Chapter I

INTRODUCTION

1.1. Objectives and Scope

Breast cancer is the cancer with the highest prevalence, and ranks second in all cause cancer mortality in women. It is also the major cause of death in women between the ages of 40 to 59 [104]. Breast cancer is the most diagnosed cancer. In India breast cancer is the leading cause of cancer related morbidity in women, breast cancer’s relative risk in India is about 0.33 [136].

A review of the declining breast cancer rates in developed countries shows that most of the reductions in breast cancer mortality in the last several decades, are attributable to early detection and improved adjuvant treatment with hormonal and chemotherapy after initial surgery. Therefore the first priority in reducing breast cancer mortality in low and middle income countries is to ensure that most women can be diagnosed early and that an effective adjuvant treatment is available. Extensive research has been focused on early detection of breast cancer, and available evidence has shown that if diagnosed early, the survival rate increases to about 98%, from 23%[84].

Currently, the common radiological imaging modalities used to detect breast cancer is X-ray mammography, Ultrasound (US), and Magnetic Resonance Imaging (MRI). Multimodal imaging techniques provides more accurate analysis. However, no imaging method is specific enough to provide complete definitive diagnosis. Sonography has been a popular imaging technique because it provides real-time information, noninvasive, relatively inexpensive, and safe. Ultrasound Elastography (UE) is believed to produce the best results in detecting cancer and reducing unnecessary biopsy.
Segmentation of breast images is essential for diagnosis of the stage of breast cancer. If segmentation is manually done, the process becomes repetitive, monotonous, markedly cumbersome and arduous. Manual delineation is too time consuming and idiosyncratic.

Delineation of tissue formation contours and discernment of contour variations by the radiologist is prone to error and may give rise to potentially avoidable delineation faults. Efforts have been made to find efficient methods for unsupervised/automatic breast image segmentation. This is envisaged to solve the problem of unnecessary biopsy, and the need for second readers in support of radiologists - resulting in reduced cost and recalls.

The main objective of this research is to develop an automatic segmentation method for UE breast images to maximize identification of cancerous abnormalities. In this context the research aims to automatically delineate and detect tumor contours in UE breast images using statistical texture and edge based analysis, and wavelet based image segmentation. Automatic delineation is achieved through feature extraction, selection and segmentation processes. This research proposes the use of Discrete Wavelet Transform (DWT) for multiscale image analysis, statistical texture and edge analysis and K-means algorithm for image segmentation.

The developed approach has been tested with real case studies using 100 UE images of both benign and malignant tumors.

1.2. Anatomy and Cancer

Cancer is a category of diseases that results in uncontrolled cell division and in the end forms a tumor (lump or mass). This section explains the breast anatomy and the occurrence of cancer.
1.2.1. Breast Anatomy

The breasts have a pointed shape and are found, side by side, inside the subcutaneous layer of the upper chest region, anteriorly to the “pectoralis major” muscle. The base is rounded and is 10-12cm in diameter, with a variable volume. Non-lactating breast weighs about 150 to 225g, while a lactating breast weighs up to 500g. Mature breast are made up of glandular tissue (20%), fat (80%) and connective tissue. The outside of breast tissue is primarily fat, with glandular tissues making up the central area.

The anatomy of the female breast is given in Figure 1.1. Each breast is made up of about 15 to 25 lobes sections; this is shaped by groups of lobules, and the milk producing glands. Individual lobule is made of grapelike bunch of acini (also known as alveoli), the empty sacs that produce and contain breast milk. A thin tube called ducts which bear milk to the nipples connects the lobes and the lobules. The pigmented region adjacent the nipple is known as areola. Connection and fatty tissues fills the remaining space between the lobes and ducts [47].

