Oncologists world over are concerned about the high growth rate of breast cancer cases among womanhood. As this research is intended to develop techniques to detect breast cancer at an early stage, a medical perspective of breast cancer is presented in this chapter. Anatomy of female breast is explained in the beginning. The current most popular and cost effective breast imaging modality is the x ray images of breast called mammograms. The symptoms of breast cancer and biopsies required are explained. Different abnormalities that are visible in mammograms are also mentioned.
This research work is aimed at developing a new computer aided method for the early
detection of breast cancer. Therefore this chapter provides a brief insight into the
medical perspective of breast cancer.

Breast cancer is one of the best-studied human tumors, but it remains poorly
understood. Although it is certain that, breast cancer is the result of DNA alterations
(damage or mutation) that lead to uncontrolled cell proliferation, the actual etiology
of breast cancer remains obscure. A basic understanding of the anatomy and histology
of the breast is important for an understanding of the pathologic processes that occur
and are helpful for image interpretation (Kop 2007).

2.1 Anatomy of female breast

The breast generally refers to the front of the chest and medically specific to the
mammary gland (Med 2009). The breast is a mass of glandular, fatty, and fibrous
tissues positioned over the pectoral muscles of the chest wall and attached to the chest
wall by fibrous strands called Cooper’s ligaments. A layer of fatty tissue surrounds
the breast glands and extends throughout the breast. The fatty tissue gives the breast a
soft consistency (Bel 2009). The cross sectional view of female breast is given in fig
2.1.

Each breast has 15 to 20 sections, called lobes that are arranged like the
petals of a daisy. Each lobe has many smaller lobules, which end in dozens of tiny
bulbs that can produce milk. The lobes, lobules, and bulbs are all linked by thin tubes
called ducts. Toward the nipple, each duct widens to form a sac (ampulla). During
lactation, the bulbs on the ends of the lobules produce milk. Once milk is produced, it
is transferred through the ducts to the nipple (Bel 2009). These ducts lead to the
nipple in the center of a dark area of the skin called the areola (OSU 2011).

There are no muscles in the breast, but muscles lie under each breast and
cover the ribs. Each breast also contains blood vessels and vessels that carry lymph.
The lymph vessels lead to small bean-shaped organs called lymph nodes, clusters of
which are found under the arm, above the collarbone, and in the chest, as well as in
many other parts of the body (OSU 2011).
The shape and appearance of the breast undergo a number of changes as a woman ages. In young women, the breast skin stretches and expands as the breasts grow, creating a rounded appearance. Young women tend to have denser breasts (more glandular tissue) than older women (Bel 2009).

A woman’s breasts are rarely balanced (symmetrical). Usually, one breast is slightly larger or smaller, higher or lower, or shaped differently than the other. The size and characteristics of the nipple also varies from one woman to another. During each menstrual cycle, breast tissue tends to swell from changes in the body’s levels of estrogen and progesterone. The milk glands and ducts enlarge, and in turn, the breasts retain water (Bel 2009).

During pregnancy, a variety of breast changes occur. Typically, breasts become tender and the nipples become sore after a few weeks of conception. The
breasts also increase in size very quickly. The nipples also become larger and more erect as they prepare for milk production.

The breasts’ glandular tissue, which has been kept firm so that the glands could produce milk, shrinks after menopause and is replaced with fatty tissue. The breasts also tend to increase in size and sag because the fibrous (connective) tissue loses its strength. It is easier for the radiologists to detect cancer on older women’s mammogram films, since the breast becomes less dense after menopause. The abnormalities will be more visible as breast is less dense. Since the risk of breast cancer increases with age, all women should undergo annual screening of mammograms after the age of 40, and continue monthly breast self-exams and physician-performed clinical breast exams every year.

2.2 Breast Cancer

Cancer begins in the cells which are the basic building blocks of the body and it is named after the place from where it originates. Normally, body forms new cells as needed, replacing old cells that die (NLM 2010). This is a normal, controlled process. However, there is a chance that this orderly process could be disturbed and cells begin to reproduce in an abnormal way (Min 2003). New cells grow even when it is not needed. These extra cells can form a mass called a tumor (NLM 2010).

Tumors can be benign or malignant. Benign tumors remain similar to the tissue of their origin. Generally, benign tumors are not cancerous while malignant ones are. Cells from malignant tumors can invade nearby tissues. They can also break away and spread to other parts of the body (Kop 2007).

