A PILOT STUDY OF

POWER DOPPLER SONOGRAPHY USING TUMOUR VASCULARITY PATTERN IN DIFFERENTIATING BENIGN FROM MALIGNANT BREAST LESION

BY
DR. SITI NOR BADRIATI SHEIK SAID

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ACHIEVEMENT

This paper was presented in the 11th National Conference on Medical Sciences held in School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kelantan on 20-21 May 2006.

To

Umi and Abah

Your unselfish love and support guide me through life;

My son; Ahmad

Your smiling face never failed to enlighten my day

I hope you will forgive me the time when I was not available throughout these years

although you would have needed me;

&

To the fond memory of my late husband

Our great love has kept me going through life.

I know you would have been proud of me

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ABBREVIATIONS

AP	Anteroposterior
ASR	Age-standardised Incidence Rate
BI-RADS	Breast Imaging Reporting and Data System
B-mode	Brightness mode
CA	Cancer
DCIS	Ductal carcinoma in situ
FNAC	Fine needle aspiration cytology
HPE	Histopathological examination
HUSM	Hospital Universiti Sains Malaysia
ICC	Intraclass Correlation Coefficient
IDC	Invasive ductal carcinoma
MRI	Magnetic Resonance Imaging
NPV	Negative Predictive Value
PACS	Picture Archiving and Communication System
PPV	Positive Predictive Value
PRF	Pulse Repetitive Frequency
SPSS	Statistical Software for Social Sciences
TDLU	Terminal ductal-lobular unit
US	Ultrasonography
USM	Universiti Sains Malaysia

ABSTRACT

Bahasa Malaysia

Tajuk: Kajian awal mengenai peranan sonografi power Doppler menggunakan corak saluran darah dalam membezakan ketumbuhan payudara benign dan malignan (kanser).

Tujuan:

1. Mengira sensitiviti, spesifisiti, nilai ramalan positif (PPV) dan nilai ramalan negatif (NPV) corak salur darah lesi payudara menggunakan power Doppler sonografi dalam membezakan ketumbuhan benign dan malignan.
2. Mencari hubungkait saiz dengan corak salur darah lesi payudara benign and malignan.

Metodologi: Kelulusan Jawatankuasa Etika dan keizinan pesakit diperolehi. Kajian prospektif selama 16 bulan ini dijalankan di Hospital USM, Kubang Kerian, Kelantan daripada Julai 2004 sehingga Oktober 2005. Seramai 40 orang pesakit yang mempunyai ketulan payudara menjalani pemeriksaan power Doppler sonografi menggunakan transduser 13.5MHz. Ciri-ciri power Doppler yang dianalisa termasuk kadar arus, taburan, morfologi dan kehadiran salur darah penetratif. Pemeriksaan FNAC dan/atau HPE dilakukan ke atas semua kes. Perbandingan corak salur darah dan HPE (Histopathological examination) dianalisa. Sensitiviti, spesifisiti, nilai ramalan positif (PPV) dan nilai ramalan negatif (NPV) dikira menggunakan jadual diagnostik.

Keputusan: Kehadiran salur darah dikesan dalam 13 lesi payudara malignan dan 16 lesi benign. Saiz min lesi lesi vaskular ialah 30.5mm dengan 1.8mm deviasi standard. Saiz lesi mempengaruhi kadar arus dengan nilai p 0.005. Kehadiran salur darah penetratif dan salur darah tidak sekata mempunyai nilai p yang signifikan (0.011 dan 0.004). Tiada corak salur darah yang spesifik untuk lesi benign mahupun malignant. Nilai ramalan positif corak salur darah, kadar arus, taburan dan salur darah penetratif adalah rendah iaitu 50.0%, 54.5%, 56.0% and 63.1% masing-masing. Sebaliknya kadar ramalan negatif adalah tinggi bagi taburan pinggiran (100%), arus rendah (88.9%) and salur darah sekata (87.5%).

Kesimpulan: Kajian salur darah menyokong diagnosa lesi benign tetapi hanya menyumbang maklumat terhad dalam membezakan lesi payudara benign dan malignan.