![Figure 1.1. Anatomy of the female breast](image)

The lymphatic supply of the breast is multifarious. Almost 75% of the lymphatic drainage gets to territorial nodes in the axilla. The axilla comprises of a variable number of nodes, usually between 30 and 60. Other metastatic routes include lymphatic adjacent to the internal mammary vessels. After direct spread into the mediastinum, lymphatic drainage may
go to the intercostal glands, which are located posteriorly along the vertebral column, and to sub-pectoral and sub diaphragmatic areas. Lymph drainage usually flows toward the most adjacent group of nodes. This idea represents the foundation for sentinel node mapping in breast cancer. In most cases breast cancer spreads in a systematic manner within the axillary lymph node basin based on the anatomic relationship between the primary tumor and its associated regional (sentinel) nodes [83]. Nonetheless, lymphatic metastases from one specific area of the breast may be found in any or all of the groups of regional nodes. The use of sentinel node biopsy has been confirmed in women with breast cancer. All of the women studied had positive nodes. However, in only 3% of these women, the only positive nodes occur outside of the axilla. Metastases from one breast across the midline to the other breast or chest wall occur occasionally [81].

Breast tissue is sensitive to the cyclic changes in hormonal levels. The epithelium of the breast responds to fluctuating levels of estrogen and progesterone similar to other hormonally sensitive tissue. The stromal of the breasts and the myoepithelial cells of the breasts also respond to estrogen and progesterone. Women often experience breast tenderness and fullness during the luteal phase of the cycle. The average increase in volume of the premenstrual breasts is 25 to 30mL, as measured by water displacement techniques [49]. Premenstrual breast symptoms are produced by an increase in blood flow, vascular engorgement, and water retention. There is a corresponding enlargement in the lumina of ducts and an increase in ductal and acinar cellular secretory activity. During the follicular phase, there is parenchymal proliferation of the ducts. During the luteal phase, there is dilation of the ductal system and differentiation of the alveolar cells into secretory cells. The alveolar elements respond to both estrogen and progesterone. When menstruation begins, there is a regression of cellular activity in the alveoli and the ducts become smaller. Over
time, the fibrous tissue surrounding the lobules increases in density and amount and in the postmenopausal woman, the breast lobules and ducts atrophy [100].

Accessory breasts or nipples can occur along the breast or milk lines, which run from the axilla to the groin. Supernumerary nipples (polythelia) or breasts (polymastia) are common anomalies, which may be well developed and functional or rudimentary. They occur in approximately 1% to 2% of women of European descent and 5% to 6% of Asian women [59].

Underdevelopment of one breast in relationship to the other is a common anomaly. It has been noticed that of 8408 mammograms recorded, 3% were notable for asymmetrical volume reduction relative to the contralateral breast [33]. This asymmetry represented a benign, normal variation unless an associated palpable abnormality was present.

1.2.2. Breast Cancer

Breast cancer sets out in the breast tissues, made up of milk producing glands, known as lobules, together with connecting ducts from the lobules to the nipples. The rest of the breast comprises of connective, lymphatic and fatty tissue. Based on the origin, breast cancer can be classified into two (a) ductal and (b) lobular. Ductal carcinoma accounts for about 80-90% and lobular carcinoma make up 10-20% cases of breast cancers [134]. According to the World Health Organization (WHO), cancer is the leading cause of death worldwide and continues to increase due to aging world population as well as environmental changes and lifestyle consequences from smoking and alcohol use. About 1.4 million new cancer cases and 360,000 cancer mortality were recorded in 2008 [21]. Currently, women world over are struggling with the challenges of living with breast cancer. The odds ratio of developing breast cancer in a lifetime is about 0.17 (1 in 6). Almost every woman stands the chances of developing breast cancer. There are several known risk factors associated with breast cancer.
that affects the general population. Yet, majority of breast cancer cases occur in women with no known risk factors aside gender and age. High prevalence and mortality of breast cancer in women has been an issue of concern and has been a subject of enormous research. Breast cancer incidence is about 100 percent more in women than in men [57].

Breast cancer risk factors include diet, physical activity, body mass index, prenatal conditions, and exposure to estrogen. A family history of cancer is the chief risk factor. High fat diet and red meat are risk factors for breast cancer. High intake of alcohol and caffeine are also considered as high risk factors, while phytoestrogens and high intake of calcium (vitamin D) are believed to offer protective effects. Hormonal situations are considered as a vital risk factor. Extended exposure to high concentration of estrogen regulated by the onset of menstruation, pregnancy, and menopause raises the risk of breast cancer. The level of testosterone is also associated with increase in rate of breast cancer in some research, although consistency is lacking in these studies [101].

