CHAPTER 1
INTRODUCTION

Cancer is one of the biggest threats to human life. According to the World Health Organization (WHO) cancer is the leading cause of death worldwide, accounting for 7.6 million deaths (around 13% of all deaths) in 2008. But it is projected to continue rising, with an estimated 13.1 million deaths in 2030. Cancer is the general term that refers to cells which grow larger than 2mm in every three months. It multiplies out of control and spreads to other parts of the body. Collection of cancer cells form tumor which destroys the healthy tissue. The formed tumor breakaway and spreads to other parts of the body which is called as metastasis. Cancer arises from one single cell. The transformation from a normal cell into a tumor cell is a multistage process, typically a progression from a pre-cancerous lesion to malignant tumors. Most kind of cancer is named after the part of the body where it started. Breast cancer begins in the breast tissue, it may spread to lungs but still it is breast cancer not lung cancer.

Breast cancer is defined as an abnormal growth of cells in the breast that multiply uncontrollably, new cells grow when they are not needed and old cells do not die when they should. Breast cancer can occur in both men and women, however for every one hundred females with breast cancer only one male will contract the disease, as a result only female breast cancer is taken in to account in this research work.

Breast cancer is the first leading cause of cancer death particularly for women in all over the world. According to the World Health Organization 1.38 million women were diagnosed with Breast cancer in 2008 accounting for nearly quarter of cancers diagnosed in women. According to Medindia “Breast cancer in India rising rapidly”, it is rapidly becoming the number
one cancer in females and pushing the cervical cancer to second place. According to Tata memorial hospital the breast cancer has been reported to occur in 1 woman out of 1000 during 1974-78. But today in India it occurs 1 in 10, which shows the necessity of taking preventive steps against this dangerous disease.

According to the American Cancer Society (ACS), about 1.3 million women will be diagnosed with breast cancer annually worldwide, about 465,000 will die from the disease. But ACS reported that breast cancer death rates have been dropping steadily since 1990, because of earlier detection and better treatments. At present vaccination is available to prevent some kind of cancers such as lung cancer, cervical cancer. But in the case of breast cancer the root cause is still unknown. Hence the proper preventive measures are absent. However complete curing of breast cancer is possible if it is detected in its earlier stages. Early detection will improve the survival rate of patient by 95%. Hence earlier detection is the only way to reduce the mortality rate.

At present mammogram readings are performed by the radiologists and mammographers will examine the mammograms visually for the presence of deformalities that can be interpreted as cancer. But reading mammogram image for cancer detection is challenging task as the image occasionally show low contrast difference especially on dense breast. It will be time consuming to train an expert person in this area. Manual reading may result in misdiagnosis due to various factors such as eye fatigue. Hence the effectiveness in the performance of the radiologists varies from 65 to 85%. There are two types of errors occur while reading mammograms, False Positive(FP)which consists of the detection of a sign that appears to be malignant which usually lead to unnecessary intervention and False
Negative(FN) which are detection of malignant signs that are classified as benign by radiologist which leads to unnecessary delay in treatment.

To overcome the above problem in diagnosing breast cancer and to improve the diagnostic accuracy and efficiency of screening mammography, Computer Aided Diagnosis (CAD) techniques are introduced. Over the past two decades many attempts have been made by computer scientists to assist radiologists in detection and diagnosis of masses by developing computer aided tools for mammography interpretation. Image processing and intelligent synthesis are two main streams of computer technologies that have been constantly explored in the development of computer aided mammography systems. Although there are several image processing methods are proposed for the detection of mass in mammogram, the detection rate is still not high. The standard algorithms that can produce invariable result for all kind of mammograms are still not available. Hence in this research work it is aimed to develop a fully automatic Mammogram screening system with improved accuracy and capable of producing the invariable result over all kind of mammograms.

In this thesis Chapter 1 is the introductory chapter which gives the detailed introduction about the Breast Cancer, Computer Aided Diagnosis tool, and digital image processing and also explains the need for CAD as a second reader. Chapter 2 is about the literature survey which explains briefly about other existing works in this field. Chapter 3 is about methodology which explains the available existing methods to design CAD, it also explains the reason behind selecting the particular methods in this research work. In chapter 4 the first approach which is named as 3SMDT is explained in detail. Chapter 5 deals with MDTC and the final approach MDTR is explained in Chapter 6. Chapter 7 describes the comparative study
of all the three approaches, and their test results against the same set of 400
digital mammogram images. MDTR is selected to be the best of three
methods in all aspects. Chapter 8 compares the results of MDTR with other
existing techniques. Conclusion and Future work is given in Chapter 9.

1.1 WORLD WIDE STATISTICS OF BREAST CANCER

According to a study conducted by World Health Organization
(WHO) the most prevalent cancer type was found to be breast cancer. In the
incidence of new cases, breast cancer is the most encountered cancer type
for women in both developed and developing countries. The mortality of
breast cancer is also very high with regard to other cancer types. Figure 1.1
shows the result of the above study. Breast cancer continues to be one of the
most common cancers and a major cause of death among women
worldwide. According to the current statistics of the Centers for Disease
Control and Prevention, breast cancer is the most common cancer in women
accounting for 32 percent of all female cancers. The National Cancer
Institute estimates that about 1 in 8 women in the United States
(approximately 13.3 percent) will develop breast cancer during her lifetime.
The graphical representation of incidence and mortality rate is shown in Fig
1.2 and 1.3., which explains about the comparative study of breast cancer
with other cancer types.
Fig. 1.1 Estimated numbers of new cancer cases (incidence) and deaths (mortality) by WHO (GLOBOCAN 2008(IARC)).

Fig. 1.2. Incidence rate of all cancer types ((GLOBOCAN 2008(IARC))
According to the American Cancer Society, about 1.3 million women will be diagnosed with breast cancer annually worldwide about 465,000 will die from the disease. Breast cancer rates have risen about 30% in the past 25 years in western countries. The incidence of breast cancer increased by approximately 4% during the 1980s but leveled off to 100.6 cases per 100,000 women in the 1990s. Breast cancer incidence rates vary considerably, with the highest rates in the developed world and the lowest rates in Africa and Asia as shown in table 1.1 below. Incidence is generally high in the developed countries and markedly lower in developing countries, though differences in population sizes mean that approximately equal numbers of cases were diagnosed in the developed and developing regions in 2008 (around 690,000 cases each).
Table 1.1. Cancer Incidence, Mortality and Prevalence Worldwide

<table>
<thead>
<tr>
<th>Breast (All ages)</th>
<th>Incidence</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>18.7</td>
<td>5.5</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>19</td>
<td>14.1</td>
</tr>
<tr>
<td>India</td>
<td>19.1</td>
<td>10.4</td>
</tr>
<tr>
<td>Japan</td>
<td>32.7</td>
<td>8.3</td>
</tr>
<tr>
<td>Brazil</td>
<td>46</td>
<td>14.1</td>
</tr>
<tr>
<td>Singapore</td>
<td>48.7</td>
<td>15.8</td>
</tr>
<tr>
<td>Italy</td>
<td>74.4</td>
<td>18.9</td>
</tr>
<tr>
<td>Switzerland</td>
<td>81.7</td>
<td>19.8</td>
</tr>
<tr>
<td>Australia</td>
<td>83.2</td>
<td>18.4</td>
</tr>
<tr>
<td>Canada</td>
<td>84.3</td>
<td>21.1</td>
</tr>
<tr>
<td>Netherlands</td>
<td>86.7</td>
<td>27.5</td>
</tr>
<tr>
<td>UK</td>
<td>87.2</td>
<td>24.3</td>
</tr>
<tr>
<td>Sweden</td>
<td>87.8</td>
<td>17.3</td>
</tr>
<tr>
<td>Denmark</td>
<td>88.7</td>
<td>27.8</td>
</tr>
<tr>
<td>France</td>
<td>91.9</td>
<td>21.5</td>
</tr>
<tr>
<td>United States</td>
<td>101.1</td>
<td>19</td>
</tr>
</tbody>
</table>