ABSTRACT

English

Topic: A pilot study of power Doppler sonography using tumour vascularity pattern in differentiating benign from malignant breast lesions.

Objective:

1. To determine the specificity and sensitivity of the criterias of the tumour vascularity pattern using power Doppler sonography in differentiating benign and malignant breast lesion.
2. To find any association between tumour vascularity pattern and size of benign and malignant breast lesion

Methods and Materials: Ethics committee approval and informed consent were obtained. This study was carried out in Hospital USM, Kubang Kerian, Kelantan for 16 months from July 2004 until October 2005. Power Doppler sonography using 13.5MHz transducer was prospectively performed on a total of 40 patients with breast lesion. The tumour vascularity criterias assessed were the flow, distribution, vessel morphology and presence of penetrating artery. FNAC (Fine needle aspiration cytology) and/or HPE (Histopathological examination) were done for all cases. The power Doppler criterias and HPE were analysed using univariate analysis. The sensitivity, specificity, positive predictive value and negative predictive value calculated using diagnostic table.

Result: There was detectable blood flow in 13 infiltrating ductal CA and 16 benign lesions. The mean size of vascular lesion was 30.5mm with 1.8mm standard deviation. The size of the lesions may have played a part in the vascularity of the lesion with a p value of 0.005 for flow characteristics. In the vascular lesions, irregular vessel and presence of penetrating artery showed a significant p value of 0.004 and 0.011. There was no single vascularity pattern which was specific for benign and malignant breast lesion. The descriptors of vessel morphology, flow, distribution and penetrating artery were not found to be highly predictive of malignancy with positive predictive value of 50.0%, 54.5%, 56.0% and 63.1% respectively. High negative predictive values were interestingly noted in the following descriptors: peripheral distribution (100%), low flow (88.9%) and regular vessel (87.5%).

Conclusion: Power Doppler US provided only limited additional information in differentiating benign solid breast lesions from malignant lesions. Vascular assessment was helpful only when it supported a benign morphology.

SECTION ONE:

INTRODUCTION

1 INTRODUCTION

Breast cancer is the third most common cancer worldwide and the commonest cancer in women. The Second Report of the National Cancer Registry cancer incidence in Malaysia showed that 3738 female breast cancer cases were reported in 2003, making it the most commonly diagnosed cancer in women. It accounted for 31.0% of newly diagnosed female cases with the overall age-standardized incidence rate (ASR) of 46.2 per 100,000 populations (Hisham and Yip, 2004).

The present screening modality for breast cancer is mammography combined with clinical breast examination. Mammography is nowadays available in most centres. It is superior in detecting microcalcification. Limitation of mammography lies in its difficulty in assessing dense glandular tissue. In addition, there is still a large 'grey zone' of indeterminate mammographic features.

Since past decade, breast ultrasonography has been proven to be helpful as an adjunct to mammography in predicting more accurately if a lesion is benign or malignant.
Improvements in technology have made high resolution B-mode US scanners available for clinical use. Unlike mammography, it does not involve ionizing radiation. This high resolution technique allows better detection of small breast lesions, which can be easily missed by clinical examination and mammography in dense breast parenchyma and it improves the analysis of sonomorphologic details. Sonographic features like margin, echotexture, through transmission of sound and parallel orientation are used to determine

a benign versus malignant nature of a mass (Raza and Baum, 1997). Yet, even with this high resolution technique, the diagnosis remains uncertain in some cases as there is overlap in the sonographic findings between benign and malignant solid breast lesions.

Magnetic Resonance Imaging (MRI) of the breast has emerged as a very powerful breast imaging technique in the past decade. It provides better soft tissue contrast resolution than conventional mammography and ultrasound. Even so, the use of MRI is limited due to its cost effectiveness, availability and lack of clinical efficacy in a screening setting.

One important observation that had been concluded in the studies of breast malignancy was that the malignant tumours directly stimulate the growth of new blood vessels by secreting angiogenesis factors which subsequently led to hypervascularisation of the tumour (Milz *et al.*, 2001). These new vessels of malignant tumours differ from the physiologic vascular architecture. Recent studies showed that, it is characterised by a higher capillary density, chaotic branching, vessel loops and arteriovenous shunts (Guita *et al.*, 1999). Therefore, the ability of colour Doppler sonography to detect neovascularization provides a potential role in distinguishing benign from malignant lesions.