Early menstruation and first time full-term pregnancy are positively associated with increased risk of breast cancer. Oral contraceptives data showing association with breast cancer risk are somewhat controversial. Some studies [88] reported an increased risk of breast cancer among oral contraceptive users, but other researchers, reported no significant association in oral contraceptive users. The two new research reviews gave no data to support that oral contraceptives can be attributed to increase in breast cancer.

Conventional wisdom sees breast cancer as a disease of the developed world, but 69% of all breast cancer related mortality occurs in the developing countries, moreover, survival rate in these countries are relatively poor. The lifetime risk of developing breast cancer for women in developing countries is 0.048 and 0.018 in developed countries. Figure 1.2 shows that Breast cancer is the leading cause of cancer related morbidity among women in India, with a relative risk of 0.033 of developing breast cancer. For the year 2015, there will be an
estimated 1,55,000 new cases of breast cancer and about 76000 women in India are expected to die of the disease. The gap only seems to be widening, which means that one need to work aggressively on early detection.

The breast cancer with the highest incidence is ductal cancer. This cancer is seen in the ducts of the cells. Lobular cancer starts in the lobes of the breast and is commonly found in both breasts more than other types of cancer. Breast cancer rarely starts in the connective tissues. Cancer originating in connective tissue is known as sarcoma. 1 in 100 (1%) cases of breast cancer is sarcoma. Phyllodes tumor and angiosarcoma are the frequently occurring forms of sarcoma. Cancer can also be categorized as invasive (infiltrating) and non-invasive (in situ).

In situ is used to refer to “the original place” and simply means cancer which have not spread outside their point of origin. Invasive breast cancer however spreads or invades other tissues in the breast or other parts of the body. Inflammatory breast cancer is a type of breast cancer that is rare and is described by redness and swollen breast. The different types of infiltrating cancers, their incidence and proportion survived are shown in Table 1.1.

Invasive ductal carcinoma which has the highest incidence of breast cancer accounts for about 75% of breast cancer cases. The invasive ductal carcinoma not otherwise specified (IDC NOS), and other carcinomas accounts for less than 5 percent of diagnosed breast cancer.
Table 1.1. Incidence and outcome of histological types of invasive (infiltrating) breast cancer.

<table>
<thead>
<tr>
<th>Histopathological type of invasive breast carcinoma</th>
<th>Frequency (%)</th>
<th>10-year Overall Survival (OS) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal carcinoma not otherwise specified (IDC NOS)</td>
<td>50-60</td>
<td>35-50</td>
</tr>
<tr>
<td>Inflammatory carcinoma</td>
<td>1-6</td>
<td>30-40</td>
</tr>
<tr>
<td>Apocrine carcinoma</td>
<td>1–4</td>
<td>Like IDC NOS</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>5-7</td>
<td>50-90</td>
</tr>
<tr>
<td>Metaplastic carcinoma</td>
<td>&lt;5</td>
<td>Unknown</td>
</tr>
<tr>
<td>Micropapillary carcinoma</td>
<td>1-2</td>
<td>Unknown</td>
</tr>
<tr>
<td>Tabular carcinoma</td>
<td>1-2</td>
<td>90-100</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>5-15</td>
<td>35-50</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>0.1</td>
<td>85-100</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td></td>
<td>85-95</td>
</tr>
<tr>
<td>Neuroendocrine carcinoma</td>
<td>2-5</td>
<td>Unknown</td>
</tr>
<tr>
<td>Mammary Paget disease</td>
<td>1-4</td>
<td>40-50</td>
</tr>
</tbody>
</table>

1.3. Breast Pathologies

Throughout a women’s life, breast tissue remains sensitive to hormonal changes, even during the menstruation, pregnancy and lactation. There may be abnormal proliferation of
cells in the breast called neoplasm. A breast neoplasm can be benign or malignant[10,74, 76]. Tumor is any form of swelling, neoplastic or not. Some neoplasms such as leukemia and carcinoma in situ do not form a tumor.

