ULTRASOUND MEDICAL IMAGING SYSTEMS USING TELEMEDICINE AND BLOCKCHAIN FOR REMOTE MONITORING OF RESPONSES TO NEOADJUVANT CHEMOTHERAPY IN WOMEN’S BREAST CANCER: CONCEPT AND IMPLEMENTATION

A thesis submitted
to Kent State University in partial fulfillment of the requirements for the degree of
Masters of Science in Computer Science

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April 2017
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DEDICATION

First and foremost, I would like to thank Allah (God) for all what I am and all what I have. I am delighted to express my deep and sincere gratitude to my thesis advisor Professor Austin Melton, he has been my inspiration and mentor; I would like to thank you for encouraging my research and for allowing me to grow as a researcher. Besides my advisor, I would like to thank my committee members: Professor Angela Guercio, Professor Gokarna P. Sharma for serving as my committee members. I also want to thank you for letting my defense be an enjoyable moment, and for your brilliant comments and suggestions, thanks to you.

I would like to thank my family specially my parents, for allowing me to realize my own potential. All the support they have provided me over the years was the greatest gift anyone has ever given me.

My warm and special gratitude to Mrs. Susan Schmidt, for her love and care, her mighty heart means a lot to me, I love you so much.

My emotional and irreproachable gratitude to Marcy Curtiss, The Administrative Secretary, for her never-ending help, support and advices that I cannot mention here all.
Last but not least, my unique gratefulness goes out to Muntadher Sallal, my precious gift from God; my best friends Maha Thafar, Salwa Aljehane, Hanan Muhajab, Rasha Obaid, and Liz Schmidt, they have always been there when I needed them. Without whom I would have struggled to find the inspiration and motivation needed to complete this thesis.

God bless you all.
ACKNOWLEDGEMENTS

I owe my most and special appreciation to Dr. Nancy Gantt, Professor of Surgery, NEOMED Co-Medical Director, Joanie Abdu Comprehensive Breast Care Center, Youngstown, Ohio, for her mighty heart and kindness when I approached her searching for types of breast cancer treatment. I would like to pay my gratitude to AMD Global Telemedicine which has provided me information about telemedicine carts and systems which can be used in my thesis; they both deserve my recognition.

Safa Shubbar
April 7, 2017
Kent, Ohio
Preface

I decided to explore telemedicine for the remote monitoring of responses to treatment in women who suffer from breast cancer, hence this thesis topic. This research sums up the knowledge I have acquired in Image Processing and Telecommunications and Networking over several years, taking into account the modern technology in health care (specifically in medical imaging). After reviewing the most common breast cancer imaging techniques (e.g., Mammogram, MRI, PET, etc.), I found that the ultrasound imaging technique would be the best choice for this thesis for several reasons. First, there is no harmful radiation in an ultrasound and thus is considered a safe screening tool. Second, it is useful in examinations on patients with dense breasts or breast implants. Third, the image resolution and contrast is high, which produces a clear distinction between healthy tissue and suspicious areas. It is used along with Telemedicine, or the intelligence of sharing medical and clinical information over a distance through teleradiology, along with blockchain technology and smart contract to ensure the validity and security of the patient’s data. With this, I felt like my dream was realized; I would finally propose a project that women in developing countries and isolated rural areas can benefit from. This work would be the concrete basis for our future career. Precisely, what we have done so far gives a narrowed-down direction towards a successful PhD. This PhD would contribute into deeply addressing, improving, and evaluating issues that might appear with our current work.
CHAPTER 1
Introduction

1.1 Problem Description and Motivation

Several global and national non-profit organizations have participated in finding solutions cancerous deaths, but the number of female victims of breast cancer is constantly growing. In 2017, the American Cancer Society (ACS) and the National Cancer Institute (NCI) estimate that there will be 252,710 new breast cancer cases, and about 40,610 women will die of breast cancer in the United States. This is a considerable number, considering the new technology and the advanced research institutions which are now available. More specifically, in the developing countries, substantial numbers of women are dying from breast cancer every year due to a lack of early detection and diagnosis methods as well as limited or no availability of necessary equipment. Therefore, early breast cancer detection is the first crucial step towards breast cancer treatment; it plays an essential role in breast cancer diagnosis and treatment.

Breast cancer screening is vital for the purpose of detecting breast cancer. Mammography and sonography are the most common screening methods. Mammography is the most important tool that is used by medical professionals to reveal, diagnose, and evaluate breast cancer. Conventional mammography is an X-ray photograph of the breast. This technique has been used for over 50 years for diagnosing breast disease [1]. It is able to detect breast cancer even when the lump is very small and not concrete. Indeed, several
studies have shown that lives can be saved through regular examinations by mammography. However, it has some limitations for breast cancer detection. Although it may be very sensitive, mammography is less sensitive of women with dense breast tissue (often, young patients), and thus can be inaccurate when detecting breast cancer in these patients [2]. Most cancerous tumors arise in dense tissue, so detection for women in this riskier category is quite challenging. Cancer detection with mammography is problematic when the breast tissue of younger women (under age 30) tends to be dense and full of milk glands. In mammograms, glandular tissues look more dense and white, appearing much like cancerous tumors [3]. Furthermore, a breast tumor might not appear on the mammogram. This is known as a false negative, as it can be hidden by normal breast tissue. In the case of "false alarms" or false positives, a mammography can identify an abnormality that looks like a cancer but turns out not to be one. A misdiagnosis or false positive means more tests and follow-up procedures, which are stressful for patients. Such tests and procedures, however, must be done in order to compensate for these limitations, more than is often necessary for mammography to make a proper diagnosis [4]. In fact, nearly two-thirds of the lesions that are sent for biopsy are benign. Many factors lead to this high failure rate, including low quality in mammography that show things like a low conspicuity of mammographic lesions, noisy images, and the overlying and underlying structures that obscure the region of interest (ROI) features [5]. Therefore, finding a solution to tackle the aforementioned limitations is considered the main challenge that must be faced in this field. Because an ultrasound has a distinct feature of not being limited by denser breasts, it is deemed as an important addition to mammography in order to detect, characterize, and
localize breast lesions. In addition, it has no radiation or compression [6]. Accordingly, sonography is more effective for women who are younger than 30 years of age [3]. Research results [7] have revealed that using ultrasound imaging is the best approach to get a higher detection accuracy of malignant tumors in the denser portions of breast parenchyma.

Ultrasound imaging seems to be more suitable for wide-scale screening and diagnoses due to its positive aspects such as being portable, using inexpensive equipment, and needing no ionizing radiation. On top of that, breast sound wave examinations are playing an increasingly important role in detecting breast cancers, due to the fact that an ultrasound can detect lumps which are obscured in mammography by dense tissue [8].

In this research, several previous studies that were conducted on breast cancer screening are reviewed. These studies are based on using different image processing techniques that help in early detection as well as diagnoses of breast cancer. In addition, the use of ultrasound imaging to improve the interpretation of breast images is explained in this work. Furthermore, we illustrate how sonography imaging makes it easier to detect lumps obscured by dense tissue [8].

Developed countries and several non-governmental organizations, side by side with the World Health Organization (WHO), have embarked on strengthening health care through the financing of medical research. This strengthening happens especially in developing countries, where there is limited access to hospitals and the necessary medical care is not always available. In this thesis, a method of automatic breast abnormality detection in breast ultrasound images is presented. In addition, we identified whether these
abnormalities are lesions or not. However, establishing a remote healthcare plan to monitor cancerous tumor treatments is considered the main intended goal of this work. It will be achieved by using telecommunication infrastructure and blockchain technology. Blockchain technology is deemed as one of the main components of Bitcoin cryptocurrency. The smart contract concept is a collection of code that is governing something important or valuable in the blockchain. Although there are quite a number of men who develop breast cancer, this thesis focuses on female victims of breast cancer.

1.2 Structure of the Thesis

The remainder of this thesis research consists of six chapters. In this section we provide a brief overview of the chapters.

**Chapter two:** Details the background information of breast cancer; breast anatomy, and abnormalities of the breast to educate women and encourage them to have a breast self-examination done on a regular schedule. This section also specifies the stages of breast cancer. It provides elemental education about the disease, including the causes, symptoms, diagnoses, and estimates of new cancer cases and deaths of breast cancer and of other common cancers in females, and finally treatment options (especially neoadjuvant chemotherapy).

**Chapter three:** Reviews the previous research and studies that were done in the area of breast cancer imaging techniques such as Scintimammography, Microwave Imaging, and Thermal infrared imaging to name a few. This chapter also discusses the review of the
imaging techniques currently being used (including their advantages and disadvantages) and discusses why ultrasound imaging is being considered in recent years. It also includes a comparison between the screening techniques with their limitations. In addition, different methods of pre-processing and segmentation are studied, and the advantages and disadvantages of those methods are discussed. Existing methods for feature extraction are also examined. Finally, the methods used to classify lesions in breast ultrasound images, along with the advantages and disadvantages of each method, are considered.

**Chapter four:** Reviews the previous research and studies done in the area of breast cancer imaging techniques such as those Scintimammography, Microwave Imaging, Thermal infrared imaging to name few. This chapter also discusses the review of the imaging techniques currently being used and their advantages and disadvantages and discusses why ultrasound imaging considered in recent years and the comparison between the screening techniques with their limitations. In additional to different methods of pre-processing and segmentation are studied, and the advantages and disadvantages of those methods discussed. We also discuss existing methods for feature extraction. Finally, we discuss the classification methods to classify lesions in breast ultrasound images, and we also discuss advantages and disadvantages of each method.

**Chapter five:** This chapter is the core part of this thesis. Telemedicine through mainly Teleradiology is examined; however, the real-time application is also mentioned in this chapter for future use when needed. This section also defines telemedicine with its uses. Real time and store-&-forward techniques used to share radiological images are mentioned,
along with how broadband networks have contributed to the success transmission of information of any form. In the same way; this work has suggested using any of the mentioned transmission channels along with the blockchain technology and smart contract for the electronic health records. Using Patient Assessment Terminal (PAT), a telemedicine cart from AMD global telemedicine, is also suggested. After reviewing some of the existing software for telemedicine solutions for the cancer patient, the use of AGNES Interactive software from AMD global telemedicine, along with a 5-18 MHz transducer for breast and small parts scanning, is recommended because this equipment is portable and does not require an ultrasound machine.

Chapter six: Gives the conclusion and future work recommendations and suggestions to develop an automated method of identifying types of tumors in breast ultrasound images such as Luminal A, Luminal B (HER2 negative), Her2 Positive, and Basal-like (usually triple-negative). As the blockchain contains a history of all transactions and grows in size with each new transaction, the scalability of block chain matters, and overcoming the scalability issue is part of our future work.

This research work also contains an appendix for additional information about the images processed results, MATLAB codes, and the existing telemedicine solutions for patients.
CHAPTER 2

2. Background information

This chapter gives an overview regarding the breast and its anatomy, the normal and abnormal configuration of the breast, and ultrasound and breast imaging. It also details the theory of breast cancer along with its symptoms, and it discusses methods of diagnosis in addition to ultrasound.

2.1 Anatomy of Breast

Breasts are cone-shaped structures on the anterior of the lateral chest wall. They are mostly made up of fat cells called adipose tissue. In general, the second or third rib (level of the clavicle) marks the upper boundary of the breasts which extend to the sixth or seventh rib (the underarm and across to the middle of the ribcage) [9]. A healthy female breast consists of 12–20 conical lobes. A lobe's base lies on top of the chest muscles and ribs, while the apex of lobe is located at the areola and nipple. Each of these lobes consist of many smaller lobules. A breast lobule is a gland that produces milk in nursing women. Both the lobes and lobules are linked by milk ducts, which serve as tubes to carry the milk to the nipple. Basically, these breast structures are where a cancerous tumor begins to form [9]. Breasts contain no muscle, but muscles are located under each breast, covering the ribs. The size and weight of breasts differ among individuals and with individuals themselves at different periods of their lives. Typical breast measurements are 10-12 cm long and 5-7 cm thick [9]. Figure 2.1. defines the anatomy of the female breast [10]. Breasts
are small in size before adulthood, enlarging during adolescence. Breast size also increases during pregnancy and especially after childbirth. Breasts become atrophic at the old age. Overall, the left breast is larger than the right breast.