1.2 BREAST STRUCTURE

The breast is held in place by the chest muscles that cover the ribs. Each breast is made up of fifteen to twenty lobes with lobules containing smaller lobules. Tiny glands within these lobules are what produce milk, which flows from the lobules through thin tubes called ducts to the nipple. The nipple is in the center of a dark area of skin called the areola. Fat fills the spaces between the lobules and ducts. The breasts also contain lymph vessels which lead to lymph nodes. The lymph nodes trap bacteria, cancer
cells, or other harmful substances. Most breast cancers begin in the ducts, some in the lobules and the rest in other tissues. Figure 1.4 below depicts the internal structure of the breast. Milk production is the main function of the breast.

![Fig. 1.4. Internal breast structure](image)

### 1.3 Breast cancer visual symptoms

Breast cancer can have a number of different symptoms, the most common of which is a lump in the breast although some 90% of breast lumps are benign. Other symptoms include a change in how the breast or nipple feels a change in the shape or size of the breast, nipple turned inwards towards the breast, change of skin color or a fluid discharge through the nipple. These symptoms are shown graphically in Figure 1.5.
1.4 RISK FACTORS OF BREAST CANCER

All the following are identified as risk factors of Breast Cancer

a) Age: One of the best-documented risk factors for breast cancer is age. The incidence of breast cancer is extremely low before age 30 (incidence <25 cases per 100,000), after which it increases linearly until the age of 80, reaching a plateau of slightly less than 500 cases per 100,000.

b) Reproductive Factors: Brinton et al (8) examined the relationship between reproductive factors and the risk of breast cancer in a series of studies. The results indicated that women who began menstruating before
the age of 12 had a relative risk for invasive breast cancer of 1.3 compared to those who began after the age of 15. At the other end of the reproductive period, those who did not reach menopause until age 55 or after (late menopause) showed a relative risk of 1.22 compared with those who experienced menopause before the age of 45 (early menopause). Brinton et al epidemiological study in 1983 demonstrated that the risk of breast cancer increased if a woman was nulliparous or experienced her first live birth at or after the age of 30. Compared to a woman with a first live birth at an age less than 20, the relative risk for the nulliparous woman was 1.67, and the risk for the woman giving birth at or after the age of 30 was 2.2.

c) **Family History:** Many studies have attempted to define levels of risk associated with varying degrees of positive family history. The degree of risk was a function of the type of relative affected (first or second degree), the age at which the relative developed cancer, and the number of relatives affected. Compared to individuals with no family history of breast cancer, they estimated a relative risk of 1.8 associated with a first-degree relative who developed breast cancer at 50 years of age or older compared with a relative risk of 3.3 for a first-degree relative who developed breast cancer at an age less than 50 years. The BRCA1 and BRCA2 genes are associated with an inherited susceptibility to breast and ovarian cancers. Initial studies indicated that the increased risk for carriers of BRCA mutations was very high, with an expected lifetime incidence of cancer approaching 90% by the age of 70.

d) **Hormone Replacement Therapy:** In the United States in 1995, nearly 40% of postmenopausal women used hormone replacement therapy (HRT) for the control of menopausal symptoms and the prevention of osteoporosis. For every five years a woman uses estrogen, the risk of breast cancer
increases six percent. But for every five years a woman takes both estrogen and progestin, called combined therapy—today's standard hormone replacement therapy to ease the symptoms of menopause, the risk of breast cancer rises 24 percent. The average breast cancer risk with estrogen progestin use was 1.24 (95% CI = 1.03 1.50) in four randomized trial. Estrogen progestin users are significantly more likely to be estrogen receptor (ER) positive. Hormone therapy in younger postmenopausal women increases the risk of breast cancer and pulmonary embolism and reduces the risk of cardiovascular events, colon cancer and hip fracture. The probability of a mortality benefit in this population was 1.0 which outweighed the increase in deaths from breast cancer.

e) **Oral contraceptives and Breast Cancer. (OCS):** It is uncertain whether the use of an oral contraceptive increases the risk of breast cancer later in life, when the incidence of breast cancer is increased. A population-based, case control study found that the risk of breast cancer among former and current users of oral contraceptives of 35 to 64 years of age was not associated with a significantly increased risk of breast cancer RR = 1.0 (95 percent confidence interval, 0.8 to 1.3).

f) **Pregnancy and Breast Cancer:** The only factor known to consistently decrease lifetime breast cancer risk regardless of ethnicity is early childbirth. Women who have undergone a first full-term pregnancy/birth (FFTB) before 20 years of age have a 50% reduced lifetime risk of developing breast cancer when compared with nulliparous women. These parity-specific effects on breast cancer risk are limited to hormone-responsive breast cancer as highlighted in a recent meta-analysis study which investigated parity and age at first full-term pregnancy/birth (FFTB) among Positive Estrogen-Progesterone Receptor, and among Negative Estrogen-Progesterone
Receptor, respectively (ER+/PR+ and ER\textsuperscript{+} /PR\textsuperscript{+}) breast cancer factors. Each birth reduced the risk of breast cancer by 11%. The protective effect was maintained within the ER+/PR+ group.

**g) Breastfeeding and Breast cancer:** Collaborative Group on Hormonal Factors in Breast Cancer and breastfeeding reanalyzed data from 47 epidemiological studies in 30 countries. They found that 16% and 14% of women in the breast cancer and control groups were nulliparous, 71% and 79% of women in the breast cancer and control groups, respectively, had never breastfed. The average lifetime duration of breastfeeding was 9.8 and 15.6 months for women with breast cancer and women in the control group, respectively. In all women, the Relative Risk (RR) of breast cancer decreased with increasing duration of breastfeeding respectively.

**h) Smoking cigarettes and tobacco smoke:** Tobacco smoking has been suggested as a cause of breast cancer. In the evaluation of IARC, smoking and tobacco smoke are judged to be carcinogenic to humans. Chemical carcinogens in tobacco smoke can cause mammary tumors in animals. However, epidemiological studies of smoking and breast cancer have produced inconsistent results. A recent pooled analysis of 53 epidemiological studies showed no increased risk of breast cancer associated with smoking. However, passive smoking has been suggested to be associated breast cancer risk rather consistently. Thus, the risk of active smoking may be canceled out by the passive smoking risk in the control group. Some studies suggested that longer duration or high intensity of smoking may be associated with an increased risk of breast cancer.