1.3.1. Granulomatous Lobular Mastitis

Granulomatous Lobular Mastitis is described by multiple, continuing active, necrotizing, granulomatous blisters revolving around the segmental ducts and connected lobules producing a lobulocentric diseases pattern. It induces a breast mass, often resembling carcinoma in women who have attained child bearing age. Granulomatous Lobular Mastitis usually occurs in women that are parous or taking oral contraceptives.

1.3.2. Fibroadenomas

Fibroadenomas are firm, rubbery, freely mobile, solid, usually solitary breast masses. They are the second most common type of benign breast disease. Fibroadenomas most frequently present in adolescents and women in their 20s. Typically the painless mass is discovered accidentally. Growth of the mass is usually extremely slow, but may be quite rapid. Fibroadenomas do not change in size with the menstrual cycle, and they do not produce breast pain or tenderness.

Approximately 30% of fibroadenomas will disappear and 10% to 12% become smaller when followed for many years. Pathophysiologically, fibroadenomas should be considered as an abnormality of normal development rather than true neoplasm. However, the long-term risk of invasive breast cancer is approximately twice that for control patients. Women with fibroadenomas should be made aware of this risk and encouraged to maintain annual mammographic screening.
1.3.3. Intraductal Papilloma

The classical symptom of an intraductal papilloma is spontaneous bloody discharge from one nipple. This symptom usually appears in a woman in the premenopausal age group. The discharge from the nipple is spontaneous and intermittent. The consistency of the discharge associated with an intraductal papilloma can be watery, serous, or serosanguineous. The amount of discharge varies from a few drops to several milliliters of fluid. Approximately 75% of intraductal papilloma is located beneath the areola. Often these tumors are difficult to palpate because they are small and soft. During examination of the breast, it is important to circumferentially put radial pressure on different areas of the areola. This technique helps to identify whether the discharge emanates from a single duct or multiple openings. If the discharge is from a single duct, then intraductal papilloma and carcinoma maybe involved in the differential diagnosis. If multiple ducts are involved, the diagnosis of carcinoma is more likely. Intraductal papilloma is usually microscopic but may grow to 2 to 3 mm in diameter, extending radially from the alveolar margin.

Treatment of an intraductal papilloma is extirpation biopsy of the duct involved and minute amount of surrounding tissue. However, these tumors normally revert in women who have passed menopause and occasionally diminish in size in premenopausal women. It is advisable to remove them.

1.3.4. Fat Necrosis

Fat necrosis is rare but important because it is often confused with carcinoma. The patient presents with a firm, tender, indurate, ill-defined mass that may have an area of surrounding ecchymosis. Sometimes the area of fat necrosis liquefies and becomes cystic in consistency. Mammography may demonstrate fine, stippled calcification and stellate contractions. Occasionally there is skin retraction, which further confuses the pre biopsy
diagnosis. The usual cause of fat necrosis is trauma. However, the majority of women do not remember the event that injured the breast. Treatment of fat necrosis is excisional biopsy. There is no relationship between fat necrosis and subsequent breast carcinoma.

1.3.5. Breast Paget’s disease

Mammary Paget’s disease is an uncommon kind of breast tumor that is linked with roughly 3% of all breast cancers. It occurs more frequently in women than in men; however it also diagnosed in men. This disease was first described as a skin disorder by Velpeau in 1856. However, in 1874 Sir James Paget described the relationship between Mammary Paget’s diseases and breast cancer. Paget described the skin changes that occurred in 15 women between the ages of 40 to 60 years [89]. These women first showed changes in the skin around the nipple-areolar complex, this changes with time progressed to breast cancer. All the patients had itching skin disorder like rash and nipple discharge, which were not responding to common treatment, and progressed to cancer within a year.

Most of the patients diagnosed with Paget’s disease also have a tumor in the breast. In many cases, 90% of the patients diagnosed with Paget’s disease subsequently develop invasive or non-invasive carcinoma. About 50% of patients with Paget’s disease also show palpable mass in their breast. The age distribution of Paget’s diseases is equivalent to that of breast cancer, and can affect young or older women. The early signs of Paget’s disease are itching, and skin lesions around the nipple-areolar complex. In advanced stages of the disease the lesions often progress to ulceration and results in nipple retraction and bloody nipple discharge.
1.4. Imaging of the Breast

Breast imaging has undergone tremendous changes since the advent of mammogram over a quarter of a century ago. The art of breast imaging is rapidly progressing as new modalities are evolved. The technological advancements have helped to individualize the evaluation of breast lesions as well as treatment, improving efficacy while minimizing morbidity and mortality. A summary of selected latest developments in breast imaging highlights the evidence supporting them and their potential future application in breast imaging.