![Anatomy of Female Breast](image)

(a) Front View  (b) Side View

**Figure 2.1. Anatomy of Female Breast [10]**

### 2.2 Abnormalities of a breast

Several changes may occur in women's breasts during the menstrual cycle, pregnancy or aging period. Breast tumors, which are extraordinary changes occur in the breast and these changes may be malignant (cancerous) or benign (non-cancerous). Breast abnormalities can be divided into 2 categories: breast masses (lumps) and microcalcifications.
2.2.1 Breast masses (lumps)

A lump is a bump or thickening that looks different from the surrounding breast tissue. It is usually denser in the center than on the edges. A mass may be discovered in a breast during a breast self-examination or during a routine clinical examination. Breast lumps are relatively common and usually not cancerous. Lumps may be either painless or painful, and accompanied by nipple discharge or changes in the skin, such as redness, tightened skin, irregularities, or a dimpled texture like the skin of an orange. Breast masses are often fluid-filled vesicles (cysts) or solid lumps, which are usually fibroadenomas (a ball of fibrous tissue). Both fibroadenomas and cysts are non-cancerous, or benign. Benign breast tumors are non-cancerous disorders that do not extend outside of the breast to other organs. They are not life threatening, are easily removed, and do not need follow-up treatments.

Shapes and margins are the most important features that indicate whether a mass is benign or malignant. Figure 2.2. shows that the mass shape can be round, oval, lobular, or irregular [11]. Circumscribed round and oval lumps are usually non-cancerous (benign), while irregular shapes more likely indicate malignant tumors [11]. The margins can be circumscribed, micro-lobulated, obscured (partially hidden by nearby tissues), spiculated (characterized by lines radiating from the mass), or indistinct (ill-defined) as shown in Figure 2.3. When the margins are circumscribed, the likelihood that the mass is a malignancy is very low.
Figure 2.2. Breast Mass-shapes [11]

- Round
- Oval

- Lobular
- Irregular

Figure 2.3. Breast Mass-margins [11]

- Circumscribed
- Micro-lobulated
- Obscured
- Ill-defined
- Spiculated
2.2.2 Microcalcifications

Microcalcifications are tiny spots of calcium deposits. They are too small to be felt, but they can be seen on a mammogram. Microcalcifications are usually harmless and show up as small, bright white spots [12]. However, when they show up in certain patterns such as clusters in one region of the breast or are all in a line, they might be an early sign of breast cancer. Microcalcifications may result from injury or nursing. In these cases, they are probably benign. Microcalcifications are not indicative of the amount of calcium in a woman’s body. However, they can occasionally indicate a suspicious area which may contain cancerous cells [12].

2.3 Breast Cancer

2.3.1 Definition

As previously discussed, it is imperative that all people throughout the world learn more about cancer, especially breast cancer, so that they are better prepared to take precautions to fight against the disease and its consequences. The National Cancer Institute (NCI) refers to “cancer” as a collection of related diseases. In all types of cancer, some of the body’s cells begin to divide without stopping and spread into surrounding tissues [13]. According to the National Breast Cancer Foundation, breast cancer is defined as a disease in which malignant (cancer) cells form in the tissues of the breast [14]. Although male breast cancer is relatively rare, it does occur in both men and women. Breast cancer is considered the most common type of cancer among females. In fact, four out of every 10 female cancer survivors in the United States have recovered from breast cancer [15]. It is
a neoplastic development of tissue in the breast. Tumors usually form cells, which can be seen on an x-ray or felt as a mass. Strange changes in the breast can be either non-cancerous or malignant (carcinogenic); malignant cells can invade into surrounding tissues or propagate (metastasize) to other areas of the body. Breast cancers may start in any part of the breast. Furthermore, they may be named either as “ductal cancers” which start in the ducts that carry milk to the nipple, or “lobular cancers” which begin in the glands that make breast milk. Also, there are a few kinds of cancers named “sarcomas” and “lymphomas” which start in other tissues in the breast but are not considered as breast cancer. However, it is important to know that most breast lumps are not cancerous, but benign. Despite the fact that benign breast tumors grow in an abnormal way, they do not spread over distant areas of the body. Moreover, there are not life threatening. However, any breast mass or change should be examined by health caregivers to decide whether it is benign or cancer, and whether it might affect the patient’s future risk of cancer. Figure 2.4. shows the relationship between the lymph nodes of the breast [16]. Breast cancer may spread out through the lymph system as well. This system contains lymph nodes, lymph vessels, and fluid that spread across the body. Moreover, the lymph system has tissue fluid and waste products. Lymph nodes are basically small, grain-shaped groups of immune system cells that are linked by lymph vessels. Lymph vessels are quite similar to small veins. The key difference between lymph vessels and veins is that veins carry blood while lymph vessels carry a clear fluid called lymph away from the breast. Breast cancer cells may enter the lymph system through lymph vessels and start to grow in lymph nodes.
The presence of breast cancer cells in one or more lymph nodes usually affects treatment plans and increases the likelihood of finding cancer in other organs. A healthy body is usually able to repair DNA when it becomes damaged, while DNA is irreparable in cancer cells which makes the body weaker.

2.3.2 Causes and Symptoms

2.3.2.1 Causes

The causes of both general and breast cancer remain unknown. However, according to the National Cancer Institute (NCI), some research has shown that there are certain risk factors linked to the disease that may increase a person’s likelihood of developing cancer. Each kind of cancer has its own risk factors such as alcohol, tobacco, and dieting routines. Cancer risk factors also include things are difficult to control or change by people, like
race, age, family history, etc. [17]. Since the attention here is focused on breast cancer, one of the important factors that plays a key role in developing breast cancer is hormones, but how that happens is not quite understood. Some factors that might increase the possibility of having breast cancer are listed below [18,19]:

**a. General**

- Age: Older women have a higher chance of having breast cancer. Women over 60 have been diagnosed and found to have cancer, but it is very rare in women under 45.
- Gender: Any woman is at risk of getting breast cancer. Although nearly 2,000 men get breast cancer each year, this disease infects women 100 times more than men.

**b. Genetics**

- Family history: Women with a close blood relative (a mother, sister or daughter) who has or had breast cancer have approximately twice the risk of developing breast cancer during their lifetimes. However, more than 8 out of 10 women who have a close relative with breast cancer will never develop it.
- Inherited factors: Some inherited genetic mutations (changes) may increase breast cancer risks; for instance, mutations in the BRCA1 and BRCA2 genes are the most
common inherited causes.\textsuperscript{1} Other gene mutations may also increase breast cancer risks.

- Race: African-American women are less likely to get breast cancer than white women. However, African-American women have a higher probability of dying from this disease; this is due to the rapid growth of the tumor in these women.

c. **Body**

- Obesity: Fat tissue may contribute to increasing estrogen levels after menopause. Increasing the levels of estrogen may increase the risk of breast cancer. Also, weight gain during adulthood and excess fat around the waist play an important role in increasing the risk of developing this disease.
- Not having children: Having no children or having the first child after age 35, may increase the risks of breast cancer. On other hand, breastfeeding may help to reduce breast cancer risks.
- High breast density: Women with dense breast tissue (less fatty tissue and more glandular and fibrous tissue) are more likely to develop breast cancer than women with less dense breasts.

\textsuperscript{1}“BRCA1 and BRCA2: Cancer Risk and Genetic Testing,” National Cancer Institute, April 7, 2015, https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet#q1
• Some breast changes: Certain benign (noncancerous) growths raise the risk of breast cancer.

• Menstrual history: Women who begin menstruation before age 12 years old and/or have menopause after age 55 have a slightly higher risk of developing breast cancer.

d. Lifestyle

• A sedentary lifestyle: Like any other health problem, physical activity in the form of exercising regularly for four to seven hours weekly may help to lower the risk of getting breast cancer.

• Heavy drinking: An excessive alcohol intake is clearly associated with an increased risk of breast cancer. The risk increases with the amount of alcohol consumed.

e. Previous treatment

• Birth control pills: Studies have shown that using birth control pills within the past 10 years may increase the risk of developing breast cancer. However, the risk decreases over time after the use of contraceptives stops.

• Combined post-menopausal hormone therapy (PHT): One of the factors that increases the risk of breast cancer is using a combined hormone therapy after menopause. Also, combined HT raises the likelihood of finding the cancer at a more advanced stage.

• Diethylstilbestrol exposure (DES): Between 1940 and 1971, this drug was commonly given to pregnant women to avoid miscarriage. It may slightly increase
the risk of developing breast cancer not only for the mother but also for any babies in the womb.

- Radiation exposure: Women at any age who have had radiation therapy in the chest area as a result of treatment for another cancer have a significantly higher chance of developing breast cancer.

### 2.3.2.2 Symptoms

Breast cancer is the most invasive cancer in women, both in the US and worldwide. Breast cancer in its early stages is usually painless or does not cause symptoms. For this reason, regular breast exams and mammograms are very important. This enables the detection of cancers without immediate symptoms. A new mass in the breast that women or doctor can feel is the most common symptom of breast cancer. Such masses are usually hard and painless, but some may be painful. Though not all masses are cancer, it is important to have a medical professional check out any new lump or mass right away.

According to the American Cancer Society, any of the following extraordinary changes in the breast can be a sign of breast cancer [20]:

- Change in the breast size (swelling in or around the breast, collar bone, or armpit)
- Shape
- Breast warmth and itching
- Breast pain
- Nipple changes (pain or the nipple turning inward)
- Nipple or breast skin redness or thickening
• Scariness
• Nipple discharge (especially if the fluid is bloody, clear-to-yellow, or green)

2.3.3 Stages of Breast Cancer

The staging of breast cancer is a procedure taken by the healthcare team to find out how far cancer has progressed when it is found [21]. The stage of the disease significantly affects the determination of the disease treatment plan and the success of the plan. Stages of breast cancer range from 0 to 4, where each stage represents a progression of the cancer. Breast cancer is assigned to the stage based on where it begins in the breast and how much of the breast and other parts of the body are affected by it [21]. Figure 2.5. shows the stages of breast cancer based on the National Breast Cancer Foundation (NBCF).

Figure 2.5. Stages of Breast Cancer Based on the NBCF [21]
• **Stage 0 breast cancer (carcinoma in situ)**

  a. Noninvasive

  b. Cancer Cells Location: lining of the breast milk duct or lobules (not spread to the surrounding tissue)

  c. Treatment options: surgery, radiation, or a combination of both. No need for chemotherapy.

• **Stage 1 breast cancer**

  a. Invasive

  b. This stage is divided into two groups

     ➢ **Stage 1A**: The tumor size is less than 2 cm (0.8 in). The cancer cells have not yet spread into the surrounding breast tissue or lymph nodes.

     ➢ **Stage 1B**: Lymph nodes have small clusters of cancer cells with an approximate size ranging from 0.2 mm to 2.0 mm.

  c. Treatment options: surgery, radiation, a combination of both, or hormone therapy. No need for chemotherapy.

• **Stage 2 breast cancer**

  a. Invasive

  b. This stage is divided into two groups

     ➢ **Stage 2A**: can be broken down into a number of cases:
1) No tumor is present but the cancerous cells have spread to less than four axillary lymph nodes.

2) The tumor size is less than 2 cm (0.8 in). The cancerous cells have spread in less than four axillary lymph nodes.

3) The tumor size is between 2 cm (0.8 in) and 5 cm (2 in) but have not yet spread to the axillary lymph nodes.

➤ *Stage 2B*: can be broken down into:

1) The tumor size is between 2 cm (0.8 in) and 5 cm (2 in), and cancerous cells have spread in less than four axillary lymph nodes.