**i) Radiation Exposure:** Therapeutic radiation exposure to monitor or treat disease is now the most significant cause of radiation-induced carcinogenesis. Multiple fluoroscopies are a significant risk factor for breast
cancer the relative risk for 1 Gy (SI unit gray) of radiation exposure at a latency period of 10 years was estimated to be 1.61.

j) Physical activity and Obesity: The International Agency for Research on Cancer estimates that 25% of breast cancer cases worldwide are due to overweight/obesity and a sedentary lifestyle. The preponderance of epidemiologic studies indicates that women who engage in 3, 4 hours per week of moderate to vigorous levels of exercise have a 30%-40% lower risk for breast cancer than sedentary women. Women who are overweight or obese have a 50%-250% greater risk for postmenopausal breast cancer.

1.5 HISTORICAL OVERVIEW

The recorded history of breast cancer traces back thousands of years. It is no surprise that from the dawn of history doctors have written about cancer. Incidents of breast cancer have been documented back to the early Egyptians when the popular treatment was cautery of the diseased tissue. Surgery was practiced but it was an extremely radical treatment considering there was no anesthesia or antisepsis available. The oldest description of cancer (although the term cancer was not used) was discovered in Egypt and dates back to approximately 1600 B.C. The Edwin Smith Papyrus describes 8 cases of tumors or ulcers of the breast that were treated by cauterization, with a tool called “the fire drill”. The writing says about the disease, “There is no treatment”.

The origin of the word cancer is credited to the Greek physician Hippocrates (460-370 B.C.), the "Father of Medicine." Hippocrates used the terms carcinos and carcinoma to describe non-ulcer forming and ulcer-forming tumors. In Greek these words refer to a crab, most likely applied to the disease because the finger-like spreading projections from a cancer
called to mind the shape of a crab. Carcinoma is the most common type of cancer. According to the doctrines of the Greek physician Caudius Galen (130-200 AD), whose works on physiology and anatomy dominated medical thought until the Middle Ages, melancholia was the chief factor in the development of breast cancer. Special diets were the recommended treatment. However, other treatments included exorcism and the use of topical applications which were seldom preferred by patients.

During the Renaissance, Andreas Vesalius recommended mastectomy as well as ligatures (sutures) to control the bleeding rather than cautery. Recognition that breast cancer could and did spread to the regional auxiliary nodes was first recognized by the physician LeDran (1685-1770). Dr. LeDran was likely the first to associate poor prognosis with the spread of breast cancer to the lymph nodes.

The famous Scottish surgeon John Hunter (1728-1793) suggested that some cancers might be cured by surgery and described how the surgeon might decide which cancers to operate on. If the tumor had not invaded nearby tissue and was “moveable”, he said, “There is no impropriety in removing it”. During the mid 1800’s, surgeons first began to keep detailed records of breast cancer. Those statistics indicate that even those treated by mastectomy had a high rate of recurrence within eight years—especially when the glands or lymph nodes were affected. Nevertheless, the common treatment was to remove the breast and the surrounding glands in an effort to stave off any further tumor development.

In 1894 William Roentgen discovered X-rays. This paramount discovery shed light on the detection of many diseases as well as breast cancer. Some years later, in 1913, Albert Solomon, a pathologist in Berlin, produced images of 3,000 gross mastectomy specimens. He observed black
spots at the centers of breast carcinomas (microcalcifications). Between the 1930’s and the 1950’s treatment and detection improvements were noticeable. This was the time when Stafford Warren (Rochester memorial Hospital, New York) developed a stereoscopic system for tumor identification. Also, doctors started classifying the stage and progression of breast cancer. In 1949 Raul Leborgne (Uruguay) emphasized breast compression for identification of calcifications. In 1940s-1950s breast self-examinations were advocated.

In 1960 Dr. Robert Egan (Houston) adapted high-resolution industrial film for mammography, allowing simple and reproducible mammograms with improved image detail. And in 1963 the first randomized controlled trial of screening by the Health Insurance Plan of New York found that mammography reduced the 5-year breast cancer mortality rate by 30 percent. Major improvements in mammography equipment, such as reduced radiation dosage, digital imaging, and computer-aided diagnosis help for the improved and early detection of breast cancer.

1.6 BREAST CANCER TYPES

Based on cellular morphology, breast tumors are of ductal origin (ductal carcinomas) or of lobular origin (lobular carcinomas). Breast tumors are classified into invasive (infiltrating) carcinomas capable of metastasizing and noninvasive disease which can invade beyond the basement membrane (ductal carcinoma in situ) [DCIS]. Ductal carcinoma comprises (70-80%) as shown in table 1.2 which is considered to be the most common histological type with variable prognosis, ranging from indolent to rapidly progressive tumor. The continued growth in mammographic evaluation and technology has resulted in an increase in the diagnosis of ductal carcinoma in situ of the breast (DCIS) due to the presence of microcalcifications.
Lobular Carcinoma forms (10-15%). Lobular carcinoma in situ (LCIS) is associated with an increased risk of developing invasive disease either ductal or lobular, they are more likely to be bilateral compared with ductal carcinoma (DC), and they are difficult to diagnose. Special subtypes (<10%) include papillary, tubular, and medullary carcinomas and are usually with favorable prognosis.

A relatively rare subtype (1%) is inflammatory Breast Cancer. It is an aggressive subtype. Clinically it is associated with cutaneous erythema of the breast and the cutaneous edema "peau d'orange" It can occur in women of any age. Paget's disease of the breast consists of the infiltration of the nipple areolar complex epidermis by adenocarcinoma cells and accounts for approximately 2-3% of breast carcinomas. Clinically, this is seen as an eczematous eruption of the nipple that may be associated with erosion or ulceration. It is often associated with underlying ductal carcinoma in situ (DCIS). Cystosarcoma phylloides are typically large, fast growing masses that form the periductal stroma of the breast. They account for less than 1% of all breast neoplasms, 90% are benign.
### Table 1.2. Percentage of malignant breast tumors

<table>
<thead>
<tr>
<th>Type of Carcinoma</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ carcinoma</td>
<td>15%-30</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>80%</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>20%</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td>70%</td>
</tr>
<tr>
<td>Ductal carcinoma (no special type)</td>
<td>79%</td>
</tr>
<tr>
<td>Lobular carcinoma</td>
<td>10%</td>
</tr>
<tr>
<td>Tubular/cribiform carcinoma</td>
<td>6%</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>2%</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>2%</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>1%</td>
</tr>
</tbody>
</table>


### 1.7 Breast Cancer Stages

Cancer **stage** is based on four characteristics:

- the size of the cancer
- whether the cancer is invasive or non-invasive
- whether cancer is in the lymph nodes
- whether the cancer has spread to other parts of the body beyond the breast

The following words are also used to describe the stage of the breast cancer:

- **Local**: The cancer is confined within the breast.
- **Regional**: The lymph nodes, primarily those in the armpit, are involved.
- **Distant**: The cancer is found in other parts of the body as well.
Sometimes doctors use the term “locally advanced” or “regionally advanced” to refer to large tumors that involve the breast skin, underlying chest structures, changes to the breast's shape, and lymph node enlargement that is visible. The stage of the breast cancer can help to understand the prognosis (the most likely outcome of the disease) and make decisions about treatment, along with all of the other results in pathology report.

There is another staging system known as TNM to describe the cancer. This system is based on the size of the tumor (T), lymph node involvement (N), and whether the cancer has spread, or metastasized, to other parts of the body (M).

