Chapter 2

DIGITAL MAMMOGRAMS AND PLACENTAL SONOGRAMS – AN OVERVIEW OF THE BACKGROUND

2.1 Introduction

Recent developments in computer technology have tremendous impact on medical imaging. Modern radiological modalities perform well when integrated with computers. The recent improvements in breast cancer screening and foetal monitoring result from the developments in modern imaging technology. There has been a significant increase in the area of Computer Aided Diagnosis of both breast cancer and placental maturity analysis. This chapter gives a concise background of the problem under study.

2.2 Digital Mammogram for Breast Cancer Detection

Rapid and uncontrolled growth of abnormal cells results in cancer. The division and proliferation of cells lead to the formation of tumor. Depending on the biological behavior of a tumor it can be classified into benign or malignant. If the tumor does not invade to surrounding tissue it is called benign and if it invades and metastasis to surrounding, it is a malignant tumor [12]. The four predominant types of cancer are Carcinomas, Sarcomas, Leukemias and Lymphomas. Breast cancer is a type of Carcinoma. According to 2013 statistics of American Cancer Society [13], approximately 2,32,340 new cases of invasive breast cancer 64,640 non invasive breast cancer and 39,620 breast cancer deaths are expected to occur in U.S. women. In 2011 the statistics were 2,30,480,
57,650 and 39,520 respectively [14]. In 2005, 211,240 new cancer cases and 40,410 cancer death are reported [15] and in 1999, it was 175,300 and 43,300 respectively [16]. According to the breast cancer statistics in INDIA, 144,937 women were newly detected with breast cancer and 70,218 women died of breast cancer in 2012. In 2008, the numbers were 115,251 and 53,592 respectively [17]. These statistics alarm the urgency in early detection of breast cancer. In this section a brief view of risk factors, symptoms, diagnosis, treatment of breast cancer, importance of digital mammography and need of computer aided diagnosis of breast cancer are discussed.


Figure 2.1 Characteristics of benign and malignant tumors
2.2.1 Breast anatomy

Anatomically breast is located within the superficial fascia of the anterior thoracic wall. It overlay the pectoral muscle and extends from the level of second and third rib to the intra mammary fold, which is at the level of sixth or seventh rib of human rib cage. Each breast has fifteen to twenty lobes of glandular tissues that radiate and open at the nipple. The lobules that are present in the small chamber of lobes contain clusters of alveolar glands that produce milk. The alveolar gland passes milk to lactiferous duct. The breast anatomy is given in Fig. 2.2. Breast cancer can arise in different areas of breast like duct and lobules. The epithelial cells present in the lactiferous ducts or lobules can easily develop to malignant tumor. According to the involvement of different tissues and the severity, breast cancer is classified into ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), lobular carcinoma in situ (LCIS), invasive lobular carcinoma (ILC) and inflammatory breast carcinoma (IBC).

(Source: https://en.wikipedia.org/wiki/Breast)

Figure 2.2 Breast anatomy

1. Chest
2. Pectoralis muscles
3. Lobules
4. Nipple
5. Areola
6. Milk duct
7. Fatty tissue
8. Skin
2.2.2 Breast cancer risk factors and symptoms

In the current decade rapid improvement has occurred in understanding the cause and diagnosis of breast cancer [18]. Gender and age are the strongest risk factors. Family history with genetic mutation in BRCA1 and BRCA2 increases the chance of developing breast cancer. Reproductive functionalities such as nulliparity, late age at first pregnancy, early menarche and late menopause are also shown to increase risk. Breast density is a powerful risk factor for diverse subtypes of breast cancer. Environmental causes like exposure to radiation, use of pills and hormone replacement therapy, life style, alcohol consumption, high intake of fat and animal protein, smoking and obesity are also some established risk factors of breast cancer. Maintaining a healthy life style by balancing the weight, increasing physical activity, avoiding alcohol and smoking and the like can reduce breast cancer risk. Any change in the size or shape of breast, change in armpit, change in nipple, thickening or presence of lump in the breast and puckering appearance of the skin are some of the common symptoms of breast cancer.

