cancer that most commonly affects women (Fitzmaurice et al., 2017). The burden of breast cancer has increased globally in recent years: in 2012, it affected 1.7 million women resulting in 521,000 deaths while in 2015, an estimate of 2.4 million cases was reported with 523,000 deaths (Fitzmaurice et al., 2017; Torre et al., 2017). The disease burden is increasing in developing countries where an incidence of 1.7 million cases and 70% deaths are expected in 2020 (Rivera-Franco et al., 2018). Out of the 1.7 million cases reported globally in 2012, 56.8% were from low-and middle-income countries where young women are more affected by the disease (LMICs) (Akarolo-Anthony et al., 2010; Cumber et al., 2017; Ginsburg, 2013). Furthermore, the mortality rate of breast cancer in LMICs is surpassing that of high-income countries (HICs) with a five-year survival rate of less than 40% in Sub-Saharan Africa (Cumber et al., 2017; Gutnik et al., 2016).

In South Africa, breast cancer remains the most burdensome cancer. According to the South African National Cancer Registry report of 2017 and the facts sheet, breast cancer is the most prevalent cancer (Cancer Association of South Africa (CANSA), 2017a, 2017b). The age-adjusted incidence rate of the disease was 31.4 per 100 000 women with a lifetime risk of 1 in 29 (Lince-Deroche et al., 2017). Women in rural communities have limited access to advanced technological services like screening mammography (Cubasch et al., 2018; Ramathuba et al., 2015). Rural communities, especially in LMICs, often have limited access to breast cancer screening services, limited resources in the form of specialized human resources, equipment and space. These services are only accessible in tertiary, secondary or specialist hospitals which are mostly situated in urban areas (Lince-Deroche et al., 2017). Therefore, rural women who have limited finances, access to transport, and time and family issues to access these breast cancer screening services situated in the urban centers are often diagnosed with late stage disease (Dickens et al., 2014; Lince-Deroche et al., 2017). Yet it is well documented that late-stage diagnosis results in poor treatment outcomes (Tiezzi et al., 2017).

Although mammography is the gold standard for breast cancer screening (Moseley, 2016), it sometimes gives false negative results for younger women (especially those younger than 50 years) with dense breast tissue (Padia et al., 2017). Alternative breast cancer screening methods include breast self-examination (BSE) and clinical breast examination (Rivera-Franco et al., 2018). However, CBE has low sensitivity (44.6% to 65.9%) depending on a clinician's experience in finding palpable masses (Ghartey et al., 2018; Wishart et al., 2010). Furthermore, the efficacy of BSE is not compelling since it is reported to increase benign breast biopsies and anxiety in women (Shah et al., 2017; Thomas et al., 2002). A breast cancer screening method that is reliable, effective and affordable, as well as accessible to rural South African communities, would promote early detection of breast cancer. Ultrasound has been reported to be a viable breast cancer screening modality for rural South African health facilities due to its relatively low cost, especially with the invention of portable ultrasound systems (Andreoni et al., 2015; Dickerson et al., 2017). Additionally, ultrasound has higher sensitivity in detecting breast cancer or other breast abnormalities in dense breast tissue as compared to mammography (Dickerson et al., 2017). Thus, ultrasound is used as an adjunct to mammography.

In the rural health facilities, there are majorly general doctors, ultrasonographers or midwives and these are non-specialist in ultrasound, but they can be trained to perform ultrasound scan. Thus, Dickerson et al. (2017), in their study reported the feasibility of training a non-specialist to perform breast ultrasound. However, interpretation of the results from the scan and reporting of the results are limited to only specialists (radiologists or oncologists) who are normally not accessible in rural healthcare facilities. The integration of portable ultrasound with a mobile device may provide a platform for the non-specialist to consult with the specialist on interpretation and reporting. Advances in mobile or portable device technology have enabled the proliferation of mobile health (mHealth) services. mHealth is a component of electronic health which involves the delivery of healthcare services using mobile technologies (Leon et al., 2012). Mobile or portable technologies used in mHealth include mobile phones, smartphones, tablets, personal computers like laptops, portable media players, and their mobile applications. With mHealth, data can be collected, stored and transmitted to a specialist for further analysis and management of a patient. mHealth has the potential to improve access to specialist services hence strengthening the services provided at non-specialist centers such as primary healthcare facilities in rural settings.

Integration of mHealth technologies with ultrasound includes the incorporation of a mobile or portable device and its application into an ultrasound system to provide a platform via which the non-specialist can consult with the specialist (Brunette et al., 2010). Such a platform would enable a bidirectional telecommunication of the non-specialist with the specialist where the non-specialist sends patient data (images and other information) to the specialist who responds with a report to the non-specialist via the platform.

1.1 Aim and objectives

The aim of the study was to develop a prototype mHealth-based portable ultrasound platform for breast cancer screening for remote consultation of a non-specialist with a specialist to improve access to the screening services in rural South Africa.

The aim was achieved through the following objectives:

- To review existing mHealth/internet-based portable ultrasound platforms with remote consultation, with regard to their design as well as their potential to improve access to breast cancer screening.
- To design and develop a prototype of a mHealth-based portable ultrasound platform for breast cancer screening.

1.2 Overview and significance of the study

A review of existing internet-based portable ultrasound platforms was carried out to gain evidence of how such platforms can improve access to the ultrasound services such as breast cancer screening. The findings from the review informed the development of a platform suitable for breast cancer screening. A prototype application was designed and developed as a web application. The application was integrated with a mobile-based portable ultrasound and it resulted in a web-based portable ultrasound platform for breast cancer screening. The developed platform may enable a non-specialist clinician trained in breast ultrasound to provide breast ultrasound services with remote support from a specialist. In addition, the application may provide breast cancer screening services to South African women in rural areas. This will

result into improved access to screening services which may enable earlier detection of breast cancer amongst rural South African women thus reducing the devastating outcomes of late-stage presentation.

1.3 Organization of the dissertation

The dissertation is organized as indicated below.

- Chapter 2 presents a literature review providing an overview on breast cancer with specific reference to etiology, causes and existing breast cancer screening methods. The benefits and limitations of these methods are discussed, as are alternative methods with specific focus on mHealth and portable ultrasound.
- Chapter 3 presents a systematic review of the evidence on the ability of internet-based portable ultrasound platforms to improve access to ultrasound services. The chapter reviews existing mHealth-based portable ultrasound platforms and their design, as well as the way in which they have improved access to ultrasound services.
- Chapter 4 discusses the design and development of a web-based application for a mHealth-based portable ultrasound platform.
- Chapter 5 discusses the integration of the developed web-based application with a mobile-based portable ultrasound to implement a mHealth-based portable platform for breast cancer screening.
- Chapter 6 discusses the findings of the study and concludes the dissertation.

Chapter 2 Literature review

This chapter discusses breast cancer and the need to improve access to breast cancer screening services. The discussion starts with the etiology and causes of breast cancer and the existing screening methods, followed by breast ultrasound, mHealth and portable ultrasound.

2.1 Breast Cancer

Breast cancer refers to cancer that originates from the breast tissue, most commonly from the inner lining of the milk ducts or the lobules that supply the ducts with milk (Akram et al., 2017; Feng et al., 2018; Sharma et al., 2010). Figure 1 shows the anatomy of the breast depicting a normal and a cancerous breast. Based on pathological features, breast cancer may be non-invasive (in situ), invasive or metastatic (Feng et al., 2018). Non-invasive breast cancer is a condition where the cancer cells are confined to the ducts and do not invade surrounding fatty and connective tissues (Akram et al., 2017; Sharma et al., 2010). There are two forms of non-invasive breast cancer; ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). DCIS is the most common form of non-invasive breast cancer, which is confined to the ducts (90%). DCIS has high potential to develop into invasive cancer if not detected and treated early (Feng et al., 2018). In invasive breast cancer, the cancer cells have broken through the duct and lobular wall and invade the surrounding fatty and connective tissues of the breast (Sharma et al., 2010). The common subtypes of invasive breast cancer are categorized into invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) (Strehl et al., 2011). Metastatic breast cancer is advanced cancer where the cancer cells spread to the lymph nodes and organs (Feng et al., 2018).

Tumor size (T),lymph node involvement (N) and the presence of distant metastases (M), denoted as (TNM) staging is used to define the severity of a person's breast cancer (McGuire et al., 2015). The staging of breast cancer by TNM includes stages 0, I, II, III, IV; stage 0 is non-invasive, stages I, II, III are invasive and stage IV is metastatic (Lince-Deroche et al., 2017).

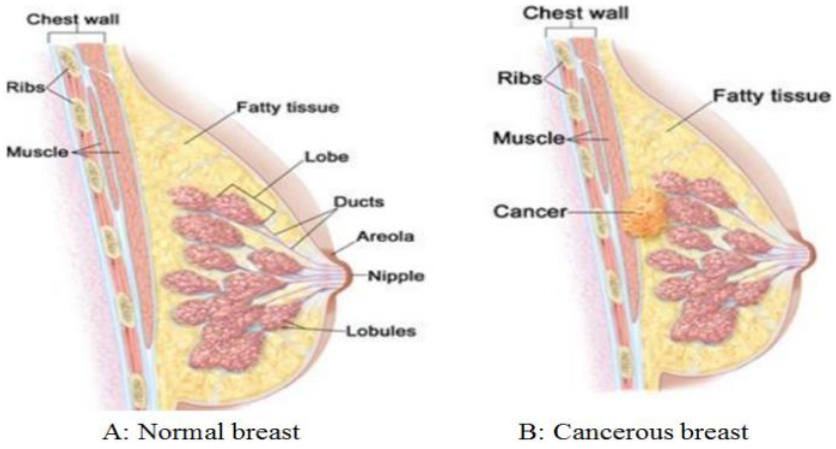

Figure 1: Anatomy of breast tissue(A) (Breast Health, 2015) and (B) (National Cancer Institute, 2019)

The causes of breast cancer are not known but there are risk factors, which may increase the chances of developing the disease. These include genetic mutations, reproductive factors, hormone replacement therapy, contraceptive use, exposure to radiation, exposure to diethylstilboestrol, benign breast conditions, family history, physical inactivity, obesity, alcohol consumption and smoking (Brewer et al., 2017; Eliassen et al., 2010; Engin, 2017; Feng et al., 2018; Kispert et al., 2017; Sharma et al., 2010).

2.2 Screening for breast cancer

The breast cancer screening methods proposed to support LMICs like South Africa are mammography, clinical breast examination and breast self-examination (Corbex et al., 2012; Rivera-Franco et al., 2018). Table 1 describes each method, its mode of operation and its advantages and limitations.

Table 1: Breast cancer screening methods proposed for LMICs

Method	**Operation**	**Advantages**	**Limitation**
Mammography	The gold standard breast cancer screening method (Moseley, 2016). Internal visualization of the breast using low-dose x-rays (Rivera-Franco et al., 2018).	Reported to consistently reduce breast cancer-related mortality rate (Megan Winner, 2017).	Relatively expensive and requires infrastructure setup and skilled personnel to operate it. Performs poorly in women younger than 50 years because of high density of the breast tissue, which may suppress the underlying tumour leading to false negative results (Padia et al., 2017). The false negative results may lead to an additional examination which increases exposure to X-ray radiation (Miglioretti et al., 2016). The procedure is painful due to compression of the breast (Újhelyi et al., 2018).
Clinical breast examination	Performed by a trained clinician. Includes detailed history and physical examination of the breast in different positions (Rawashdeh et al., 2019).	Affordable	Difficult to standardize because it depends on the clinician's expertise in finding palpable masses (Megan Winner, 2017).
Breast self-examination	Performed by the woman herself to feel lumps or other abnormalities within the breast. Recommended monthly every second week of a woman's menstrual cycle (Kocic et al., 2011).	Affordable	Unreliable because it is performed by a non-trained person. Increases the number of benign breast biopsies (Megan Winner, 2017). Increases anxiety (Pippin et al., 2020; Thomas et al., 2002).

Screening mammography is the most reliable method for breast cancer screening. The equipment utilized is expensive for low-resource settings, due to the cost of acquisition and maintenance. Poor performance in women with dense breast tissue is another limitation. Breast compression causes discomfort and fear. Figure 2 illustrates patient undergoing mammography examination where the breast is compressed between plates. As a result of the pain, patients may avoid mammography.

Figure 2: Mammography examination (Centers for Disease Control and Prevention, 2018)

Clinical breast examination and breast self-examination are the alternate breast cancer screening methods to mammography as described in Table 1. However, the limitations of these two methods directly affect their reliability for screening.

2.3 Ultrasound

Ultrasound has been reported to be a viable option for early detection of breast cancer due to its ability to detect breast cancer within dense breast tissue and its affordability (Dickerson et al., 2017). The affordability of ultrasound is contributed by the technology of the modality. Ultrasound technology involves the application of sound waves by mechanical compression or rarefaction of the medium using an ultrasound probe (Merritt, 2017). The basic components of an ultrasound system include the transmitter that energizes the transducer, the transducer which converts electrical energy to mechanical energy and vice versa; the receiver and processor which detects and amplifies the backscattered energy and manipulates the reflected signals for display; the display which presents the ultrasound image or data in a suitable form for analysis and interpretation (Merritt, 2017).

The scanning device used in ultrasound is the probe or transducer which, when placed on or in the body, transmits sound pulses and receives echoes from within the tissue or organ under examination (Szabo et al., 2013). Ultrasound transducers produce sound waves at high frequencies above the threshold of human hearing. These transducers are designed with different operating frequencies for specific clinical applications. The frequency range for an ultrasound transducer used in clinical imaging is 1MHz to 20MHz, although specialized transducers for specialized applications may have higher frequencies (Szabo et al., 2013). The current technology of transducers uses multiple piezoelectric elements arranged into arrays (Merritt, 2017). Transducers may be differentiated by the array arrangement and typically include (Merritt, 2017; Szabo et al., 2013):

- Linear arrays have their individual elements arranged in a linear order. They are used for scanning small parts and for vascular and obstetric applications.

- Curved arrays are shaped with convex curves and used in various applications with the larger curved arrays for general abdomen, obstetrics and transabdominal pelvic scanning. The small high frequency curved arrays are used in transvaginal, transrectal and pediatric imaging.
- Phased arrays are used to scan neonatal heads, intercostal areas to evaluate the heart, liver or spleen, and other areas with limited access.
- Specialized types including 2D mechanically scanned linear arrays and mechanically scanned convex arrays have also been produced.

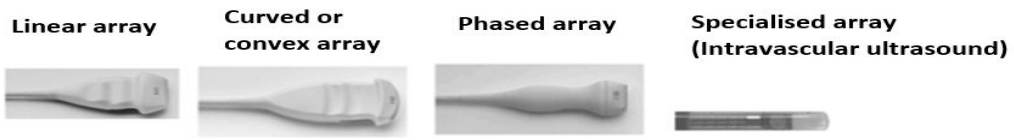

Figure 3: Different transducer arrays(Szabo et al., 2013)

The other major transducer property is the penetration depth, which decreases with increasing frequency. Superficial organs such as the breast, have lower penetration depth and therefore are imaged at higher frequencies ranging from 10MHz to 15MHz while deeper structures in the abdomen require higher penetration depth thus, are imaged at lower frequencies ranging from 2.5MHz to 3.5 MHz (Lieu, 2010). The images generated from the ultrasound scan are displayed on the screen or monitor for interpretation in the following modes: A (amplitude) mode where the amplitude is recorded as the position and strength of the reflecting structure in a 1D ; M (motion) mode for assessment of the motion patterns of specific reflectors and determining anatomic relationships from characteristic patterns of motion; and B (brightness) mode which uses brightness to represent the strength of a backscattered signal in a 2D image (Merritt, 2017).

2.3.1 Breast ultrasound

In ultrasound imaging, the breast is divided into zones including perimammary, mammary and retromammary as illustrated in Figure 4A for breast zonal anatomy (Carpentier et al., 2017). The zone most affected by breast cancer is the mammary zone with echogenic fibrous connective tissue and hypoechogenic glandular tissue. The transducer used for breast imaging is a high frequency transducer operating at a center frequency of at least 12 MHz to achieve an optimum penetration depth (Jordana Phillips, 2018). This type of transducer is typical in evaluating the mammary zone in an average range of 3cm to 4cm for dense breasts (Carpentier et al., 2017). B-mode imaging is the common imaging mode for breast ultrasound and produces 2D real-time images at frame rates of 15 to 60 frames per second (Candelaria et al., 2013; Merritt, 2017). In B-mode display, the breast tissue affected with cancer will appear darker due to the weak signals of the reflected echoes (hypoechogenic) while the normal breast tissue will appear brighter due to the stronger signals of the reflected echo (hyperechogenic) (Candelaria et al., 2013). This is also illustrated in Figure 4B with the hypoechogenic section marked A. Obtaining high quality signals or images, requires optimization of the gain setting, focal zone selection and field of view (American College of Radiology, 2016).

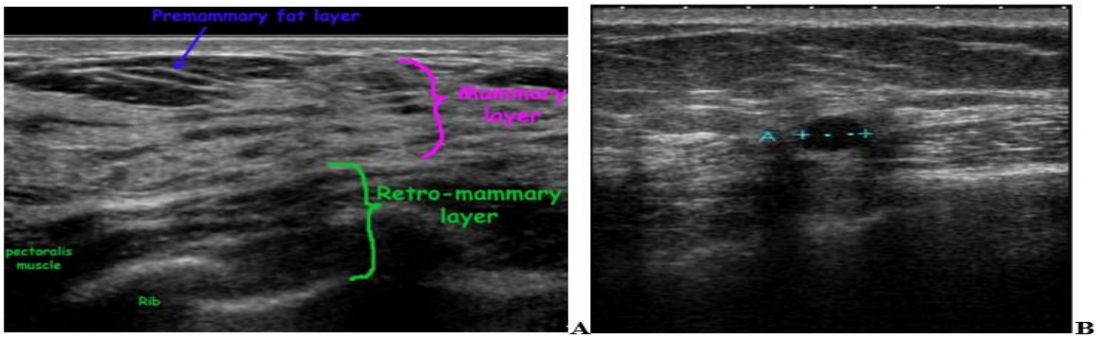

Figure 4: A: Breast zonal anatomy (Ultrasoundpaedia, 2018) and B: B-mode image display differentiating hypoechoic from hyperechoic breast tissue (Athanasiou et al., 2009)

2.3.2 Comparison of ultrasound with mammography

A study carried out by Tan et al. (2014) showed that ultrasound had a sensitivity of 40% higher than that for mammography in the detection of breast cancer in women with dense breasts. Additionally, ultrasound does not require breast compression and therefore does not cause discomfort. Mammography however causes pain due to compression of the breast (Újhelyi et al., 2018). Ultrasound does not deliver ionizing radiation as is the case with mammography (Miglioretti et al., 2016). Advances in ultrasound technology have led to portable ultrasound systems, which do not require any designated space because of their compactness; they utilize small and light devices (the probe and the display monitor) rendering them mobile as compared to the traditional console style ultrasound system (Andreoni et al., 2015). Moreover, portable ultrasound systems incorporate rechargeable batteries which make them feasible for low-resource settings with poor electricity (Becker et al., 2016). Training of a non-specialist to perform ultrasound is more feasible than training a non-specialist to perform screening mammography (Dickerson et al. (2017). However, non-specialists do not interpret and report the ultrasound results. In South Africa, only radiologists are responsible for interpretation of breast imaging including ultrasound (Louw, 2018). Other African countries like Uganda have a similar approach where only radiologists can review the ultrasound images for diagnosis (Scheel et al., 2016).

2.4 mHealth

Recently, mHealth has been used for various applications such as remote clinical data collection; dissemination of data to practitioners, researchers and patients, patient reminders, education and awareness, managing emergency response services such as for road accidents; remote monitoring of vital signs and diagnosis. mHealth for diagnostic remote support enables patients obtain specialist support without the need to incur transport expenses (Vesel et al., 2015). There is a surge of such mHealth innovations in African countries (B. Malila). In South Africa, there are several mHealth innovations, which have been developed (Botha et al., 2016), and some are still under development including piloting. The high proliferation of mobile phones and interest of the use of mobile technology by the health sector is the significant contributor to mHealth innovations in South Africa (Botha et al., 2016). Also, there is acceptance of usage of mHealth technologies by the South African rural healthcare workers to improve healthcare delivery (Anstey Watkins et al., 2018). One of the mHealth innovations which has been developed and implemented in South Africa is MomConnect, which has successfully supported more than 1.8 million South African mothers to access health-related information and has also supported mothers with HIV to access information (Pillay et al., 2016).

MomConnect shows how healthcare service delivery can benefit from mHealth technology. A study carried out by Spence et al. (2016) showed how mHealth enabled collection of reliable and sustainable data for scoring injury severity in a high-volume trauma center in South Africa.

The benefits of mHealth have triggered breast cancer-related mHealth interventions to improve breast cancer awareness and access to screening (Broach et al., 2016; Vithana et al., 2015). Ginossar et al. (2017) in their review of breast cancer-related mHealth innovations, revealed 101 applications developed by 2015 for strategies such as education, behavioral change, fundraising and providing information about breast cancer screening and treatment. These studies suggest that mHealth may be a promising intervention for promoting access to quality and affordable breast cancer screening services. It is also possible that if mHealth is integrated with ultrasound, it may make previously inaccessible ultrasound services accessible for breast cancer screening through data transmission for telemedicine consultation.

2.4.1 Data transmission

In telemedicine consultation, a non-specialist consults with the specialist who responds with results to the non-specialist. through two possible modes of data transmission, namely synchronous and asynchronous (Aziz et al., 2015). The same modes are applied to mHealth, which is a form of telemedicine. Synchronous mode is a real-time form of telemedicine where the non-specialist and specialist communicate at the same time (Daniel et al., 2015). This may comprise video conferencing, phone conversation or online chatting. Although video conferencing may be an opportunity for the non-specialist to obtain real-time guidance from the specialist, the unstable internet in a rural setting (Goodridge et al., 2016) may limit the quality of transmitted images (Pian et al., 2013). Additionally, the specialist may not have time to interpret or analyse the examinations performed by the non-specialist. Moreover, there is a possibility of misinterpretation and misreporting of the results by the non-specialist while using a phone conversation or online chatting.

Asynchronous mode is a store-and-forward form of telemedicine, where the non-specialist and the specialist do not communicate at the same time (Daniel et al., 2015). After obtaining the required patient data (images, other clinical information or reports), the data are stored and then transmitted (Aziz et al., 2015). This method also allows time for the specialist to interpret and analyse the results. Despite the advantages of the asynchronous mode of data transmission, its efficiency may be limited by the size of the data to be transmitted. This is because large data require large internet bandwidth for efficient transmission. Data compression may be necessary to reduce the data size and economize internet usage while enabling efficient transmission of data (Bairagi et al., 2008; Kaur et al., 2015).

There are two methods of data compression, namely; lossy and lossless compression (Kaur et al. (2015). In lossy compression, the file size is reduced with loss of some data, while in lossless compression, the file size is reduced without data loss (Gupta et al., 2016). Although lossy compression is more economical than lossless compression, it causes degradation in image quality. On top of data compression, ensuring security of this patient data is important. Since patient data must remain confidential, encryption of the data is necessary to avoid its access by uncredentialed users or hackers (Guillén et al., 2012). Data transfer protocols such as secure file transfer protocol (SFTP) and secure hypertext transfer protocol (HTTPS) enable secure data transmission over the internet (Gupta, 2015; Singh, 2013). SFTP uses a security layer called secure shell (SSH) to encrypt data (Gupta, 2015). In addition to the data transfer

protocols, the use of transmission control protocol over internet protocol (TCP/IP) gives a guided transmission of data to the correct destination (Harini et al., 2016).