However, the lack of evidence documenting the ability of Doppler sonography to distinguish with adequate sensitivity and specificity between benign and malignant neoplasm limits its role clinically. Some of the past studies have given results; but unsatisfactory results also have been claimed by some studies. As the study using colour Doppler alone has come out with less promising results, Power Doppler sonography is

applied in this study due to its advantages such as high sensitivity to slow flow, no angle dependency and no aliasing (Zwiebel, 2000).

So far, there is no published study in Malaysia on prediction of breast malignancy using power Doppler sonography. By identifying patient that has low risk for malignancy, unnecessary biopsies can be avoided and an option of follow up can be offered to the patient as an alternative to biopsy. At the same time a high detection rate of early stage of breast cancer can be achieved.

SECTION TWO:

LITERATURE REVIEW

2 LITERATURE REVIEW

2.1 Normal breast anatomy and physiology

2.1.1 Anatomy of the normal breast.

The female breast consists of three major components: breast parenchyma, subcutaneous tissue and skin. The breast parenchyma lies between the subcutaneous tissue and the fascia of the pectoralis major and serratus anterior muscles. The suspensory ligaments of Cooper span from the dermis to the deep fascia thus supporting the framework of the breast. Small branching lymphatics and blood vessels course through the retromammary space between the posterior surface of the breast parenchyma and the fascia of the pectoralis major (Figure 1).

The breast consists of 15 to 25 lobes, each of which is drained by a collecting duct terminating in the nipple. The collecting duct has several branches, which end in a terminal ductal-lobular unit (TDLU), the basic functional unit of the breast (Figure 2). The TDLU is composed of a small segment of terminal duct and a cluster of ductules (acini), which are the actual secretory units. The functional structures are surrounded by a varying amount of fat and collagenous tissue. The acini (blind ending sacs) consist of layers of two types of cells (epithelial and myoepithelial) that surround a lumen. The acini are lined by a single layer of cuboidal epithelium which merges into the columnar epithelium of smaller ducts and finally into the stratified squamous epithelium of the major lactiferous ducts.