1.4.1. Ultrasound Imaging

Early research using ultrasound to detect breast masses started with John Wild in the 1950s [87]. His idea was creation of a medical device that can effectively detect breast masses. Little did he recognize that the United State Food and Drug Administration (FDA), in 2012, would give approval for the first automated breast ultrasound device for use in screening of patients with dense breasts [135]. Ultrasound as an adjunctive diagnostic tool to mammography is well documented. Nevertheless, the use of ultrasonography as a screening tool remains a subject of rigorous research [46].

After mammography, sonography is the most important breast imaging modality. It most important roles include

- Diagnosing cysts
- Characterizing masses that are incompletely assessed by mammography (Breast Imaging Reporting And Data System (BI-RADS) 3, 4 and 5 as in Table 1.3)
- Complementary assessment in women with dense tissue and high risk
- First imaging choice in symptomatic women under the age of 40 years
- First imaging modality for visualization of the axilla
Ultrasound utilizes high-frequency sound waves to yield images of the breast. Figure 1.3 shows the normal breast scan (Source: American College of Radiology (ACR)). The fibroglandular parenchyma is echogenic (the arrows) and adjacent to hypoechoic fat. Ultrasound technology is presently employed to distinguish the cystic versus solid nature of a clinically palpable mass or to further describe irregular mammographic results. Ultrasound features are used to distinguish benign masses from malignant and adjunct assessment for pathologic lymphadenopathy.

![Figure 1.3. Scan showing the mid transverse of a normal breast.](image)

Ultrasound features guarded for malignancy consist of supposed margins, taller than wide dimensions, shadowing of the posterior acoustic, or calcification. Benign appearances consist of hyperechogenicity, elliptical shape, taller than wide dimensions, well-confined margins, and a tinny echogenic casing. The manifestation of interior echoes shows that a mass is solid, but could still be benign.

Ultrasound screening is yet to be fully recommended, but results from studies shows that addition of ultrasound to screening mammography in women with dense breasts might raise the sensitivity up to 96.6%. Though from findings screening mammography can detect 4
to 5 cancers/1000 women screened per year, this is doubled with further 3.25 cancers/1000 women when screening ultrasound is incorporated in women with dense breast with no other risk factors [118]. Berg et al.[17] reported similar figures (4.2 cancers/1000 women) when ultrasound is incorporated with screening mammography in patients with high risk. The cancers found were small and without node. Figure 1.4 shows the confirmed malignancy of a cancer patient’s left breast. The tumor shows a hypoechoic mass with fine irregularities of the margin. Multiple echogenic areas flanges a clear indication of malignancy in breast carcinoma.

Other uses of ultrasound screening include guidance in interventional operations like biopsy, abscess drainage and cyst aspiration.

### 1.4.2. Sonoelastographic Imaging

Normal tissue is generally softer than breast cancer tissue, which are generally hard. The knowledge about this feature is widely used in physical examination. Elastography makes use of the differences in the physical attributes of elasticity and strain of masses and normal tissue to produce diagnostic information. Elasticity is the tendency of a tissue to return to its original size and shape after it has been stretched or compressed [125]. Figure 1.5 shows the tissue differentiation in an elastographic breast image (Source: ACR). A-D in Figure 1.5 represents different types of tissues in a breast. A, C refers the increased stiffness while B, D has less stiffness. This can be found from the dual color image, blue indicates the high stiffness in the tissue. The grayscale image has different variations for the same stiffness depending on the dense fatty breast tissue.