2.4.2 mHealth and ultrasound

The implementation of data transmission for a non-specialist's consultation with a specialist using asynchronous mode may be via email, a web-based application (Caffery et al., 2004), or a mobile-based application accessible on any mobile or portable computing device. The data transmission process will be completed when the patient has been able to access the results from the non-specialist. However, most of the patients in LMICs especially in rural communities are limited by finances and knowledge to use internet based services (Barreiro et al., 2020; Moskalenko et al., 2020) such as email or web-application. Access of results by individual patients would be more affordable through text messages or by visiting the healthcare facility. Although the healthcare facilities may afford to use email or web-application to enable non-specialist consultation with specialist email implementation has more security challenges (Cush, 2014) than web application (Mata Miquel, 2015). The integration of the data transmitting application with mobile device and an image acquisition device (portable ultrasound) provides a mHealth-based portable ultrasound platform.

A conventional portable ultrasound has its probe dedicated to a specific model of an imaging system (display and processing unit), and hardwired onto the processing unit of the imaging system (Jones, 2014). Figure 5 shows three conventional portable ultrasound systems. The use of a conventional portable ultrasound systems in mHealth presents challenges. In addition to the mobile device that hosts the transmitting application, conventional portable ultrasound may require components such as storage media or a wireless or internet connection to export the ultrasound images from the imaging system to the mobile device (Swanson et al., 2016). This makes the implementation of a mHealth-based portable ultrasound platform with a conventional portable ultrasound cumbersome. However, a fully integrated mobile-based portable ultrasound would have its mobile or portable computing device serving as the imaging system as well as the host for the data transmitting application. A probe interconnects with the mobile or portable computing device via a universal serial bus (USB) or wireless connection; Bluetooth or Wi-Fi. Figure 6 shows Food and Drug Administration (FDA) approved mobile-based portable ultrasound systems with USB and wireless probes. A Wi-Fi connection has a high energy consumption (Khan et al., 2017) which leads to battery drainage, thus is not feasible for a rural setting with unstable electricity.

Figure 5: Conventional portable ultrasound systems with probe hardwired onto the processing unit; GE Logiq Book and GE Vscan from (GE Healthcare) and Acuson P10 (Healthineers, 2019).

Figure 6: Mobile-based portable ultrasound systems with flexible probes; Philips Lumify from (Philips Lumify, 2019a), IntersonSeeMore from (Interson, 2019), Clarius from (Clarius Mobile health, 2018)and Sonon from (Healcerion, 2017).

2.5 Summary

Breast cancer is a global public concern which is even more significant in the LMICs especially in the rural communities of these LMICs. Patients in the rural communities such as South African rural communities have limited access to breast cancer screening services. Improving access to, and reducing the cost of, screening services, could improve the health outcomes. Researchers have reported the feasibility of ultrasound to detect breast cancer in young women with dense breast tissue and its affordability as compared to mammography. However, the interpretation of ultrasound images requires specialists who are not accessible in rural healthcare settings. Non-specialists may be able to provide breast cancer screening services if they could easily access support from specialists. Innovative solutions are required to enable improved access to breast cancer screening services by the rural women. mHealth is a promising solution for improving access to health services such as breast cancer screening using ultrasound, by enabling a non-specialist to consult with a specialist. Implementation of mHealth with portable ultrasound systems may provide a mHealth-based portable ultrasound platform which is cost effective and accessible, ultimately promoting early detection of the disease.

Chapter 3 Systematic review

This chapter reviews the evidence from portable ultrasound platforms and their ability to improve access to patient care. The evidence was generated through a systematic review methodology.

3.1 Methods

3.1.1 Research question

The systematic review was guided by the question: *"How do portable ultrasound platforms, used for remote consultation of specialists by non-specialists, improve access to ultrasound services?"*

The PICO approach– Participants (P), Intervention (I), Comparator (C) and Outcome (O) was used to guide the search strategy and eligibility criteria:

- Participants: patients receiving portable ultrasound services from non-specialists supported remotely by specialists.
- Intervention: mHealth- and internet-based portable ultrasound platforms.
- Comparator: conventional ultrasound, or portable ultrasound without remote consultation
- Outcome-improved patient care

3.1.2 Search strategy

The following databases were searched: PubMed, Academic search premier, Engineering Village, Scopus, Cochrane Library and Web of Science. Studies conducted in both low-and middle-income countries and high-income countries were included. Relevant studies from the period of 2004 to 2019 in the English language were reviewed following defined eligibility criteria. Table 2 is a detailed description of the eligibility criteria defined by the PICO elements population, intervention, and outcome. We considered studies from a start date of 2004 because portable ultrasound systems were introduced in 2004 (Andreoni et al., 2015). Grey literature and reference lists of the relevant full text articles were consulted to obtain further studies. Initially, our intention was to extract studies on the implementation of only mHealth as an intervention and only for breast cancer screening. However due to the scarcity of the studies realized from a preliminary search with PubMed, we decided to consider studies for implementation of both mHealth and internet-based portable ultrasound interventions for any clinical condition. Details of the search terms used for the databases and grey literature are indicated in Appendix 1.

Table 2: Eligibility criteria

Characteristic	Inclusion criteria	Exclusion criteria
Population	Studies involving patients receiving direct ultrasound services from non-specialists remotely supported by specialists.	Studies involving patients receiving ultrasound services directly from specialists.
Intervention	Studies including mHealth-based or conventional portable ultrasound platforms implemented with the following technologies were considered: Mode of data transmission: asynchronous data transmission; via mHealth systems, or via internet-based platforms accessible via dedicated application interfaces Mobile or Portable device: smartphone, or tablet or laptop Ultrasound: conventional portable ultrasound, or mobile-based portable ultrasound.	Studies using platforms implemented with conventional console type ultrasound or only portable ultrasound without internet-based data transmission or platforms using any form of synchronous data transmission or platforms using asynchronous mode through email, SMS, shared folders etc.
Outcome	Studies, which reported improved patient care, measured through increased patient attendance, improved patient management through referrals, treatment or discharge, early detection, reduced waiting time, improved quality of care.	Studies which did not report the impact of the intervention through improved patient care and management.

3.1.3 Selected studies

Potentially relevant studies from the databases were retrieved using the search terms indicated in Appendix 1. The studies were saved in the Endnote reference manager for further screening. The author and an additional researcher independently screened the studies by title and abstract to generate relevant studies. The researchers made final assessment for inclusion of the studies using full text articles. Each author independently documented the reasons for exclusion of the studies.

3.1.4 Data extraction

Data were extracted from the relevant full text articles by the author and the second researcher independently. The two researchers discussed the results of the extracted data to come to a consensus. Any discrepancies were resolved by intervention of the third author. The data extraction form presented in Appendix 2 was used to extract data from relevant full text articles under the following themes:

- Author and year of study
- Study setting
    - Country of study
    - Type of healthcare facility/environment (mobile facility e.g. ambulance, primary healthcare facility, secondary healthcare facility, tertiary healthcare facility)
    - Setting of healthcare facility (rural or urban)

- Participant: patients, non-specialist, specialist
- Intervention: mHealth-based or internet-based portable ultrasound platform (defined by modality of platform; mobile application or web application; modality of portable ultrasound; conventional portable or mobile-based; and type of mobile or portable computing device)
- Clinical application for the platform
- Type of outcomes measured
- Findings/results

Data for the included studies were entered into an excel sheet to assess the full text articles with reference to the inclusion criteria.

3.1.5 Data analysis and synthesis

The data generated from included studies were analysed using a qualitative approach. This involves describing the data under the following themes; study setting (LMICs or HICs, rural or urban), type of participants (patients and their clinical conditions, non-specialist, and specialist), intervention (modality of the platform, mobile device and portable ultrasound), study outcomes due to the use of the intervention with specific consideration of impact on patient attendance, early detections, impact on patient management (referrals, treatment etc.), quality of care and turnaround time.

3.2 Results

This section presents the results of the systematic review. As shown in Figure 7, a total of 274 studies were obtained: 250 from the databases and 24 from grey literature. Duplicates were removed, leaving186studies. The 186 studies were then screened by title and abstract, leaving 36 results for full text screening. Six eligible full text papers remained. Three more eligible studies were obtained from the reference lists of these eligible papers, resulting in nine eligible full text studies. Full text studies which did not meet the inclusion criteria were excluded and are indicated in Table 8 (Appendix 3).

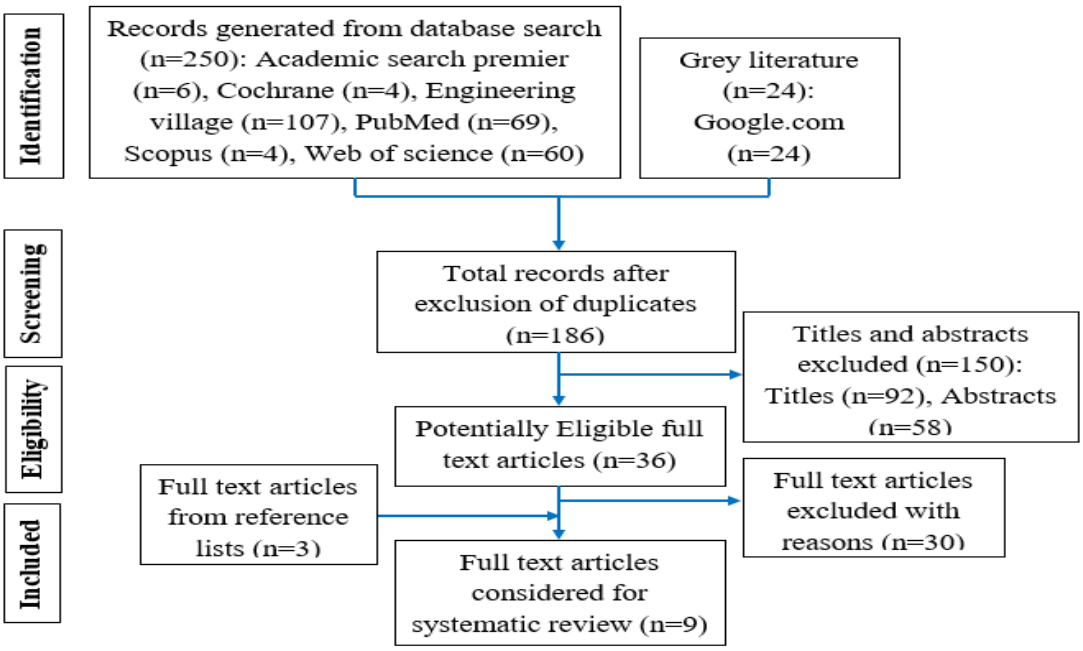

Figure 7: PRISMA flow chart

3.2.1 Study setting

For the reviewed studies, 89% (n=8) were conducted in LMICs with 87% (n=7) in rural settings. Only one study (11%) was conducted in a high-income country. These study settings are described in Table 3.

Table 3: Study settings of included studies

Country income level	Country	Healthcare setting – rural/urban	Author & year of study
LMICs	Brazil	Not specified	(Lopes et al., 2018)
	Honduras	Rural	(Choi et al., 2011)
	India	Rural	(Singh et al., 2013)
	Kenya	Rural	(Vinayak et al., 2017)
	Peru	Rural	(Ferrer et al., 2017)
	Uganda	Rural	(DeStigter et al., 2011)
	Uganda	Rural	(Ross et al., 2013)
	Uganda	Rural	(Ross et al., 2014)
HICs	Spain	Not specified	(Evangelista et al., 2016)

3.2.2 Study participants

The study participants were assessed according to clinical conditions (cardiovascular diseases and obstetrics) assessed with the intervention. This assessment is depicted in Table 4. For all the studies, there was prior training of the non-specialists in ultrasound image acquisition.

Table 4: Descriptive analysis of the study participants

Patient's clinical condition	Non-specialist	Specialist	Country &Reference

Cardiovascular disease	Imaging technician screening students at Belohorizonte school	USA and Brazil expert echocardiologists	Brazil, (Lopes et al., 2018)
	Cardiology fellow with limited echocardiography training	USA expert echo cardiographers	Honduras, (Choi et al., 2011)
	Sonographers in rural India	Worldwide physicians	India, (Singh et al., 2013)
	Primary healthcare family doctors in referrals areas of Barcelona and remote Vielha	Expert cardiologists	Spain, (Ross et al., 2013)
Obstetrics	Midwives at satellite clinics for Agakhan Hospital	Expert radiologists at Agakhan Hospital	Kenya, (Vinayak et al., 2017)
	Midwives at a rural healthcare facility in Churcampa Huancavile	Expert radiologists in Lima Peru	Peru, (Ferrer et al., 2017)
	Nurse midwives at a rural healthcare facility: Nawanyago level III	Expert radiologists in USA and ECURIE Mengo Hospital	Uganda, (DeStigter et al., 2011)
		Expert radiologists at ECURIE Mengo Hospital	Uganda,(Ross et al., 2014)
		Expert radiologists at ECURIE Mengo Hospital and an expert sonographer at Nawanyago Mission Hospital	Uganda, (Ross et al., 2013)

3.2.3 Intervention

(Ross et al., 2014; Ross et al., 2013) implemented the same platform used by DeStigter et al. (2011). In each of the studies, the intervention was implemented with a portable ultrasound system, a mobile/portable computing device and data transmission application. For two studies, it was not clear what kind of device was used to provide access to the data transmission application (Evangelista et al., 2016; Singh et al., 2013). Table 5 presents a descriptive summary of the interventions. In the nine reviewed studies, seven different platforms were identified; two studies.

Table 5: mHealth-based portable ultrasound platform implementation for the nine studies

Author & year of study	**Portable ultrasound**	**Mobile/ Portable computing device**	**Data transmission technology**	**Modality of viewing application/software**
(Choi et al., 2011)	Conventional: GE Vscan	Laptop	mVisim server	mVisum application on smartphone
(DeStigter et al., 2011; Ross et al., 2014; Ross et al., 2013)	Conventional: laptop ultrasound	Netbook	Custom-built compression and transmitting software	Server
(Evangelista et al., 2016)	Conventional: GE Vscan	Not reported	Study cast/CoreConnect; cloud-based	Study cast/CoreWeb
(Ferrer et al., 2017)	Convectional: Mindray P20	Tablet	Cloud-based server.	Interface software for diagnosis

(Lopes et al., 2018)	Conventional: GEVivid Q	Laptop	Verizon cloud; cloud-based	VitelNet
(Singh et al., 2013)	Conventional: GE's Vscan, Vivid Q, and Vivid I	Not reported	Study cast/CoreConnect; cloud-based	Studycast/CoreWeb
(Vinayak et al., 2017)	Mobile-based: Philips VISIQ ultrasound probe	Tablet	Web link; web-based	Web link

3.2.3.1 *Portable ultrasound*

As shown in Table 5, eight studies implemented the intervention with conventional portable ultrasound (Choi et al., 2011; DeStigter et al., 2011; Evangelista et al., 2016; Ferrer et al., 2017; Lopes et al., 2018; Ross et al., 2014; Ross et al., 2013; Singh et al., 2013) while one study used a mobile-based portable ultrasound (Vinayak et al., 2017). The studies which implemented a conventional portable ultrasound also used exporting components to export the images from the ultrasound to the mobile device. DeStigter et al. (2011), Ross et al. (2013) and Ross et al. (2014) in their studies, used a wireless ethernet to transfer the patient's images to the mobile device. While Ferrer et al. (2017) used a video capture card and Lopes et al. (2018) used a USB flash drive. It was not clear which exporting components were used by Choi et al. (2011), Singh et al. (2013) and Evangelista et al. (2016).

3.2.3.2 *Mobile/Portable computing device and Data transmission*

Portable devices (tablets, laptops, netbook) were used to access/host the data transmission application onto which the images were uploaded for transmission. Vinayak et al. (2017) and Ferrer et al. (2017) used tablets in their respective studies. In the studies by DeStigter et al. (2011), Ross et al. (2013) and Ross et al. (2014), a netbook was used as the device providing access to a web-based platform. Choi et al. (2011) and Lopes et al. (2018) used a laptop computer. The laptop hosted the software EchoPACS which converted the images to DICOM format before uploading them onto the data transmission application (Lopes et al., 2018). For two studies (Singh et al., 2013) and (Evangelista et al., 2016), it was not clear which type of device was used. However, the portable nature of the ultrasound suggests the use of a portable computing or mobile device at the site of image acquisition, therefore studies were included.

As shown in Table 5, the intervention was implemented with different data transmission applications. Five of the platforms (Choi et al., 2011; Evangelista et al., 2016; Lopes et al., 2018; Singh et al., 2013; Vinayak et al., 2017) were implemented with commercially available applications with servers for data transmission while the rest were implemented with custom-built applications. In the Choi et al. (2011) study, the data were first compressed to MPEG 4 for videos and JPEG for still images and then uploaded onto the mVisum server for access by the specialist. The specialist accessed the patient's data on their smartphone using the mVisum application. The authors reported a minimal loss in image quality as compared to the images which were viewed using the Vscan's Gateway workstation. Secure data transmission was established using Secure Socket Layer (SSL) (Zhao et al., 2015).

Singh et al. (2013) and Evangelista et al. (2016) used the commercially available web-based application called CoreConnect and the respective specialists accessed data via CoreWeb software accessible on the cloud. Secure data transmission was attained by SSL. The specialist reported back to the non-specialist using a web-based report. Lopes et al. (2018) used Verizon commercially available cloud-based software.

The DICOM images were uploaded onto the software for transmission to the specialist. The specialist accessed the patient's data via another cloud-based server called Vitel Net. Studies such as this one that used commercially available software, transmitted data using broadband internet.

In the study by Vinayak et al. (2017), the specialist accessed the images from the Philips medical solutions software. Although Vinayak et al. (2017) did not report how data were managed for transmission (compression, encryption), they reported no degradation in image quality. DeStigter et al. (2011), Ross et al. (2013) and Ross et al. (2014) used a custom-built software server which compressed the DICOM images to MPEG 4 format before transmission to the specialists. The images were accessed by the specialists via the server and downloaded onto their respective Picture Archiving Communication Systems (PACS).

Ferrer et al. (2017) used an application that compressed the images using an h.264 algorithm, and encrypted the images and other patient information using an algorithm based on Advanced Encryption Standard (Hameed et al., 2018). They uploaded the encrypted data onto a cloud-based server for access by the specialist. The application also included user guide for the non-specialist to acquire quality images using volume sweep imaging. In this study, the specialist reported back to the non-specialist using a web-based report accessible onto the mobile device via a cloud-based server.

3.2.4 Outcomes

All the nine studies reported positive outcomes for using the intervention. Three studies reported on the impact on patient management and referrals (DeStigter et al., 2011; Evangelista et al., 2016; Singh et al., 2013). The outcome of early detection was reported in three studies: early detection of rheumatic heart disease (Lopes et al., 2018); early identification of pregnant women at high risk (Vinayak et al., 2017); and early detection of twins (Ferrer et al., 2017). Two studies reported on increased confidence in delivery of care (Ross et al., 2013; Vinayak et al., 2017). Two studies reported on the outcome of increased patient attendance (DeStigter et al., 2011; Ross et al., 2013) which resulted in an increased number of patients receiving other services (Ross et al., 2014) outside the ultrasound service. One study for echocardiography examination reported reduced waiting time as compared to the waiting time for conventional ultrasound (Evangelista et al., 2016). Choi et al. (2011) reported the ability to detect abnormalities as they would be detected on a workstation.

3.3 Discussion

The systematic review has highlighted the scarcity of published literature in the area of internet- or mHealth-based portable ultrasound for breast cancer detection. The review yielded no eligible studies on breast cancer. Nine studies addressing other health conditions in two clinical areas - cardiovascular disease and obstetrics -met the inclusion criteria. Participants were patients receiving direct support from non-specialists who consulted with specialists via the intervention. Obstetrics was addressed most frequently. The use of portable ultrasound in obstetrics has reached the stage of implementing a quality assurance platform (Swanson et al., 2016) to support obstetric services in LMICs. Likewise, in the included studies, the intervention was mostly implemented in LMICs especially in African countries. Although, no study was done in South Africa, for all the studies done in the rest of the African countries,

implementation was specifically in the rural areas. This suggests that the intervention addresses a need to improve access to healthcare services in rural healthcare settings.

Most of the studies implemented the intervention with conventional portable ultrasound and only one study used the mobile-based portable ultrasound. The reason for this imbalance may be that the technology for cost effective implementation of the latter has become available more recently. However, Choi et al. (2011) ‘s observation of the high cost required to implement their platform may foster implementation of such platforms with mobile-based portable ultrasound. This is because mobile-based portable ultrasound platforms require less components (only the exporting component such as a flash disk) as compared to conventional portable ultrasound which require a mobile device and an exporting component.

The data transmission technology used in the platforms was through dedicated applications with servers for specialist access either through a web-based or cloud-based link, rather than through a mobile technology application. The strategic implementation of such data transmission technology as opposed to a using mobile application may be due to limitations of mobile operating systems or concerns with security. Five of the platforms were implemented with commercially available applications with servers for data transmission (Choi et al., 2011; Evangelista et al., 2016; Lopes et al., 2018; Singh et al., 2013; Vinayak et al., 2017), while the rest of the platforms were implemented with custom-built applications. Custom-built applications allow designers to design according to user needs. Addressing user needs is key for implementation of mHealth technologies for LMICs or developing countries to increase scalability and usability (Niemöller et al., 2016). The incorporation of an image acquisition protocol in two studies supported the non-specialist in acquiring images appropriately. The outcomes showed improved patient care as measured through impact on patient management and referrals, early detection, improved quality of care, increased patient attendance, and reduced waiting time. Despite the outcomes showing positive impact of the intervention, the review showed several limitations. Firstly, the number of eligible studies retained in the review was small. Secondly, different clinical conditions were addressed in the nine studies reviewed, limiting the generalizability of the findings. Thirdly, the solutions implemented had different image formats and transmission bandwidths; discussion of these was beyond the scope of the review.

3.4 Conclusion

Although the review did not yield results on the use of portable ultrasound for breast cancer screening, implementation of such platforms with other clinical conditions has shown that they have the potential to improve access to ultrasound services by enabling a non-specialist to consult with a specialist to provide services by way of data transmission for telemedicine consultation. Also, the lessons learnt from the review show that implementation of a platform with a mobile-based portable ultrasound may be more cost effective as compared to using a conventional portable ultrasound. The cost effectiveness of the platform would in turn increase the accessibility, scalability and usability of the platform. Furthermore, it has been learnt that implementing the platform with an application which is accessible on any mobile device would increase the accessibility of the platform. Thus, increasing the accessibility of the services provided by the platform to the intended population.

The aim of this study in this dissertation was to develop a mHealth-based portable ultrasound platform for breast cancer screening. This platform is developed according to the evidence and lessons learnt from the

reviewed studies to create a platform that may increase accessibility of the services to the rural South African women.