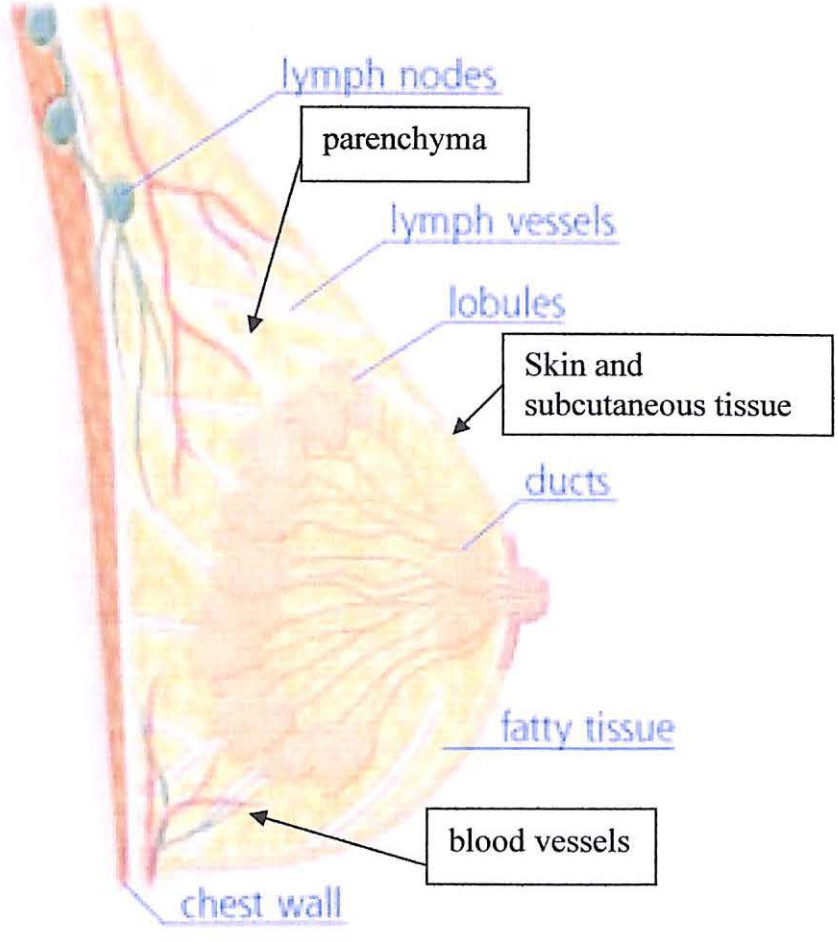

Figure 1: Anatomy of the female breast

(Adapted from internet: Anonymous www.ribbonofpink.com)

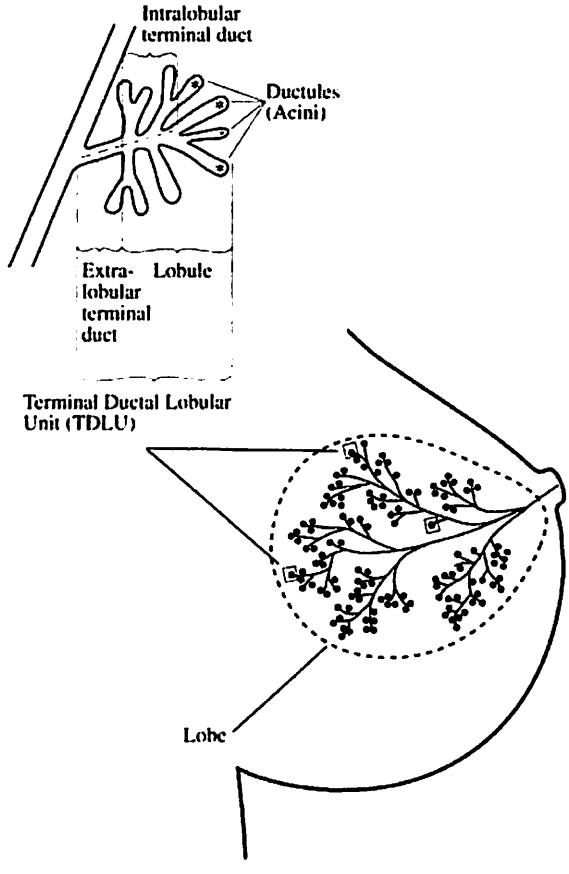

Figure 2: Anatomy of the human breast, a lobe and a TDLU

(Adapted from (Tabar, 1998)

The breast parenchyma consists of glandular tissue and ductal tissue. The fatty and fibrotic tissues which surround and extend into the lobules constitute the stroma. Both are contained within a sac formed when the superficial pectoral fascia splits into superficial (anterior) and deep (posterior) layers. Cooper's ligaments are tent-like projections of the superficial layer of the superficial fascia through the subcutaneous tissue to the skin.

The blood supply to the breast is derived from the branches of the internal mammary artery (which pierce the intercostal spaces and traverse the pectoralis muscle), lateral thoracic branch of the axillary artery and the perforating branches of the anterior intercostals arteries (Figure 3). Venous drainage accompanies the arteries to the axillary and subclavian veins and the azygous system (Figure 3). The primary lymphatic drainage is to the axillary lymph nodes (draining the lateral aspect of the breast) and the secondary lymphatic drainage is to the internal mammary nodes which drains the medial aspect of the breast (Figure 4). This is reflected in the lymphatic spread of cancer. In the absence of axillary lymph node metastases, the internal mammary nodes were involved in 13% of medial cancers and in 4% of lateral cancers.