Elastography is classified into Shear-Wave Elastography (SWE) and Compression Ultrasound Elastography (CUE). SWE is achieved once “an acoustic pressure wave prompts slow-moving lateral waves inside the tissue, and the speed of propagation of the shear wave
is relative to the square root of the tissue’s elastic modulus”. Strain or Compression is accomplished by pressure employed by the operator of the ultrasound or originating from the patient like cardiac pulsation or respiration. Images are constructed on computing the proportional tissue displacement induced. This qualitative measure is limited by user-related differences in transducer placement, pressure applied, and reproducibility. However, results with compression elastography in characterization of breast masses were promising with similar sensitivity and specificity compared with conventional ultrasonography.
Images from compression elastography were formed as color maps of the compression results overlaid on the gray-scale images. Malignant masses were harder than benign masses and seemed larger than the equivalent mass seen on orthodox morphologic ultrasound images. Table 1.2 shows the comparison of the results of compression and shear wave elastography [15, 25, 77, 98, 131]. This is also reported in SWE and may be as a result of local effect of the mass on the adjoining tissues or tumor range further than what is discernible on ultrasonography.

SWE is done using conventional linear array probe, permitting it to be incorporated into ultrasound examination with real-time acquisition of the data. This allows for reproducibility of the results. The average time added to the examination is about 3 to 5 minutes. However, compression elastography, consistency is not operator dependent [40]. Data acquired are quantitative, constructed on the velocity of the induced wave in tissue.

Preliminary research in using UE showed promising results in decreasing unnecessary biopsies and unnecessary recalls. This probable benefit is greatest for the Breast Imaging Reporting And Data System (BI-RADS) category 3 and 4 lesions. The information rendered by morphologic research and elastography are corresponding to each other and has potential of improving administration of BI-RADS category 3 and 4A lesions, in particular.

Table 1.2: Comparison of CUE and SWE.

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CUE</td>
<td>70.1</td>
<td>95.7</td>
<td>88.2</td>
<td>87.1</td>
<td>88.5</td>
</tr>
<tr>
<td>CUE</td>
<td>86.5</td>
<td>89.8</td>
<td>88.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SWE</td>
<td>97</td>
<td>83</td>
<td>91</td>
<td>88</td>
<td>95</td>
</tr>
<tr>
<td>US</td>
<td>87</td>
<td>78</td>
<td>83</td>
<td>84</td>
<td>82</td>
</tr>
<tr>
<td>SWE</td>
<td>97</td>
<td>83</td>
<td>-</td>
<td>88</td>
<td>95</td>
</tr>
</tbody>
</table>
Elastography results is cautioned not to be used in downgrading BI-RADS 4B, 4C, or 5 lesions or alter management in BI-RADS category 2 lesions as shown in Table 1.3 (Source: ACR).

Like other imaging modalities, suspicious findings should mostly motivate management. The blend of morphologic ultrasonography and elastography increases

Table 1.3.Harmonized BI-RADS assessment categories and management recommendations.

<table>
<thead>
<tr>
<th>Category</th>
<th>Assessment</th>
<th>Management</th>
<th>Likelihood of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 0</td>
<td>Incomplete — Need Additional Imaging Evaluation</td>
<td>Recall for additional imaging</td>
<td>N/A</td>
</tr>
<tr>
<td>Category 1</td>
<td>Negative</td>
<td>Routine screening</td>
<td>Essentially likelihood of malignancy 0%</td>
</tr>
<tr>
<td>Category 2</td>
<td>Benign</td>
<td>Routine screening</td>
<td>Essentially likelihood of malignancy 0%</td>
</tr>
<tr>
<td>Category 3</td>
<td>Probably Benign</td>
<td>Short-interval (6-month) follow-up or continued surveillance</td>
<td>&gt; 0% but ≤ 2% likelihood of malignancy</td>
</tr>
<tr>
<td>Category 4A</td>
<td>Suspicious</td>
<td>Tissue diagnosis</td>
<td>&gt; 2% but &lt; 95% likelihood of malignancy</td>
</tr>
<tr>
<td>Category 4A</td>
<td>Low suspicion for malignancy</td>
<td>Tissue diagnosis</td>
<td>&gt; 2% to ≤ 10% likelihood of malignancy</td>
</tr>
<tr>
<td>Category 4B</td>
<td>Moderate suspicion for malignancy</td>
<td>Tissue diagnosis</td>
<td>&gt; 10% to ≤ 50% likelihood of malignancy</td>
</tr>
<tr>
<td>Category 4C</td>
<td>High suspicion for malignancy</td>
<td>Tissue diagnosis</td>
<td>&gt; 50% to &lt; 95% likelihood of malignancy</td>
</tr>
<tr>
<td>Category 5</td>
<td>Highly Suggestive of Malignancy</td>
<td>Tissue diagnosis</td>
<td>≥ 95% likelihood of malignancy</td>
</tr>
</tbody>
</table>
specificity and allows for earlier diagnosis of breast cancer. Information acquired with elastography that has potentials as a significant factor in prospective management assessments includes shape of the zone stiffness, stiffness and maximum stiffness [24].