Chapter 4 Design and development of a web application for a mHealth-based portable breast ultrasound platform

This chapter discusses the development of a data transmission application for a mHealth-based portable ultrasound platform suitable for breast cancer screening, which comprised the second objective of the research project. The design was informed by the findings of the systematic review presented in the previous chapter. The development was achieved through the following stages:

1. Definition of design requirements
2. Design of a prototype of the application
3. Development of the prototype of the application
4. Integrating the application with the mobile-based portable ultrasound

4.1 Design requirements

The requirements for the design of the data transmission application discussed here were established after consideration of the literature and the results of the systematic review. A data transmission application may take the form of a mobile application or a web application (Selvarajah et al., 2013). In case of a mobile application, access to the platform may require a specific mobile device with a specific operating system (either android based or iOS based) as used by GE applications (GE Healthcare) and Philips Lumify (Philips Lumify, 2019b) or other dedicated applications . While a web application is not specific to a certain operating system as it does not reside on a local server. The application is accessible on any mobile or portable computing device (smartphone, tablet laptop etc) using browsers such as google. Thus, in this dissertation a web application was developed to enable data transfer between the non-specialist and the specialist. The data would finally be transferred to patient in form of a report from the non-specialist by either a phone call or direct visit at the healthcare facility. The application comprises of a frontend and a backend. The backend includes a database and a server. The application is accessible on any mobile device via a browser.

The following design requirements were defined for the development of the application:

1. Accessibility: the app would be designed and developed as a web application to ensure that it would be accessible on any mobile/portable computing device.
2. Cost effectiveness: the web app would be designed for asynchronous data transfer, which is more cost effective in terms of bandwidth requirements.
3. Effectiveness of the application dependent on the users' relationship with the application: the app would be designed with simple icons for ease of use.
4. Implementation with any portable ultrasound device that is compatible with a mobile device: the app would be designed as a web application operating under a browser so that it would be accessible on any mobile device compatible with different portable ultrasound probes.
5. Backend: the web application would be created with backend services that would enable patient data to be exchanged between users and would provide database storage services and user authentication.

4.2 Web application overview

A web application was preferred over a mobile application to provide a platform that would be accessible on various mobile/portable computing devices. This was also intended to enable a user to select their preferred vendor for the components (mobile/portable computing device and portable ultrasound).

Figure 8 illustrates how the application would be implemented to perform the following functions: (i) enable a non-specialist to upload patient data (image and other identification information) for sending to a specialist; (ii) enable the specialist to download patient data sent by the non-specialist for interpretation and reporting; and (iii) enable the non-specialist to access the specialist report for reporting the results to the patient. The functions of the application would be implemented via two main web pages; one to enter patient data and one to download patient data on both the non-specialist and specialist ends. This is depicted in Figure 8.A user signs in via the sign in page to access the main pages of the application.

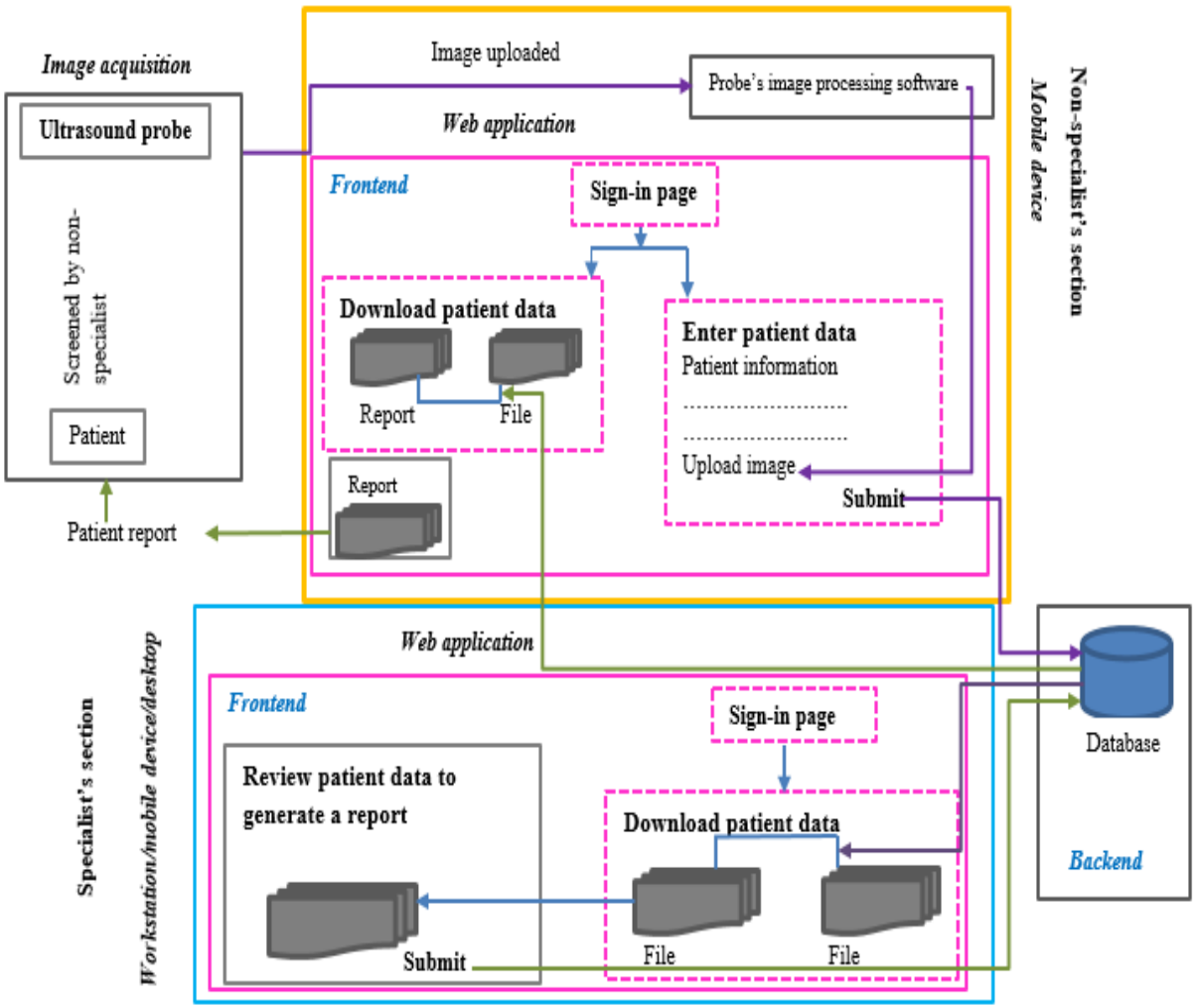

Figure 8: Web application for portable ultrasound

Table 6 describes the four functions of the web application to enable a non-specialist to consult with a specialist.

Table 6: Functional requirements of the application

Functionality	User	Description and requirements	User tasks
Enter patient data	Non-specialist	Enter patient information (identification and family history on cancer) and upload patient images. Upon signing in, the application prompts the user to the functionality page to *"Enter patient data".*	1.Sign in 2.Enter patient data 3. Submit
Download patient data	Specialist	The application enables the user to download patient data sent by the non-specialist. Upon signing in, the application prompts the user to the functionality page to access the task: *"Download patient data"*.	1.Sign in 2. Download patient data
Review patient data to generate report	Specialist	After downloading the patient data, the user is required to review the patient information and images to generate a report and upload it for access by the non-specialist.	3. Edit patient file, update the file as a report. 4. Submit
Download patient data	Non-specialist	The application enables the user to download the patient report provided by the specialist. Upon signing in, the application prompts the user to the functionality page to access the task: *"Download patient data"*.	1.Sign in 2. Download patient data; download patient report.

4.3 Design of the web application

The design of the application was based on the design specifications described in section 4.1. The design of the application included design of the frontend which was represented by mock-up prototypes of web pages. The web pages formed the user interface (UI). The interaction of the user with the web pages and their transition from one web page to another formed the user experience (UX). The UI and UX were designed using Adobe XD (Adobe, 2019), an open source tool. The UI design resulted in a low-fidelity mock-up prototype while the UX design resulted in a high-fidelity mock-up prototype of the application. The functionality of the application required backend services, which are described in the development (section4.4)

The web application was named *Breast Tele-ultrasound app*, referring to its purpose of supporting breast health and the application of telemedicine technology in the provision of ultrasound services. The main colors considered for the design of the user interface of the web application were; shocking pink defined by hex code #F916C7, white defined by hex code #FFFFFF and deep coffee defined by hex code #763F3F (Design Colors, 2021). #F916C7 is close to the color normally used to denote breast cancer. #FFFFFF was used for the text inside the #F916C7 color code, for clear and bright visibility. While #763F3F was used for the rest of the text used in the application. The web application encompassed the following pages: home page, registration page, sign-in page, user profile page, and the functionality pages (*Enter patient data* and *Download patient data*).

4.3.1 Home page

The home page is the first landing page when the user opens the application. Figure 9 shows the home page. Its purpose is to give information about the application, such as how the application would be used and who should use it.

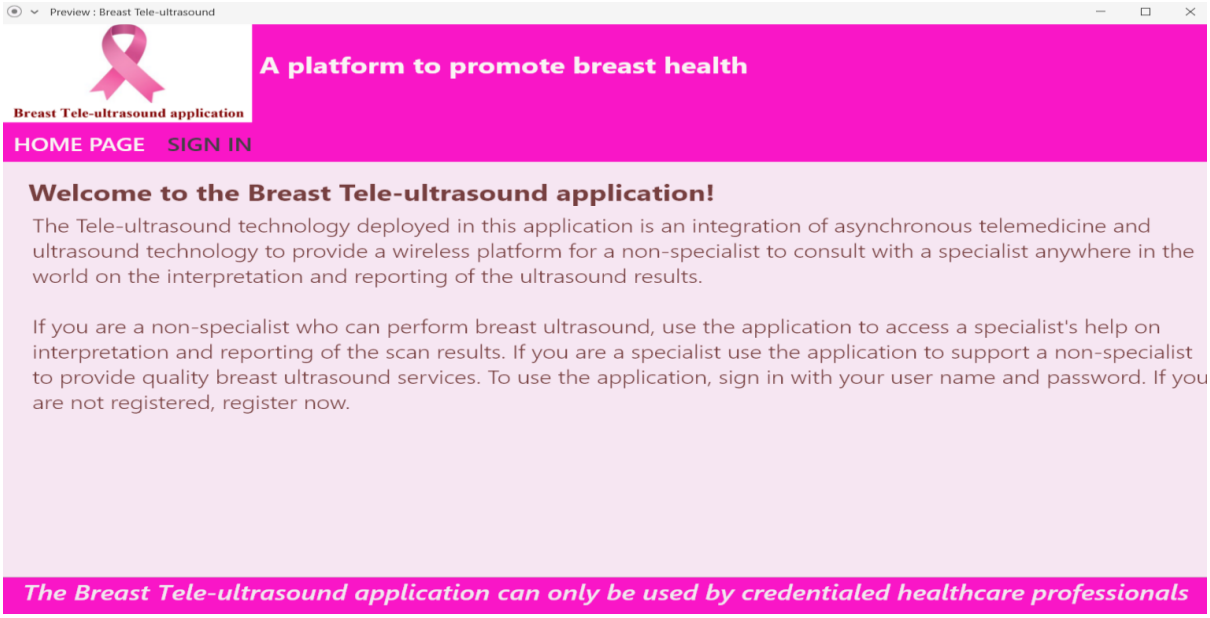

Figure 9: Home page

4.3.2 Registration page

The purpose of the registration page is to enable a user to register to be authenticated before using the application. The user would register with their username and password to obtain an account that would be used for signing in. Figure *10* shows the registration page.

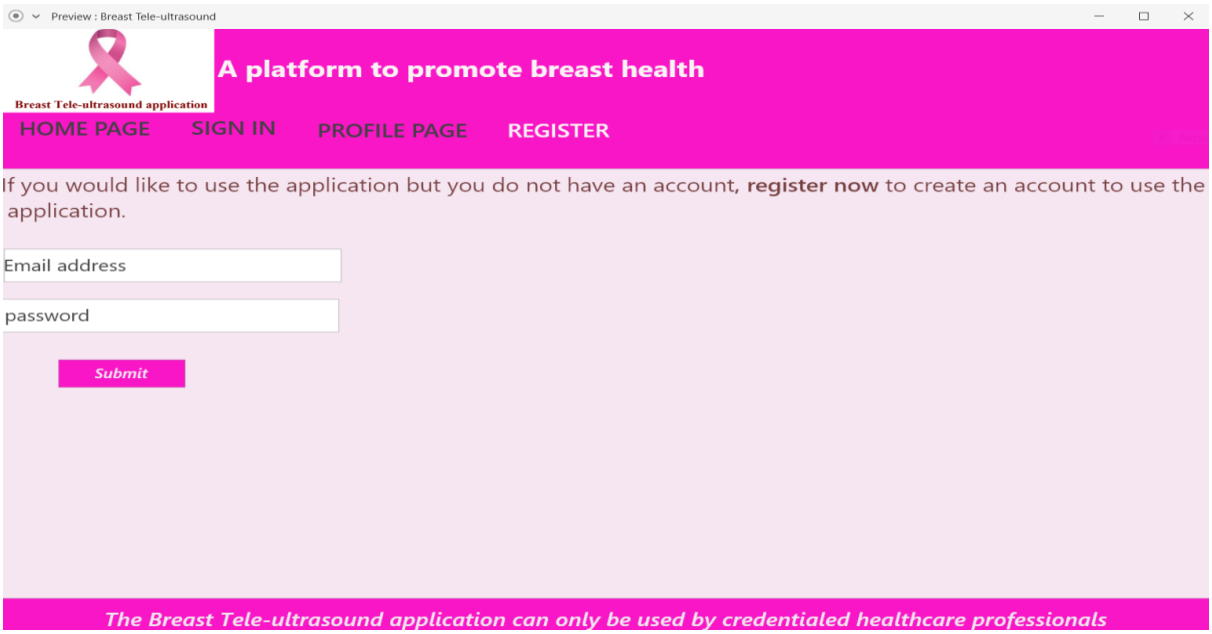

Figure 10: Registration page

4.3.3 Sign-in page

The purpose of the sign-in page is to allow a user to sign in to use the application. Signing in authenticates the user and gives them functionality according to their information used during registration; username and email address. Figure 11shows the sign-in page.

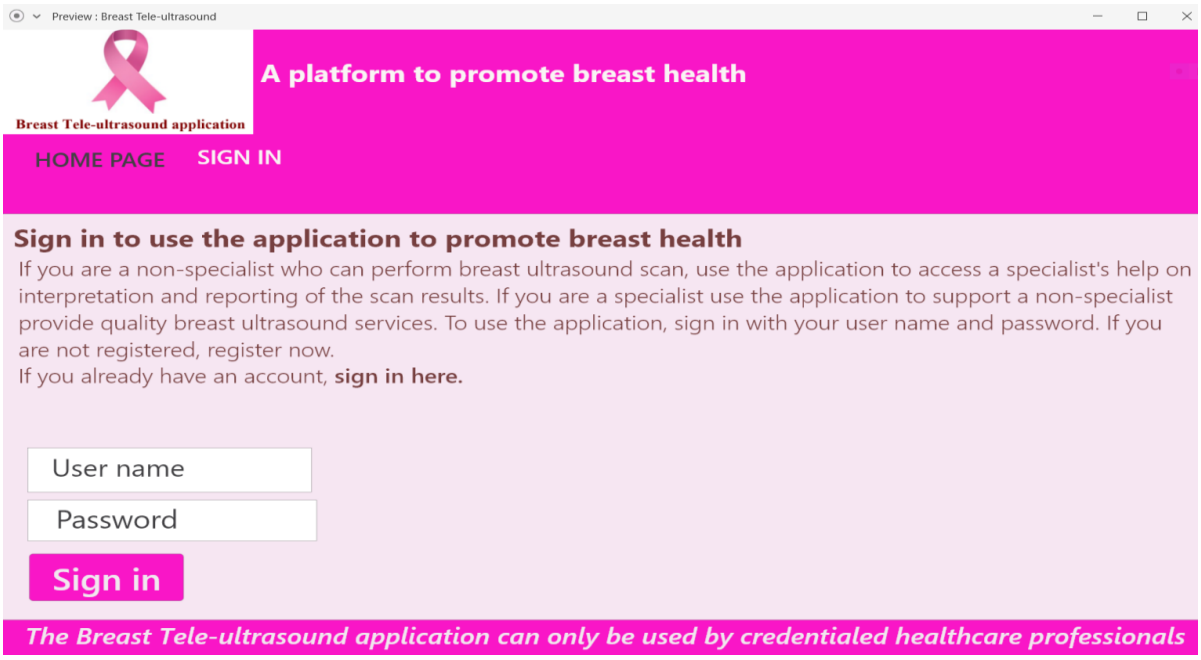

Figure 11: Sign in page

4.3.4 Profile page

The purpose of the profile page is to allow a user to update their profile data by changing the password. Figure 12 shows the user profile page. This page can only be accessed after the user has signed in.

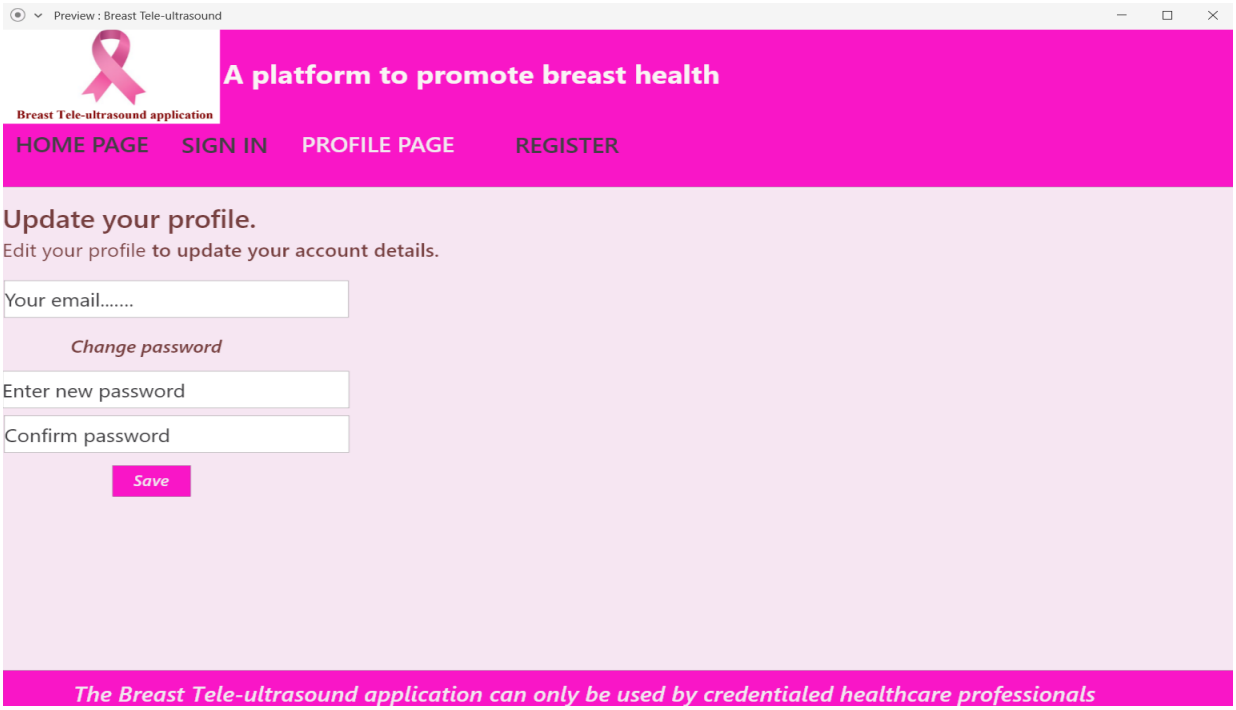

Figure 12: User profile page

4.3.5 Functionality page

After signing in, a user would be taken to the functionality page that provides access to the tasks to be performed. The functionality pages include the *Enter patient data* and *Download patient data* pages.

4.3.5.1 *Enter patient data page*

The purpose of the Enter patient data page is to enable a user (a non-specialist) to enter patient data including patient clinical information and the ultrasound image generated from the scan. Figure 13 shows the *Enter patient data* page.

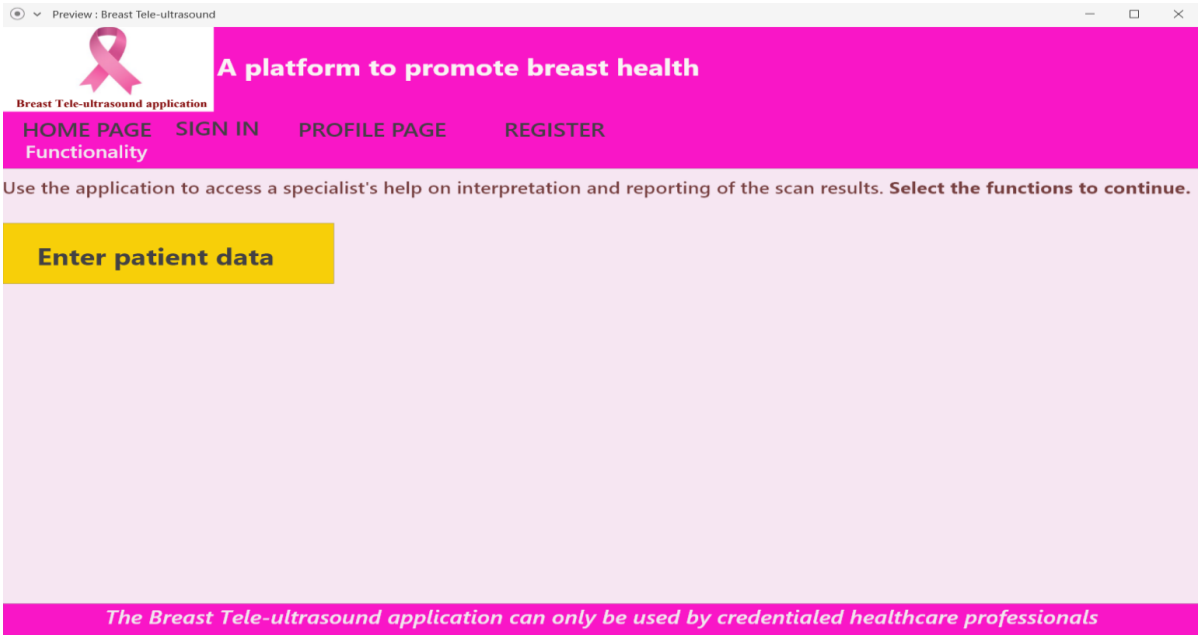

Figure 13: Enter patient data page

After scanning the patient using portable ultrasound, the image saved on the mobile device would be uploaded onto the web-based application. The information about the patient would also be captured. Figure 14 demonstrates the data entered on the page, namely patient information captured, and an image uploaded.