2.2.3 Diagnosis methods

Advancing the frontiers of medical imaging requires the knowledge and use of latest imaging technologies. Diagnosis techniques should be able to characterize the tumor. It should be able to identify and map the structural and morphological differences in tumor like solid mass, calcium deposits, breast asymmetries, architectural distortion and angiogenesis. Above all, the diagnosis methods should be practical, inexpensive and harmless. Mammography, MRI, Ultrasound, PET are the commonly available methods used for breast cancer diagnosis [19].
Mammography

Mammography allows intervention at an early stage of cancer progression. Early detection of lesions using mammogram reduces disease specific mortality. Mammogram findings vary depending on the physical, mechanical and biological characteristics of tissue under examination. The principles and use of mammography are detailed in section 2.2.6.

MRI

Magnetic Resonance Imaging (MRI) provides excellent identification of structural abnormalities in breast. Compared with ultrasound and mammogram, MRI offers improved visualization of multi focal and multi-centric lesions, high sensitivity, and determination of chest wall invasion which leads to excellent staging of breast cancer. The cost of MRI is high compared to other diagnostic methods.

PET

Positron Emission Tomography (PET) uses a radioactive material to produce 3-D image of the functional characteristics of the body. Computerized reconstruction of the image provides better recognition. It performs excellent in neo-adjuvant chemotherapy (change in metabolism) compared to other diagnostic methods. Anatomic and metabolic functions of the organ can be obtained by combining PET with MRI and CT.

Ultrasound

Ultrasound imaging is used as an adjuant to mammography. In case of a doubt lesion, after mammogram, ultrasound can be used to detect whether the lesion is a cyst or solid mass. According to the nature of the tissue, the
response of the ultrasound varies. The use of 3D ultrasound imaging permits proper localization of tumor and measurement of tumor volume.

**Other Common Systems**

Scintimammography is a nuclear medicine approach that relies on the emission of radioactive substances from tracers that are injected into the body. The effect of tracers is more pronounced in cancerous tissue than in normal tissue. Therefore malignant tissues can be easily distinguished from benign tissues. Following are some of the techniques that are under active investigation. Magnetic Resonance Spectroscopy (MRS), Thermography, Electrical Impedance Imaging, Electronic Palpation and Full Field Digital Mammography (FFDM).

**2.2.4 Treatment and prevention**

Depending on the stage and biological characteristic of the tissue, the physician will recommend the type of treatment best suited for the patient. The patient’s age, preference of treatment, general health, size of tumor, involvement of lymph node and presence of hormone receptors play a vital role in physician’s decision making. The main treatments are surgery, radiotherapy, chemotherapy, hormone therapy and targeted therapy. Either one of these or a combination of more than one can be applied for immediate cure.

**2.2.5 Importance of digital mammography**

- Small, safe dose of radiation is used.
- Less Expensive.
- Can identify breast cancer when it is very small - 2 to 3 years before you can feel it.
2.2.6 Principles of digital mammography

Mammogram provides information about breast morphology, normal anatomy and gross pathology. Mammographic unit use X-rays to produce images of the breast. Mammographic system includes an X-ray generator, an X-ray tube and gantry, and a recording Medium [20]. The X-ray generator modifies received voltage to supply the X-ray tube with the power required to generate an X-ray beam. Low energy X-rays are generated by the X-ray tube when a stream of electrons, step up to high velocities by a high-voltage supply from the X-ray generator, bump with the tube’s target anode. The cathode includes a wire filament that, when heated, produces the electron source. The target anode is struck by the impinging electrons. X-rays leave the tube through a port window of beryllium. The filters in the pathway of X-ray beam adjust the X-ray spectrum. The incoming X-rays are shaped by either a collimator or cone apertures and then passed through the breast. Fig. 2.3 explains the basic principle of mammogram image formation.