Elastography of calcified lesions can render some diagnostic measures. Elastogram stiffness of tissue with mammographic calcifications is different for benign and malignant lesions. Benign lesions are less stiff than malignant. Ductal Carcinoma In Situ (DCIS) has transitional stiffness amid invasive carcinoma and benign lesions. Benign proliferative lesions, non-proliferative lesions, and DCIS all show less stiffness than invasive carcinoma.

Elastography may also be beneficial for patients undertaking neoadjuvant chemotherapy. Research shows that elastography gives higher response rate to neoadjuvant chemotherapy in patients having soft malignancies than those with hard malignancies. Tumor stiffness is a typical of the extracellular matrix; quantifiable variations in stiffness may serve as pointers of tissue response.

Overlap in elasticity between benign and malignant lesions presents itself as a limitation. False-negative findings occur in DCIS, early stage of invasive carcinoma, carcinomas with large necrotic areas, mucinous carcinomas, papillary carcinomas, and medullary carcinomas. False-positive findings occur in stiff benign processes such as fibroadenoma, surgical scar, post radiation skin thickening, inflammation, fat necrosis, hyalinized fibroadenoma and fibrocystic lesions; and processes of questionable malignant potential such as papilloma and radial scars.

Limiting factors found for sensitivity and specificity of elastography consist of deepness of the lesion from the skin, thickness of the breast at the location of the lesion, and diameter of the lesion as well as transducer length. Thick breast tissue diminishes both sound and elastic waves. As stated earlier, compression elastography reproducibility is also limited
by operator-caused modifications and absence of quantitative information leading to major variation in acquisition and interpretation of image.

1.5. Structure of the thesis

This thesis is organized as follows.

Chapter 1 deals with the scope and objectives of the thesis, the basic concepts of breast anatomy, pathology and cancer. This is followed by describing the role of sonoelastography in breast cancer detection.

Chapter 2 reviews the main existing approaches in this research area, referring to the multi-feature unsupervised segmentation of breast images. In particular three categories of features are outlined: (i) wavelet features, which are primarily used to detect global cyclicity in an image, an ideal descriptor of directionality of cyclic 2-D patterns in an image, (ii) texture feature, the mapping of the spatial variation in gray values (pixel intensity); and (iii) edge features, the smooth transition of gray values across a number of pixels. Feature selection is also discussed in the context of reducing computational complexities. Existing approaches to segmentation of breast images is also discussed here.

Chapter 3 covers the discussion about the multi-feature, wavelet based proposed methods for UE breast image segmentation, and the proposed MM-LBP. The proposed schemes are;(i) Feature set optimization using statistical measures for UE image segmentation, (ii) Multi-scale texture analysis for UE image segmentation, and (iii) Novel MM-LBP method are analyzed using 100 UE breast images of both benign and malignant tumors. The first twoschemesselects the ranked features andthen a K-means algorithm is applied for segmentation, while the third scheme proposes a novel method by extracting features and then thresholding for improving the segmentation accuracy.
Chapter 4 presents the results from the multi-feature analysis, wavelet analysis and analysis of the optimal features from both multi-features and wavelet based features. It thereby contains the results of the proposed methods and explains the best features for UE breast image segmentation that may emerge in this context. The result of the proposed MM-LBP is also provided for evaluation.

Chapter 5 gives the summary of results by pointing out the research impacts. It also gives a list of undetermined matters that flow from this thesis, which represents areas of research needs for future work.