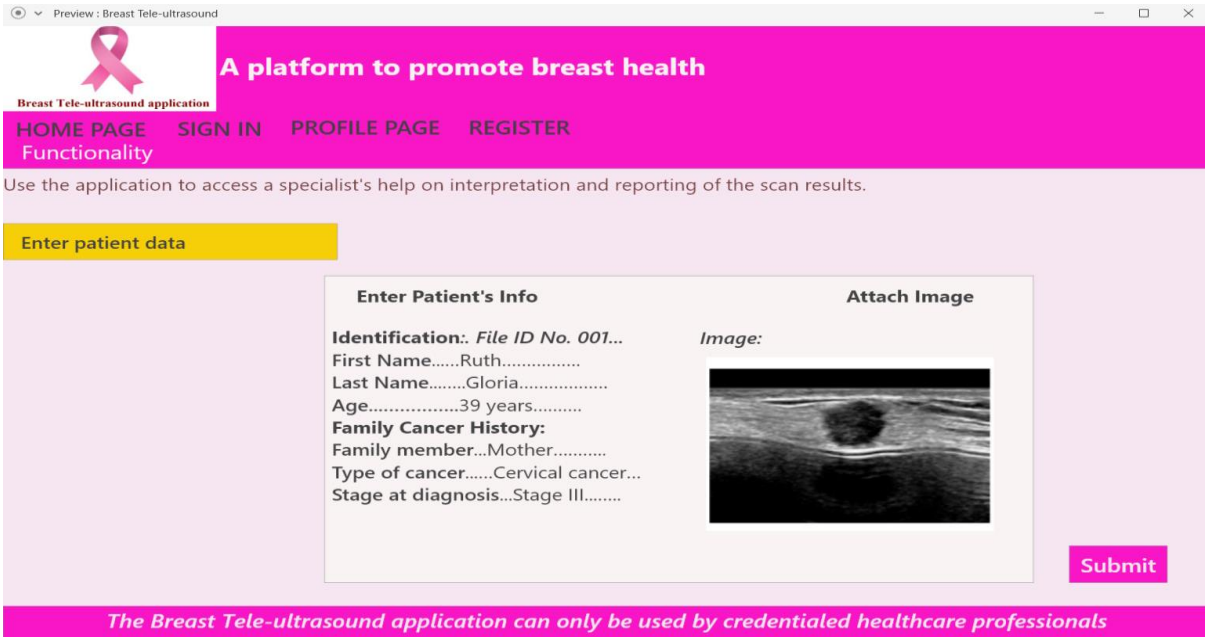

Figure 14: A demonstration of the data entered on the page

4.3.5.2 *Download patient data page*

The purpose of the *Download patient data* page is to enable a specialist to download patient data sent by a non-specialist for review and also enable a non-specialist download patient report sent by the specialist. After the data have been entered, they would be stored in the database. When the specialist signs in, they would be taken to the *Download patient data* page, shown in Figure *15*, to access the data uploaded by the non-specialist. Figure 16 demonstrates the data to be downloaded by the specialist on the *Download patient data* page. On this page, the specialist would select the patient File: ID No. to access their data for review and reporting.

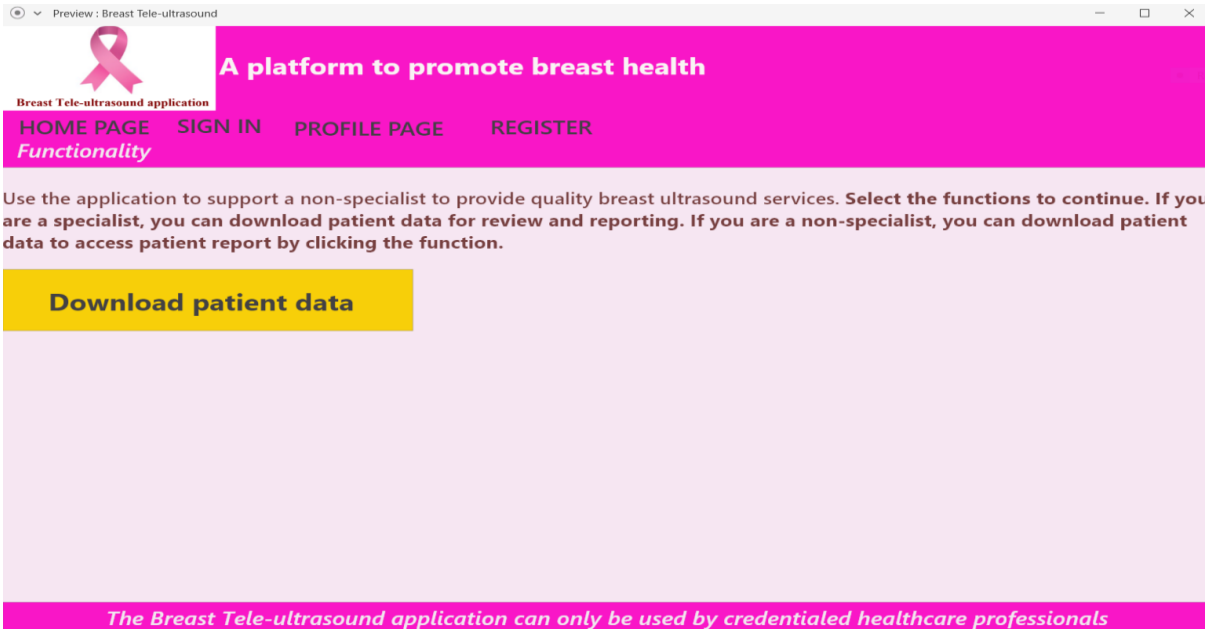

Figure 15: Download patient data page

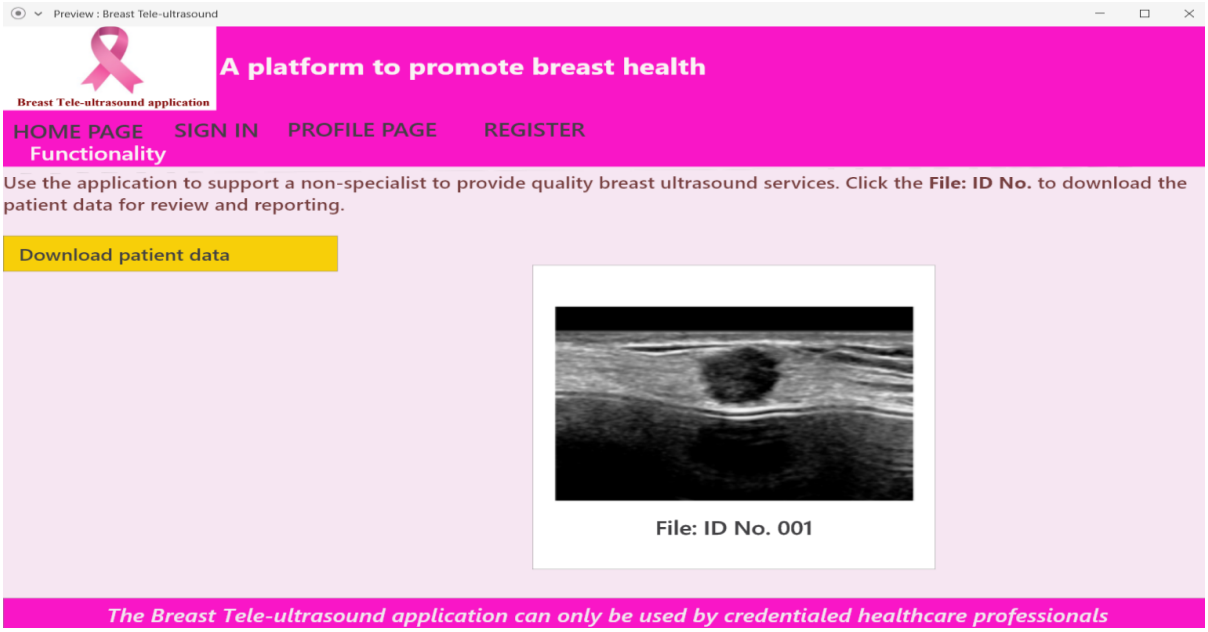

Figure 16: A demonstration of the data to be downloaded by the specialist

After downloading the data, the specialist would interpret the image and also use the other patient information to generate a report, which will be submitted for access by the non-specialist. The report would include the specialist findings as indicated in Figure 17 below.

Figure 17: Patient data after review by the specialist

To access the report generated by the specialist, the non-specialist would sign in and be taken to the functionality page where they would select the *Download patient data* function to access page shown in Figure *15*. On this page, the patient data, which was previously named File:ID No. before its review by a specialist, appears as a report with the name Report: ID No. (Figure *18*), which provides the non-specialist access to the report, depicted in Figure *19*.

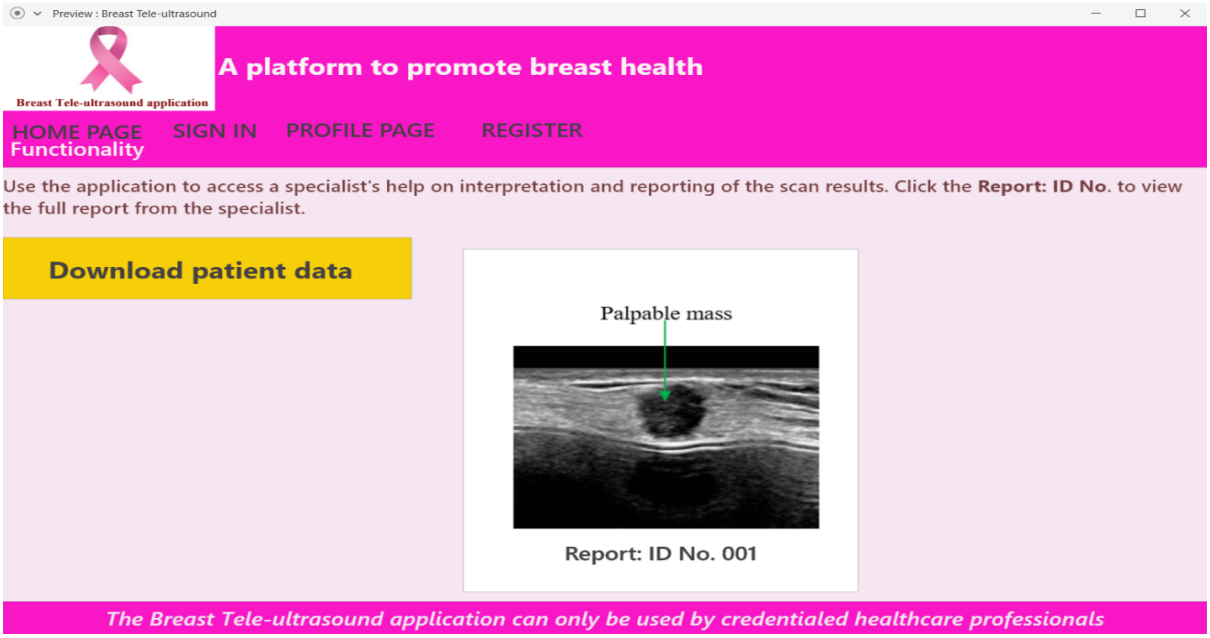

Figure 18: Access to the report to be downloaded by the non-specialist

Figure 19: Patient report

4.3.1 User experience design

To assess the flow of the web pages of the application, a UX (user experience) design was created using Adobe XD. Adobe XD has a wire-framing tool, which was used to interlink the web pages to create a workflow. The UX is shown in Appendix 4 (Figure 50). The UX design formed the high-fidelity prototype of the web application. The UX designs for anon-specialist using the application to upload patient data for access by a specialist, and for a specialist using the application to access patient data from the non-specialist and review the data to generate a report for access by a non-specialist, are illustrated in Appendix 4 (Figure 50 Figure 51 Figure 52 Figure 53).

The UX design helped to identify the following design errors;

- The web pages didn't have the option that would enable a user to return to the home page.
- There was no possibility for a user to sign out from the appropriate pages.
- There was no link between the sign-in and registration pages.

These errors were resolved during the development stage, discussed in Section 4.4.

4.4 Development of the application

The high-fidelity design described in section4.3 and illustrated in Appendix 4 (Figure *50*, Figure *51*,Figure *52*,Figure *53*), were transformed into real-world prototypes by coding. These high-fidelity designs were developed into web pages for the frontend of the application, which would constitute the user interface for the users to perform their respective tasks. The frontend was created using Visual Studio IDE (https://code.visualstudio.com). The data entered by the user could be stored using backend services. The backend as a service was implemented using Google Firebase (https://firebase.google.com) to provide data storage services and authentication of the users.

4.4.1 Backend development

The backend was implemented using Firebase. The data stored included the patient data and user information. Figure 20 shows an example of patient data stored. These data were captured via the frontend and stored in the database. The data were stored as; title defined by "Report: ID No.", patient information as content, image "bus 2 PNG" presented as file reference (fileref). The data may be accessed through a hyperlink.

Although firebase automatically encrypts data using https data transfer protocol, security rules were also applied to ensure security of patient data. Data compression did not form part of the scope of work of this research study.

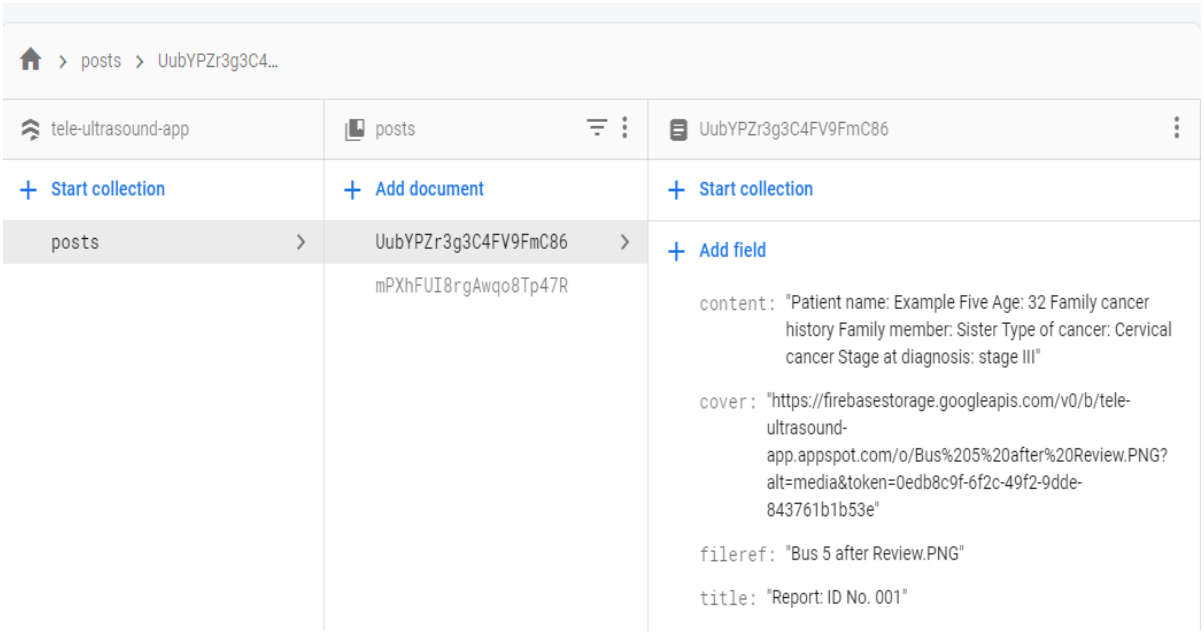

Figure 20: Data storage

The backend was also intended to provide user authentication. Figure 21 shows an example of the users authorized to use the application. These users were captured in the database by their names, email and password.

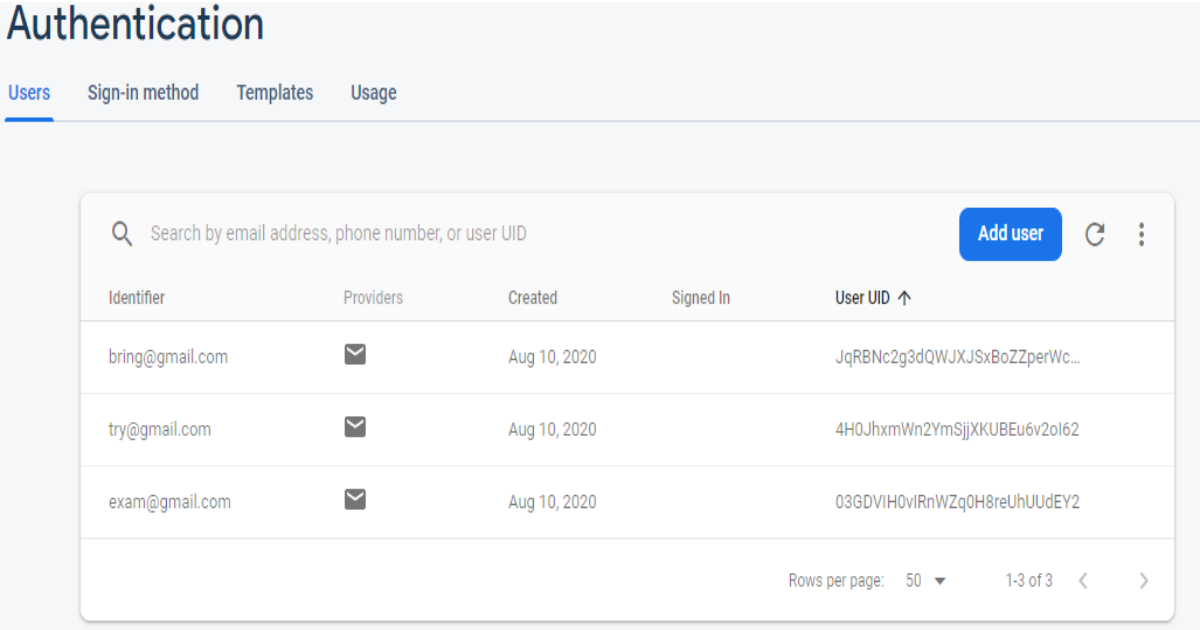

Figure 21: A list of authenticated users; captured by their email and password

4.4.2 Frontend development

The frontend was developed using Visual Studio IDE. The high-fidelity mock-up prototypes of the web pages described in section 4.3were transformed into real-world prototypes in the form of the frontend. This included presentation of the web pages, using HTML, styling of the web pages using CSS and real programming of the web pages to present them as interactive pages using JavaScript. Each of the web pages developed is described in this section with their respective illustrations presented as screenshots.

4.4.2.1 *Home page*

The home page (Figure 22) is the first page that can be accessed by a user on opening the application. The page also includes the information about the app. A menu bar was included on the page to enable the user to access the sign-in page (Figure *23*).

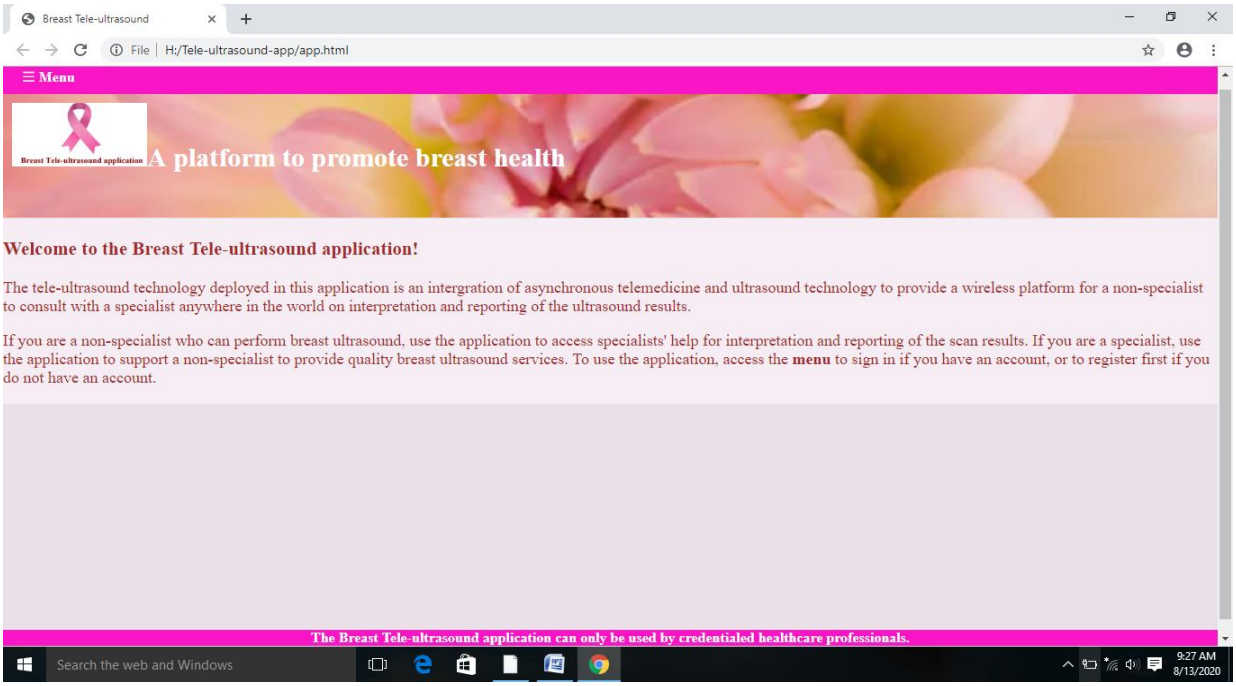

Figure 22: Home page

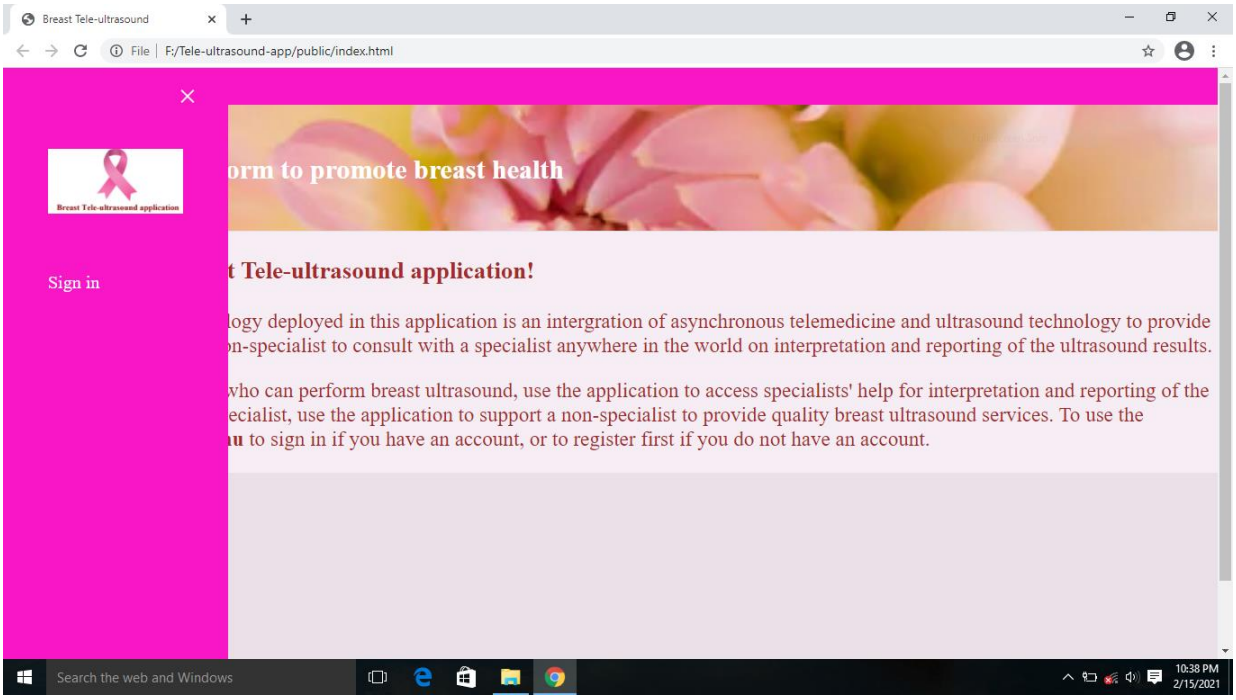

Figure 23: Access to sign in page

4.4.2.2 *Sign-in page*

The *Sign-in* page (Figure 24) enables a user to use the application by signing in with their email and password. On this page, a user registers with their email address and password to get an account and when

they click the register button, they are registered. After registration they could proceed to sign in with their registered email address and password by clicking the sign in button. A user could use this sign in page, to sign out by clicking the sign out button and the user is taken to the home page as shown in Figure *23*. The home page can also be accessed on this page via the menu bar as shown in Figure 25.