**Stage 0**

Stage 0 is used to describe non-invasive breast cancers, such as DCIS (ductal carcinoma in situ). In stage 0, there is no evidence of cancer cells or non-cancerous abnormal cells breaking out of the part of the breast, in which they started, or getting through to or invading neighboring normal tissue.

**Stage I**

Stage I describes invasive breast cancer (cancer cells are breaking through to or invading normal surrounding breast tissue) in which:

- the tumor measures up to 2 cm AND
- no lymph nodes are involved

Microscopic invasion is possible in stage I breast cancer. In microscopic invasion, the cancer cells have just started to invade the tissue outside the lining of the duct or lobule, but the invading cancer cells can't measure more than 1 mm.
Stage II
Stage II is divided into subcategories known as IIA and IIB.
Stage IIA describes invasive breast cancer in which:
• no tumor can be found in the breast, but cancer cells are found in the lymph nodes under the arm (axillary) OR
• the tumor measures 2 cm or smaller and has spread to the axillary lymph nodes OR
• the tumor is larger than 2 cm but not larger than 5 cm and has not spread to the axillary lymph nodes
Stage IIB describes invasive breast cancer in which:
• the tumor is larger than 2 cm but no larger than 5 cm and has spread to the axillary lymph nodes OR
• the tumor is larger than 5 cm but has not spread to the axillary lymph nodes
Stage III
Stage III is divided into subcategories known as IIIA, IIIB, and IIIC.
Stage IIIA describes invasive breast cancer in which either:
• no tumor is found, but cancer is found in axillary lymph nodes, which are clumped together or sticking to other structures, or cancer may have spread to lymph nodes near the breastbone OR
• the cancer is any size and has spread to axillary lymph nodes, which are clumped together or sticking to other structures
Stage IIIB describes invasive breast cancer in which:
• the cancer may be any size and has spread to the chest wall and/or skin of the breast AND
• may have spread to axillary lymph nodes, which are clumped together or sticking to other structures, or cancer may have spread to lymph nodes near the breastbone

Inflammatory breast cancer is considered at least stage IIIB. Typical features of inflammatory breast cancer include:

• reddening of a large portion of the breast skin
• the breast feels warm and may be swollen
• cancer cells have spread to the lymph nodes and may be found in the skin

Stage IIIC describes invasive breast cancer in which:

• there may be no sign of cancer in the breast or, if there is a tumor, it may be any size and may have spread to the chest wall and/or the skin of the breast
• the cancer has spread to lymph nodes above or below the collarbone
• the cancer may have spread to axillary lymph nodes or to lymph nodes near the breastbone

Stage IV

Stage IV describes invasive breast cancer that has spread beyond the breast and nearby lymph nodes to other organs of the body, such as the lungs, distant lymph nodes, skin, bones, liver, or brain.

“Advanced” and “metastatic” are the words used to describe stage IV breast cancer. Cancer may be stage IV at first diagnosis or it can be a recurrence of a previous breast cancer that has spread to other parts of the body.
TNM staging system

TNM (Tumor, Node and Metastasis) is another staging system researchers use to provide more details about how the cancer looks and behaves. Sometimes clinical trials require TNM information from participants.

The TNM system is based on three characteristics:

- size (T stands for tumor)
- lymph node involvement (N stands for node)
- Whether the cancer has metastasized (M stands for metastasis), or moved beyond the breast to other parts of the body.

The T (size) category describes the original (primary) tumor:

- **TX** means the tumor can't be measured or found.
- **T0** means there isn't any evidence of the primary tumor.
- **T** means the cancer is "in situ" (the tumor has not started growing into healthy breast tissue).
- **T1, T2, T3, and T4:** These numbers are based on the size of the tumor and the extent to which it has grown into neighboring breast tissue. The higher the T number, the larger the tumor and/or the more it may have grown into the breast tissue.

The N (lymph node involvement) category describes whether or not the cancer has reached nearby lymph nodes:

- **NX** means the nearby lymph nodes can't be measured or found.
- **N0** means nearby lymph nodes do not contain cancer.
- **N1, N2, and N3:** These numbers are based on the number of lymph nodes involved and how much cancer is found in them. The higher the N number, the greater the extent of the lymph node involvement.
The M (metastasis) category tells whether or not there is evidence that the cancer has traveled to other parts of the body:

- **MX** means metastasis can't be measured or found.
- **M0** means there is no distant metastasis.
- **M1** means that distant metastasis is present.

Once the pathologist knows T, N, and M characteristics, he or she can use them to assign a stage to the cancer. For example, a T1 N0 M0 breast cancer would mean that the primary breast tumor is less than 2 centimeters across (T1), has not involved the lymph nodes (N0), and has not spread to distant parts of the body (M0). This cancer would be grouped as stage I.

1.8 **BENIGN AND MALIGNANT TUMORS**

Masses and Microcalcifications are the two important signs of breast cancer in Mammogram. Microcalcifications are nothing but the collection of calcium cells. Sometimes it may look like cancer cells, but it is not the actual sign of cancer. Masses are quite subtle, and often occur in the dense areas of the breast tissue, they have smoother boundaries than microcalcifications, and have many shapes such ascircumscribed, speculated, lobulated or ill-defined. The circumscribed ones usually have distinct boundaries, 2–30 mm in diameters, and are high-density radiopaque, the speculated ones have rough, star-shaped boundaries, and the lobulated ones have irregular shapes. Benign and malignant are another confusing terms while speaking about cancer. The difference is mentioned as follows,

A benign tumor is not cancerous because:

1. They do not grow in an aggressive manner and if removed normally do not grow back.
2. Benign tumors do not invade healthy surrounding tissue.
3. Benign tumors do not metastasize i.e. spread to other parts of the body.

A malignant tumor is cancerous because:

1. If the tumor is removed it can still grow back.
2. Malignant tumor cells can invade and damage surrounding tissue.
3. Malignant tumor cells can metastasize.

Fig.1.6. (a) Benign mass mammogram, (b) Malignant mass mammogram

Fig.1.7. (a) Benign calcification, (b) Malignant calcification
Understanding and differentiating the benign and malignant is the most important and complicated part of Breast cancer diagnosis. Because sometimes misunderstanding of their appearance will lead to misdiagnosis. Mammogram samples of Benign and malignant tumor is shown in Fig 1.6. Calcification part of benign and malignant type is clearly shown in Fig1.7.

1.9 IMPORTANCE OF EARLY DIAGNOSIS OF BREAST CANCER

There are two components of early detection efforts as follows,

**Early diagnosis:**

The awareness of early signs and symptoms (for cancer types such as cervical, breast colorectal and oral) in order to get them diagnosed and treated early before the disease becomes advanced. Early diagnosis programmes are particularly relevant in low-resource settings where the majority of patients are diagnosed in very late stages and where there is no screening.

**Screening:**

Screening is defined as the systematic application of a test in an asymptomatic population. It aims to identify individuals with abnormalities suggestive of a specific cancer or pre-cancer and refer them promptly for diagnosis and treatment. Screening programmes are especially effective for frequent cancer types for which a cost-effective, affordable, acceptable and accessible screening test is available to the majority of the population at risk.