When a tumor spreads to other parts of the body and grows, invading and destroying other healthy tissues, it is said to have metastasized. This process is called metastasis, and the result is a serious condition that is very difficult to treat (MNT 2004).

Alterations of considerable extent are present in the mammary duct epithelium of each breast which contains a primary carcinoma, whether infiltrating or non-infiltrating (Gal 1969).
At present, high quality mammography is the diagnostic method with the proven highest accuracy in finding early breast cancer at the lowest cost–benefit and harm–benefit ratios (Tab 2003). If it is detected at an early stage, the survival rate of the patients can be increased.

On mammogram films, breast masses, including both non-cancerous and cancerous lesions, appear as white regions. Fat appears as black regions on the films. All other components of the breast (glands, connective tissue, tumors, calcium deposits, etc.) appear as shades of white on a mammogram. In general, for younger woman the breasts are denser. As woman ages, her breasts become less dense and the space are filled with fatty tissue shown as dark areas on mammography x-rays (Bel 2009).

If two or more readers review these mammogram images, it reduces the failure to perceive an abnormality. Unfortunately, two radiologists reviewing every image are not practical. Nevertheless, it is a way to reduce the chance of overlooking a cancer on a mammogram. Computer-aided diagnosis (CAD) comes as a help in this problem. Double reading, may mean a review by two readers to reduce errors of perception, or it may be considered as double interpretation, where the second reader may decide on the concerns raised by the first reader as warranted or not (Kop 2007).

The most popular methods for interpreting mammograms presented in the Atlas of mammography by Tabar (Tab 2001) are discussed in the next section.

2.3 Breast Imaging

Different breast imaging (Pau 2005) modalities which help in the diagnosis of breast cancer are discussed in this section.

2.3.1 Magnetic Resonance Elastography (MRE)

In this technique, mechanical vibrations are applied to the breast’s surface that propagates through the breast as a three-dimensional, time-harmonic spatial displacement field varying locally with the mechanical properties of each tissue region. These data are used to optimize a Finite Element (FE) model of the breast’s
three-dimensional mechanical property distribution by iteratively refining an initial estimate of that distribution until the model predicts the observed displacements as closely as possible.

2.3.2 Electrical Impedance Spectroscopy (EIS)

EIS passes small AC currents through the pendant breast by means of a ring of electrodes placed in contact with the skin. Magnitude and phase measurements of both voltage and current are made simultaneously at all electrodes. The observed patterns of voltage and current are a function of both the signals applied and of the interior structure of the breast. EIS is referred to as electrical impedance spectroscopy because AC currents can be applied to the breast at a wide range of frequencies.

2.3.3 Microwave Imaging Spectroscopy (MIS)

Like EIS, MIS interrogates the breast using EM fields. It differs in using much higher frequencies (300–3000 MHz). In this range it is appropriate to treat EM phenomena in the breast in terms of wave propagation rather than voltages and currents. The technologies and mathematics used in EIS and MIS are, therefore, divergent, despite the fact that both exploit EM interactions in tissue.

2.3.4 Near Infrared Spectroscopic Imaging (NIS)

In NIS, a circular array of optodes (in this case, optical fibers transcribing infrared laser light) is placed in contact with the pendant breast. Each optode in turn is used to illuminate the interior of the breast, serving as a detector when nonactive. A two or three-dimensional FE model of the breast’s optical properties is iteratively optimized until simulated observations based on the model converge with observation.
2.3.5 Ultrasound

An ultrasound device that uses high frequency sound waves which bounce off tissues and echoes are converted to pictures. The pictures produced show whether a lump is solid or filled with fluid. This exam may be used along with a mammogram (Bel 2009).

2.3.6 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) uses a powerful magnet linked to a computer (Bel 2009). MRI makes detailed pictures of breast tissue. MRI may also be used along with a mammogram.

The most common breast imaging modality is the mammogram and is explained in the next section.

2.4. Mammography

Mammography is a radiographic examination that is specially designed for detecting breast pathology. It is the single most important technique in the investigation of breast cancer. It can detect disease at an early stage when therapy or surgery is most effective (Dou 2009), (Bic 2010). A mammogram is a picture of the breast that is made by using low-dose x-rays (Bel 2009).