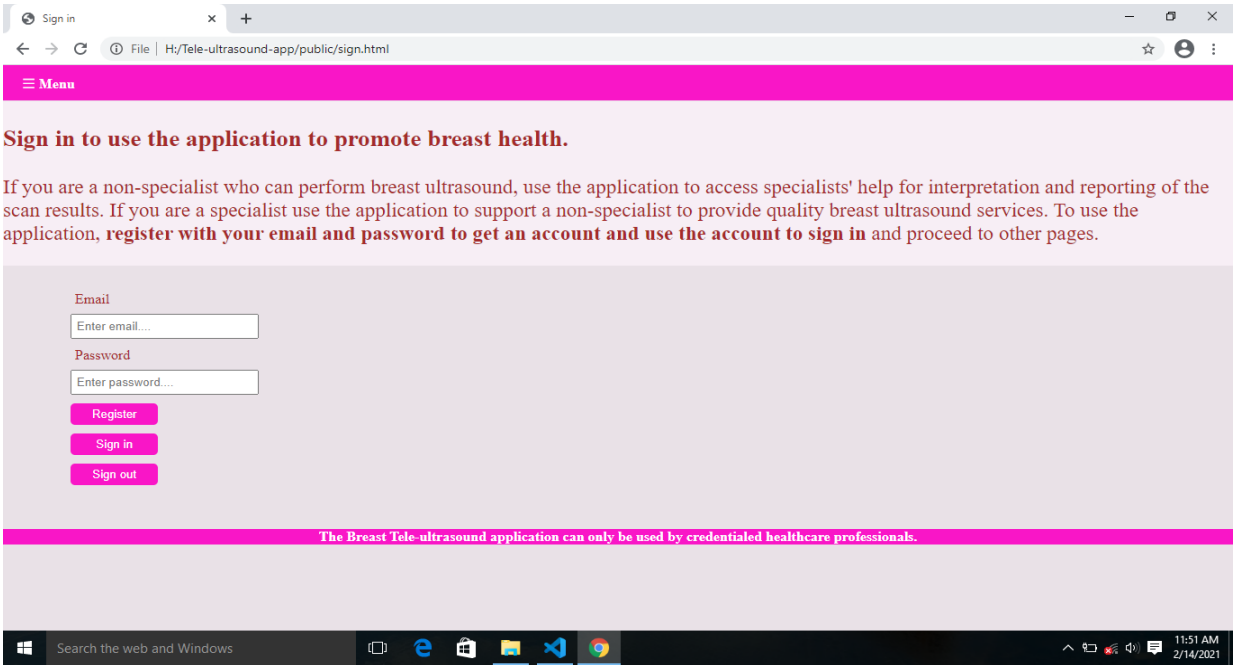

Figure 24: Sign in page

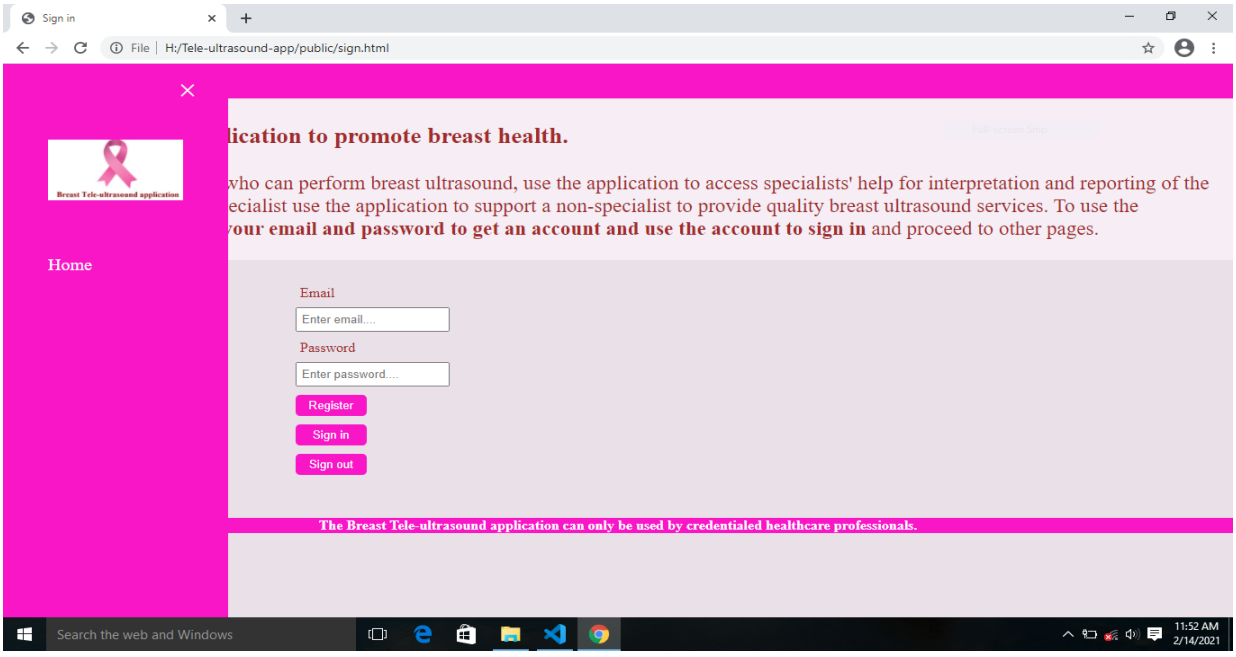

Figure 25: Access to home page from sign in page

After signing in, the user would be taken to the *Tasks* page (Figure 27) accessed by clicking the menu bar of the *Download patient data* page (Figure 26). From the *Tasks* page, a user may access the *Profile page* (Figure 28) to update their account details. On the *Tasks* page, a non-specialist would access the *Enter new data* page where they would enter patient data.

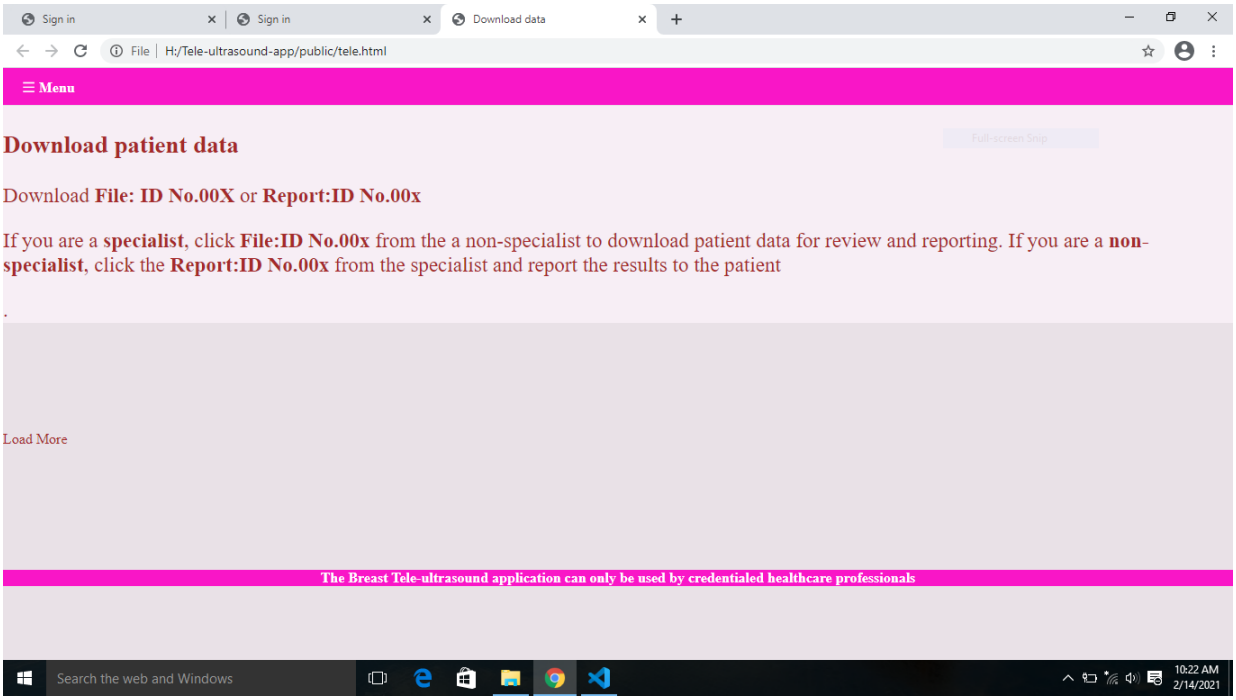

Figure 26: Download patient data page

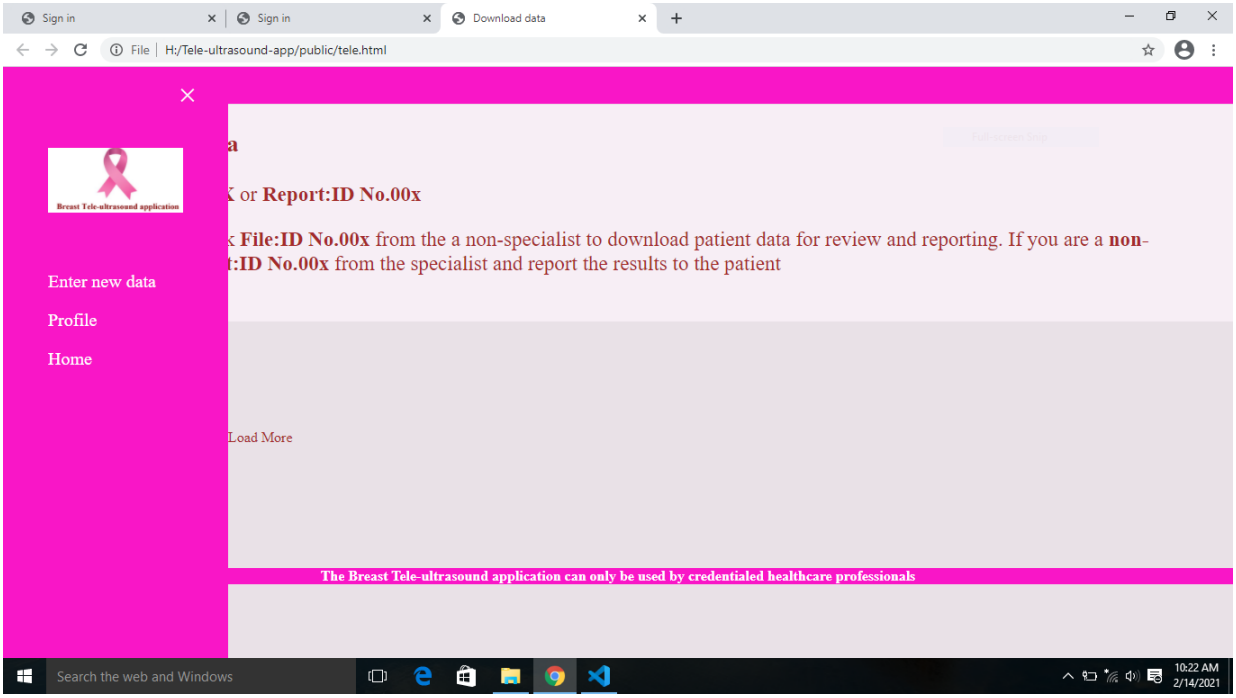

Figure 27: Tasks page

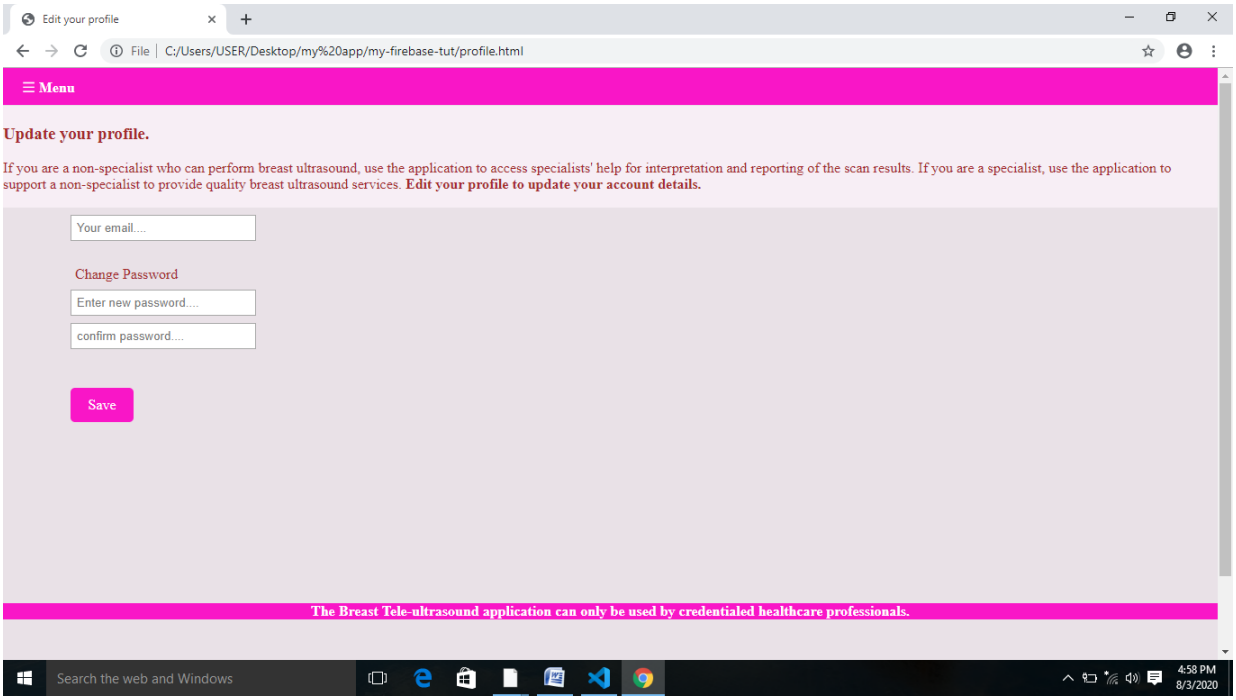

Figure 28: Update profile

4.4.2.3 *Enter new data page*

When a non-specialist signs in, they would be prompted to the *Download patient data* page (Figure 26) from which they would click the menu bar to access the *Enter patient data* page (Figure 29), where a non-specialist may enter patient data including patient information and the image generated from the scan.

The patient ID No. would be entered as *File:ID No.00x*. X is an integer from 1…..n. The rest of the data would be entered in the space for *Enter data.* The image would be uploaded by clicking the *Choose file* button, and this would link to where the file was saved. The user would click the *Submit* button to upload the data. A demonstration of data entered onto the *Enter patient data* page is shown in Figure 30.

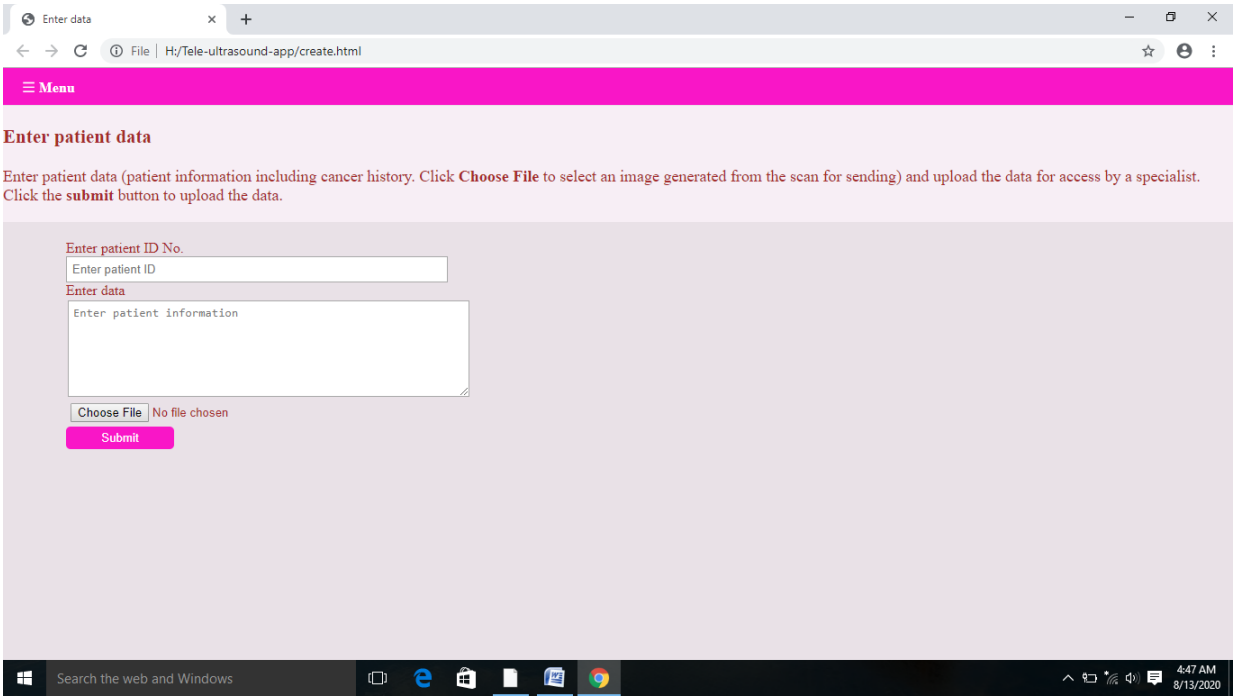

Figure 29: Enter patient data page

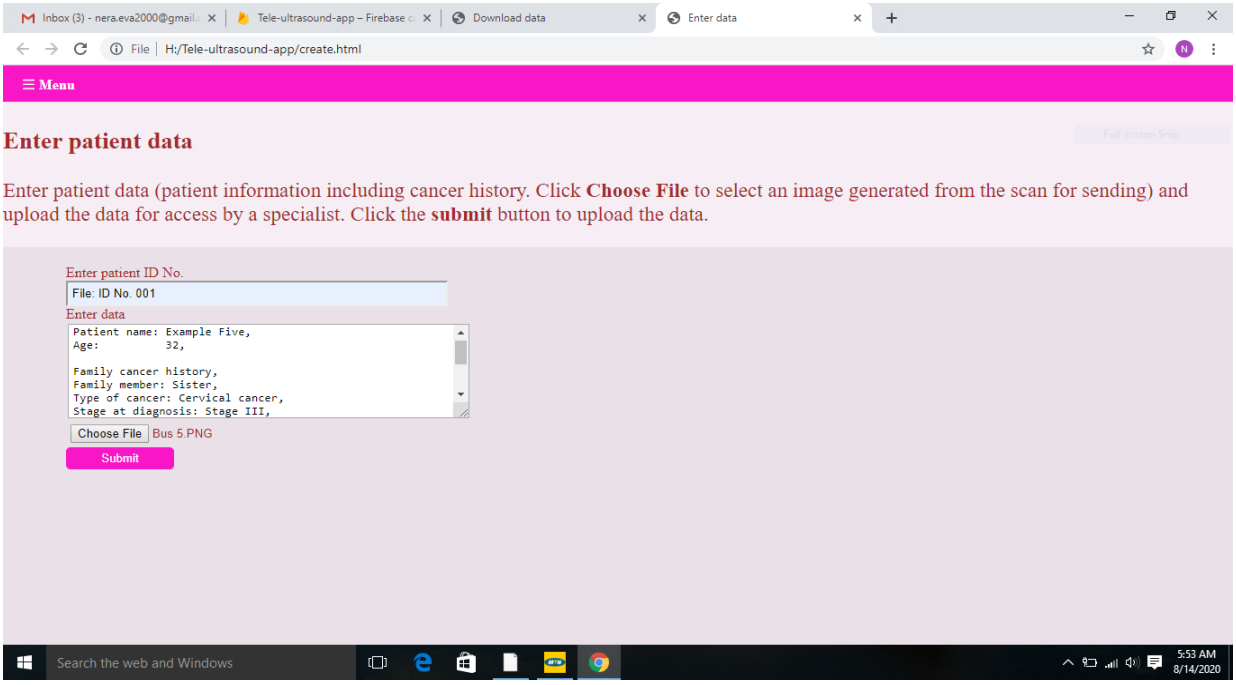

Figure 30: Demonstration of the Enter data page

The data entered by the non-specialist would be stored in the database shown in Figure 31 for the backend database. Figure 32 shows the data storage for the backend. This stored data would be accessed by the specialist on the download data page Figure 26 after signing in. Figure 33 is a demonstration of the *Download data page* where data uploaded by the non-specialist is accessed by the specialist.

The specialist would click the *File: ID No.00x* to download the data including the image and other patient information for review. Figure 34 shows data downloaded by the specialist by clicking *File: ID No. 001*.