2) The tumor size is larger than 5 cm (2 in) but have not spread to the axillary lymph nodes.

c. Treatment options: Radiation, hormone therapy, chemotherapy, and surgery.

• *Stage 3 breast cancer*

a. Invasive

b. This stage is divided into three groups based on the tumor size, the locations and numbers of lymph nodes to which the cancerous cells have spread, and also whether the chest wall has been affected or not.

➤ *Stage 3A*: can be broken down into a number of cases:

1) The tumor size is less than 2 cm (0.8 in) and the cancer has spread to 4-9 nearby lymph nodes.
2) The tumor size is larger than 5 cm (2 in) and lymph nodes have small clusters of cancer cells with an approximate size ranging from 0.2mm to 2.0 mm.

3) The tumor size is larger than 5 cm (2 in) and the cancer has spread to 1-3 lymph nodes under the arm or near the breastbone.

➤ **Stage 3B:** The tumor can be any size and cancer has spread to the chest wall or breast skin, or up to 9 lymph nodes near the breastbone.

➤ **Stage 3C:** Can be broken down into a number of cases:

1) No tumor is found in the breast but the tumor may be any size and the cancer has spread to the chest wall, the breast skin, or 10 or more lymph nodes under the arm.

2) No tumor is found in the breast but the tumor may be any size and the cancer has spread in the lymph nodes near the collarbone area.

3) No tumor is found in the breast but the tumor may be any size and the cancer has spread in the lymph nodes under the arm and near the breastbone.

c. Treatment options in this stage may consist of a combination of two or more of the following treatments: mastectomy, radiation, hormone therapy, chemotherapy, and surgery (this option may need a treatment method to reduce the breast cancer before the surgery).
• **Stage 4 breast cancer**
  
  a. invasive
  
  b. Stage 4 breast cancer is the most advanced stage. In this stage, cancer has spread to other organs in the body, most often the brain, lung, bones, and liver.
  
  c. This stage of breast cancer is considered incurable. However, patients with Stage 4 breast cancer may respond to some of treatment options that can extend the patient’s life for several years, but this requires personal motivation and excellent health care.

**2.3.4 Breast Cancer Formation**

Breast cancer is a malignant tumor that grows in the breast tissue. Breast cancer is the most common type of cancer among women in America. The rates of developing breast cancer are higher than those for any other cancer, besides lung cancer [22]. The most common type of breast cancer occurs when cancer cells develop in the milk ducts (ductal carcinoma). Cancer cells may also develop in the glands (lobular carcinoma), often in both breasts. Provocative breast cancer is a singular kind of breast where the breast is temperate, red, and inflated. This is additionally more prevalent in African-American females than in white females. Generally, African-American females are more probable to expire of breast cancer. The likelihood of getting and dying from breast cancer is less in Hispanic, Asian, and Native-American females [22].

In 2016, over 2.8 million females in the U.S who either have or have had breast cancer. This involves females presently being taken care and females who have completed
treatments. A female’s likelihood of having breast cancer roughly doubles when she has a family member (mother, daughter or sister) with breast cancer. Fewer than 15% of females who acquire breast cancer have a relative detected with it [22].

However, about 5-10% of breast cancers can be linked to gene mutations (abnormal changes) inherited from one’s mother or father. The rate of breast cancer in females in their twenties is very low, and it gradually increases after the age of 45. The rate of cases increases significantly after the age of 50, indicating the necessity of yearly check-ups throughout a woman's life [22]. Breast cancer occurs almost entirely in females, although men have also been diagnosed with it.

It is still difficult to understand the main cause of breast cancer and how to change or eliminate the causes of this malignancy. An ideal way to cope with the problem is to take necessary and appropriate measures regarding early diagnosis and treatment. In 2017, the American Cancer Society has stated that [23]:

- About 252,710 new cases in women would be diagnosed.
- About 40,610 females would die from breast cancer.
- About 2,470 new cases in men would be diagnosed.
- About 460 men would die from breast cancer.

The information on this page refers only to the common cancer cases in women, particularly those of breast cancer [23]. Table 2.1., made by the American Cancer Society, shows common cancer types, estimated new cases, and estimated deaths in females [23].
Table 2.1. Estimated Common Cancer New Cases and Deaths in Females, US, 2017 [23]

Based on table 2.1. Figure 2.6 shows the percentage of diseases recorded by the American Cancer Society, signifying that at least 38% women diagnosed with cancer have breast cancer.
Figure 2.6. Most Commonly Diagnosed Cancers in Females, US 2017

As shown in table 2.1, breast cancer is the second leading cause of death in women after lung cancer. Figure 2.7 shows that at least 19% of women who die from cancer die from breast cancer.
Figure 2.7. The Most Common Deadly Cancers in Females, US 2017

2.3.5 Breast Cancer Treatment

Breast cancer continues to be one of the most important health issues in women’s lives, not only because it is the most common cancer in women but also because it is the second leading cause of death in women after lung cancer. An early detection and diagnosis of breast cancer and other types of cancers plays the main role in increasing the rate of survival. Breast cancer examination methods include a breast self-exam (BSE) which each woman must do once a month at home, and a Clinical Breast Exam (CBE) by a healthcare
expert who has been trained to recognize various kinds of abnormalities. Treatment options depend on upon multiple factors, including [24,25]:

- The tumor’s stage,
- The type of tumor, such as Luminal A, Luminal B, Her-2 Positive, and Basal-like (usually triple-negative),
- The patient’s age, menopausal status, general health, and preferences,
- The existence of changes in inherited breast cancer genes, such as BRCA1 or BRCA2.

Doctors generally recommend surgery to remove the tumor for both ductal carcinomas in situ (DCIS) and early-stage invasive breast cancer. To guarantee that the whole tumor is removed, the surgeon would likely remove a little zone of strong tissue around the tumor. Despite the surgical goal to remove the visible cancer, microscopic cells may remain, either in the breast or elsewhere. Under certain conditions, this may suggest other procedures that could be relied upon to kill or remove any remaining malignant cells. For large cancers or those that are growing quickly, doctors may endorse a systemic treatment with chemotherapy or a hormonal treatment before the surgical procedure (also known as a neoadjuvant treatment) [26-31].

After a surgical procedure, the purpose of accompanying treatments for managing early breast cancer is to cut down the risk of repetition and get rid of any infected cells. Treatment given after a surgical procedure is called adjuvant treatment [32], and it might contain radiation therapy, chemotherapy, targeted therapy, and/or hormonal therapy. Whether adjuvant treatment is required depends on the likelihood that any tumor cells stay
in the breast or the body, and that the given treatment would work to treat the damaged cells. Although adjuvant treatment reduces the threat of the cancer returning, it might not thoroughly eliminate the risk [33].

Recently, medical imaging possibilities through bioinformatics have been included and endorsed by research institutions. These institutions, together with the National Cancer Institute (NCI) and the American Cancer Society (ACS) want to promote a greater use of breast images produced from x-rays (mammogram), ultrasounds, MRIs, etc. In this context, this study examines the detection of cancerous tissues from ultrasonic images by using the SVM algorithm and Agnes software to monitor and measure diseased breast tissues. This requires advanced medical equipment and high speed internet connections to facilitate the work by the patient and nurses who provide health care. This way, women in remote areas with few opportunities to benefit from health care technology can, in fact, receive care from telehealth technology. This benefit can be achieved through the use of appropriate devices in combination with tools for detecting and finding tumor sizes. From the user side, ultrasound equipment that will help to take digital images is necessary. Hence, images and information about the tumor size will be sent remotely through the Agnes software to a doctor who will then review the patient’s progress offline.²

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² See chapter 5 for more information on Agnes software
2.4 Neoadjuvant Chemotherapy

Chemotherapy is the use of a cancer cell-killing drug treatment that can be administered either in a vein or by mouth. The drugs circulate through the blood stream to the cancer cells in most parts of the body [34]. Neoadjuvant chemotherapy refers to the systemic therapy of breast cancer before surgical therapy [26]. Reducing the size of the tumor (shrinking of the malignant lesion) may lead to a decrease in the required extent of the surgery. A tumor mass that has a required mastectomy, or total removal of the breast, may be treated by lumpectomy with clear margins. Tumor shrinkage can facilitate the surgical procedure, along with improving the postoperative QOL (Quality of life) for the patient. Neoadjuvant chemotherapy provides the possibility of treating both a woman’s whole body and any micrometastases at distant sites. Unfortunately, chemotherapy can be associated with many serious side effects that may lead to a worsening of the patient’s overall health status [27,28]. Neoadjuvant chemotherapy is performed in cycles with a resting phase after each treatment cycle. The important criteria to determine the eligibility of a patient for surgery are the response to the chemotherapy, and patient health/performance status [26]. Significant survival benefits have been established from using neoadjuvant chemotherapy in breast [29] and lung cancers [30,31]. Doctor N. Gantt (personal communication, January 30, 2017), said “actually we have not really proven an overall survival benefit in breast cancer in large studies. That data may be forthcoming with the increasing utilization of Pertuzamab with Taxotere/Carboplatin/Herceptin in the neoadjuvant setting.”
2.4.1 Possible Side Effects of Neoadjuvant Chemotherapy for Breast Cancer.

There are many side effects caused by chemotherapy treatments. The drug types, the given dose, and the length of treatment period play major roles in these side effects. Most of them usually disappear after treatment is finished. Some of the most common possible side effects include [28,35]:

- Hair loss (Alopecia) and nail changes
- Neuropathy (neuropathy can be persistent)
- Mouth sores
- Loss or increase appetite
- Fatigue
- Diarrhea
- Easy bleeding
- Nausea and vomiting
CHAPTER 3

Literature Review

3.1 Breast Cancer and its Diagnosis Using Screening Techniques

Several studies have been conducted in the field of bioinformatics on cancer. The National Cancer Institute has prioritized the development of advanced techniques, playing a key role in contributing to early detection and diagnosis. Previous works include: Scintimammography (nuclear imaging, also known as a Miraluma test or Sestamibi breast imaging [36]), is a kind of breast imaging technique which is carried out through a standard gamma camera used to detect cancer cells in women who either have had abnormal mammograms (Scintimammography is not used as an alternative to a mammogram), or who have dense breast tissue. During the test, the patient is injected with a small amount of radioactive substance called technetium 99. It is taken up by cancer cells so that pictures of the breast can be taken by a gamma camera to detect cancer cells [37].

Thermal infrared imaging (TII) is another method of breast cancer imaging where the infrared image provides more dynamic information of the tumor by making the tumor appear in the IR image as a high temperature spot [38].

Another method of breast cancer imaging includes Microwave imaging. In this technique, the breast tumors exhibit electrical properties that differ from those of healthy breast tissues [39].
Positron Emission Tomography (PET) is a nuclear medicine technique that provides information about the diseased and healthy breast tissues by the use of a powerful camera inside the human body to capture images, showing the chemical functions of the body [40].

Several research studies and surveys have been conducted worldwide for the detection of breast cancer. Different tools and procedures to detect and diagnose the disease often include at least one of the following techniques:

- Mammography
- Magnetic Resonance Imaging (MRI)
- Ultrasound

Specifically, mammograms are conducted on women who do not exhibit symptoms of breast cancer. An ultrasound screening procedure is used if a patient is diagnosed with a cancer, or if an abnormality has been found. If the previous screening methods failed to provide definitive information regarding breast cancer, then a medical biopsy may be taken by a surgeon. This is done by removing a sample of breast tissue, and then testing the biopsy to determine whether the tissue is benign or cancerous. The advantages and disadvantages of existing screening tools are as follows

3.1.1 Mammography

A mammogram is an X-ray image of the breast. Currently, this is the recommended method used by doctors for breast cancer screening for women who have no symptoms of
breast cancer or its symptoms. This technique is designed to look only at breast tissue. The mechanism of this machine involves compressing the breast between 2 plates, applying low doses of X-rays to it [41]. Figure 3.1 shows a mammography imaging unit [42]. The emissions from the X-ray pass through the breast, and captured images are either stored onto film or directly onto a computer as digital images. Although there is a highly reasonable probability of the mammogram detecting significant changes in the breast such as calcifications and masses, harmful ionizing radiation is used in X-ray mammography. This radiation, along with the painful process of applying pressure to the breast between plastic plates, are drawbacks for this technique [43].
a. Advantages

- Good sensitivity.
- High-quality results
- Forming an image takes only a short time.

b. Disadvantages

- Less effective for patients with dense breast cancer.
- The procedure of compressing the breast between the plates is painful for the patient.
- The use of ionizing radiations in the process makes the X-ray mammogram unsafe and potentially harmful.