X-ray mammography is one of the most challenging areas in medical imaging. It is used to distinguish subtle differences in tissue type and detect very small objects, while minimizing the absorbed x-ray dose to the breast. Since the various tissues comprising the breast are radiologically similar, the dynamic range of mammograms is low. Most modern x-ray units use molybdenum targets, instead of the usual tungsten targets, to obtain an x-ray output with the majority of photons in the 15–20 keV range (Dou 2009).
To see lesions in dense fibro glandular tissue, the x-ray beam should be sufficiently energetic to penetrate these tissues. The American College of Radiology (ACR) recommends that the least penetrated tissues on a film/screen mammogram (the whitest areas) measure 1.0 or higher on a densitometer. This is a level at which structures can be seen through the dense (white) portions of the mammograms. There must also be sufficient penetration on a digital mammogram so that structures are also visible in the least penetrated areas (Kop 2007), (Bus 2002).

However the interpretation of screening mammograms is a repetitive task involving subtle signs, and suffers from a high rate of false negatives (10–30% of women with breast cancer are falsely told that they are free of the disease on the basis of their mammograms (Mar 1979), and false positives (only 10–20% of masses referred for surgical biopsy are actually malignant.

### 2.5 Finding Breast Changes

Screening is looking for cancer before a person has any symptoms (Bel 2009). This can help to find cancer at an early stage. When cancer is found early, it is easier to treat. By the time symptoms appear, cancer may have begun to spread. Three tests are commonly used to screen for breast cancer:

- **Mammogram**: Taking the x-ray of the breast.
- **Clinical breast exam (CBE)**: A clinical breast exam is an examination of the breast by a doctor or other a health professional. The doctor will carefully feel the breasts and under the arms for lumps or anything else that seems unusual.
- **Breast self-exam (BSE)**: Breast self-exam refers to examination to check their own breasts for lumps or anything else that seems unusual.

While screening mammography attempts to identify breast cancer in the asymptomatic population, diagnostic mammography are performed to further evaluate abnormalities such as a palpable mass in a breast or suspicious findings identified by screening mammography. In screening mammography, two x-ray images of each breast, in the mediolateral oblique and craniocaudal views are
routinely acquired. Early detection of cancer gives the patient the best chance to have the disease successfully treated. The American Medical Association, American Cancer Society, and American College of Radiology have recommended yearly mammogram for women, after the age of forty.

### 2.5.1 Medio Lateral Oblique and Cranio Caudal

Screening mammography involves taking two views of the breast, from above (cranial-caudal view, CC) and from an oblique or angled view (mediolateral-oblique, MLO) (NLM 2010) and is shown in fig. 2.2.

The mediolateral oblique view (MLO) is taken from an oblique or angled view. During routine screening mammography, the MLO view is preferred over a lateral 90-degree projection because more of the breast tissue can be imaged in the upper outer quadrant of the breast and the axilla (armpit).

The cranio-caudal view (CC) images the breast from above. With the CC view, the entire breast parenchyma (glandular tissue) should be depicted. The fatty tissue closest to the breast muscle should appear as a dark strip on the x-ray and behind that it should be possible to make out the pectoral (chest) muscle. The nipple should be depicted in profile.

![Fig 2.2](image)

Fig 2.2 Two views of the breast (a) Cranio Caudal View (b) Medio Lateral View
2.5.2 Symptoms

Symptoms of breast cancer can vary depending on the stage it is in. There may not be visible symptoms in the early stages of breast cancer. Usually there is no pain or any other sign associated with breast cancer.

As the cancer grows it can cause changes in the breast (Bel 2009). Some of them are:

- A lump in or near the breast or under arm
- Thick or firm tissue in or near the breast or under arm
- Nipple discharge or tenderness
- A nipple pulled back (inverted) into the breast
- Itching or skin changes such as redness, scales, dimples, or puckers
- A change in breast size or shape

Since risk of breast cancer increases with age, monthly breast self-exams and physician-performed clinical breast exams every year are preferred (Bel 2009).

Once a change in the breast is sensed, biopsy and histological examination are generally necessary to determine whether the abnormality identified by the imaging methods is benign and harmless or malignant and life threatening.