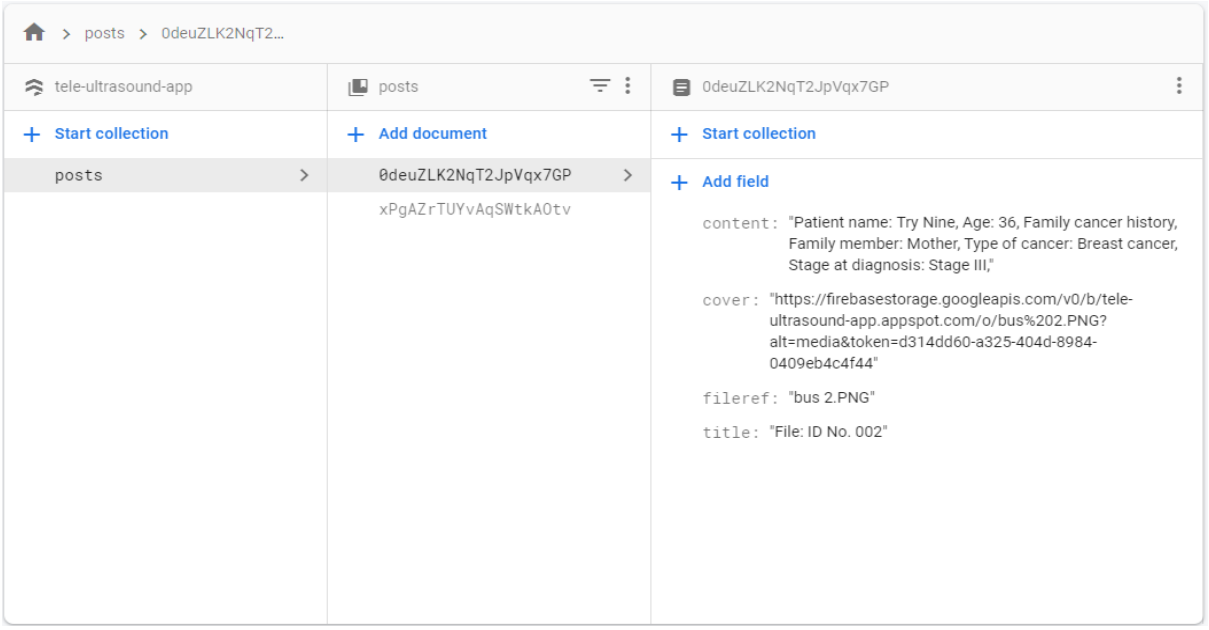

Figure 31: Demonstration of the data stored in the database

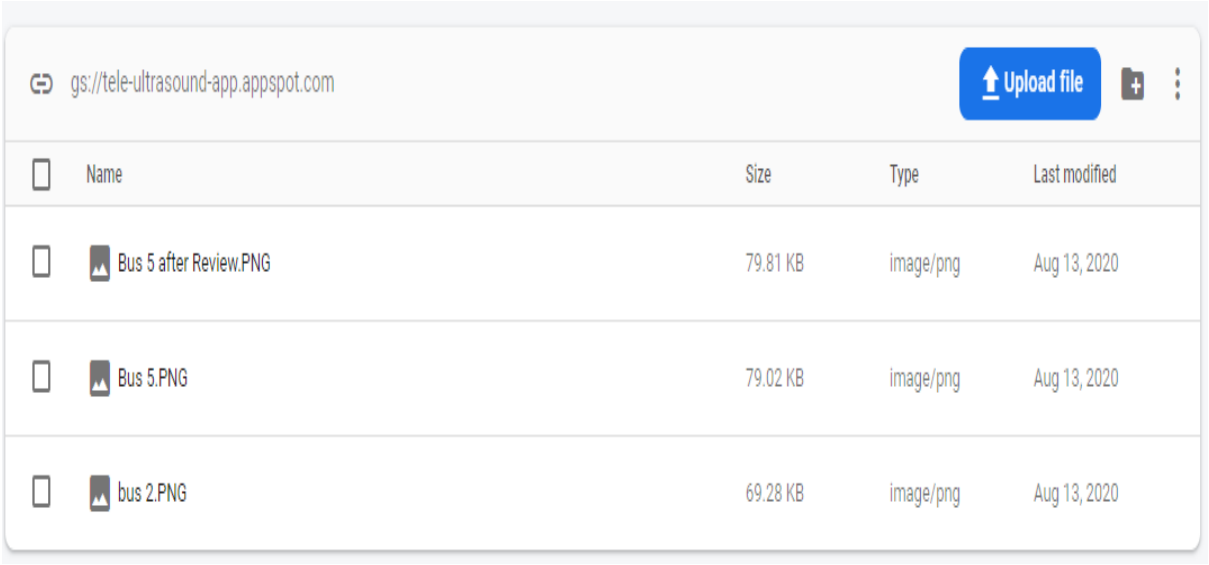

Figure 32: Data storage

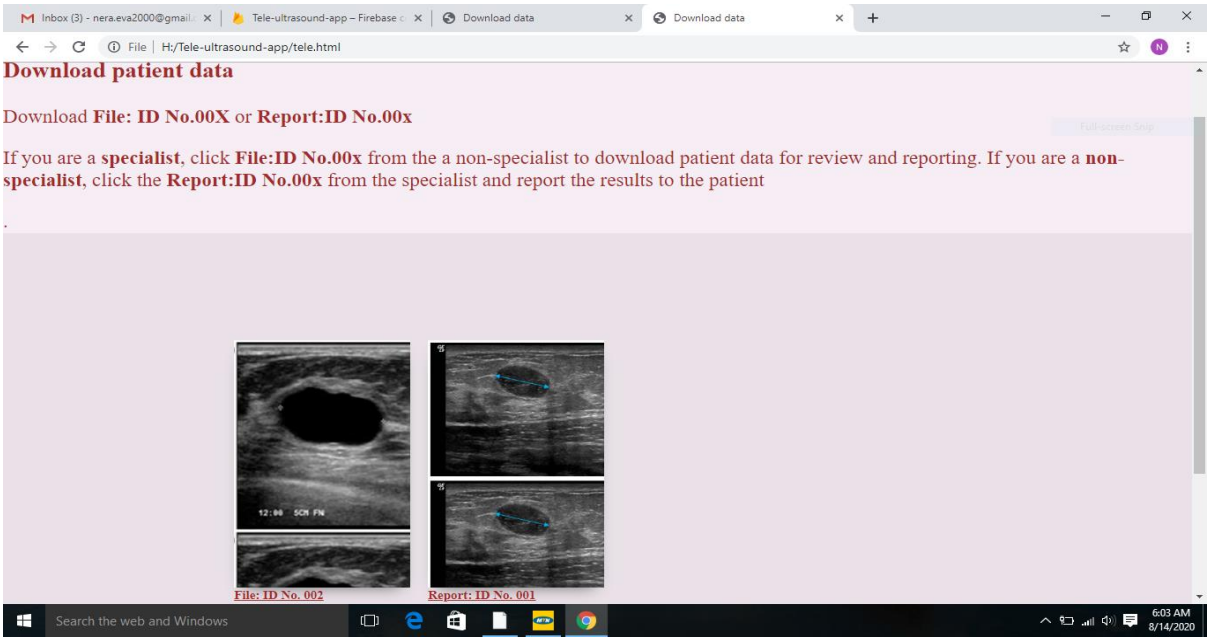

Figure 33: Demonstration of the download data page

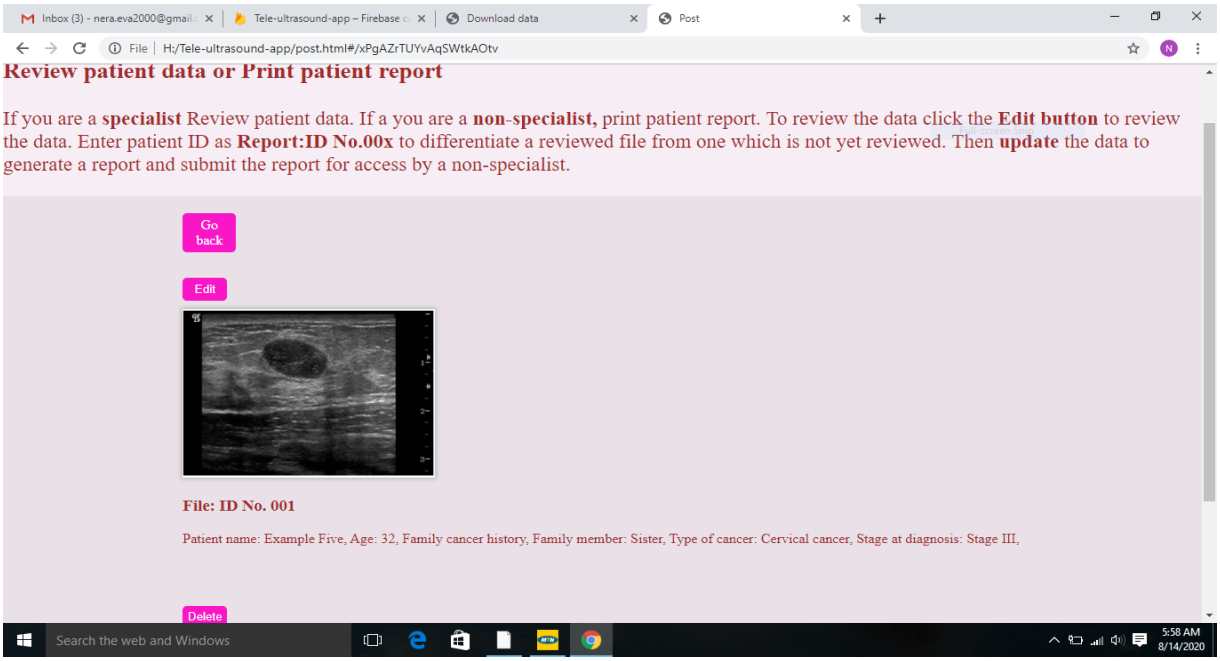

Figure 34: Demonstration of data downloaded by specialist

The specialist clicks the *Edit* button and reviews the image and the other patient information (Figure 35) to generate a report, which is saved in the database when clicking the *Update post* button. This report may be downloaded by the non-specialist from the *Download patient data* page shown in Figure 33. Figure 36shows the report downloaded by the non-specialist.

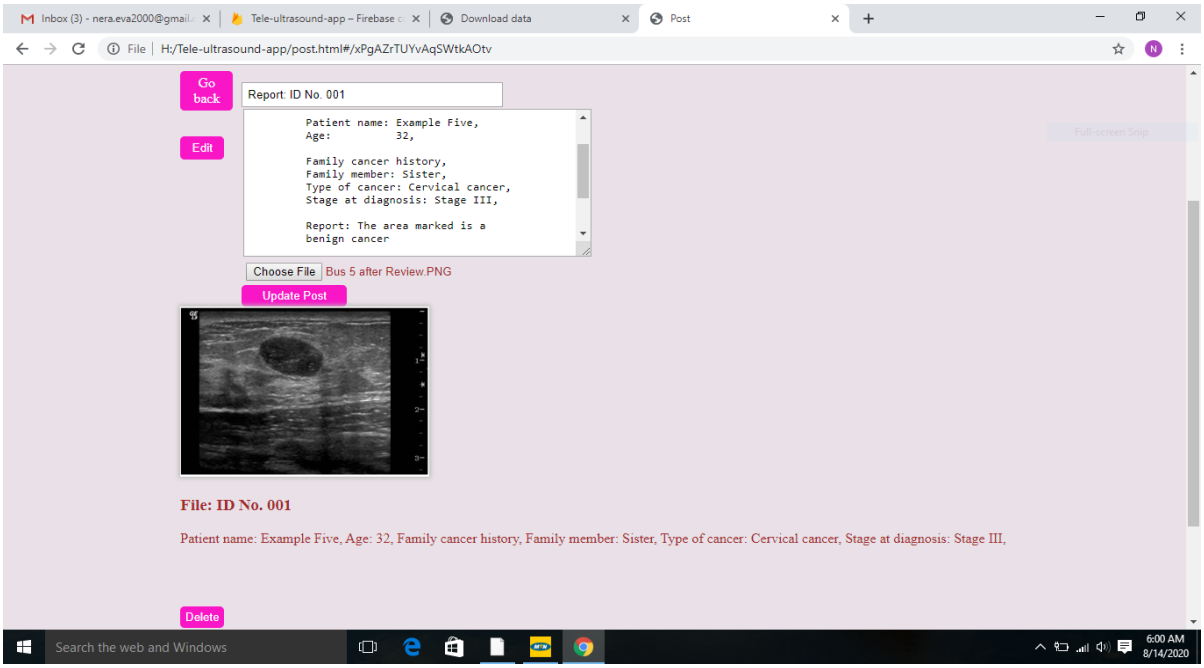

Figure 35: Demonstration of data reviewed by specialist

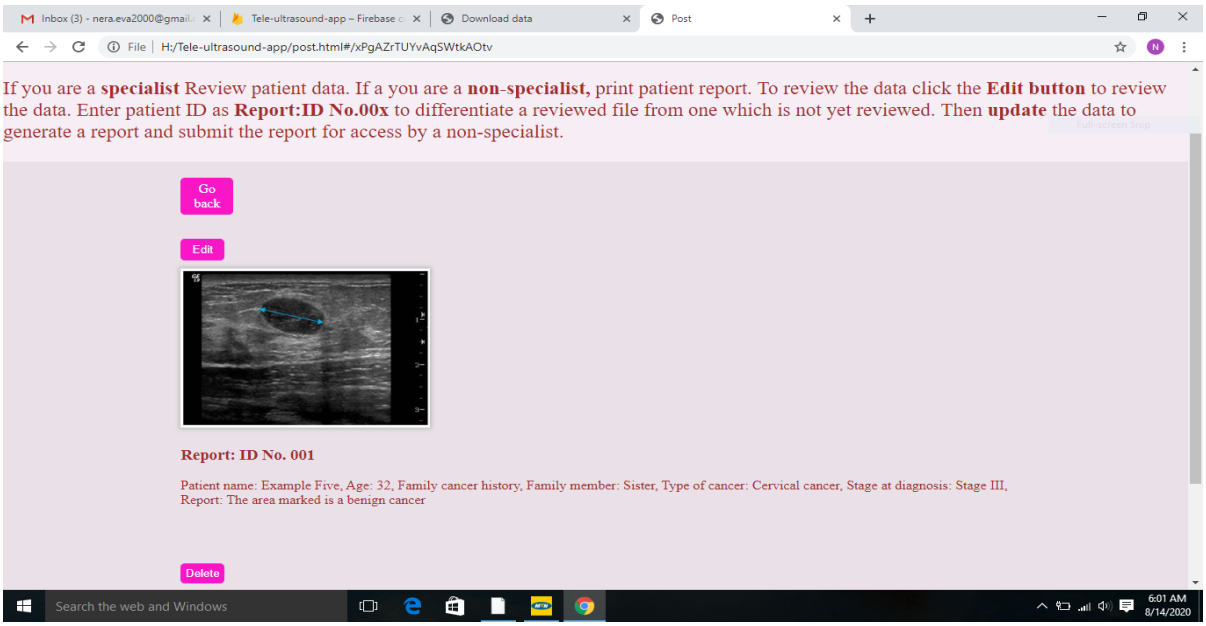

Figure 36: Demonstration of report downloaded by non-specialist

The *Enter data page* and *Download data page* are the main pages via which the non-specialist would consult with a specialist to enable improved access to breast cancer screening services. Integration of the web application using these web pages with a portable ultrasound platform for breast cancer screening is discussed in the following section.

Chapter 5 Integration of the web-based application with a portable ultrasound system

This chapter describes the integration of the developed web-based application with a portable ultrasound system to implement a mHealth-based portable ultrasound platform. Ultrasound images were generated and uploaded onto the application to demonstrate a non-specialist consulting with a specialist for provision of breast cancer screening services.

5.1 Materials

1. A phantom breast with model breast lumps was used as the source of image to be uploaded onto the application. The phantom breast was accessed at the Clinical Skills Centre of the Faculty of Health Science at the University of Cape Town.
2. A mobile-based portable ultrasound system; Philips Lumify (https://www.usa.philips.com/healthcare/sites/lumify) was used for image acquisition. An ultrasonographer assisted the researcher to acquire an image of the phantom breast.

Description of the phantom breast and the portable ultrasound system is well detailed in Table *7*.

Table 7: Study materials

Material		**Specifications**
Phantom breast		Model: BCT100
Portable ultrasound system	Mobile device: Tablet	Model: Samsung SM-T515
	Portable ultrasound	Philips Lumify L12-4 BJ2WWE

5.2 Methods

5.2.1 Image acquisition

A phantom breast with breast model lumps was scanned using the Philips Lumify mobile-based portable ultrasound system as shown in Figure 37 to generate an image.

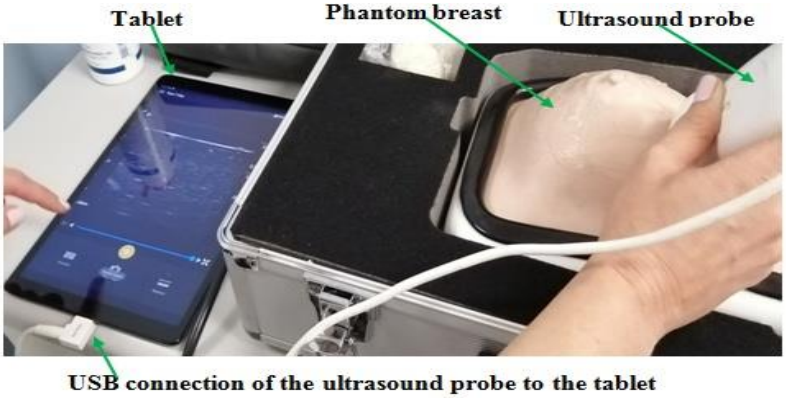

Figure 37: A tablet integrated with a portable ultrasound probe to scan a phantom breast

5.2.2 Ethics approval

No ethics approval was required as this was a bench-top study with no human subjects included as participants. An application was submitted to get approvals for amendment of the study. Further to this the corona virus disease impeded some of the research activities planned and therefore the changes to the initial proposal.

5.2.3 Implementation of the platform

The implementation of the app was done by the author and this demonstrated how a non-specialist would use the app to send patient data to a specialist who reviews the data and responds back to the non-specialist with a report. Thus, in this implementation study, the author acted as a non-specialist and a specialist and the two users were differentiated by their different sign in accounts. To demonstrate the implementation of the app, the flow included;

1) a non-specialist uploads patient data onto the app for access by a specialist,
2) the specialist downloads the data, reviews the data, generates a report and uploads the report onto the app for access by the non-specialist
3) the non-specialist downloads the report to share the results with the patient.

5.2.3.1 *Non-specialist uses the app*

The non-specialist used the app to upload patient data for access by a specialist. The user downloaded the app as depicted in Figure 38 via the link; https://tele-ultrasound-app.web.app. The user signed in as depicted in Figure 39 to access the Enter patient data page. At this page, as depicted in Figure 40, patient data were entered as follows; at the section of Enter patient ID No. the patient ID was entered as *File: ID No.007*, at the section of Enter data, data was entered as phantom number (Phantom 1) and at the *choose file* section, an image for phantom 1 was selected and submitted by clicking the *submit* button. The page demonstrated how the data would be entered. The data submitted were accessed on the download data page shown in Figure 41 and this enabled the user to confirm that data were submitted. The user then signed out via the sign in page accessed through the menu bar of the home page.

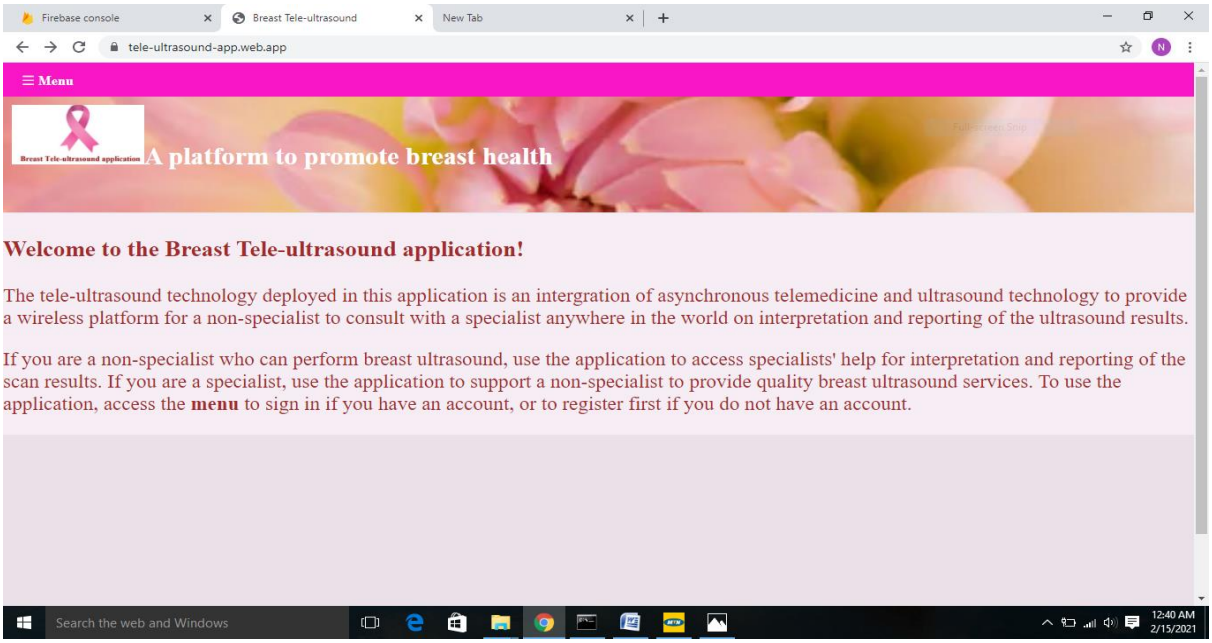

Figure 38: Breast Tele-ultrasound app (home page)