3.1.2 Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging is a non-invasive medical technique used by physicians to diagnose and monitor treatment for medical conditions. MRI uses strong and powerful magnets, radio frequency pulses, and a computer to form high quality images to produce detailed pictures of soft tissues and internal body structures. This machine does not use X-rays (ionizing radiation). The images produced by the MRI allow physicians to evaluate different parts of the body and determine whether there is the presence of disease in an organ or not. The MRI system is placed in a protected room where the device operates at high frequencies. This helps to avoid any intervention of other sound-waves from the
environment [44,45]. Figure 3.2. shows the magnetic resonance imaging machine (MRI) [46]

During the examination, the patient lies on a table (bed) as shown in Figure 3.2. Furthermore, small scanners are placed around the breast to monitor and enhance the quality of the obtained image. Several images are usually required to complete the examination, which takes a long time to complete a single test [46]. The MRI machine produces a loud pounding sound, in addition to the buzzing noises during the screening process. This makes it imperative for the patient to wear ear caps to help block out the sound [46].

![Magnetic Resonance Imaging Machine (MRI)](image)

**Figure 3.2. Magnetic Resonance Imaging Machine (MRI) [46]**

- **Advantages**
  - Non-invasive and painless
  - Non-ionizing imaging technique
  - MRI proved effective in screening women with dense breasts.
• Ability to capture images from different orientations
• The possibility of revealing small tumors and multifocal breast cancer. Multifocal cancer [47] in which the breast has more than one tumor, all of which originated from a single original tumor. The tumors are probably being in the same quadrant of the breast.
• Can determine if the cancer has reached to the chest wall.
• Can detect breast implants and ruptures.

b. Disadvantages

• Extremely expensive
• It is very noisy for the patient
• Fixed and immobile
• MRI is not able to detect calcifications.
• Patients may feel scared of being in a confined space (claustrophobia).
• Compared to X-ray and ultrasound scanning techniques, MRI is time-consuming.

3.1.3 Ultrasound Imaging

Ultrasound imaging is considered to be a safe screening tool, as it does not cause discomfort to patients, and is suitable for women with dense breasts and breast implants [48]. Ultrasound uses ultrasonic waves (non-harmful radiation) with a frequency range of 1MHz to 15MHz for examining an internal body structure. Such a technique is used to determine whether the region consists of a cancerous tissue or not. Ultrasound images can
be obtained from any orientation or angle. In case a solid tissue is found during the examination, a biopsy (sample) will be required to determine whether it is cancerous in nature. The ultrasound procedure is usually performed by radiologists, or physicians who are specialists in the application and interpretation of various medical imaging methods. To conduct a sonography, a portable probe known as a transducer is typically used. It is placed directly on and moved over the patient. Figure 3.3 shows an ultrasound imaging system [49].

Figure 3.3. Ultrasound Imaging System [49]
a. Advantages

- There is no harmful radiation and thus is considered a safe screening tool.
- Useful in examinations on patients with dense breasts or breast implants.
- Image resolution and contrast is high, which produces a clear distinction between healthy tissue and suspicious areas.

b. Disadvantages

- The procedure is dependent on radiologists who specialize in the application and interpretation of various medical imaging methods.
- Difficulty of detecting deep-lying lesions.
- Difficulty of distinguishing between certain solid masses and others.

3.1.4 Comparison Between the Most Common Screening Techniques

Early detection and diagnosis of breast cancer has significantly improved the chances of a quick and successful treatment, as well as the long-term welfare of the patient. The screening techniques used for breast cancer detection are X-ray mammography, ultrasounds, and MRIs. The comparison between these techniques is discussed in subsections 3.1.4.1 to 3.1.4.3 [43-49]:

3.1.4.1 A Comparison of Mammogram with Ultrasound and MRI Techniques

X-ray mammography is the most commonly used technique in breast cancer detection and is deemed as the basic method for early stage breast cancer screening. During
the examination, the breast is compressed between two plastic plates. Then, X-rays pass through the breast to form an image that can be stored either onto film or as digital images directly onto a computer. Compared to other techniques, X-ray mammography technique is considered to be the “Gold Standard” for the detection of breast cancer, as it offers several benefits. These include high-resolution images, a high sensitivity of detection, and a formation of images in a short time period. Despite the positives that have been mentioned for this technique, it has several drawbacks compared to other existing screening techniques. Besides being relatively expensive, the pain associated with compressing the breast and the lowered accuracy in detecting abnormalities in patients with dense breast cancer are both disadvantages of this procedure. Unlike the MRI and ultrasound techniques, mammograms use ionizing radiation in the process, making it potentially harmful. In addition to this, mammograms are unable to detect tumors near the chest wall or arm.

3.1.4.2 Ultrasound Comparison over Mammography

Compared to X-ray mammography, ultrasounds are considered a good screening tool, as they do not cause discomfort to patients and are suitable for women with dense breasts or breast implants. Testing with the ultrasound technique uses ultrasonic waves (non-harmful radiation) with a frequency range of 1MHz to 15MHz for examining an internal body structure. Along with X-ray mammography, ultrasound images also have a high contrast and resolution, yielding a high discrimination between healthy tissue and
suspicious areas. However, it is hard for an ultrasound to detect tumors located deep in the breast when compared to an MRI.

3.1.4.3 MRI Comparison over Mammography and Ultrasound

An MRI is a non-invasive medical technique that uses strong and powerful magnets, radio frequency pulses, and a computer to form high quality images to produce more highly detailed pictures of soft tissues and internal body structures than those from an X-Ray mammography. It accurately distinguishes between soft and hard tissues due to the strong magnets’ sensitivity as compared to ultrasound. As in ultrasounds, an MRI is very useful for women with dense breasts and breast implants. Since it does not use X-rays (ionizing radiation), it can also detect a tumor without any adverse side effects. Unlike X-ray mammography and ultrasounds, MRI images can be obtained from different orientations to estimate the exact location of tumors and detect multifocal cancers. However, an MRI machine requires a large area in which to be placed, making it immobile and unsuitable for large-scale screening programs. During the MRI scanning process, a patient must be placed down in a large cylindrical-shaped structure. This may cause a claustrophobic effect on patients because of their fear of being in a confined space.

These techniques mentioned above, and others not mentioned here have contributed to the accurate and efficient detection of breast cancer. This thesis uses a computer-aided diagnosis to improve the visualization of digital images obtained from ultrasound machines. Ultrasound is one of the most useful diagnostic tools for breast cancer, especially for younger patients with dense breasts. Ultrasound is mostly used to distinguish between
solid and cystic masses, as well as to help differentiate between malignant solid tumors and benign tumors. A cystic mass is a cyst-like structure which is usually filled with a liquid, a semi-solid, or gaseous materials much like in a blister. For women younger than 30, ultrasonography is probably used as the primary clinical examination to determine whether there is a mass or a nipple discharge. Breast cancer tends to occur in women after menopause. Therefore, doctors try not to use mammograms with young women in order to avoid exposure to unnecessary radiation.

3.2 Introduction of Breast Cancer Computer-aided Detection (CAD)

Breast ultrasound CAD systems in conjunction with a radiologist might be used to evaluate ultrasound images and detect breast cancer [50]. A breast ultrasound CAD system is very useful to improve the quality of an ultrasound image, increase the image contrast, and determine the lesion location automatically [51-53]. The most important advantage of CAD systems is significantly reducing the workload for the specialist and improving the diagnosis and accuracy of detection [50].

3.2.1 Stages in CAD

There are four stages for ultrasound images in a computer-aided diagnosis system These stages are as follows:

3.2.1.1 Pre-processing: This stage is used to enhance and reduce noises in the ultrasound image without compromising important features.
3.2.1.2 **Segmentation**: This stage is used to detect non-interlaced segments that can be distinguished from the background. Those segments could be lesions.

3.2.1.3 **Feature extraction**: This stage extracts the data from each segment that is obtained in the previous stage, which will then be used to distinguish between benign and malignant tumors in the classification stage.

3.2.1.4 **Classification**: Classification is the final stage, where lesions are classified into one of two categories: benign and malignant.

### 3.2.2 Detecting Tumor from Ultrasound Images

#### 3.2.2.1 Pre-processing

Due to a different source of interventions, ultrasound images are usually deteriorated from noise, which usually appears as dark and bright spots (or speckle). Such spots are undesirable, as speckle makes it difficult in finding the fine details to detect and diagnose low-contrast lesions. Thus, pre-processing is an important stage to eliminate the noise [54,55].

Several image enhancement algorithms have been introduced, each one belonging to either the spatial-domain or transform-domain-based category. In spatial domain algorithms, image operations are performed on a local region or a whole image based on the image statistics. This category includes methods such as image averaging, histogram equalization, nonlinear median filtering, and using edge detection and morphology operators for image sharpening [56].
The transform-domain-based algorithms include image operations in the transform domain. This method facilitates the extraction of image features that cannot be obtained from the spatial-domain. This category includes methods such as the wavelet domain and Fourier [57]. Image enhancement algorithms aim to improve the quality of the image by the use of mathematics; the result is an image containing specific features that appear more clearly and are more distinct than those in the original image.

A speckle reduction method of ultrasound images was implemented in Matlab [58] based on Wiener filtering, median filtering, and wavelet transform methods. The Wiener filtering is considered an optimal linear filter used to minimize the mean-square error value [59,] but it has some limitations.

The median filter is a nonlinear method used to reduce noise from images by moving through the original grey image pixel by pixel, replacing each pixel’s value by the median value in a specific neighborhood. This method is widely used and works well in reducing noise and preserving edges of the image [60].

Noise reduction by using frequency domain filters is easier than filtering in spatial-domain, where noises can be identified easily in the frequency domain. For example, by transforming an image into a Fourier domain, the high-frequency components can identify image edges, details, and noise, while low-frequency components identify blurred or smooth regions of the image. Based on that, we can design filters to remove noises according to image frequency components [61], where high-pass filtering will usually emphasize the image sharp details and edges by reducing low-frequency components, and
where low-pass filtering will smooth or blur images by reducing high-frequency components.

3.2.2.2 Segmentation

Some of the segmentation methods that have been used in breast ultrasound images will be reviewed here. A simple histogram thresholding [62] can detect the boundary of the lesion. In this method, the over-simplified approach results in an inaccurate boundary. This method can be used either as an intermediate step or be combined with post-processing procedures such as morphological operations [63] to provide a rough contour. The disadvantage of histogram thresholding is that it is very sensitive to noise, so it is not accurate for breast ultrasound images which are very noisy [64].

Markov random fields (MRF) [65] is one of the model-based methods including commonly-used models such as level set citeZaina and active contours. The main idea of Markov random fields is to solve the problems with traditional segmentation methods based on intensity. A difficulty associated with this model is robust smooth segmentation. Speckle noise in ultrasound image MRF does not work well because this may lead to a loss of important structural details in the image. Also, these methods are time-consuming to run, and require an initial contour or region of interest. For those reasons, model-based methods might not be suitable for breast ultrasound images [66].