2.5.3. Biopsy

If a breast lump is suspicious, a sample of tissue or fluid must be taken and tested by a pathologist (Bel 2009). There are four methods for biopsy:

*Fine needle aspiration (FNA)*

A very fine needle is used to remove out some fluid and/or cells, which will be examined under a microscope. FNA is the fastest and easiest method of breast biopsy, and the results are rapidly available.
Core needle biopsy

The needle used during core needle biopsy is larger than the needle used with FNA. The surgeon puts this needle through the skin and into the suspicious regions in the mammograms which are palpable and non-palpable tissue samples are taken. The sample is then sent for lab tests.

Vacuum-assisted biopsy (Mammotome or minimally invasive breast biopsy)

This relies on the suspicious regions identified by the stereotactic mammography or ultrasound imaging. The computer coordinates will help the physician to guide the needle to the correct area in the breast. Vacuum-assisted biopsy is a minimally invasive procedure that allows the removal of multiple tissue samples. After the biopsy is complete, the tissue samples will be sent to the pathology laboratory for diagnosis.

Open surgical (excisional or incisional)

During an excisional surgical biopsy, the surgeon will attempt to completely remove the area of concern (lesion), often along with a surrounding margin of normal breast tissue. An incisional surgical biopsy is similar to an excisional biopsy except that the surgeon removes only the part of the breast lesion and is usually only performed on large lesions.

2.6 Normal mammograms

Unfortunately, there is no normal appearance on a mammogram that can be memorized. What constitutes “normal” varies within a wide spectrum. In addition, the appearance of the breast differs during pregnancy and in the post partum period. This spectrum is due to the difference in the breast composition. Snippets of normal mammograms are shown in fig 2.3.
A breast with a high composition of adipose tissue will appear darker on a mammogram than a breast with a high composition of connective tissue stroma (tighter). Other normal variations of breast tissue include asymmetric patterns and asymmetric size. Although the breasts usually develop symmetrically, differences in the symmetry of the breast tissue patterns or breast size are not necessarily abnormal. Without other indices of an abnormal process, such asymmetry may simply be a development phenomenon.

2.7 Abnormalities in the breast

This section describes the different abnormalities that are seen in the mammograms.

2.7.1 Calcifications

A calcification is a deposit of the mineral calcium in the breast tissue. Calcifications appear as small white spots on a mammogram (Bel 2009). There are two types:

*Macrocalcifications* are large calcium deposits often caused by age. These are not usually cancerous.

*Microcalcifications* are tiny specks of calcium that may be found in the area of rapidly dividing cells. If they are found grouped together in a certain way, it may be a sign of cancer.
Calcium in the diet does not create calcium deposits (calcifications) in the breast. A cluster is typically defined as 3 to 5 microcalcifications within 1 square centimeter region. Up to 50% of malignant masses demonstrate clustered microcalcifications and in a number of cases the clusters are the only signs of malignancy.

Suspicious calcifications occur in about one third of breast cancers and may develop prior to the invasive phase of tumor growth (in situ cancer) when cancer is most curable. Calcium deposits are easy to be seen in x-rays because they are much denser (have higher x-ray stopping power) than all types of soft tissues in the breast. Calcifications associated with cancer are usually very small. However, calcifications commonly occur in benign breast processes where they may be confused with cancer. Examples of malignant and benign microcalcifications are shown in fig. 2.4 and 2.5 respectively.

Malignant microcalcifications vary extremely in form, size, density and number. They are usually clustered within one area of the breast, often within one lobe. They are two types: granular and casting.

**Pleomorphic or heterogeneous calcifications (granular):** These are tiny calcifications with dot like or elongated shape and are innumerable. They are varying in size, usually less than 0.5mm. Fine and/or branching (casting) calcifications: these are thin irregular calcifications that appear linear, but are discontinuous and under 0.5mm in width. They are often associated with cancer and clearly merit immediate biopsy.
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**Fig 2.4** Examples of Malignant Microcalcifications (a) Original Mammograms with Malignant Microcalcifications (b) Region containing Microcalcifications (c) Some snippets of Malignant Microcalcifications

**Fig 2.5** Examples of Benign Microcalcifications (a) Original Mammograms with Benign Microcalcifications (b) Region containing Microcalcifications (c) Some snippets of Benign Microcalcifications
Benign microcalcifications are characterized by homogeneous shape, density, sharp outline or radio lucent density. They are usually larger than that associated with malignancy. They are coarser, often round with smooth margins and they are easily seen.