![Mammogram Unit](image1)

**Figure 2.3** Mammogram image formation

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2.2.7 Breast abnormality detection using digital mammograms

Early screening using X-ray mammography could reduce death rate due to breast cancer by detecting and treating when cancers are very small [21]. Mammographic examination generally consists of two views; Craniocaudal (CC) and Mediolateral Oblique (MLO) as in Fig. 2.3. Mammography interpretation involves screening for abnormal tissues and diagnosis of the detected abnormalities. According to Breast Imaging Reporting and Data Systems (BIRADS), the major signs in X-ray mammogram are masses, microcalcification clusters, architectural distortions and bilateral asymmetry. In diagnostic mammogram the morphology of benign and malignant tissues is different. It is depicted in Fig. 2.4. In the examination of mammogram images, the following abnormalities are taken care of:

1. Soft tissue density especially if borders are not well defined.
2. Clustered microcalcification in specific areas.
3. Calcification within or closely associated with a soft tissue density.
4. Asymmetric density or parenchymal distortions.

Breast cancers are radiodense which appears as bright spots in mammogram and fat is radiolucent that appear in colour ranging from dark grey to black. Dense fibroglandular fat tissue can obscure small cancers. The proportion of fat to fibroglandular tissue is called breast density. Women with dense breast have a higher percentage of fibroglandular tissue than fat tissue. The mammographic breast composition defined by BIRADS [22], which is a quality assurance tool, designed to standardize mammographic reporting is as follows.
Type 1: The breast is entirely fat. 
Type 2: Scattered fibroglandular densities, 25 % to 50%. 
Type 3: Heterogeneously dense breast tissue, 51 % to 75%. 
Type 4: Extremely dense, > 75 % glandular. 

**Mass**

Mass is a space occupying lesion seen at least in two different mammographic projections. Mass is called an asymmetric density when seen only in a single projection. Mass can be mainly divided into the following three categories.

1. **Spiculated Mass**

   It is an indication of invasive breast cancer characterized by radiating spicules from a central soft tissue.

2. **Circumscribed Mass**

   It is an indication of a benign condition with well defined or sharply defined margin. Features such as number, margin and density need to be carefully analysed.

3. **Non specific soft tissue densities**

   This is the main reason for small cancers. These appear in some specific areas.

   In general, masses with irregular shape and ill defined or speculated margin are more likely to be malignant and masses with circumscribed oval shape are usually benign.
Figure 2.4 Sample mammogram images of malignant and benign masses

**Microcalcifications**

These are tiny flecks of Calcium, which show up as bright white spots on mammogram [23]. Microcalcifications are characterized by their distribution, that is, they appear either isolated or in clusters. The morphology of malignant microcalcification and benign microcalcification is different. Size of an individual microcalcification varies from 0.1 to 10 mm with an average diameter of about 0.5 mm. The presence of three or more microcalcifications within 1 cm² defines a cluster. The size, shape, contrast and distribution of location of microcalcification in a cluster are used for characterizing the individual and cluster regions of microcalcification. The characteristics of malignant microcalcification are, they are numerous in number, more densely packed, small, varying in size and orientation [1]. Benign calcifications are larger, more rounded, smaller in number, less densely packed and more homogeneous in size and shape as in Fig.2.5.
Digital Mammograms and Placental Sonograms - an Overview of the Background

Architectural Distortion

The normal architecture is distorted with spiculations radiating from a point and focal retraction or distortion of the edges of the parenchyma.

Focal Asymmetry

Focal asymmetry and global asymmetry are the two types of bilateral asymmetries present in mammogram images. Focal asymmetry is difficult to describe as it lacks borders and conspicuity of a true mass. When the amount of fibroglandular tissue in one breast is high compared to the other in the same area, it leads to global asymmetry [24].

In general the presence of defined margin around suspicious area indicates a benign lesion [25]. Usually malignant lesions may not have defined margin. The benign tumor is relatively slow in growing and does not invade to surrounding tissue. In contrast malignant tumors have rapid growth and are able to metastasis.
Limitations of Mammography

- Normal breast structures may obscure cancerous lesions particularly in dense breast with high composition of fibroglandular tissues.
- Superimposed tissue can cause unnecessary recall after diagnosis.
- Complex structures can mask abnormality.
- Inter-intra observer variability is high.
- Low positive predictive value for biopsy recommendations.
- Chances of misinterpretation leading to high false positive and false negative.
- Wrong interpretations may sometimes lead to over diagnosis and over treatment.