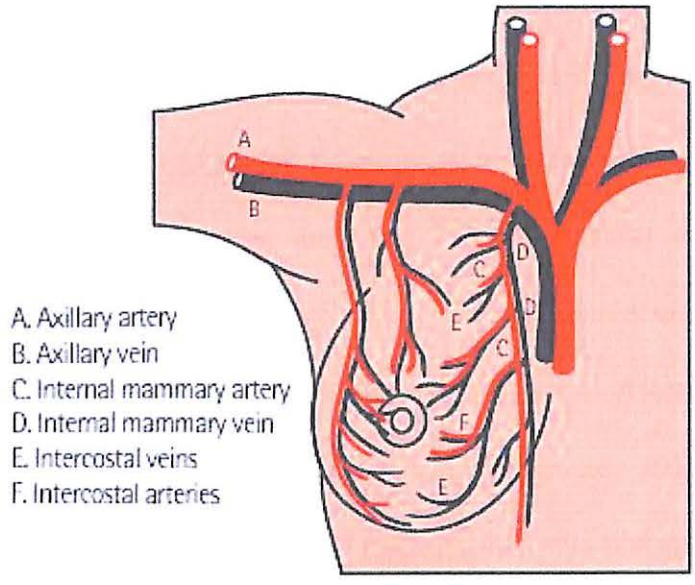

Figure 3: Breast vascular supply

(Adapted from internet: Anonymous www.breastdiseases.com/anat.htm)

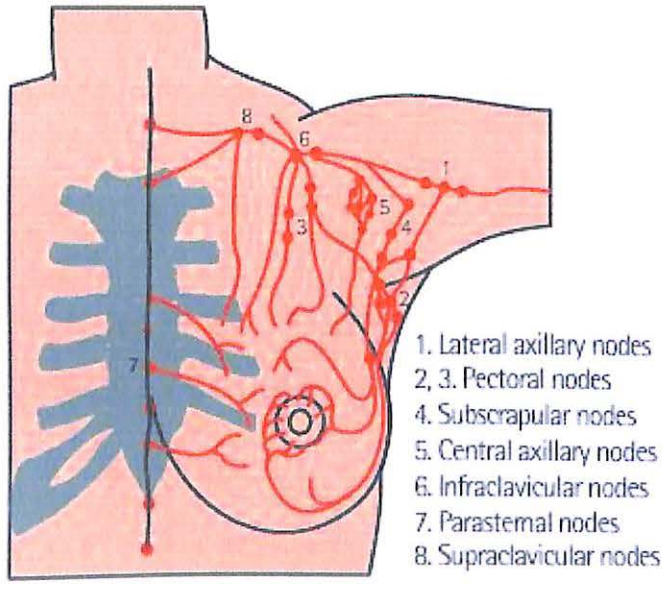

Figure 4: Breast lymphatic drainage

(Adapted from internet: Anonymous www.breastdiseases.com/anat.htm)

2.1.2 Normal breast development and physiology

At puberty, the breast develops under the influence of the hypothalamus, anterior pituitary, and ovaries and also requires insulin and thyroid hormone. During each menstrual cycle 3 to 4 days before menses, increasing levels of estrogen and progesterone cause cell proliferation and water retention. After menstruation cellular proliferation regresses and water is lost. During pregnancy cellular proliferation occurs under the influence of oestrogen and progesterone, plus placental lactogen, prolactin and chorionic gonadotropin. At delivery, there is a loss of oestrogen and progesterone, and milk production occurs under the influence of prolactin. At menopause involution of the breast occurs because of the progressive loss of glandular tissue.

2.2 Breast pathology

2.2.1 Benign breast diseases

Most benign lesions can actually be regarded as aberrations of normal processes. In hyperplastic breast conditions, there is more glandular and fibrotic tissue than expected for the patient's age and parity. The tissue is also morphologically abnormal. There are five main types: adenosis (epithelial hyperplasia of the lobules), papillomatosis (epithelial hyperplasia of the duct), fibroadenoma, papilloma and fibrocystic condition (Grainger *et al.*, 2001).

Adenosis may be seen as patchy or homogenous areas of increased echogenicity which may contain punctuate adenosic microcalcifications (1mm or less) with symmetrical distribution in both breasts. Histologically, adenosis represents an increase in the number of lobules and acini within each lobule. These acini show epithelial proliferation and dilatation. Adenosis tends to regress with age, especially after the menopause. In sclerosing adenosis subtype, there is a predominant connective tissue proliferation which is thought to represent a late stage where the epithelial elements have regressed and are replaced by fibrosis. It may represent as a discrete mass with smooth and well demarcated margins, which may be straight, curved or even rounded (Grainger *et al.*, 2001).