Dokur and Olmez [67] suggest a segmentation method of ultrasound images based on a neural network. After dividing images into blocks of squares, the discrete cosine
transform (DCT) is used to extract the features from each block. After that, the three-layer hybrid neural network can be trained to classify these blocks into foreground and background. A neural network is one of the machine learning methods and by using such methods, we can combine various lesion characteristics. However, the disadvantages of this method are that it requires a long training time and the test image comes from a training images set. This method is also machine dependent, meaning that it is possible to get different results depending on different types of ultrasound machines.

### 3.2.2.3 Feature extraction

After segmentation, we need to categorize the lesions into benign or malignant by finding some features in the region. These features such as boundary, shape, and internal structures play an important role in breast cancer diagnosis.

Singh et al. [68] discuss that the texture features extraction has a very strong power for classification and is not time consuming. Chen et al. [69] studies different texture features, including 2D normalized auto-covariance coefficients, BDIP (Block difference inverse probabilities), GLDM (Gray-level difference matrix), SGLDM (Spatial gray-level difference matrices), and NGTDM (Neighborhood gray-tone difference matrix). These features are used to process ultrasound images. After extracting these features, they applied the PCA (principle component analysis) to reduce the dimensions.

### 3.2.2.4 Classification

The main objective of this study is to assist radiologists in interpreting ultrasound images. After extracting features from the image, we need to implement one of the
classification methods to determine whether the lesion is suspicious or not. Image classification is one of the traditional problems in image processing. Several methods for solving this problem currently exist, such as K-nearest neighbor (k-NN), adaptive boost (Adaboosted), Artificial neural network (ANN), and Support Vector machine (SVM) [70,71].

The k-NN is a conventional non-parametric classifier, meaning that it does not make any assumptions about the distribution of basic data. This is a very useful feature, since not all the practical data in the real world tends to follow typical theoretical assumptions. The k-NN classifier assigns the input image to a class by calculating the distance between the feature vector of the training image dataset and the feature vector of the input image. K is an integer that decides how many instances influence the classification [70].

An artificial neural network (ANN) [71] is a brain-style mathematical model, and it has the ability to capture complex and nonlinear interactions between factors. The goal of the ANN is to get a meaningful output from the inputs. It has also been used for many applications such as visual information, recognition, and predication. Researchers have developed the structure of various ANNs to improve the quality of medical images and analyze the survival problems. An ANN analysis also shows when the disease is expected to recur after surgery [72].

An adaboost classifier can be used in conjunction with a set of weak classifiers to improve their performance and construct a “strong” classifier. They are called weak classifiers because their performance is slightly better than a random predictor. An
adaboost is an iterative learning algorithm, so at each iterative step the weak classifier with the smallest weighted error is selected. Weak classifiers classify or label the sub-window of an image belonging to an object or noise class by comparing a single feature to the threshold $\theta$ value. If the feature is above the threshold value then it belongs to the positive. Otherwise, the feature belongs to the negative $[70,73]$.

A support vector machine (SVM) $[74]$ is considered to be one of the best-known methods in image classification. This method constructs an optimal separating hyperplanes in high-dimensional feature space. Data points are viewed in different classes, $(x_1,y_1), (x_2,y_2),...(x_p,y_p)$, where $x_i$ are the feature values, and $y_i$ is the class label (usually $+1,-1$). Images of which feature vectors are located on one side of the hyperplane belong to class $+1$, with the other images belonging to class $-1$.

### 3.2.3 Summary

Several pre-processing techniques have been introduced. However, each has some limitations. Some techniques remove important information in the ultrasound images, while others do not provide a good separation between background and foreground. This shortage requires using better pre-processing methods to preserve important information in the ultrasound image and improve the quality of the image.

In segmentation, some techniques are unsuitable for ultrasound images because these techniques are very sensitive to noise. Other segmentation methods are time-consuming to run. Also, the performance of some techniques is not good when the training dataset is small. These problems suggest using a technique that is suitable for ultrasound
images and not sensitive to noise.

Among classification methods that have been introduced, some methods appear to be unsuitable to perform on medical imaging applications. It seems that the ANN and SVM perform well in applications for medical imaging.
CHAPTER 4

The Methodology of the Proposed Technique

The revealing of structures is very important for diagnosing a huge number of diseases, including breast cancer in breast ultrasound images. With a lack of clarity in nature and few variations or saturation in noise, even most standard techniques of image processing do not give their best results in these images. The computer-aided diagnosis (CAD) systems are very sensitive to noises, and in ultrasound images, noise is inevitable. Also, some of the CAD methods produce different outputs from various types of ultrasound imaging systems. It is suggested to use a method for the referred problems that is able to provide a clear background and foreground separation of the ultrasound images. Figure 4.1. shows the methodology of the proposed technique.
1. **Image loading**: This algorithm will read the ultrasound input image file to be processed.

2. **Image denoising using wavelets**:

   In medical image processing, speckle noise reduction has become a very necessary and difficult task during the diagnosis. Noise in ultrasound imaging is an inherent property, and the poor quality of images is one of the main defects in ultrasound images, including all parameters that cause these noises (e.g., echoing, older machinery, external sound interferences, electrical interferences) [75]. Noise tends to reduce the diagnostic value of
this imaging method by reducing the image accuracy and contrast. Due to this, speckle denoising is an important precondition when using ultrasound imaging for tissue diagnosing [56]. In medical literature, speckle noise is referred to as “texture”, and may possible include useful and important diagnostic information. In general, physicians prefer the original noisy images over smoothed versions because the filters that smooth out these images may destroy some relevant image details. Subsequently, it is important to develop noise filters which can ensure the preservation of features that are important to the physician. In this work, a simple pre-processing procedure is introduced, where the images are modified based on the acquired radio frequency in a way to ensure to preserve important anatomical information in images while removing noise. In this way, the preprocessing based on a wavelet denoising method assumes the noise to be Gaussian or white and greatly improves the quality of resulting images [56].

Recently the wavelet transform has entered the area of image denoising (especially in medical imaging field), and its position is now strongly recognized as a dominant denoising tool for improving images from noisy data [60,76]. Several characteristics of the wavelet transform to make this method attractive for denoising include the following features:

- Multi-resolution: analyzing the images’ details of different sizes in appropriate resolution scales.
- Edge detection: where large wavelets coincide with image edges.
- Edge clustering: within each sub-band, the edge coefficients tend to form clusters connected spatially.
The wavelet transforms into a multi-resolution noise filter tool [60]. A speckled image is commonly modeled as: V1=f1*γ, where f={f1,f2,…fn} is a noise-free ideal image. V={v1,v2,v3,..vn} Speckle noise. And γ={γ1, γ2,.. γn} is a unit mean random field. Wavelet denoising general procedure is [77]:

- Perform a multilevel wavelet decomposition, where at each level the decomposition is characterized by a low pass filter and high pass filter. The low pass filter can create an approximation co-efficient, and the filtered part of the image with a high pass filter will contain values called details with only high intensity gradients. Approximation values are used to find the low frequency components, while details are used when it is necessary to look at the image details for speckle patterns or edges where values change rapidly.
- Remove noise from the coefficients.
- Reconstruct the denoised image or signal by applying the transformed inverse wavelet transform.

3. Image Enhancement Using Imadjust Function

Medical images that have been used for the analysis may have some weaknesses such as low or blurred contrast. Because of this, intensity image enhancement techniques needed to be used. In this work, the adjust image intensity values (imadjust) tool in Matlab was utilized. An imadjust function is the basic tool of gray-scale images intensity transformation.
Syntax:

\[ J = \text{imadjust} (I, \text{low-in high-in}, \text{low-out high-out}, \text{gamma}) \]

This function maps the intensity values of the image I to a new value in image J. The effects are that values between low-in and high-in map to values between low-out and high-out, while values below the low-in map to low-out and values above high-in map to high-out.

- If gamma < 1 the mapping is weighted toward higher (brighter) output values
- If gamma > 1 the mapping is weighted toward lower (darker) output values
- To avoid the argument gamma defaults to 1 and it will be a linear mapping

This work presents the usage of the syntax: \( J = \text{imadjust} (I) \), where imadjust function is just stretching the highest and lowest values of the image to obtain an intensity range of the image to fill the entire range (0-255) then visually observing that the darkest pixels turn to black, while the brightest pixels become white.

4. Segmentation of Breast Abnormalities Using K-means

Image segmentation, also called labelling, is the process of partitioning the individual elements of digital images into multiple groups (sets of pixels) so that all elements in a group have a common feature. The common features in medical images are usually elements that belong to the same tissue type [78]. Medical images often contain a lot of information, but not all structures are of interest. Segmentation allows for the removal
of unimportant information while keeping structures of interest. In this work, we employed the k-means clustering algorithm, a least-square supervised partitioning method that divides the input data into K classes based on inherent distances from each other. The algorithm consists of two steps: in the first step the mean of each cluster is calculated. The second step computes the distance of each point from each cluster and takes this point to the cluster which has the nearest centroid from that particular point [79].

To define the distance of the nearest centroid, there are different methods used for this purpose. Euclidean distance is one of the most used methods. The algorithm for K-means clustering is as follows [79]:

1) Input: K (number of clusters), data points \([x_1,x_2,\ldots,x_n]\)

2) Place centroid \([\mu_1, \mu_2,\ldots, \mu_k]\) in random locations

3) Repeat until convergence
   - For each point of an image, calculate the distance \(d\) between each point \(x\) and the center \(\mu\) by use the Euclidean distance as follows:
   \[
d = \sum_{j=1}^{K} \sum_{i=1}^{n} ||x_i - \mu_j||^2
   \]
   where \(d\) objective function, \(K\) number of clusters, \(n\) number of data points, \(x_i\) data point \(i\), and \(\mu_j\) centroid for cluster \(j\)

   Then assign the point \(x\) to the cluster which has the minimum distance to \(x\),

   \[argmin\ (d)\], \(argmin\) is an argument of the minimum value

4) After all points have been assigned, re-calculate the new centroid position for each cluster as follows:
New centroid $\mu = \text{mean of all points in the cluster,}$

$$\mu_j = \frac{\sum_{x_i \rightarrow \mu_j} x_i}{n}$$

Where: $\mu_j$ new centroid for cluster j, n number of data points in cluster j, $x_i$ data point in cluster j

5) Stop the process when none of the cluster assignments changes centroid.

6) Reform the cluster points into images

If we compare K-means with another clustering method, it has many advantages in terms of being fast and easy to implement [80]. K-means also has some drawbacks. For example, where the initial centroid is randomly chosen then different results will be received for different initial centers. To solve this problem, the initial centers would be chosen carefully [81]. Computational complexity also needs to be considered while designing the K-means clustering algorithm. Computational complexity occurs where K-means complexity depends on the number of iterations, the number of clusters, and the number of data points [81].

$O (\text{the number of iterations} \times \text{the number of clusters (K)} \times \text{the number of data points (X))}$, This show how much computation time needs to be used in order to calculate the distance between each point in the input data and all the clusters’ centroids.
5. Classification of the Tumor Using Support Vector Machine (SVM) Algorithm

Image classification is one of the conventional problems in image processing. An image classifier has to automatically categorize the features of input images into classes. The commonly used classifiers are K-nearest neighbor (KNN), Adaptive boost (Adaboost), Artificial Neural Network (NN), and Support Vector Machine (SVM) [70,71]. Support Vector Machine [74] is one of the supervised pattern classifiers which has been recognized as one of the best methods for classification. SVM yields good results based on strong mathematical foundations. The working of a standard SVM classifier is simple: the classifier chooses some features in the images, and it will search for the closest features (or support vectors), then the SVM constructs a hyperplane maximizing the margin in the given training data to separate these features into two different classes in the input space by doing vector subtraction [82]. Figure 4.2 shows a separating hyperplane and margins which are the distance between the support vectors and the class boundary hyperplanes. Each point in the training set has one class label and several features [83]. Then the classifier derives the best line that divides points and perpendicular to the connecting line. When we get a new point (testing data), the SVM will have already made a line that keeps points for each class far apart from each other. This makes it so that all images of each feature vector are located on one side of the hyperplane and belonging to class 1, whereas the others belong to class 0, so it's impossible that points get mismatched with the others or cross the boundary dividing the two.
Inside the code, we have two divisions called lesion and no lesion. The lesion class has one set of features (points with particular features) identified and stored from trained images. The other set is the no lesion class. The SVM classifier analyzes the input image, automatically assigning the areas of that image to the respective class to which it belongs. If an image contains a lesion area, it can distinguish the points within both the lesion area and non-lesion area. We have used a marking technique inside the code to mark the affected area with the tumor. So the code itself identifies the area of tumor and calls in the function to mark.