*Skin calcifications*: these are typically dense smooth and lucent centers (less dense in center than margin) that are pathognomonic (appearance is always benign). They are situated in the skin, resulting from calcium deposits in hair follicles and are more common in the center of the chest at the inner edge of the breast.

*Vascular calcifications*: they are parallel paired tracks or linear tubular calcifications that are clearly associated with small arteries.

*Coarse or pop corn like calcifications*: Rounded groups of coarse calcifications develop in an involution fibro adenoma. When completely developed the appearance is reliable, but during early phases of development, calcifications in fibro adenomas may be suspicious.

*Large rod shaped calcification*: these are benign calcifications forming continuous rods that may occasionally branch. They are usually more than 1mm in diameter and may have lucent center, if calcium surrounds rather than fills an enlarged duct.

*Round calcifications*: they are smooth dense and round calcifications with size less than 1mm.

*Spherical or lucent centered calcifications*: These are benign calcifications that range from under 1mm to over a centimeter. These deposits have smooth surfaces, are round or oval and tend to have a lucent center. They arise from areas of fat necrosis, calcified ducts debris and occasional *fibro adenoma* of a duct involved irregularly by breast cancer.

### 2.7.2 Masses

The presence of a localized collection of tissue represents a mass. By ACR BIRADS definition, a mass is a space occupying lesion seen in 2 different projections (X-rays point of view). When an apparent collection is seen in only one view, it is
referred to as a mammographic density. Although the density may be of a mass perhaps obscured by overlying glandular tissue on other views, it may be nothing more than several overlapping normal areas. When a density is seen in only one view, additional views must be done to confirm the presence of a mass.

Circumscribed masses have a distinct border and are typically circular in shape. High density radio lucent /radio opaque combined masses are almost always benign.

Halo and capsules are characteristics of benign masses with rare exceptions. A halo is a narrow radiolucent ring or a segment of a ring around periphery of a tumor. A capsule is a thin curved radio opaque line that is seen only when it surrounds tumors containing fat. A cyst with smooth borders and orienting in the direction of the nipple following the trabecular structure of the breast also indicates a benign lesion. Contour density, shape, orientation and size of the mass are important factors to be considered when analyzing a visible mass. General shape of a mass is relatively non specific since both benign and malignant processes tend to arise from one spot and grow circumferentially. Examples of circumscribed and spiculated masses are shown in fig. 2.6 and 2.7 respectively.

Round and oval shapes are associated with benign processes in part because they imply a well circumscribed region, a benign sign considered in the margins section.

Fig 2.6 Examples of circumscribed mass
Round, oval and lobular shape: Masses in these categories imply a well defined smooth edge and is often benign. If their margin is not smooth, their shape alone does not tend to exclude malignancy. Mammograms with benign and malignant circumscribed masses are shown in fig. 2.8 and 2.9 respectively.

*Irregular shape:* irregular shapes tumor infiltrating edges are of more concern, because they imply indistinct and more often malignant cases.

**Fig. 2.7** Examples of Spiculated Mass

**Fig. 2.8** Benign circumscribed mass (a) Original Mammogram with Benign circumscribed mass (b) Region containing Benign circumscribed mass
2.7.3 Architectural distortions

In this case, the normal outline of tissues is distorted, sometimes with no definable mass. It includes spiculations (line radiating from a center) and retraction of normal tissue planes where it causes contraction, which can be seen before an actual mass.

Architectural distortion occurs with healing after injury including previous biopsy and so it is critical to determine if the area has been injured. Benign causes of architectural distortion such as scarring tend to remain unchanged or improve. So one has to compare and observe if changes have really occurred. Fig. 2.10 illustrates the architectural asymmetry in mammograms.
2.7.4 Spiculated lesions

Spiculated lesions appear as star shaped with blurred borders. They are almost always malignant. Generally, the lesion has a distinct central tumor mass with dense spicules radiating in all directions. The spicule length usually increases with tumor size. Occasionally translucent, oval or circular center or translucent areas within a loose structure and low density spicules characterize benign spiculated lesions. Examples of malignant and benign spiculated lesions are presented in fig 2.11.
2.8 Chapter Summary

This chapter presents a brief introduction to the breast cancer. Different breast imaging techniques that are available today are also discussed here. The most commonly used breast imaging modality is the mammography and is explained in detail. The abnormalities that can occur in the breast are described as well.