According to a study conducted by World Health Organization (WHO) due to early detection and treatment one third of the mortality can be reduced and approximately 400000 could be saved per year. Clear increases in the incidence of, and mortality from, breast cancer were
observed up to the early 1980s in both high-income and low-income countries. The subsequent advent of early detection and screening programmes in high-income countries altered the reported rates of both incidence and mortality, masking trends in the underlying risk for the disease. Mortality rates for breast cancer in western Europe and North America are in the order of 15–25 per 100 000 women, being slightly more than a third of the incidence rate, which is approximately 50–60 per 100000. Total mortality from breast cancer is already higher in the developing world. Whilst mortality is declining in most western countries, it is estimated that it will increase by over 100% in developing countries by 2020. Whereas less than one-third of women diagnosed with breast cancer in developed countries die from the disease, this proportion reaches over two-thirds in developing countries. Thus the survival rate from breast cancer in developing countries is generally poorer than in developed countries, primarily as a result of delayed diagnosis of cases. According to a study conducted in developed countries early diagnosis could save between 12 to 37 women per day. Mortality rate reduction in developed countries due to early diagnosis is shown in table 1.3.

**Table 1.3. Mortality reduction in developed country due to early detection**

<table>
<thead>
<tr>
<th>Country</th>
<th>New Cases of Breast Cancer (per day)</th>
<th>Breast Cancer Deaths (per day)</th>
<th>Lives that could have been saved through early detection (per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>527</td>
<td>110</td>
<td>37</td>
</tr>
<tr>
<td>UK</td>
<td>125</td>
<td>35</td>
<td>12</td>
</tr>
</tbody>
</table>
Breast cancer incidence rates have been rising in many African and Asian countries including Japan, where rates increased more than 140% in the Miyagi registry during the time period 1973-1977 through 1998-2002, and in India where rates increased 40% in the Chennai registry between 1983-1987 and 1998-2002. Reasons for these rising trends are not completely understood but likely reflect changes in reproductive patterns, obesity, physical inactivity, and some breast cancer screening activity. Although breast cancer incidence rates continued to increase through the late 1990s, breast cancer mortality over the past 25 years has been stable or decreasing in some North American and European countries. These reductions have been attributed to early detection through mammography and improved treatment. Thus Diagnosis of breast cancer during the early stages of disease has been positively linked to a decrease in the mortality and morbidity of the illness.

1.10. BREAST CANCER SCREENING GUIDELINES
1.10.1 American Cancer Society guidelines for Breast Cancer screening with average risk

The ACS (after updating guidelines in 2003), recommends that average-risk women should begin annual mammography at age 40 years for women in their 20s and 30s, it is recommended that clinical breast examination be part of a periodic health examination, preferably at least every three years. Asymptomatic women aged 40 and over should continue to receive a clinical breast examination as part of a periodic health examination, preferably annually.

Beginning in their 20s, women should be told about the benefits and limitations of breast self-examination (BSE). The importance of prompt reporting of any new breast symptoms to a health professional should be
emphasized. Women who choose to do BSE should receive instructions and have their technique reviewed on the occasion of a periodic health examination. It is acceptable for women to choose not to do BSE or to do BSE irregularly. Screening decisions in older women should be individualized by considering the potential benefits and risks of mammography in the context of current health status and estimated life expectancy. As long as a woman is in reasonably good health and would be a candidate for treatment, she should continue to be screened with mammography.

1.10.2 American Cancer Society guidelines for breast screening with MRI for women with increased risk, (2007-2009).

Women at increased risk of breast cancer might benefit from additional screening strategies beyond those offered to women of average risk, such as earlier initiation of screening, shorter screening intervals, or the addition of screening modalities other than mammography and physical examination, such as ultrasound or magnetic resonance imaging (MRI). Annual MRI screening is recommended for BRCA carrier, like those with BRCA mutation; first degree relative with life time risk ~ 20-25% or greater, also patients who are exposed to radiation of the chest between age 10 and 30 years, and those with Li-Fraumeni syndrome (a familial cancer syndrome in which affected relatives develop a diverse set of early-onset malignancies including breast carcinoma, sarcomas, and brain tumors)
1.10.3 USPSTF Guidelines

Preventive Services Task Force (USPSTF) in the US updated recommendation statement on screening for breast cancer in the general population. The USPSTF recommends against routine screening mammography in women aged 40 to 49 years. The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take into account patient context including the patient's values regarding specific benefits and harms. Women aged 50 to 74 years should undergo biennial screening mammography (grade B recommendation).

Daniel B. Kopans, an expert in mammography screening said that the USPSTF ignored that screening only women at high risk will miss the 75-90% of breast cancers that occur in women who are not at high risk. The USPSTF also recognizes a 30% decrease in breast cancer deaths in the U.S. since 1990, but ignores it, and ignores the 40% decrease in breast cancer deaths reported in Swedish.

1.11 SCREENING METHODS

Increased breast cancer awareness with breast self-examinations and major improvements in routine breast cancer screening had a paramount effect on early detection of breast cancer. Improvements in conventional mammography (an x-ray technique to visualize the internal structure of the breast) such as the low radiation dosage, enhanced image quality, development of statistical techniques for computer-assisted interpretation of images, long-distance, electronic image transmission technologies (telemammography / teleradiology) for clinical consultations, and improved image-guided techniques to assist with breast biopsies (the removal of cells
or tissues for examination under a microscope) continue to lower the morbidity and mortality of breast cancer. The support of research on technologies that do not use x-rays and are not used for routine breast cancer screening, such as magnetic resonance imaging (MRI), ultrasound, and breast-specific positron emission tomography (PET) may play a considerable role in further improvements of breast cancer early detection. In most cases, the earlier breast cancer is detected, the better the survival rate. At present mammography is the best available method to detect breast cancer in its earliest, most treatable stage.

1.11.1 MRI (Magnetic Resonance Imaging)

MRI is a procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI). MRI does not use any x-rays. In women with a high inherited risk of breast cancer, screening trials of MRI breast scans have shown that MRI is more sensitive than mammography for finding breast tumors. Screening studies of breast MRI in women at high inherited risk are ongoing.

MRI may be used to:
- Study lumps in the breast that remains after surgery or radiation therapy.
- Study breast lumps or enlarged lymph nodes found during a clinical breast exam or a breast self-exam that were not seen on mammography or ultrasound.
- Plan surgery for patients with known breast cancer.

Benefits of MRI:
- MRI is non-invasive and does not use radiation
- MRI does not involve radiation
• MRI contrasting agent is less likely to produce an allergic reaction that may occur when iodine-based substances are used for x-rays and CT scans
• MRI gives extremely clear, detailed images of soft-tissue structures that other imaging techniques cannot achieve
• MRI can easily create hundreds of images from almost any direction and in any orientation
• Unlike techniques that examine small parts of the body (i.e. ultrasound or mammography) MRI exams can cover large portions of the body
• MRI can determine if a cancer has spread, and help to determine the best treatment

Disadvantages of MRI:
• MRI is expensive
• MRI will not be able to find all cancers (i.e. breast cancers indicated by microcalcifications)
• MRI cannot always distinguish between malignant tumors or benign disease (such as breast fibroadenomas), which could lead to a false positive results
• MRI is not painful, but the patient must remain still in an enclosed machine, which may be a problem for claustrophobic patients
• An undetected metal implant in a patient’s body may be affected by the strong magnet of the MRI unit
• There is a small chance that a patient could develop an allergic reaction to the contrasting agent, or that a skin infection could develop at the site of injection
• If a patient chooses to be sedated for the scanning, there is a slight risk associated with using the sedation medication

1.11.2 Ultra Sound

Ultrasound is an imaging test that sends high-frequency sound waves through the breast and converts them into images on a viewing screen. The ultrasound technician places a sound-emitting probe on the breast to conduct the test. There is no radiation involved. Ultrasound is not used on its own as a screening test for breast cancer. Rather, it is used to complement other screening tests. If an abnormality is seen on mammography or felt by physical exam, ultrasound is the best way to find out if the abnormality is solid (such as a benign fibroadenoma or cancer) or fluid-filled (such as a benign cyst). It cannot determine whether a solid lump is cancerous or normal.