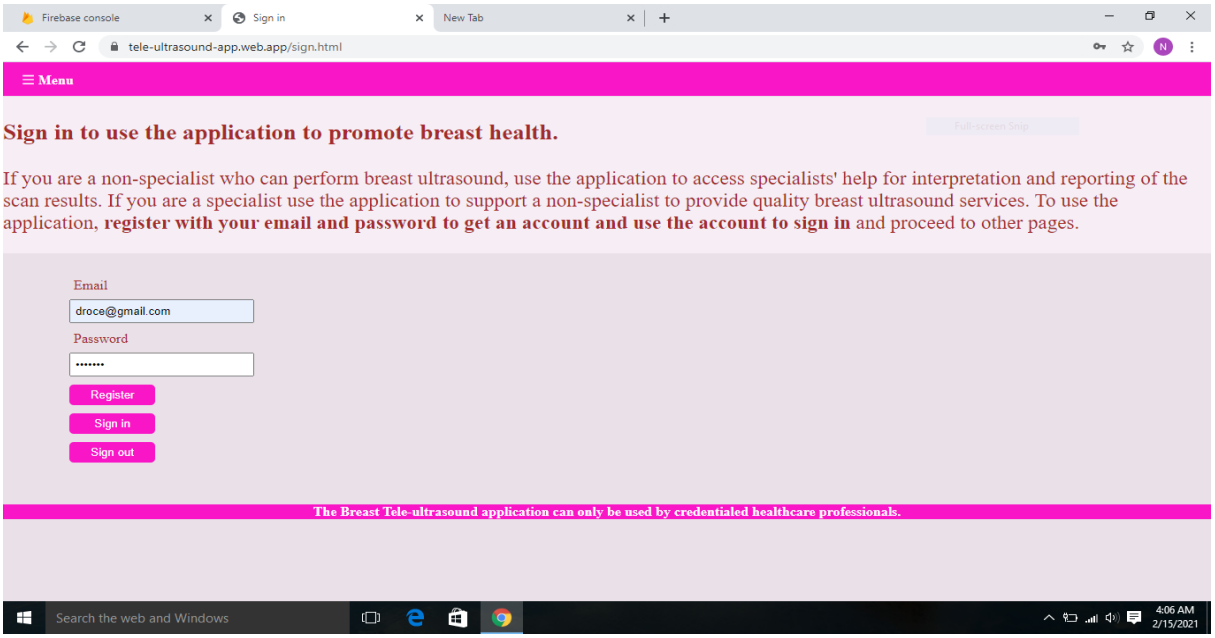

Figure 39: Implementation of the sign in page

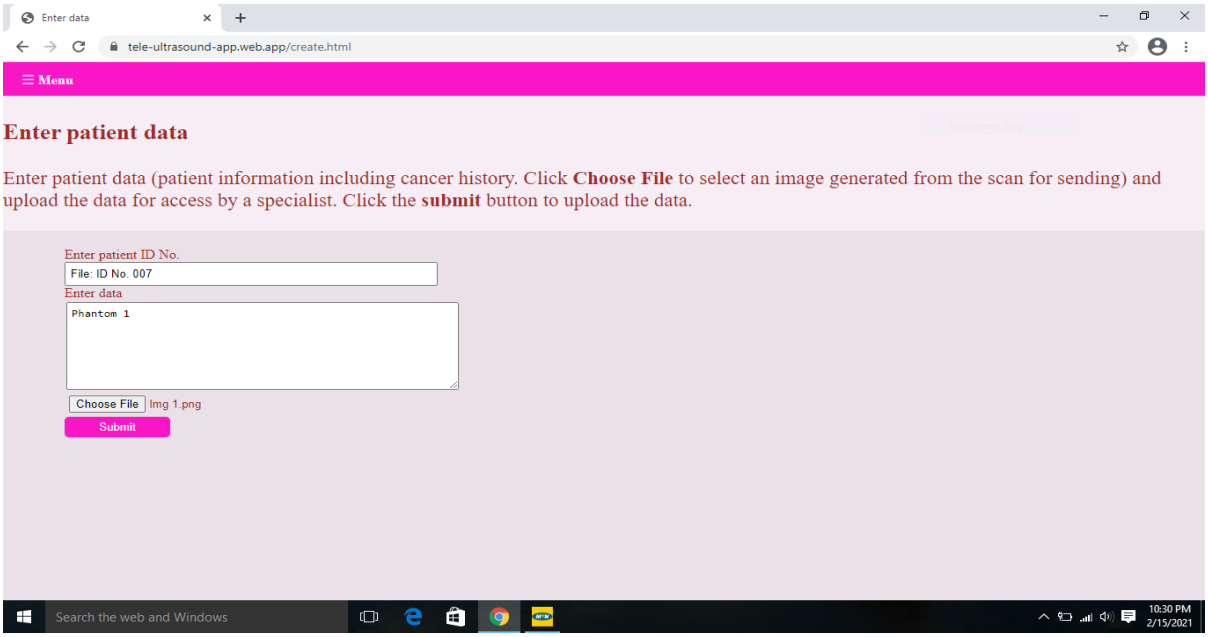

Figure 40: Implementation of the Enter data page

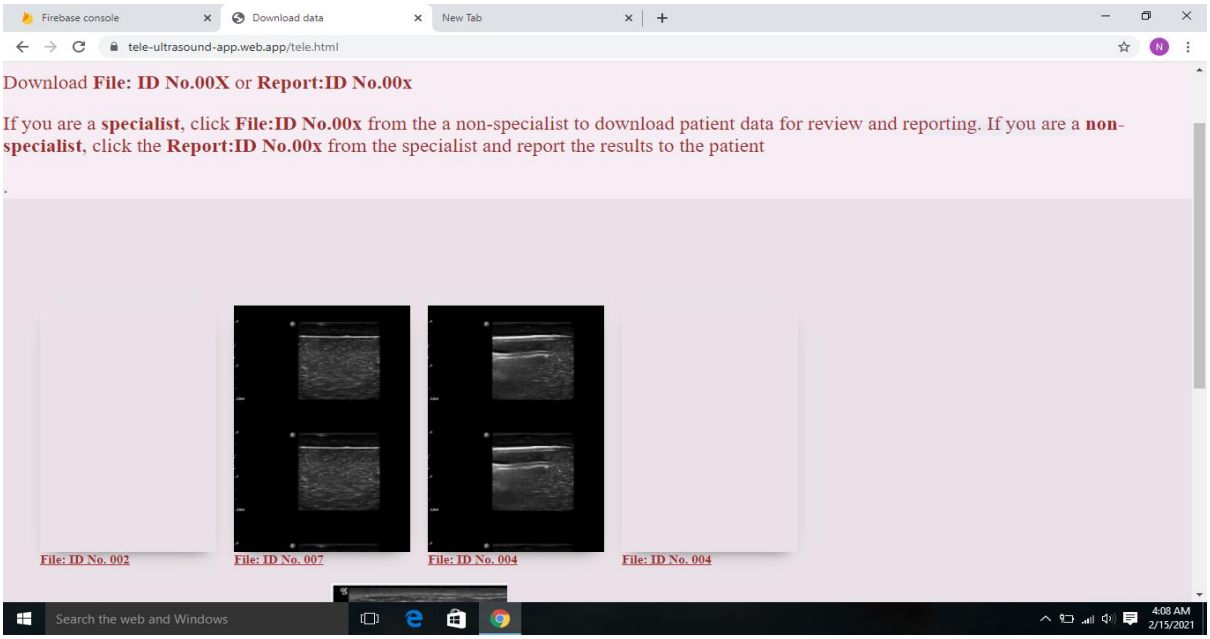

Figure 41: Non-specialist accesses data uploaded onto the app

5.2.3.2 *Specialist uses the app*

The specialist used the app to download the data sent by the non-specialist. The specialist reviewed the data, generated a report and uploaded the report onto the app for access by the non-specialist. To access the app, the specialist downloaded the app via the same web link as used by the non-specialist and signed in as depicted in Figure 42. After signing in, the user was prompted to the download data page and accessed the data uploaded by the non-specialist; *File: ID No. 007* and *File: ID No. 004* (Figure 43). The user clicked the *File: ID No. 007* and downloaded it for review as depicted in Figure 44. The file was reviewed by clicking the *Edit* button and updating of the data as depicted in Figure 45. The reviewed data were saved as *Report: ID No.007* (Figure 46) instead of *File: ID No. 007*. This report was accessed on the *Download data* page (Figure 47) and this clearly showed the difference between a reviewed data (*Report: ID No.007*) and non-reviewed data (*File: ID No. 007*). The user accessed the download data page by clicking the back button on the report page. This enabled the specialist to confirm that the original file sent by the non-specialist had been reviewed. Thus, the file not reviewed *File: ID No. 004* could easily be identified by both users (the specialist and the non-specialist). At the download data page, the user signed out by accessing the home page via which the sign in page was accessed for signing out.

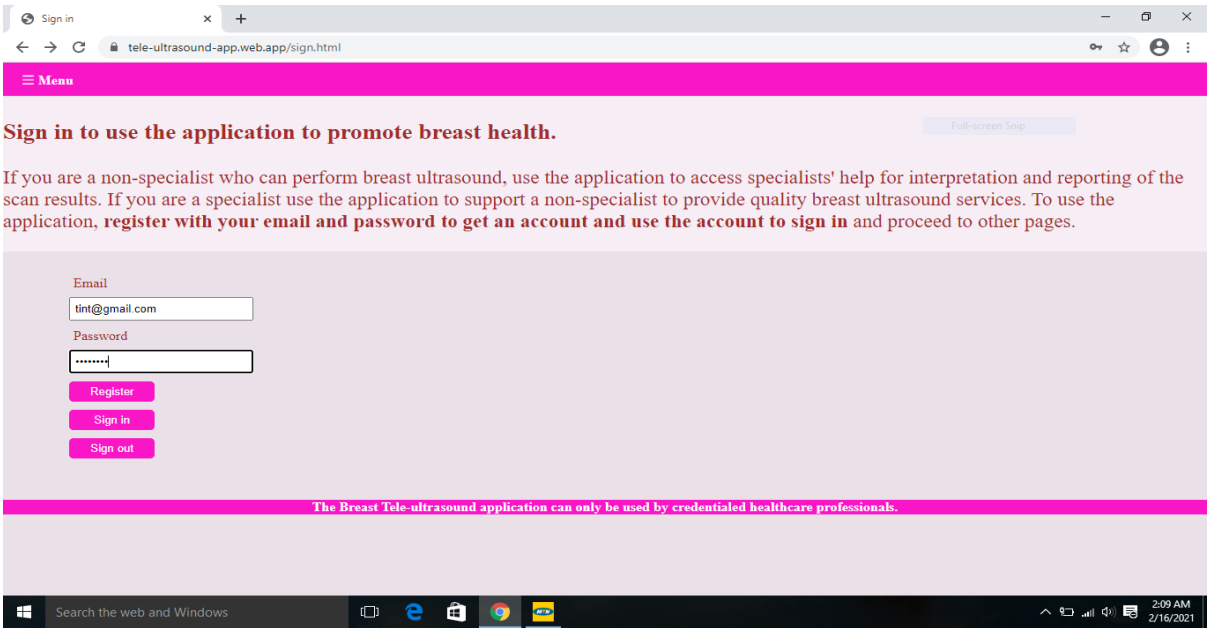

Figure 42: User signing in

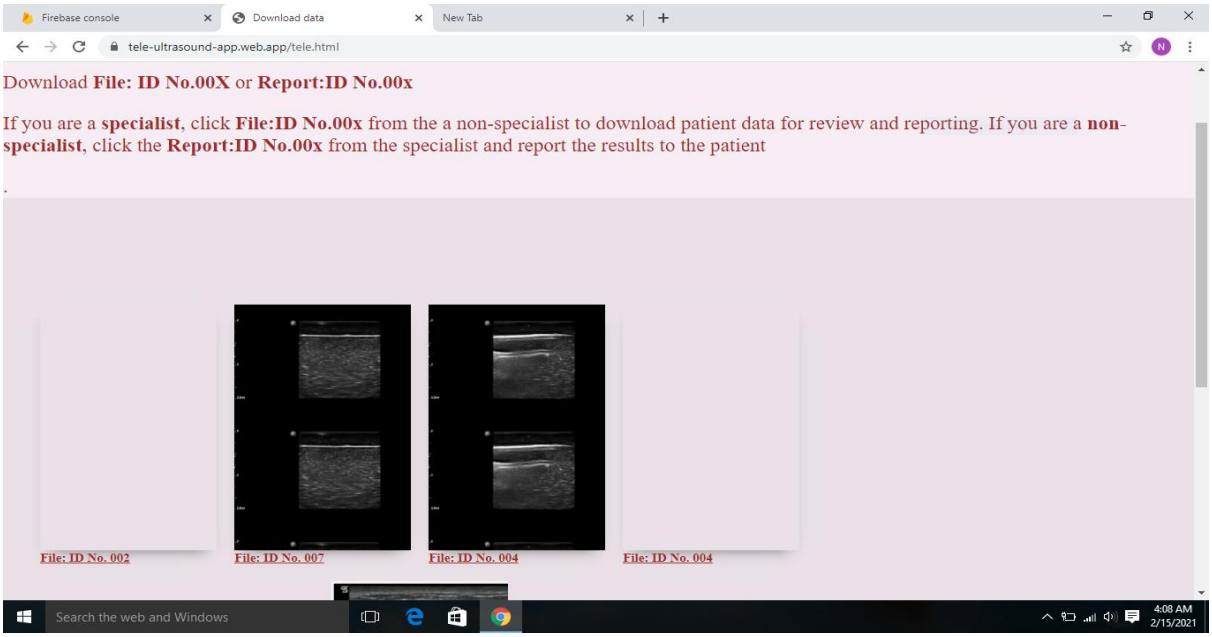

Figure 43: Specialist accesses data uploaded by the non-specialist

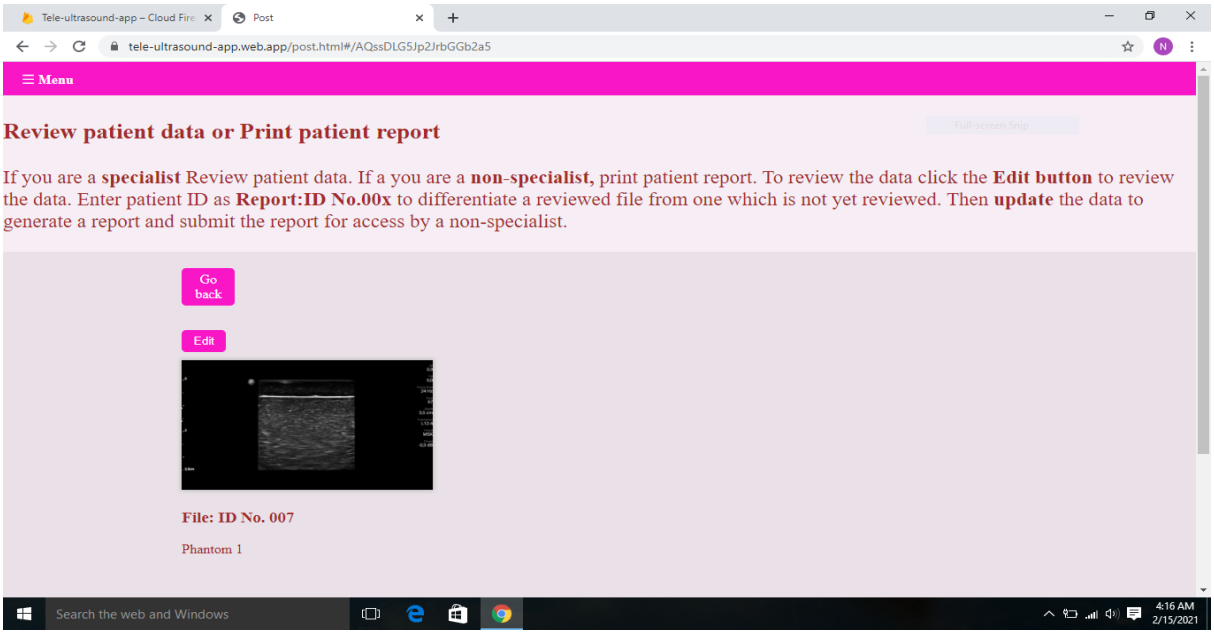

Figure 44: User downloaded data for review

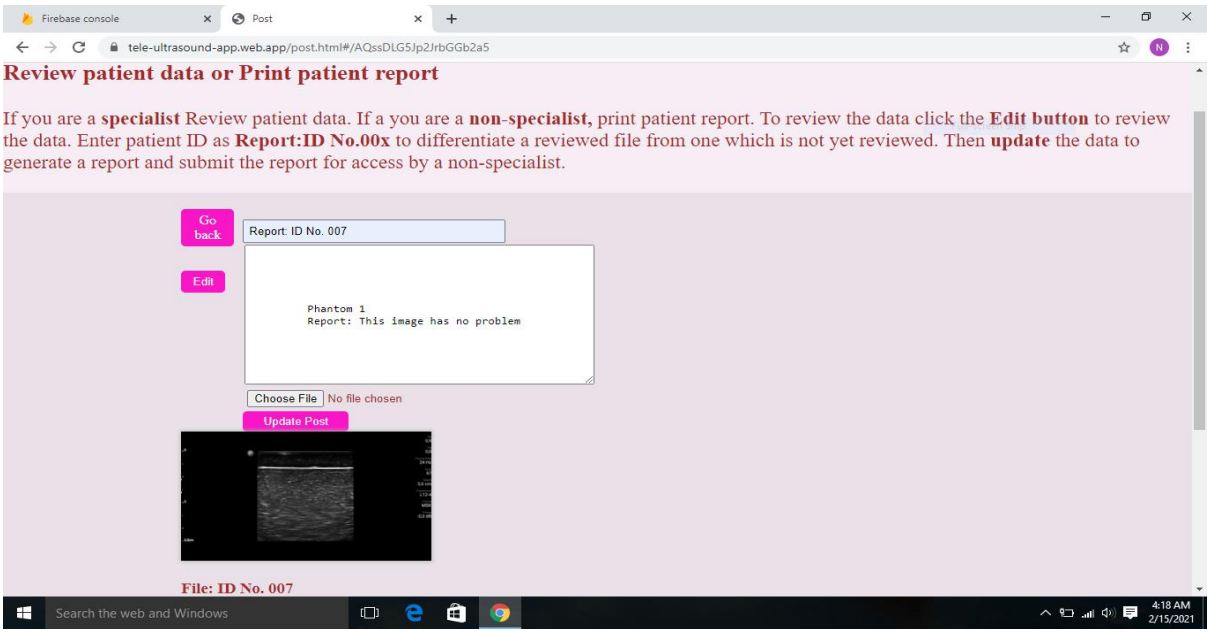

Figure 45: User reviewing data and to generate a report

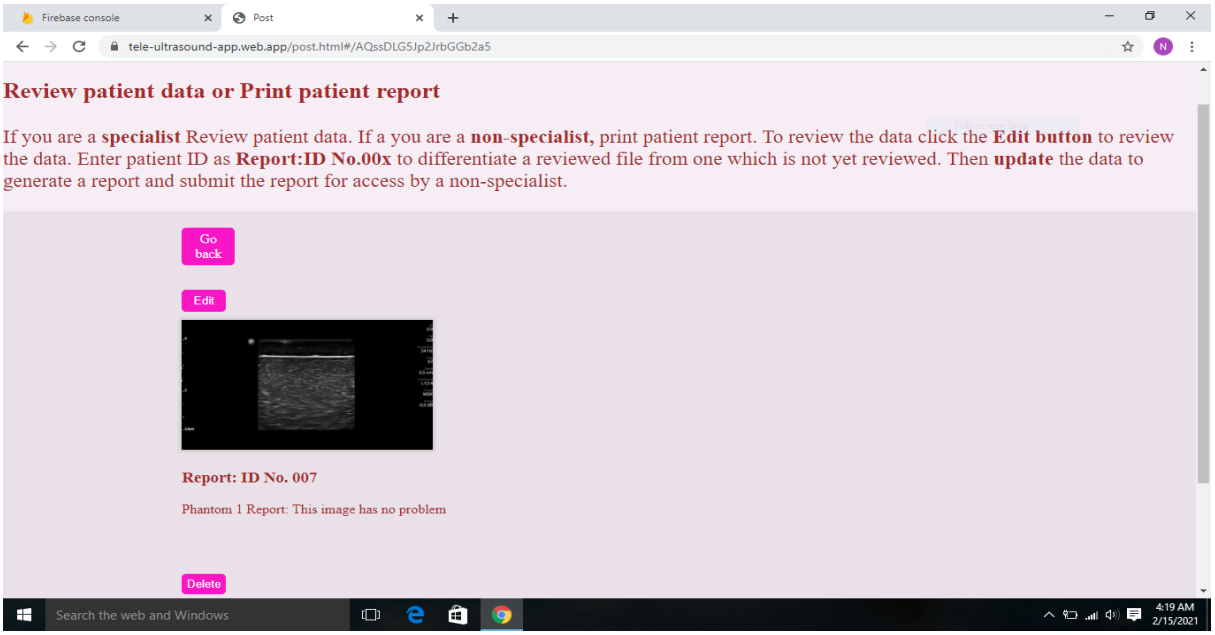

Figure 46: Report generated by the user

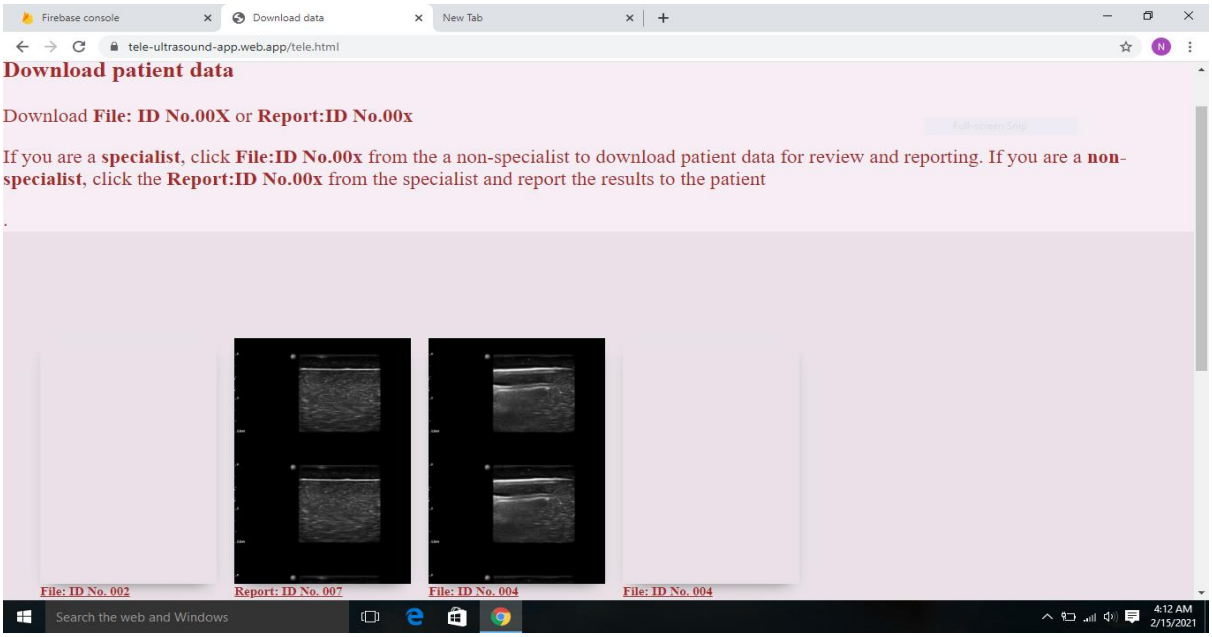

Figure 47: Download data page with reviewed data appearing as Report: ID No. 007

5.2.3.3 *Non-specialist uses the app*

The user used the app to download the report to enable the patient get their results. After downloading the app via the web link and signing in, the user was prompted to the download data page Figure 48 from which the report was downloaded. The user downloaded the report by clicking the by clicking Report: ID No. 007. Figure 49 shows the report downloaded by the user. After using the app, the user signed out by clicking the menu bar of the page which prompted the user to the home page. From the home page, the user accessed the sign in page via the menu bar which enabled the user to sign out of the app.

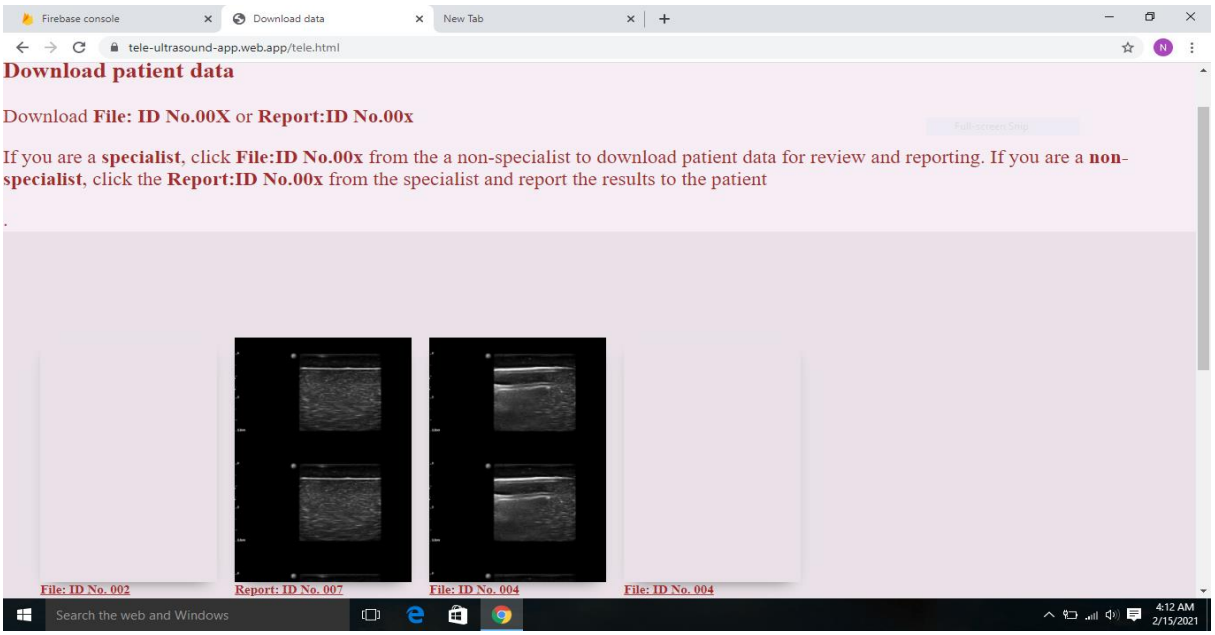

Figure 48: Non-specialist accesses report uploaded by the specialist

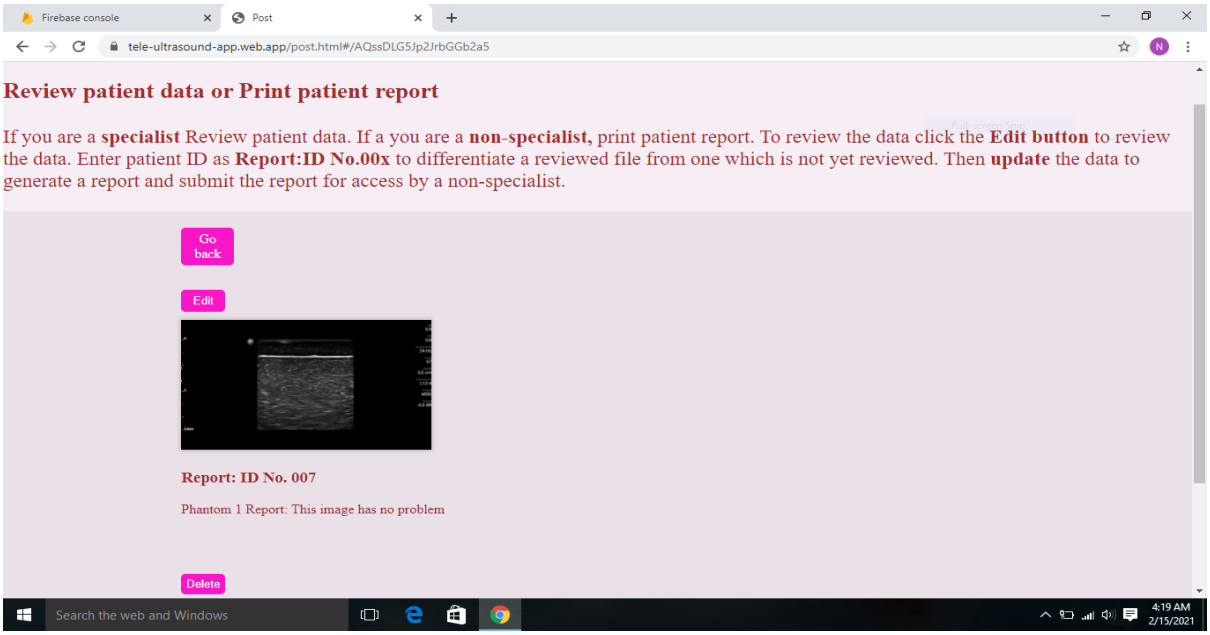

Figure 49: Report downloaded by user

5.3 Discussion

The design and development of the application called the Breast Tele-ultrasound app demonstrated in this chapter is intended to provide a probable solution that would enable rural South African women access breast ultrasound services in their proximity for early detection of breast cancer. In this thesis it has been documented that rural South African women have limited access to breast cancer screening services because these services are only accessible in the urban centers where there are equipment and specialists. Therefore, women who are limited with finances, transport and time are often diagnosed with late stage breast cancer which has resulted into poor treatment outcomes such as mortalities.