2.2.8 Computer Aided Diagnosis (CAD) in breast cancer screening

Computerized image analysis has been used over the past twenty years in order to achieve good results in diagnosis. Generally CAD systems are of two types: Computerized Aided Detection (CADe) and Computerized Aided Diagnosis (CADx) [1]. Both CAD schemes are useful for better localization and characterization of abnormalities. CADe schemes are used in screening mammography and CADx schemes are used in diagnostic mammography. CAD involves selection of different cases, interpretation of cases using computer algorithms, validation of algorithm, case performance evaluation by radiologist and final performance evaluation by clinical trials. Different steps like thresholding, Region of Interest (ROI) extraction, calculation of intelligible features to discriminate the segmented structures and
classification of lesions using extracted features can be done with high precision using CAD systems [26].

**Advantages of CAD**

- CAD can reduce the oversight of suspicious lesions.
- It can provide additional information for making biopsy recommendation.
- It improves radiologist’s detection accuracy.
- CAD provides a second opinion by overcoming the limitations posed by human visual system.
- It helps in correct decision making even at the presence of overlapping tissue parenchyma.
- Assist radiologists in the interpretation of radiology images and directs their attention to the ROI.
- The results are reproducible and realistic.
- It can easily identify signs of pathology which the radiologist can further review.
- It reduces cost of double reading by improving the accuracy of individual reading.

**2.3. Placental Sonograms**

In this section we discuss the principles of ultrasound imaging, use of ultrasound imaging in obstetrics, relevance of placental grading and need of automated grading of placental sonograms.
2.3.1 Principles of ultrasound imaging

Ultrasound imaging uses [27] sound waves of frequency in the range 1 to 15 MHz. Compared with existing medical imaging modalities, it is real time, inexpensive, non ionizing and safe. Parameters that are described by ultrasound are pressure, density, propagation direction, wavelength and particle displacement. Ultrasound is a kind of sinusoidal pressure wave. In ultrasound machines, the images of the biological tissues are constructed by transmitting focused beam of sound waves into the human body using a transducer. The sound waves that are reflected back determine the structure of the tissue being imaged. Fig. 2.6 explains the process of ultrasound image formation [28].

![Ultrasound image formation](image)

The transmit voltage applied to the transducer generates acoustic pressure at the phases of the transducer. A fraction of the waves from the propagated sound waves are reflected back on reaching the tissue surface depending on the acoustic impedance of the tissue along the path of the beam. The echo signals that are reflected back are converted to electrical signals. These signals are amplified and processed to produce ultrasound
images. The brightness of the formed image depends on the reflected echoes. The delay between pulse transmission and pulse reception, and the speed of propagation can be used for calculating the depth of the feature.

Ultrasound has two modes. A - mode (Amplitude mode) and B - mode (Brightness mode). The uses of A - mode are detection of eye tumor, liver cirrhosis and myocardial infarction whereas B - mode is used to produce 2-D Tomographic images by sweeping the beam repeatedly back and forth through the anatomical structure. Example:- Foetal monitoring.

### 2.3.2 Ultrasound in obstetrics

Ultrasound imaging has been actively applied to abdominal, breast, heart, blood vessel, and foetus imaging. It provides correct visualization of the internal parts of the body, measures blood flow and elasticity. The advances in healthcare over decades have resulted in the development of various computerized methods and tools to support foetal monitoring. Ultrasound is the ideal imaging technique for foetal monitoring. Structural anomalies of the foetus are best seen on ultrasound scan and therefore clinicians suggest that all mothers should be offered at least one thorough ultrasound scan at around 18-20 weeks or earlier [29]. Foetus’s growth pattern is well explained in ultrasound. Prenatal diagnosis is very important as it can identify an early gestation abnormality.