6. Tumor Size Determination Using Regionprops Function

Having the original image in a binary form such as this will make it easy for other functions built into Matlab to quickly analyze the region and a host of different information. The regionprops function is the tool that will provide the MajorAxisLength of the region...
under the observation/target area. The function ‘regionprops’ is used to measure the image properties.

\[ \text{STATS} = \text{regionprops}(L, \text{properties}), \]

returns measurements for the set of properties specified by properties for each connected component (object) in the binary image. It measures a set of properties for each labeled region in the label matrix L. Positive integer elements of L ('Centroid', 'Major Axis Length', 'Minor Axis Length') correspond to different regions.

center = stats.Centroid (rw,:);
diameter = mean([stats.MajorAxisLength(rw) stats.MinorAxisLength(rw)],2);
The diameter is now displayed in the Command Window to be approximately “xxx” pixels across.

Details of normal and cancerous tissues were analyzed and interpreted in the pictured Figures \(^3\). The SVM algorithm explained in detail in this chapter has been a successful tool to identify and early detect diseased tissues. Initially, we trained the SVM algorithm on diseased and healthy breast images stored as a training set. From the results, scanned images compared against both normal and cancerous images in the training set. The regionprops tool is used to find the tumor size only with images that classified as a cancerous image. With these image processing methods, we can provide the patient’s caregiver with identified diseased tissues using Telemedicine.

\[^3\] See appendix A for the proposed technique results.
CHAPTER 5

Telemedicine

5.1 What is Telemedicine?

Telemedicine (also known as "e-health") is a subset of telehealth. While telehealth is a broad term that covers all health services (public health, health care, and health education) provided using telecommunications technology, telemedicine is a bidirectional and real-time interactive communication [84]. Telemedicine allows for consultation between a patient and caregiver and vice versa in order to evaluate, diagnose, and treat patients at a distant location. Clinical experts can see patients in multiple sites wherever they are needed rapidly and efficiently without having to travel or leave their facility [85]. This can be done through the use of communication technology such as telephone lines, computers, cable, and internet equipment, along with medical devices to provide healthcare services. The most common intra-user devices regarding the use of telemedicine include desktop and laptop computers, faxes, mobile telephones, and video and still picture cameras [85].

Telemedicine offers solutions to reduce the cost of delivering remote care in both developed and developing countries where there is less need for buildings and staffing [85]. Telemedicine gives doctors, nurses, and local practitioners who have never met or worked together before the opportunity to consult with their peers and work as a team to provide the most efficient health care. According to AMD Global, telemedicine has become a
standard medical practice that sees daily use in several countries. In fact, more than 10,000 peer review papers have been published during the past 20 years to develop an effective and reasonable cost of telemedicine [86].

Many recent research studies conducted on the impact of telemedicine technology have made improvements to healthcare quality that have provided medical care in rural and remote places. Dharmar et al. [87], demonstrate a study that evaluates the financial impact of the spread of pediatric telemedicine program in outlying hospitals within a competitive healthcare service market from the viewpoint of tertiary children’s hospitals. The researchers compared the number of transfers, average hospital incomes, and professional billing income before and after the use of telemedicine. The results of using the telemedicine program reflected in an increase of the number of transfers and hospital income. This study also showed that using telemedicine can not only benefit hospitals in remote areas but also increase the hospital’s market share.

Rosenberg et al. [88], reported the experience of UPMC (University of Pittsburgh Medical Center) Health Plan headquartered in Pittsburgh and Pennsylvania. UPMC Health Plan is part of a wide, integrated delivery and financing system as it attempts to support primary care practices by converting standard health care for patient models into patient-centered medical homes. They suggested methods that could motivate this model, including offering customers adequate incentives along with interested providers. Here, telehealth is also used to connect care providers to patients when face-to-face visits are not possible or necessary.
5.1.1 Different Types of Telemedicine

The healthcare sector is always looking for the most efficient and effective ways in terms of cost for business dealing. Due to this idea, technology has allowed physicians to provide a variety of health care solutions for patients and hospitals in remote places. Today, there are three major kinds of telemedicine services that are being used worldwide today [84,85,89]. These kinds include:

- Store-and-Forward
- Self-Monitoring
- Interactive Services

- **Store-and-forward Telemedicine**

  This type of telemedicine is common in the medical fields of dermatology, pathology, and radiology. This technique facilitates access to medical data (e.g. medical imaging, test results, bio-signals) and patient records across large distances [90]. Using this technique, time can be saved, as well as allowing medical experts to more fully serve patients with their services. This kind of telemedicine is most advantageous where there is no need for the standard amount of attention from the delivering and receiving parties [91]. Unlike using traditional email, this technology goes further for patient privacy protection. However, since it depends on a report and documented information or images instead of a physical examination, complications such as misdiagnoses are more likely to occur. Figure 5.1. shows store-and-forward telemedicine technology [92].
Self-Monitoring

Self-monitoring, also known as remote monitoring or self-testing, is widely used in the management of chronic diseases such as diabetes mellitus, cardiovascular disease, and asthma by using a variety of technological devices [93, 94]. These devices are used to control health and clinical signs of a patient from a remote location. The benefits of self-monitoring include cost effectiveness and continuous monitoring, in addition to patient satisfaction [95]. However, this does not prevent certain risks, as the patient may provide inaccurate data from home. In general, however, the results are comparable to those obtained from a physical examination.
Interactive Services

This category of telemedicine, also called live telemedicine, allows for real time communication between providers and patients by using two-way communication channels like video consultations, phone conversations, and online chatting. Like store-and-forward technology, interactive services go further to protect patient privacy. While the other types of telemedicine generally supplement in-person care, live telemedicine serves as an alternative to in-person interactions [96].

All three categories of telemedicine mentioned here give providers better ways to provide efficient and effective care to patients more easily and less expensively than traditional methods of care.

5.2 Basic Technical Requirements for Telemedicine

5.2.1 Transmission channels

The information transmission and delivery play a major role in achieving accurate service [97]. The input and the transmission methods should be appropriate and accurate for a better output (result). Similarly, for the sake of taking full advantage of the opportunities of telemedicine technology, each of these techniques should be fully investigated. As mentioned earlier, telemedicine is a set of both telecommunication technologies and medicine. There are two ways to transmit data: dial-up services and fixed communication lines. Dial-up services (i.e. dial-on-demand) can use a standard telephone and cellular service, ISDNs (Integrated services digital network), and some satellite
services [98]. Fixed connections provide a permanent service between specific sites, such as DSLs (digital subscriber lines), leased lines, cable, microwave links and satellite. As each type of file requires a specific form of transmission, the provider has to choose the proper transmission channel to use based on the type of information to be shared: audio, text, video, or still images. For instance, text-based information may only need a standard telephone connection, while surgical training may require the transmission of video information over more complex technology [98].

Many factors should be taken into consideration when choosing the right transmission technologies, such as internet transmission speed, accessibility and useable flexibility requirements, reliability, and overall quality [98]. Below are different techniques applied in Telemedicine: ISDN (Integrated Service Digital Network), ATM (Asynchronous Transfer Mode), Ethernet Networks, DSL (Digital Subscriber Line), Frame Relay and Fibre Channel, Optical Network Solutions, Wireless Networks, Satellite Networks, and Next Generation Networks.

5.2.1.1 ISDN

An ISDN (Integrated Services Digital Network) is a collection of digital transmission protocols put in place by the international standards body for telecommunications. An ISDN provides all types of information such as voice, text, graphics, music, video and data by using a traditional telephone system [99]. It is widely used in linking videoconferencing systems to share video, voice, and text transmissions. Figure 5.2. shows an ISDN configuration [100]. There are several kinds of ISDN
subcategories such as Primary Rate ISDN (PRI) and Basic Rate ISDN (BRI) [100]. An ISDN can be used in many applications related to telemedicine consultations and tele-education [101].

![ISDN Configuration](image)

**Figure 5.2. ISDN Configuration [100]**

### 5.2.1.2 ATM (Asynchronous Transfer Mode)

An ATM is a network transmission protocol based on encoding data into small cells or packets of a constant size (53 bytes per cell) [102]. The small, fixed cell size in ATM equipment allows for the transmission of video, audio, and computer data over the network itself. ATM is a multiplexing technology used in backbone networks where it works in higher bandwidth with a considerably low delay [100,103]; “ATM networks in telemedicine support a broad range of configurations for interlinking such sites as hospitals, healthcare clinics, medical offices, and nursing homes, these networks also enable healthcare services in a patient's home in the event of budget cuts and hospital closures as
well as provision access to diverse treatment options for patients at distant locations.” [100].

5.2.1.3 Ethernet Networks

Ethernet technology is a computer networking technology widely used due to its low cost, high speed, and ease of installation. It is an IEEE 802.3 standard that was developed by Robert Metcalfe, an engineer at Xerox, between 1973 and 1975. Figure 5.3 shows an Ethernet LAN configuration [100]. Ethernet networks are local area networks (LANs) [100]. Wireless LANs use different types of topology (bus and/or bus-star topologies) to connect various nodes in a network. In the Open Systems Interconnection (OSI) model, the Ethernet belongs to the physical and data link layers. At St. John’s Hospital, associated with the Southern Illinois University School of Medicine, Ethernet application in Telemedicine includes the Fiber Distributed Data Interface (FDDI) backbone that interferes with the Ethernet to provide an IP Multicast to access patient records [100,104].

![Figure 5.3. An Ethernet LAN configuration][100]
5.2.1.4 Digital Subscriber Line (DSL)

DSL is a technology used for providing cheap service and a communication channel with high-bandwidth [105]. DSL technologies support links to a wide range of web sites, internet services, applications such as e-mail exchange, internet telephony, and television programming. In addition, “DSL is an enabler of tele-education, teleshopping, E-banking, tele-training, VPNs (Virtual Private Networks), video gaming, teleworking, telementoring, tele-entertainment, and telemedicine” [100].

5.2.1.5 Frame Relay and Fiber Channel Technologies

Frame Relay is a data link (Layer 2) that operates at both the physical (Layer 1) and data links (Layer 2) of the OSI networking model [106]. Frame Relay is a packet-switching protocol designed to connect local area networks (LANs) across wide area networks (WANs). Frame Relay was initially designed to operate across an Integrated Services Digital Network (ISDN) where it serves as a networking solution providing the possibility of communication between several locations that support a variety of applications [107]. One of the live applications of Frame Relay is the “Veterans Health Administration (VHA), an agency of the U.S. Department of Veteran Affairs, supports utilization of a Frame Relay network that operates over fiber optic cabling, linking more than 600 VA facilities nationwide. The Frame Relay configuration enables these VA facilities to exchange data with medical centers, regional offices, and the VA Central Office.” [100].
5.2.1.6 Optical Network Solutions

Fiber Optic Networking is a means of providing and carrying data, video, and audio information in the form of light pulses by transmitting light through thin glass or plastic optical fiber [107]. Fiber optics are used primarily for long-distance transfers. LAN uses fiber in its backbone, extending it for long distances [107]. One of the applications of optical networks is “the High-Speed Connectivity Consortium (HSCC) that supports implementation of a nationwide multigigabit WDM network testbed that supports voice, video, and data transmission at 2.488 Gbps (OC-48). All-optical network offers advanced services with QoS assurances and supports applications that include data mining, electronic commerce (E-commerce), telemedicine, distance learning, video telephony, and collaborative teleworking. The University of Washington, Carnegie Mellon University (CMU), Qwest Communications, and Ciena Corporation participate in the HSCC testbed project.” [100].