Since it has been reported that non-specialist in the rural South Africa can be trained to perform breast ultrasound scan, the application developed in this thesis may enable the non-specialist access specialist support on the review and reporting of the breast ultrasound results. After performing the scan, the non-specialist would send patient data generated from the breast ultrasound scan to the specialist, via the developed application and the specialist would respond back with a report to the non-specialist. Thereafter, the non-specialist would communicate the results to the patient, either on phone or patient would pick the results directly from the non-specialist.

Design requirements were established after a systematic review of existing literature on mHealth applications and ultrasound. Obtaining of the design requirements was essential to define the right product which would meet user needs. Thus, in this design, user centeredness is critical for a feasible product (Niemöller et al., 2016). In this context, the application was designed as a web application to enable its easier accessibility (via a browser) on either a smartphone or a laptop as compared to dedicated apps like the mVisum which is only accessible on a particular smartphone with the app. Web application is also more accessible than what is used by Philips Lumify which uses a dedicated software compatible with specific model of a smartphone. The established design requirements were then transformed into a mock-up prototype of the web application to demonstrate the user interface design of the application. Designing mock-up prototypes helps to test the design requirement to ascertain the functionality of a prototype as per the user requirements (Weichbroth et al., 2015). The designed user interface of the application included the Home page, registration page, sign-in page, profile page, Enter patient data page and Download patient data page. These pages were tested by designing a user experience of the web pages. This helped to illustrate the flow of the web pages and refine the functions of each web page for an improved web application. In this context, the user experience design results enabled the improvement of the web page designs for the development of the required web application.

At the development stage of the web application, the web pages web pages were presented using HTML, styled using CSS and made interactive using JavaScript. Backend services were also implemented at this stage to enable data storage, security of data and authentication of users. Like at the initial prototyping stage, also at this stage, the web pages of the application and its backend services were tested to gain more understanding of the functionality of the web pages. Testing a product at each level of development helps to eliminate any ambiguous errors which may be realized at the last stage of development (Pereira et al., 2018). This results into quality product with minimum or no errors especially at the stage of testing the product with users or the target market. Although, in this particular design, the web application was not tested with users, the author demonstrated how the users would use the web application. Also, the functionality of the backend illustrating how it interacts with the frontend (web pages) for real-world implementation was also demonstrated. At this stage, the web application was integrated with a mobile-

based portable ultrasound platform for breast cancer screening. During this stage, each of the web pages of the web application were demonstrated where the author acted as the non-specialist and specialist. All the steps taken by the respective users were demonstrated and showed feasibility of the concept. The ability to upload images onto the application and download images from the application showed that the concept was applicable for real-world implementation. This resulted into a mHealth-based portable ultrasound platform for breast cancer screening. It is recommended that the application is tested with the real users during a clinical study to ascertain the feasibility of the application. It also recommended that an alert message is incorporated into the application to inform the users of patient data uploaded. This will further strengthen the applicability and usability of the concept.

Chapter 6 Conclusion

This chapter gives a detailed summary of the work done in this thesis to enable the development of a prototype of a mHealth-based portable ultrasound platform. The achievements, limitation and recommendations of the study are also indicated.

The purpose of the work presented in this dissertation, was to demonstrate the development of a prototype mHealth-based portable ultrasound platform for breast cancer screening for improved early stage detection of breast cancer amongst rural South African women. The objectives of the study were to review existing mHealth-and internet based portable ultrasound platforms to inform the design and development of a mHealth-based portable ultrasound platform suitable for breast cancer screening. A review of existing platforms revealed two main application areas, namely cardiovascular disease and obstetrics. Most of the platforms were implemented with conventional portable ultrasound connected to a mobile/portable computing device with data transmission over the internet, as compared to mobile-based portable ultrasound.

As compared to a mobile application-based platform, a web-based application was considered more widely accessible because it would be accessible from any mobile device with any operating system. A web-based application was therefore designed and developed for the mHealth-based portable breast ultrasound platform. Uploading of an image onto the platform's application and downloading the image from the application demonstrated the feasibility of the developed application. However, there were limitations for the developed application. One of which was that no option for any alert message for the users (for the specialist to review patient data sent by the non-specialist, and for the non-specialist to access patient report uploaded by the specialist) to prompt them to use the application respectively. Incorporation of an alert message for the respective users should be considered in the further development of the application as this strengthens the applicability, usability and feasibility of the application.

Also, the study was a bench-top test of a prototype which was only done by the author. A recommendation for future studies would be to conduct broader testing with end users (e.g. health professionals and patients). This would help improve the prototype before its clinical trial. Subsequently, a full implementation of the design would have to be tested in a clinical setting, particularly with regard to usability, workflow and the integration of the platform into the health system. Also, further research about the application should include assessments for data transmission, the associated type and speed of connectivity, and the bandwidth requirements and their feasibility in LMICs. Future work in these factors would provide guidance on the need for data compression to ensure cost effective data storage and transmission. Further development of the prototype in the market may create an affordable, accessible, reliable and sustainable solution for breast cancer screening to improve early detection of breast cancer.

Any deficiencies in data security could compromise patient safety and confidentiality. Although Google Firebase, which was used for the backend database and data storage, ensures data security via https, it is not reliable for sensitive patient data. It is recommended that the backend service be designed and developed with data encryption services to ensure data security. However, this was not a focus of this study, and should be considered in further development of the solution.

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Appendix 1

Database search: PubMed=69 results

((((((((((Telemedicine [MeSH Terms]) OR mobile application [MeSH Terms]) OR cell phone [MeSH Terms]) OR web-based medical application OR web-based process OR web-based tool OR website OR web-enabled OR mHealth OR mobile health OR mobile applications OR telemedicine OR telehealth OR telecare OR teleconsultation OR telecommunication OR telecommunications link OR tele-expertise OR mobile computing OR cloud OR cloud computing OR cloud-based application OR cloud hosting OR wireless technology OR cell phone OR smartphone OR tablet OR iPhone OR personal computer OR laptop)))) AND ((portable ultrasound OR point of care ultrasound OR pocket size ultrasound OR low cost ultrasound)))) OR ((telesonography OR remotely supported ultrasound OR tele-ultrasound OR tele-sonography OR teleultrasound OR teleradiology)))) AND ((transferring OR uploading OR storage OR transmission OR downloading OR remotely downloaded))) AND ultrasound images

Database search results: Academic Search Premier =6, Cochrane=4, Engineering Village=107, Scopus=4, Web of Science=60

(((web-based medical application OR web-based process OR web-based tool OR website OR web-enabled OR mHealth OR mobile health OR mobile applications OR telemedicine OR telehealth OR telecare OR teleconsultation OR telecommunication OR telecommunications link OR tele-expertise OR mobile computing OR cloud OR cloud computing OR cloud-based application OR cloud hosting OR wireless technology OR cell phone OR smartphone OR tablet OR iPhone OR personal computer OR laptop) AND (portable ultrasound OR point of care ultrasound OR pocket size ultrasound OR low cost ultrasound)) OR (telesonography OR remotely supported ultrasound OR tele-ultrasound OR tele-sonography OR teleultrasound OR teleradiology))AND transferring OR uploading OR storage OR transmission OR downloading OR remotely downloaded AND ultrasound images

Grey literature search

- Google.com=24

Search terms: Telemedicine, portable ultrasound, transferring ultrasound images

Appendix 2

Data extraction form

Reference:

- Author & year of study

Study setting (LMICs or HICs):

- Country
- Type of healthcare facility or environment
- Setting of the healthcare facility (Rural or urban)

Participants:

- Patients
- Non-expert primary healthcare provider
- Expert who interprets and reports the examinations

Patient's clinical condition

Intervention:

- mHealth-based portable ultrasound platform

Modality of the intervention:

1. Acquisition ultrasound
2. Mobile device
    - Smartphone
    - Tablet
    - Laptop
3. Modality of the intervention (Transmitting application)
    - web-based application,
    - mobile-based application,
    - cloud-based (web-based application with a cloud-based server) application

Outcome measures of the intervention

- Increased number of patient attendance
- Improved patient outcome
- Improved patient management
- Reduced turnaround time
- Improved trust in the care delivered

Appendix 3

Table 8: Reason for exclusion of full text articles

No	Author & year of study	Reason for exclusion
1.	Adambounou et al. (2014)	Included real-time guidance of the non-expert. It also included the use of console ultrasound GE logiq 200
2.	Adambounou et al. (2012)	Also included the use of Console ultrasound
3.	Arbeille et al. (2014)	Used console ultrasound machine used
4.	Balasingham et al. (2007)	Used console ultrasound
5.	Bharath et al. (2018)	Outcome not of interest. The outcome is assessing the quality of the region of interest in the transmitted image.
6.	Bharath et al. (2016)	Used console ultrasound Siemen S1000, and the outcome did not reflect accessibility. Non-expert not mentioned in the study.
7.	Eadie et al. (2016)	Used health humans to as patients, outcomes not of interest
8.	Grant et al. (2010)	Ultrasound used not indicated
9.	Gray et al. (2015)	Doesn't include transmission of patient data for expert interpretation
10.	Greenberg et al. (2004)	Outcomes not of interest
11.	Hassan et al. (2011)	Considered CT and MRI images and not intended for expert interpretation
12.	Holscher (2012)	Study not done to transfer patient images for expert interpretation
13.	Kim et al. (2016)	Used console ultrasound E-cube 15, By Alpinion medical systems
14.	Kolbe et al. (2015)	Included real-time support via skype.
15.	La Cruz et al. (2016)	Used CT imaging modality
16.	Martinov et al. (2012)	No results regarding patient outcomes. Only image quality
17.	Martinov et al. (2013)	Included remote expert monitoring of the examination
18.	Mort et al. (2016)	Used health volunteers as mock patients
19.	Ninos et al. (2010)	Used console ultrasound system
20.	Panayides et al. (2013)	Study done using already existing dataset, and no report on patient outcome
21.	Parsai et al. (2012)	Used console ultrasound Toshiba Xario
22.	P. Puech et al. (2007)	Study done with CT imaging modality
23.	P. A. Puech et al. (2007)	Study outcome not of interest: Study assesses the importance of the platform
24.	Ricci et al. (2004)	It is a review article
25.	Rizou et al. (2010)	CT, DX (Digital radiography) and MR imaging modalities
26.	Shen et al. (2014)	Studies evaluated on CT, DX; Digital radiography and MR imaging modalities
27.	Sibert et al. (2008)	Used a test subject instead of patients. Outcomes not of interest

28.	Siddique-e Rabbani et al. (2016)	It is a review article
29.	Triunfo et al. (2010)	Used console ultrasound and include real-time transmission of the video examinations
30.	Vaish et al. (2017)	It includes real-time transmission of the ultrasound examination. Console ultrasound used according to the image

Appendix 4

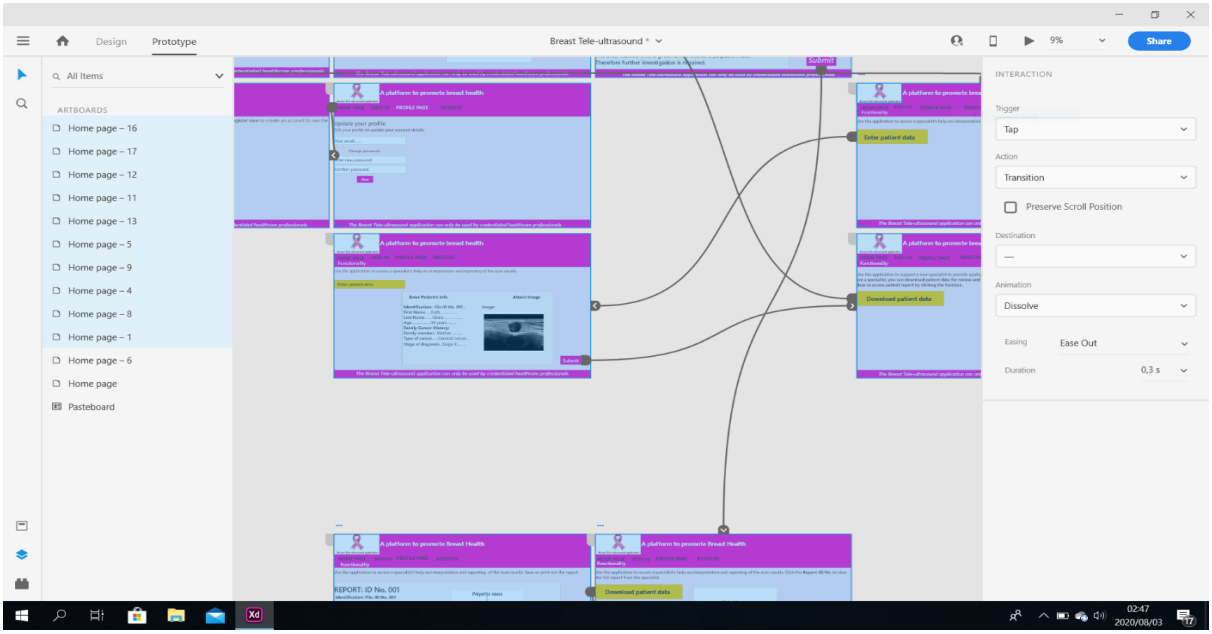

Figure 50: UX design for both the non-specialist and specialist

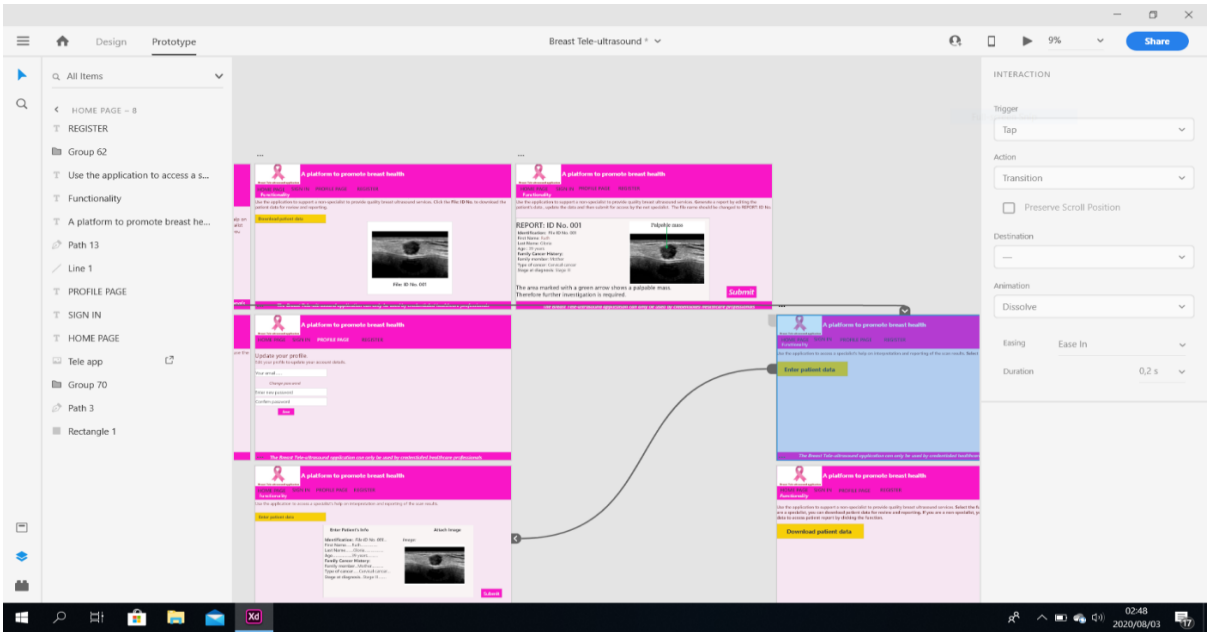

Figure 51: UX design for non-specialist to enter patient data for access by specialist

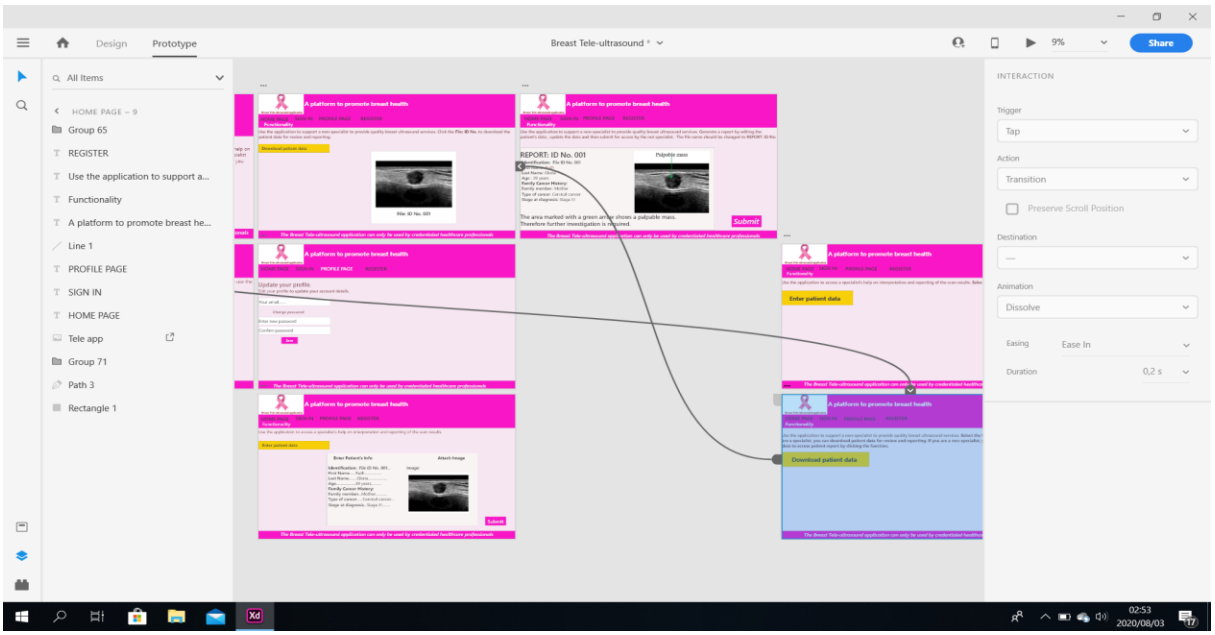

Figure 52: UX design for specialist to download patient data for review and reporting

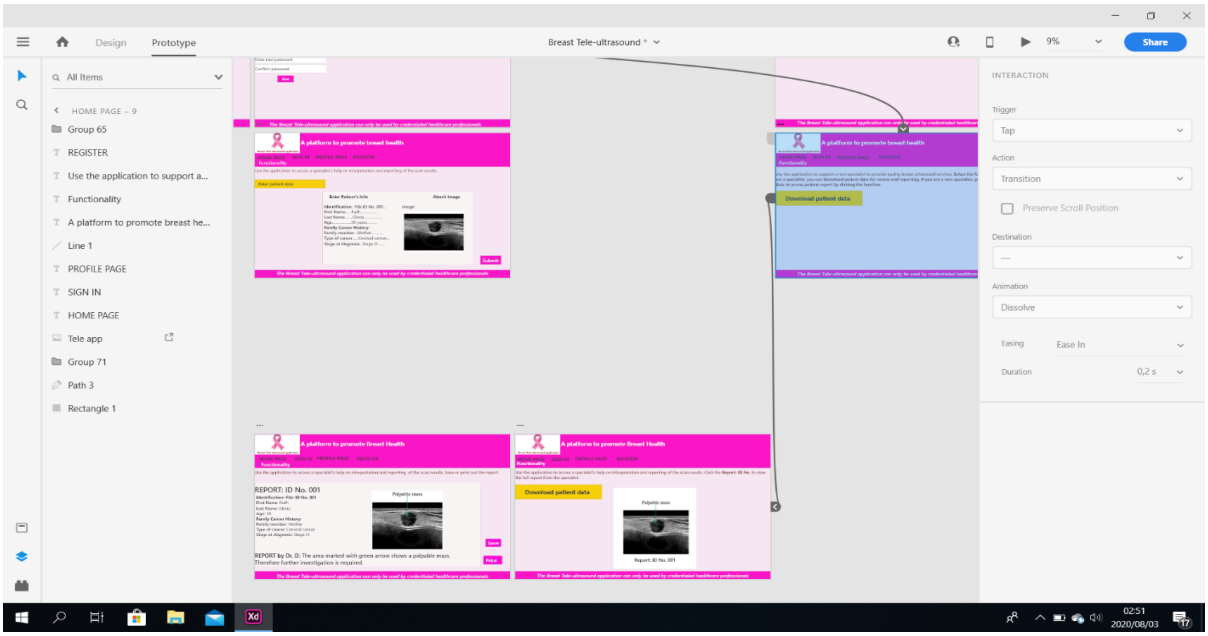

Figure 53: UX design for non-specialist to download specialist report