### 2.3.3 The Placenta

Placenta is a foetomaternal organ that is in close contact with mothers body [30]. Development of placenta begins as soon as the foetal membrane establishes close and stable contact with uterine mucosa, that is, as soon as the blastocyst implants [31]. Placenta helps to exchange respiratory gases,
nourishments, extracts waste between mother and foetus. It starts functioning close to the fourth gestational week like an endocrine organ and provides necessary support for the development of a healthy foetus [32].

Human placenta appears as a disk like thickening of the membranous sac formed by chorionic plate and basal plate [33]. Pathology of human placenta is shown in Fig.2.7. Both the sheets enclose intervillous spaces. The intervilloous space contains maternal blood which circulates around the placental villi. The villi are complex tree like projections of the chorionic plate into the intervillous space. The foetal vessels present inside the villi are attached to the circulatory system via chorionic plate and umbilical chord. The chorionic plate and basal plate are combined to each other at the placental margin and forms chorion leaves.

(Source: Benirschke et al., Pathology of the human placenta, Springer, 2006)

**Figure 2.7 Placental pathology**
Major Functions of Placenta

- Foetal oxygenation.
- Endocrinological functions.
- Protein synthesis.
- Protective functions.
- Catabolic and resorptive functions.
- Synthetic and secretory functions of liver.
- Hematopoiesis of the bone marrow during first trimester.
- Heat transfer of the skin.
- Immunological functions.

2.3.4 Placental grading

Calcification is a normal degenerative process in placenta that increases with gestational age (age between conception and birth) and appears as irregularly distributed. According to the difference in texture patterns and appearance of placental body Grannum et al. [5] grouped placenta into different grades. The characteristics during different gestational period and corresponding grades are given in Table 2.1.

### Table 2.1 Characteristics of different grades of placental images

<table>
<thead>
<tr>
<th>Grade</th>
<th>Gestational period</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero</td>
<td>Late first trimester – Early second trimester</td>
<td>Smooth chorionic plate with no indentations, homogeneous appearance of placental body.</td>
</tr>
<tr>
<td>One</td>
<td>Mid second trimester - Early third</td>
<td>Subtle indentations in chorionic plate, presence of echogenic densities, size and number of calcification increases.</td>
</tr>
<tr>
<td>Two</td>
<td>Late third</td>
<td>Marked indentations in chorionic plates, size and number of calcification increases.</td>
</tr>
<tr>
<td>Three</td>
<td>29 weeks – post date</td>
<td>Complete indentations and irregular calcifications</td>
</tr>
</tbody>
</table>
2.3.5 Importance of grading

Sonographic appearances and texture characteristics provide useful information regarding placental maturity [31]. Premature calcification can cause Inter Uterine Growth Restriction (IUGR), placental dysfunction, preeclampsia, hypertension and foetal distress in labor. Infants with IUGR show two patterns of growth, asymmetric and symmetric IUGR. The reason behind asymmetric IUGR is uteroplacental insufficiency. Sonographic assessment of the placenta should be done to find the presence of abnormal conditions such as placenta praevia, vasa praevia, placenta accrete, abruptio placenta, placental bed infraction [34]. These abnormal conditions are due to abnormal implantation of placenta, abnormal adherence of the placenta to the uterus, premature separation of the implanted placenta and so on. Therefore the examinations of morphology, anatomy, location, size and implantation, texture analysis of placenta are important. The vascular lesions in the placenta are some indications of abnormalities in complicated pregnancy. Placenta abruption is one of the main causes of perinatal morbidity and mortality.

Relevance of Grading

- If growth parameters are less compared to gestational age and if placental maturity is more it indicates an increased probability of IUGR [35].
- It helps in the diagnosis of IUGR [36].
- There exists a correlation between gestational age and placental grading.
2.3.6 Need of automated grading

- Each radiologist may have different evaluations of the same placenta, ie. high inter observer variability [30].
- Poor evaluation reproducibility.
- High subjectivity in evaluation.

2.4 Chapter Summary

In this chapter an overview of the problem domains are detailed. In the first part, the cause and effects of breast cancer, major treatment options, reason for selecting digital mammography and the importance of CAD systems are discussed. The second part discusses the use and principles of sonography in obstetrics, placental grading and need for automation.