5.2.1.7 Wireless Networks

A wireless network is an alternative to traditional networks. Wireless networks rely on radio waves instead of cables to connect devices, such as laptops, to the internet and to business networks like LAN, WAN, MAN and others [100]. Information transmitted by wireless networks can be reliably and efficiently sent abroad via cellular telephones, the internet, etc. In telemedicine, a live application of this technique can be observed when “Physicians at Good Samaritan Hospital/ Ohio, employ a broadband FWA Ethernet LAN
for accessing records of patients in cardiac and surgical units, intensive care recovery rooms, a birthing center, and hospital clinics. In addition, physicians also monitor patient medications, access intake orders, and review treatment protocols in real-time at the patient's bedside via the WLAN solution.” [100].

5.2.1.8 Satellite Networks

Satellite networks are a part of a satellite system that consists of one satellite in cooperation with multiple stations on Earth. Satellite systems use super-high radio waves and very high radio frequency bands in the electromagnetic spectrum in order to enable reliable transport of information (voice, video, data, and still images). Satellite networks are characterized by their ability to provide mobile communication services at any time and in any place, which is especially useful for rural areas. A live application of satellite networks is one of its applications is in “Telemedicine in which Sponsored by the U.S. Department of Defense, the Telemedicine and Advanced Technology Research Center (TATRC) provisions access to programs in telehealthcare, telemedicine, and medical informatics. TATRC also employs satellite services to support delivery of telemedicine treatment to U.S. military forces in Iraq, Somalia, Rwanda, Croatia, Macedonia, Haiti, Panama, Cuba, Egypt, Russia, Sweden, Kenya, and the United Kingdom.” [100].

5.2.1.9 Next Generation Networks (NGN)

Next Generation Networks (NGN) is a packet-based network that refers to the new telecommunication technology [108]. NGN supports the Next Generation Internet (NGI)
through connecting educational institutions, hospitals, and research centers all around the United States at high speeds. This encouraged the University of Iowa National Laboratory for the Study of Rural Telemedicine to use NGI to hold videoconferencing teleconsultations over the NGI between healthcare providers and patients with special needs, including persons with mental illness and children with disabilities or heart conditions [100].
5.3 Proposed Telemedicine System

The flow chart in Figure 5.4. gives an overview of our proposed telemedicine system.

Figure 5.4. Flow Chart Describing the Procedure of Breast Cancer Diagnosis, Follow-up, and Blockchain Access.
5.3.1 Telemedicine Cart

5.3.1.1 Patient Assessment Terminal (PAT)

PAT is a wall-mounted system from AMD global telemedicine that is designed for telemedicine consultations [109]. Figure 5.5. shows PAT cart [109]. This device is characterized as being unique from other healthcare wall cabinets or computer stations and is considered to be the first continually connected telemedicine wall station. Medical devices that remain connected significantly reduce the amount of effort required for setup. This benefit makes this new technology accepted among staff, in addition to providing convenience to patients who use this technology in their homes. This product has many features such as [109]:

- Two separate screens and workstations to improve the patient assessment experience. One of those screens is used to facilitate patient assessment and video consultation between patient and care provider, and the second screen serves as a documentation workspace for the clinician.
- PAT has an additional cabinet where medical equipment and telemedicine devices are conveniently located and remain connected, can be easily accessed for patient exams, and can be stored securely when not in use. This lower storage space folds down to supply connected medical equipment during exams.
- Includes an integrated PC, screen(s), keyboard, mouse, video camera system, conference speaker and microphone.
- Video conference systems can be easily integrated.
• It is Food and Drug Administration (FDA)-approved and compliant with Medical Device Data Systems (MDDS).
• The most important feature of this product is its use of AGNES Interactive. This makes it easy to capture, share, and exchange documents, medical images and data while also allowing users to participate in live video conferences and consultations over long distances.

![Patient Assessment Terminal (PAT) Image](image)

Figure 5.5. Patient Assessment Terminal (PAT) [109]

5.3.2 Telemedicine Software

5.3.2.1 AGNES Interactive

AGNES Interactive is an online telemedicine programming that enables clinicians and restorative care providers to record and share exchange reports, remedial device data, and helpful pictures instantaneously, while also participating in a live video meeting - all in a single electronic stage. Figure 5.6. shows Agnes interactive software [110]. The fundamental reason for any training in the use of telemedicine is to ensure the correct
transport of patient information that begins in one location then moves onto the following one. This is set up and operational within minutes - no back-end servers are required [110]. Once installed, the program collects the key signs data, clinical contraption diagnostics, encounter documents, and live video conferencing. After that, it securely streams that information to a remote guiding specialist [110]. Expert opinions about this are linked to the 100% live access transmission of helpful data, mobility, and quality of the medical data, as well as the ability to provide an interface for a USB-enabled stethoscope [111]. This allows for unbroken video conferencing, secure information transfer, and control structures.

Figure 5.6. Agnes Interactive Software [110]
5.3.3 Breast USB Ultrasound Probe

In this procedure, a small, portable tool called a transducer is passed back and forth over the breast. The picture produced by the ultrasound is called a sonogram or ultrasound scan. In general, with new ultrasound technology, the range of frequencies that are used for breast examination are between 12 to 15 MHz. For larger or more dense breasts, frequencies can be reduced down to 8 MHz [112]. The transducer emits inaudible and high-frequency sound waves continuously into the body. These sound waves pass through the breast tissues, and then the device listens for the varied frequencies of reflected sound waves from the tissues. The frequencies of these echoes are determined by the reflectivity of the tissues through which the sound waves pass. For breast exams, the transducer is pressed against the breast, emitting frequencies between 8-15 MHz. This provides good penetration from nearly 7-10 cm from the surface of the skin, and an excellent spatial analysis. The screen then displays real-time images of the targeted tissue [112]. Figure 5.7. shows the the portable ultrasound equipment that was used in this work. Such equipment does not require a traditional ultrasound machine [113]. The USB ultrasound probe provides high-quality ultrasound images for telemedicine applications. All that is necessary for using this USB ultrasound probe is a laptop, tablet, desktop computer, or telemedicine cart with a USB port. With this technology, we will be able to save, send and print images taken with the probe.
5.3.4 Blockchain Technology and Smart Contract for EHR

Recent research has focused on adopting major changes to the electronic health record (EHR). These changes would offer patients an opportunity to be engaged in the details of their healthcare and restore agency over their data. Specifically, a health record must meet today’s requirements, which can be achieved through adding some extra features to the current patient recording system [114]. Managing multi-institutional and lifetime medical records are deemed as the features most necessary to attach to the patient’s record. By doing this, the patient would have easy access to the past data in her record: patients don’t need to leave data scattered across various organizations, as life events take them from one provider to another [114,115].

In addition, a patient’s record would be up-to-date in terms of updating or removing rather than waiting for a certain period of time to get the record updated by the providers. This would encourage patients to update and review their full record [116]. An extra feature that has to be considered in the patient’s record relates to the security and reliability of the
patient’s data. Therefore, any technology that is adopted should manage authentication, confidentiality and data sharing—crucial considerations while handling sensitive data. However, sharing the patient’s data across different provider and hospital systems requires defining interoperability techniques that would coordinate data management and exchange.

Based on the previous information, a new system is proposed in this thesis that considers all the aforementioned features in the health record. More specifically, a new Healthcare recording system is explored that can handle a decentralized record management by use of technology that maintains a continuously-growing list of records called blockchain [117]. Blockchain technology is deemed as the most important invention in the field of cryptography and security of decentralized networks, all of which was originally associated with Bitcoin [118]. The blockchain is simply the ledger of all records, grouped into blocks (as shown in Figure 5.8). Every block is linked with previous blocks by including the unique hash of the previous block in each respective header. The first block in the block chain is known as the genesis block, and it has no references to previous blocks. A branch is a path in the blockchain which starts from a leaf block to the genesis block. Copies of Blockchain must be shared across all nodes in the network. Block chain is publicly visible and allows nodes within the network to agree to be confidential about the transfer of records between users (providers). Each block requires a degree of computational effort before it will be accepted by other nodes as valid. A group of nodes known as miners provide this effort when they solve the computational problem. For doing this, they are rewarded with an access to aggregate, anonymized data, Figure 5.9. shows the blockchain along with the miners. The solution to the problem is easy to verify but
difficult to calculate and as such the solution can be considered a proof of work (POW). Blocks are chained together, and thus, modifying a block becomes exponentially harder with the passage of time, as all subsequent blocks must also be modified.

Figure 5.8. The Blockchain Configuration
In the proposed system, both the providers and patient have access to the blockchain that stores the patient’s record. Each care provider is responsible for adding his or her patient’s record to the blockchain. The entire record will be shared across all providers (providers) without any access restrictions. However, every patient is only allowed to access her own record which has been added by her personal healthcare provider. While integrating the blockchain technology with an EHR infrastructure, the user should be aware of different risks regarding the data integrity and security, as well as patient controlled data. Therefore, in the proposed solution, attaching a very intelligent concept called a smart contract into blockchain is considered. The smart contract concept is a collection of code that governs important or valuable data in the blockchain [117,119,120].
As the patient’s record is considered important information that needs to be reliable, a smart contract will be used to regulate the patient’s access to his or her record. In other words, the smart contract will allow a patient to have conditional access to his or her record. This would help providers to assure the validity and security of the patient’s data as well as prevent any update to the patient’s record without the provider’s permission.

Furthermore, a smart contract handles functionality to enable a relationship contract between the patient and provider. This relationship contract is issued between two nodes in the system when one node stores and manages medical records for the other. It also helps to identify the records held by the provider through defining pointers and associated access permissions. Each pointer consists of a query string that, when executed on the provider's database, returns a subset of patient data [117]. Figure 5.10. shows blockchain and a smart contract.
Figure 5.10. Blockchain and Smart Contract Configuration

Over the past decade, telemedicine technology has changed and improved quickly and significantly with the explosive growth of the Internet technology and the availability of low-cost personal computers. In our network design, many sites exist, such as those shown in Figure 5.10., provider1, provider2, provider3, patient, and caregiver Telemedicine center who could be one of the providers. Services between these sites will include consultation, diagnostics, and the transfer of patient related records by using teleradiology. Teleradiology refers to the ability to obtain medical images of the internal body generated
by one of the medical imaging techniques (e.g., X-rays, MRIs, ultrasounds) in one location and their transmission over a distance to aid in the process of diagnosis or treatment by a radiologist or physician [121]. The main benefit of applying the blockchain along with the smart contract technologies to teleradiology is a truly accurate representation of the problem, by providing an integrity check on the images of the patient. Previously, radiologists and physicians had to trust that images were accurate and unchanged, but they had no evidence. Today, they have immutable proof that the images they are reading are precise and unaltered while ensuring privacy and security [121]. The algorithm will be installed in PCs in order to enable and facilitate the procedure of the transmission, sharing and manipulating breast radiological images through the svm classification method and regionprops tool to find the tumor size. The equipment at the end users consist of PCs connected to a broadband network. The remote doctor equipment consists of PCs, which are connected through a reliable, on-demand and high-speed network to efficiently handle large files, ensuring an accurate diagnosis. The software tool will be configured and installed on the PCs for the image monitoring and diagnosis. The high-speed network suitable for the ultimate telemedicine technology will be achieved through satellite and terrestrial links, ISDNs, ATM and LANs. In this thesis, the telemedicine implementation through teleradiology between the sites is accomplished in a case study: It suggests a network design that will serve small breast clinics in rural areas. This network will serve female patients in most areas of the United States through high-speed Internet, using both real-time (synchronous) and store-and-forward (asynchronous) techniques for further diagnosis.
Chapter 6
Conclusion & Future Work Recommendations

6.1 Conclusion and Summary

Breast cancer disease continues to be a worldwide concern and the most common cause of death among women. In general, the cause of breast cancer remains unknown. Early detection and diagnosis of the disease remains the only factor which contributes to the successful preservation of lives in both developed and developing countries. With the digital imaging world, this thesis suggests the ultrasound imaging method in which breast images are recorded on a high-resolution ultrasound transducer, thus converting those images into digital copies. Ultrasound imaging plays an important role in detecting breast cancer, since it is capable of detecting lumps which can be obscured by dense tissue in a mammogram. By using the computer-aided diagnosis (CAD), experts can further manipulate and process the obtained breast images. In this thesis, image classification is implemented by using the SVM method and calculating the tumor size with the regionprops tool in Matlab. The goal of this method is to eventually help different processed and scanned breast images which are derived from processing and segmenting each image to detect cancerous tumors. After that, remote health care is established to monitor women in remote areas who receive neoadjuvant cancerous treatment by using the modern telecommunication infrastructure and blockchain technology. This will reduce the need of travelling for patients and a high pay rate of experts on remote sites. The ultrasound images will be transmitted back and forth between the telemedicine center and hospitals. The
nature of this work includes sharing patient consultation and records, breast image manipulation, etc. through real-time and store-and-forward communications techniques. The proposed tool has been run successfully and meets the medical imaging and breast imaging requirements, particularly through including the study of infected areas of breast tissues in the image. Also, this thesis includes a result that shows diseased and healthy tissues.