Benefits of ultrasound:

• Can detect lesions in women with dense breasts
• Can help identify the nature of a lesion
• Widely available, and less expensive
• The only way to tell the difference between a cyst and a solid mass without using a needle to draw out fluid (non-invasive).
• Patient is never exposed to radiation during an ultrasound, allowing pregnant women to use this imaging technique.
• Can use ultrasound to detect blood flow through vessels.
• Most ultrasound exams are quick and painless.
• Ultrasounds do not cause any health problems, and there are no known harmful effects to humans.
Disadvantages of ultrasound:

• Ultrasound results may identify a potential area of concern that is not malignant. These false-positive results could lead to more procedures, including biopsies, that are not needed.
• Although ultrasound is often used in an attempt to prevent an invasive measure for diagnosis, sometimes it is unable to determine whether or not a mass is malignant, and a biopsy will be recommended.
• Many cancers cannot be detected via an ultrasound.
• Calcifications that are visible on mammograms are not visible on ultrasound scans, thereby preventing early diagnosis of the portion of breast cancers that begin with calcifications.
• Ultrasounds are not available everywhere, and not all insurance plans cover them.
• An ultrasound requires a highly experienced and skilled operator to detect a malignant lump, as well as good equipment.

1.11.3 Tissue sampling

Breast tissue sampling is taking cells from breast tissue to examine under a microscope. Abnormal cells in breast fluid have been linked to an increased risk of breast cancer in some studies. Scientists are studying whether breast tissue sampling can be used to find breast cancer at an early stage or predict the risk of developing breast cancer. Three methods of tissue sampling are under study:

• Fine-needle aspiration: A thin needle is inserted into the breast tissue around the areola (darkened area around the nipple) to withdraw cells and fluid.
• Nipple aspiration: The use of gentle suction to collect fluid through the nipple. This is done with a device similar to the breast pumps used by nursing women.

• Ductal lavage: A hair-size catheter (tube) is inserted into the nipple and a small amount of salt water is released into the duct. The water picks up breast cells and is removed

Disadvantages:

• Risk of Infection - An unavoidable disadvantage of a breast core biopsy is the small risk of infection after the procedure. Any medical procedure that breaks the skin provides an opportunity for bacteria, fungi or viruses to enter the body through the skin and colonize tissues within the breast.

• Scarring - Since a breast core biopsy uses a medium-gauge needle, patients who receive this type of breast biopsy typically develop small round scars after the procedure.

• Insufficient Tissue Collection In some cases, a breast core biopsy may have the disadvantage of not allowing the doctor to collect sufficient breast lump tissue to make a diagnosis.

1.11.4 Mammography

Mammography is one of the most important procedures in the breast cancer treatment in women. It is useful in the early detection, and diagnosis of the cancer. As a result it is absolutely necessary that mammography procedures should see the improvement in order to make it a lot more comfortable as well as secure for the women. There are several procedures that are used in mammography. The two most common methods that are
used in the mammography are the standard screen film mammography and the digital mammography.

In the standard screen film mammography an X-ray image is taken on the X-ray film. Digital mammography, also called full-field digital mammography (FFDM), is one of the most recent advances in mammography. Digital mammography is similar to conventional mammography in that x-rays are used to produce images of the breast; however, in this technology the x-ray film is replaced by solid state detectors that convert x-rays to electrical signals. These images can be displayed on the computer screen. This latest technique shows that the overall radiation dose associated with digital mammography is significantly lower than that of conventional film mammography. The radiation can be reduced by up to 50% with results as accurate as conventional mammography.

In Digital Mammography the breast image is captured using a special electronic x-ray detector, which converts the image into a digital picture. With digital imaging, the image characteristics such as brightness, contrast, magnification and orientation can be adjusted to help the radiologist during diagnosis. The key advantage of digital mammography is the ability to manipulate the image electronically.

**Advantages:**

- No waiting for the film to be developed and the radiologist can evaluate the images as they are taken. The digital images are immediately available. The patient spends less time in the exam room
- Image features can be adjusted to see subtle differences between tissues
- The digital images are easy to store and can be retrieved easily
• Digital technology provides a platform for new technologies such as CAD software for early detection of breast cancer
• Improved contrast between dense and non-dense breast tissue
• Ability to correct under or over-exposure of films without having to repeat mammograms

Although digital mammography systems are 1.5 to 4 times costlier than standard mammography equipments, this technology is gradually getting acceptance globally.

Disadvantages:
• It is less sensitive in dense breasts hence mammography can miss 10% of the cancers.
• Sometimes Mammography may misdiagnosis breast malignancies.
• Mammograms involve x-rays, Hence in continuous screening body will be exposed to more radiation

1.12 MAMMOGRAM TECHNIQUE

Mammography is at present the most reliable and widespread method for early detection of breast cancer. It is estimated that mammography can show changes in the breast for up to two years before a patient or clinician can feel them. Mammography works by using low dose x-ray to examine breasts, this is performed by a special type of x-ray machine which compresses the breast. Using x-rays as an imaging tool involves exposing the body to a small dose of ionizing radiation to produce the images. The x-rays are absorbed at different rates as they pass through various types of tissue. The variations in absorption rates provide the details of the internal breast structure. Currently both film and digital mammography are in clinical use today. Film mammography is the traditional method whereby the x-ray is made on high resolution, high contrast film. On the other hand,
Digital mammography, or full-field digital mammography (FFDM), is coming to the fore with continuing developments and advances in technology. Digital Mammography is a mammography system where the film is replaced with solid-state detectors, similar to those in digital cameras, which convert x-rays into electrical signals. These electrical signals are sent to a computer which interprets them and displays the image. One of the main advantages of using digitized mammograms is that it allows for the use of a computer-aided diagnostic (CAD) tool. Digital mammography takes an electron image of the breast and uses less radiation than film mammography, it allows image storage and transmission. Screening mammography is an x-ray study of the breast to detect breast changes in women who have no signs or symptoms of Breast Cancer. Diagnostic Mammography is an x-ray study of the Breast that is used to detect breast cancer after a lump or other signs or symptoms of BC has been found. Figure 1.8 shows example of machine for mammography.

Fig.1.8. Mammogram machine
1.12.1 Mammography Screening Process

Mammography is done by compressing the breast between two plates. Single view mammography involves taking a mediolateral view of the breast or craniocaudal view. Both views are used in screening. After the films are completed, the woman is told that she will be informed of the results within a specified period. Results are interpreted by a radiologist who should have high skills for identifying malignant and benign abnormalities. If there is any abnormality, further investigations will take place including ultrasound, fine needle aspiration, and trucut needle biopsy.