6.2 Future Work Recommendations

Future work would include a large dataset of ultrasound images. An automated method to identify types of tumors Luminal A, Luminal B (HER2 negative), Her2 Positive, and Basal-like (usually triple-negative) in breast ultrasound images will also be developed. As the blockchain contains a history of all transactions, it grows in size with each new transaction and scalability of block chain matters. Presently, all nodes are required to maintain a full copy of the ledger which places an upper limit on the number of transactions that may exist. Overcoming the scalability issue is also a part of the future work.
APPENDIX A: THE PROPOSED TECHNIQUE RESULTS

The training set consists of some instances of different categories. The class labels are designated as 0 and 1 to represent breast abnormalities as malignant and normal respectively. A total number of 8 images were used; three images were malignant, and five images were normal. Figure 1 shows samples collected in the ultrasound breast image dataset. The test images of the breast used in this research with malignant tumors shown in Figure 1 (a) come from a medical image database [122], and images of a breast with normal tissues as shown in Figure 1b come from [123]. The proposed work was implemented and tested by using Matlab 2016 environment. In this work, we have successfully used the SVM method to find the solution for the detection of breast cancer cells and classification of cancerous or normal tissues by using ultrasound images. After applying the filtering, enhancing, and segmentation methods on the isolated (crop) image that are prone to the abnormalities as shown in Figure 2 (a-c) and Figure 3 (a). The SVM algorithm will conclude to decide the breast tissues as diseased or healthy [shown in Figure 2 (d) and Figure 3 (b)] by comparing the current image classification with a stored image (training set). The essential part and purpose of this work study was to find the cancerous tumor size from the diseased image in order to make it easier for the physician to find the difference in tumor size during the follow-up procedure with the patient. Figures 2 (d) and 3 (b) show that we have used the regionprops tool in Matlab to calculate the tumor size.
Figure 1 Sample Collected Ultrasound Image Dataset (a) Images with cancerous tumor [122] (b) Images with normal tissue [123]
(a) Original image

(b) Filtered and enhanced image
(c) Segmented and classified image

(d) Status and tumor size

Figure 2 Cancer Detected Images
(a) Input normal image

(b) Filtered and enhanced image

(c) Segmented and classified image
(d) Status

Figure 3 Non Cancer Detected images
clear all;clc;%---Clear workspace and command window

%---Read image form the specified path and assign it to In

%In = uigetfile({'*.jpg;*.tif;*.png;*.gif','All Image Files';'*.*','All Files' },'Select Image File');

load categoryClassifier.mat

[FilePath PathStr FileName Ext Index] = GetFilePath();

path = strcat(PathStr,'\Processed Image');%---Path for processed image folder

path2 = strcat(PathStr,'\Enhanced Image');%---Path for processed image folder

path3 = strcat(PathStr,'\Segmented Image');%---Path for processed image folder

rmdir(path, 's');

rmdir(path2,'s');

rmdir(path3,'s');

mkdir(path);%---Creating Folder

mkdir(path2);%---Creating Folder

mkdir(path3);%---Creating Folder

In = imread(FilePath);%---Read image and assign it to In

In=imcrop(In);

I_Pre = Preprocess(In);%---Preprocessing Original Image
Ig = I_Pre.Ig; %---Assigning Image of double class to Ig

%figure(1);subplot(1,2,1);imshow(In); %---Show Original Image on first Figure window
%---Check for RGB or Gray Scale Image
if I_Pre.o==1
    title('Original Grayscale Image'); %---Title for Original Grayscale Image
else
    title('Original RGB Image'); %---Title for Original RGB Image
end

%figure(1);subplot(1,2,2);imshow(Ig); %---Show grayscale Image on first Figure window
%---Title for Grayscale double class image of an Original Image
%title('Grayscale double class image of an Original Image');

Fields = {'Filter','Level','Band','MSE','PSNR','SNR'};
%---Excel file in which performance metrics has to be written
xlswrite('Performance Metrics.xls', Fields, 5, 'A1'); %---Writing on 5th sheet
for i = 1:4;
    level = 2;
    if i == 1
        bn = 'HL';
        I_anyl = NSRFilters(In,'wlet',bn,'db1',level);
elseif i == 2
    bn = 'LH';
    I_anyl = NSRFilters(In,'wlet',bn,'db1',level);
elseif i == 3
    bn = 'HH';
    I_anyl = NSRFilters(In,'wlet',bn,'db1',level);
else
    bn = 'LH-HH';
    I_anyl = NSRFilters(In,'wlet',bn,'db1',level);
end

% figure(6);subplot(2,2,i);imshow(I_anyl);%---Show Filtered Image on sixth Figure window

FIName = strcat(path,'\',FileName,' - ','Wavelet Filter',...
                ' [Level = ',num2str(level),', Band Eliminated = ',bn,']',Ext);
imwrite(I_anyl,FIName);%---Write image file

I_anyl_histeq = imadjust(I_anyl);

FIName = strcat(path2,'\',FileName,' - ','Enhanced',...
                ' [Level = ',num2str(level),', Band Eliminated = ',bn,']',Ext);
imwrite(I_anyl_histeq,FIName);%---Write image file
\( [z1,z2]=\text{segmentation}(I_{\text{anyl histeq}}); \)

\( \text{FIName} = \text{strcat}(\text{path3},'\backslash',\text{FileName},' - ','\text{Segmented\_lesion}',... \)
\[ \text{[Level = ',num2str(level),', Band Eliminated = ',bn,','],Ext}; \]

\( \text{imwrite}(z2,\text{FIName}); \% \text{---Write image file} \)

\[ \text{FIName} = \text{strcat}(\text{path3},'\backslash',\text{FileName},' - ','\text{Segmented\_nolesion}',... \)
\[ \text{[Level = ',num2str(level),', Band Eliminated = ',bn,','],Ext}; \]

\( \text{imwrite}(z1,\text{FIName}); \% \text{---Write image file} \)

\% title(['Filtered Image using Wavelet Filter; Band Eliminated = ',bn]);

\( \text{QM(i)} = \text{MetricsMeasurement}(Ig,I_{\text{anyl}}); \% \text{---Calculating Performance Metrics} \)

\( w2f\text{mse}(i) = \text{QM}(i).M\_SE;w2f\text{psnr}(i) = \text{QM}(i).\text{PSNR}; \text{w2fsnr}(i) = \text{QM}(i).\text{SNR}; \)

\( \text{QMxls} = \{ \text{Wavelet Filter',level,bn,QM(i).M\_SE,QM(i).PSNR,QM(i).SNR}\}; \)

\( \text{index\_num} = i+1; \)

\( \text{index} = \text{num2str(index\_num)}; \)

\( \text{cell} = \text{strcat}(\text{A'},\text{index}); \)

\( \text{xlswrtie('Performance Metrics.xls', QMxls, 5, cell); \% \text{---Writing on 5th sheet} \)

end

\( \text{FIName} = \text{strcat}(\text{path3},'\backslash',\text{FileName},' - ','\text{Segmented\_lesion}',... \)
img = imread(FIName);
[labelIdx, scores] = predict(categoryClassifier, img);
status = categoryClassifier.Labels(labelIdx)
tr=strcmp(status,'lesion');
if (tr==1)

imgbw=im2bw(img,0.1);
%s = regionprops(imgbw,'centroid');
%centroids = cat(1, s.Centroid);
stats = regionprops('table',imgbw,'Centroid',...'
'MajorAxisLength','MinorAxisLength');

[MajAx, rw]=max(stats.MajorAxisLength);
center = stats.Centroid(rw,:);
diameter = mean([stats.MajorAxisLength(rw) stats.MinorAxisLength(rw)],2);
radius = diameter/2
text_str=num2str(radius);
position = [30 50];
RGB = insertText(img,position,text_str,'AnchorPoint','LeftBottom');
figure(2);

imshow(RGB)

hold on

viscircles(center,radius);

hold off

end;

%c = [1 2 3 4];

%axis square;

%figure(12);subplot(2,2,1);

%semilogy(c,w2fmse,'-ro',c,w2fpsnr,'-ms',c,w2fsnr,'-bd');

%legend('MSE','PSNR','SNR',0);

%xlabel('Cutoff Frequency');

%ylabel('Performance Metrics');

%title('Variation in performance metrics with band elimination for Wavelet Filter for second level decomposition');
APPENDIX C

Existing Telemedicine Solutions for cancer patient

Cancer patients face many issues which are usually associated with severe symptoms such as prolonged weakness, complex emotional, and psychosocial problems for which they need support. Many Internet-based support systems have been developed for cancer patients that focus on the patient through individualized information and professional online support.

WebChoice is the Interactive Health Communication Application (IHCA) and Internet-based application that is designed to support and comfort for patients with prostate and breast cancer between treatments or during rehabilitation at home [124]. This can be done by allowing them to observe their symptoms and problems. Through this application, the patient can email thoughts and questions to experts and nurses specialized in cancer treatment, and can also communicate with other patients in Eforums [124,125].

The WebChoice system received positive and negative reactions from patients. Their satisfaction was based on how frequently WebChoice system was used. In general, high-frequency users are those that gave WebChoice a pivotal role in their private life [126]. On other hand, the patients who did not use the WebChoice system frequently considered it to be complementary to their regular health services, holding an opinion that human contact remains a necessary part of health care [126].

In Telemedicine in Cancer Management article about several telemedicine projects and their outcome, Susan Royer writes that in Indiana, The United States, telehealth is used to help cancer patients in the region of pain and depression. In July 2010, research was
done to evaluate the outcome. The results were positive in terms of reducing problems related to pain and depression. The research also summarized that telehealth could be used in other cases like cancer [127]. In the United States, there are a couple of other systems for telemedicine, where the consideration has been on quality, prosperity, and just circumstances for patients living in less affluent zones.

Females with ovarian tumors and/or breast cancer in Australia were receiving telephone counselling by the clinician. The result was a reduction in travel and cost for the patients, which was exceptionally celebrated by the individuals. Despite the nonphysical contact in the telemedicine meetings, the patients felt a social closeness [127]. From this review of different telemedicine systems, it was decided that telemedicine was beneficial for patients. It can improve clinical results, in addition to patient satisfaction. It can be profitable to an extensive variety of patients, not only those living in rural zones. It was also found that the most effective method of administering telemedicine depends on the sort of sickness the patient has [127].
REFERENCES


[125] Andersen, T., & Ruland, C. M. (2009, June). Cancer patients' questions and concerns expressed in an online nurse-delivered mail service: preliminary results. In Nursing
Informatics (pp. 149-153).