Mediolateral Oblique (MLO) view  Craniocaudal (CC) view

Fig. 1.9. Illustration of two views taken in screening mammography

1.12.2 Evidence Based Benefits of Mammography

Benefits of mammography were studied over the past twenty years. The largest study was the health insurance plan of New York, in which a group of women aged between 40 and 60 was offered a mammographic screening and physical examination annually for four years. Mortality rate
was reduced by 30% for up to ten years in women invited for breast cancer screening. A Swedish trial studied single view mammography every two years for women aged 40 years, and every three years for older women. At seven years follow up there was a reduction of mortality rate of 40% for women aged over 50 years old.

The UK government established a working group to examine the benefits of breast screening. Professor Sir Patrick Forrest chaired with establishing the National Health Breast Cancer Screening Programme (NHBCSP). The committee published its findings in 1986 which shows that screening with mammography can lead to prolongation of life for women aged 50 years or over with breast cancer. In 1991 the NHBCSP, Forrest et al published the latest research findings which concluded that if 70% of the population accepts the invitation to screening with mammography, the reduction in mortality will be 25%.

Taken together, all the results confirm the conclusion from the Swedish randomized trials, that mammographic screening is an effective means of reducing breast cancer mortality. Another benefit of mammography screening was studied by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER); it shows that since the use of screening mammography has become widespread, the proportion of patients who have locally advanced disease at diagnosis has decreased. Data which encompasses approximately 14% of the U.S. population indicates that 7% of patients have stage III disease at diagnosis.

In populations that receive regular screening mammography, the percentage of patients with locally advanced disease is less than 5%. However, since only 50% or 60% of women of the study data have had a recent mammogram, the national rates are higher. According to the SEER
data, the 3- and 5-year relative survival rates for women with stage III breast cancer are 70% and 55%, respectively. Two imaging projections of each breast, craniocaudal (CC) and mediolateral oblique (MLO) views, as shown in Figure 1.9, are routinely obtained. This permits some indication of three dimensions and an understanding of overlapping structures. High-quality mammogram with high spatial resolution and adequate contrast separation allows radiologists to observe fine structures. Studies have shown that the mortality rate could decrease by 30% if all women age 50 and older have regular mammograms.

1.13 PROBLEMS WITH MANUAL VISUAL DIAGNOSIS

1.13.1 False-negative test results can occur

Screening test results may appear to be normal even though breast cancer is present. A woman who receives a false-negative test result (one that shows there is no cancer when there really is) may delay seeking medical care even if she has symptoms.

One in 5 cancers may be missed by manual mammogram reading. False-negatives occur more often in younger women than in older women because the breast tissue of younger women is denser. The size of the tumor, the rate of tumor growth, the level of hormones, such as estrogen and progesterone, in the woman’s body, and the skill of the radiologist can also affect the chance of a false-negative result.

1.13.2 False-positive test results can occur

Screening test results may appear to be abnormal even though no cancer is present. A false-positive test result (one that shows there is cancer when there really isn’t) can cause anxiety and is usually followed by more tests (such as biopsy), which also have risks.
Most abnormal test results turn out not to be cancer. False-positives are more common in younger women, women who have had previous breast biopsies, women with a family history of breast cancer, and women who take hormones, such as estrogen and progesterone. The skill of the doctor also can affect the chance of a false-positive.

1.14 COMPUTER AIDED DIAGNOSIS (CAD) SYSTEM

1.14.1 Need of CAD System

With the wide spread development of screening programs in the USA, radiologists have had to read a large number of mammograms. Reading mammograms is difficult and requires a great deal of experience. Several studies have shown retrospectively that 20% to 40% of breast cancer fails to be detected at screening due to radiologist fatigue, the complex image structure of the breast tissue, and the subtlety of the cancer. Even the most experienced mammographic readers only have a correct detection rate of 85-91%. Moreover, a study found that there is about 2.6% to 15.9% false positive reading of negative or benign mammograms by radiologists. Several studies showed that double reading by two radiologists can improve detection sensitivity up to 15%.

However, implementing double reading can be very costly, time consuming and logistically difficult. It has been proposed that a Computer Aided Diagnostic (CAD) system be used as a second reader to assist the radiologist, leaving the final decision to the human. CAD can increase the diagnostic accuracy and efficiency with high reproducibility. It has shown that the performance of a radiologist can be increased 5-15% by providing the radiologist with results from a CAD system as a second opinion. It has also been shown that a CAD system can detect approximately 50% of the
lesions which are missed at screening. The first CAD system for screening mammography approved by USA Food and Drug Administration in 1998 was the Image Checker system from R2 Technology. The Second Look system of CAD Medical Systems is a competitor of R2. Many research works are going on to implement most efficient globally accepted CAD system.

### 1.14.2 Illustration of Computer Aided Detection

Computer-Aided Diagnosis (CAD) can be defined as a diagnosis that is made by a radiologist who uses the output from a computerized analysis of medical images as a “second opinion” in detecting lesions and in making diagnostic decisions. The final diagnosis is made by the radiologist. Most of the research in Computer Assisted reading of mammogram focuses at developing methods for detection of abnormalities, like microcalcifications, clusters, densities and stellate lesions. Successful results are reported in a number of studies.

These studies demonstrated a significant increase in radiologist’s screening efficiency when using CAD. Other research in Computer Aided Diagnosis is focused at helping radiologists in interpreting abnormalities. Impressive result has been reported for computerized characterization of microcalcification clusters and masses. However, it must be noticed that the impact of these methods in a real screening program. The Computer Aided Detection will act as a second reader in assisting the radiologists. So that it would be helpful in increasing the performance and to achieve to highest accuracy in detection. This process of double checking is illustrated in Fig 1.10.
1.14.3 Performance Definitions of Computer Aided Detection

The Receiver Operating Characteristic (ROC) is often used to evaluate computer aided detection performance. The Receiver Operating Characteristic (ROC) or free-response ROC (FROC) provides the most comprehensive description of detection or diagnostic accuracy. In computer aided detection, there are two classes: one class is cancer or the abnormal class, and the other is the normal class. The following definitions are used to describe correct classification or misclassification for each class:
True Positive (TP) = An Abnormal classified as abnormal
True Negative (TN) = A Normal classified as Normal
False Positive (FP) = A Normal classified as Abnormal
False Negative (FN) = A Abnormal classified as Normal

The classification performance is described using the percentage of correct or incorrect classification of normal or abnormal data:

True positive Fraction (TPF) = Sensitivity
\[ TPF = \frac{\text{no of abnormal classified as abnormal}}{\text{total no of abnormal}} \]

True Negative Fraction (TNF) = Specificity
\[ TNF = \frac{\text{number of normal classified as normal}}{\text{total number of normal}} \]

False Positive Fraction (FPF) = 1 - Specificity
\[ FPF = \frac{\text{number of normal classified as abnormal}}{\text{total number of normal}} \]

False Negative Fraction (FNF) = 1 - Sensitivity
\[ FNF = \frac{\text{number of abnormal classified as normal}}{\text{total no of abnormal}} \]

These four fractions are not independent. TPF+FNF=1 and FPF+TNF=1.

The goal of normal mammogram identification is to maximize TNF with very low FNF. Which is the same as minimizing FPF with very high TPF.

1.15 MAMMOGRAM DATABASE

The source of the mammograms used in this project is taken from the MIAS database, DDSM database and some real time mammograms.

1.15.1MIAS database

The Mammography Image Analysis Society (MIAS) is an organization of UK research groups interested in the understanding of mammograms which has produced a digital mammography database for research purposes. The X-ray films in the database have been carefully selected from the United Kingdom National Breast Screening Programme
and digitized with a Joyce-Lobel scanning microdensitometer to a resolution of 200 µm × 200 µm. Every image is 1024 X 1024 pixels in size. The database contains left and right breast images for 161 patients. Its quantity consists of 322 images, which belong to three classes such as normal, benign and malignant. There are 208 normal, 63 benign and 51 malignant (cancerous) images. It also includes expert radiologist's markings on the locations of any abnormalities that may be present. For each image, experienced radiologists have given the type, location, scale, and other useful information of them.

The database includes a readme file, which details the (i) type of abnormality, whether it is a radial lesion, circumscribed mass, or microcalcification, (ii) the class of the abnormality i.e. benign or malignant and (iii) the location of the center of the abnormality and its diameter.

A typical mammogram from the MIAS database is shown in Figure.1.11.

![Sample Mammogram from MIAS database](image-url)
1.15.2 DDSM database

The Digital Database for Screening Mammography (DDSM) is a resource for use by the mammographic image analysis research community. Primary support for this project was a grant from the Breast Cancer Research Program of the U.S. Army Medical Research and Materiel Command. The DDSM project is a collaborative effort involving the Massachusetts General Hospital the University of South Florida and Sandia National Laboratories. The primary purpose of the database is to facilitate sound research in the development of computer algorithms to aid in screening. Secondary purposes of the database may include the development of algorithms to aid in the diagnosis and the development of teaching or training aids.

The database contains approximately 2,500 studies. Each study includes two images of each breast, along with some associated patient information (age at time of study, ACR breast density rating, subtlety rating for abnormalities, and ACR keyword description of abnormalities) and image information (scanner, spatial resolution ...). Images containing suspicious areas have associated pixel-level "ground truth" information about the locations and types of suspicious regions. Also provided is software both for accessing the mammogram and truth images and for calculating performance figures for automated image analysis algorithms. DDSM database provides two different views such as Crasino Caudal view (CC) and Madio Lateral Oblique (MLO) view of left and right breast images. Sample image of the database is shown in the Fig.1.12.
Fig. 1.12 Two views of DDSM database Mammogram (a) A1112_1 Left cc view (b) A1112_1 Left MLO view (c) A1112_1 right cc view (d) A1112_1 right MLO view

1.16 MATLAB

The majority of the system is designed by using MATLAB. MATLAB is described by Math works, the software creator, as a high-level computing language with technical applications and environment for algorithm development, data visualization, data analysis, and numeric computation. By using MATLAB for these areas of programming the
product as a whole, language and environment, can be used to great effect as extensive specialized libraries of usage definable functions are available to the user. These are implemented by simply naming and passing parameters to their function of choice.

MATLAB can be used in a large spectrum of applications, including but not limited to signal and image processing, communications, control design, test and measurement, financial modeling and analysis, and computational biology. The functions which allow users to control and build their algorithms with such ease are stored in toolboxes. These are collections of MATLAB functions which relate to a particular application of area. For example, the image processing toolbox is used in this project. The large range of toolboxes demonstrates the extent and range of situations to which the MATLAB environment can be applied to solve particular problems in its application areas.

MATLAB also provides a number of features for documenting and sharing work. MATLAB code is compatible with other languages and applications and contains specific functions for integrating MATLAB based algorithms with external applications and languages, such as C, C++, FORTRAN, Java, COM, and Microsoft Excel. This allows developers to use solutions developed in MATLAB on existing legacy systems without difficulty. The Image Processing Toolbox is used extensively in this project.

The Image Processing Toolbox (IPT) in MATLAB provides a comprehensive set of functions for image manipulation, analysis, digital imaging, computer vision, and digital image processing. The IPT capabilities include image file I/O (including DICOM files), color space transformations, linear filtering, mathematical morphology, texture analysis,
pattern recognition, image statistics and others. The IPT contains a full reference manual with mathematical descriptions of various algorithms. The Image Processing Library contains functions for performing accelerated image processing. The initial set of functionality in the library focuses on the most popular functions used in MATLAB. This library is currently included for free with all Jacket installations.

1.17 INTRODUCTION TO DIGITAL IMAGE PROCESSING

A digital image can be considered as a large array of discrete dots, each of which has a brightness associated with it. These dots are called picture elements, or more simply pixels. The pixels surrounding a given pixel constitute its neighborhood. Simply saying it is a representation of a two-dimensional image as a finite set of digital values known as pixels. Image processing is a method to convert an image into digital form and perform some operations on it, in order to get an enhanced image or to extract some useful information from it. It is a type of signal dispensation in which input is image, like video frame or photograph and output may be image or characteristics associated with that image. Usually Image Processing system includes treating images as two dimensional signals while applying already set signal processing methods to them. It is among rapidly growing technologies today, with its applications in various aspects of a business. Image Processing forms core research area within engineering and computer science disciplines too.

Image processing basically includes the following three steps.

- Importing the image with optical scanner or by digital photography.
• Analyzing and manipulating the image which includes data compression and image enhancement and spotting patterns that are not to human eyes like satellite photographs.

• Output is the last stage in which result can be altered image or report that is based on image analysis.

The continuum from image processing to computer vision can be broken up into low, mid and high-level processes.

<table>
<thead>
<tr>
<th>Low Level Process</th>
<th>Mid Level Process</th>
<th>High Level Process</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Input:</strong> Image</td>
<td><strong>Input:</strong> Image</td>
<td><strong>Input:</strong> Attributes</td>
</tr>
<tr>
<td><strong>Output:</strong> Image</td>
<td><strong>Output:</strong> Attributes</td>
<td><strong>Output:</strong> Understanding</td>
</tr>
<tr>
<td><strong>Examples:</strong> Noise removal, image sharpening</td>
<td><strong>Examples:</strong> Object recognition, segmentation</td>
<td><strong>Examples:</strong> Scene understanding, autonomous navigation</td>
</tr>
</tbody>
</table>

**Fig.1.13 Levels of Image Processing**

In the proposed research work all the above three level processes have been used to design the automatic early mass detection algorithms. Image preprocessing and noise removal comes under low level process. Segmentation comes under the mid level process and classification comes under the High level process.

**Purpose of Image processing**

The purpose of image processing is divided into 5 groups. They are:

1. **Visualization** - Observe the objects that are not visible.
2. **Image sharpening and restoration** - To create a better image.
3. **Image retrieval** - Seek for the image of interest.
5. Image Recognition – Distinguish the objects in an image.

**Applications of Image Processing**

Image processing has wide range of applications. Some of them are listed below,

- Industrial inspection (anomalies detection, measuring (bench), tracking, monitoring…)
- Medical imaging (visualization, tumor detection, reconstruction, artifact correction, diseases quantification, …)
- Satellite Imaging (weather, environmental conditions monitoring,..)
- Microscopy (pharmaceutical, micro inspection, materials characterization,...)
- Telecommunication (transmission, compression,...)
- Cinema, image synthesis, scientific visualization
- Law enforcement (license plate reading, speed, finger print)