The most common benign disorder, fibrocystic change, affects 40–50% of premenopausal women (Stevens and Lowe, 2000). It is a unified term for several proliferative, but nonneoplastic parenchymal alterations, which are usually bilateral and multifocal (Bude *et al.*, 1994). The histologic pattern in each case is varying and may include pure fibrocystic lesions (duct ectasia, cysts, fibrosis, adenosis, ductal epithelial proliferation), focal fibrosis, ductal and lobular epithelial hyperplasia (also atypical) and microcystic and fibrous mastopathy due to involutional change (Stevens and Lowe, 2000).

Breast cysts arise from adenosis when the lumina of the ducts and acini become dilated and lined by atrophic epithelium. Like fibroadenomas, cysts are often multiple and bilateral and frequently disappear or subside after the menopause. The strict ultrasound criteria for a simple cyst include well-circumscribed margins, a bright posterior wall, round or oval contours, absence of internal echoes and through transmission. If all of

these criterias are met, the accuracy of diagnosis of a simple cyst is 100% (Grainger *et al.*, 2001).

Fibroadenoma is the most common tumor in young and adolescent women. It arises as a localized hypertrophy of the TDLU and contains structures resembling terminal ducts and expanded stromal tissue (Sewell, 1995). On ultrasound, fibroadenomas have smooth, well-defined margins and are round, oval or nodular. There are internal echoes which are frequently homogenously distributed. This moderate acoustic attenuation results in intermediate strength echoes behind the mass. The sonographic appearance cannot be distinguished reliably from that of a circumscribed carcinoma. Coarse calcification in fibroadenoma is highly reflective on ultrasound, larger than benign adenosis with a more peripheral distribution. About 10% fibroadenoma will disappear per each year followed in those women who have fibroadenoma verified by fine-needle aspiration and who opt for follow up rather than for removal. Carcinoma may develop in a fibroadenoma in 1–2% of cases (Cosgrove *et al.*, 1993).

Papilloma arises in the duct epithelium as papillary projections with or without fibrous cores. It is usually a solitary tumor, but may also present as multiple lesions (Sewell, 1995). The term intraductal papilloma refers to a lesion in a cystically dilated duct. It is commonly found in the retroareolar region and becomes clinically evident when the patient presents with nipple discharge, which may be bloody or non-bloody. It is a low-risk lesion, but may develop atypical and precancerous cell populations (Sewell, 1995).

Phyllodes tumour, previously known as cystosarcoma phyllodes, arises from periductal stroma and contains sparse lobular elements. Increased cellularity of the stromal components is characteristic and separates phyllodes tumour from fibroadenoma. Although usually benign, some tumours show increased mitotic activity, pronounced overgrowth of the stroma and aggressive peripheral growth, turning it into malignancy (Sewell, 1995).

2.2.2 Breast carcinoma

Breast carcinomas are primarily divided into in situ and invasive types. Most breast cancer develops in glandular tissue and is classified as adenocarcinoma. The earliest form of the disease, ductal carcinoma in situ (DCIS), develops solely in the ducts. The most common type of breast cancer, invasive ductal carcinoma (IDC), develops from DCIS, spreads through the duct walls, and invades the breast tissue.

Invasive ductal carcinoma, which arises from the epithelium of the breast ducts, account for nearly 94% of invasive breast cancers. Invasive lobular carcinoma arises from the acini of breast lobules and accounts for 5.5% of cases. Less than 1% of invasive breast cancers are sarcomatous or other mesenchymal origin. Among infiltrating ductal carcinomas, approximately 95% are ductal NOS (not otherwise specified) or ductal with fibrosis (scirrhous). The remaining ductal carcinomas include medullary carcinoma, colloid carcinoma, papillary carcinoma, tubular carcinoma and Paget's carcinoma.

Paget's disease of the nipple is a variant of ductal carcinoma. It is a benign appearing eczematoid lesion of the nipple caused by large malignant cells (Paget's cells) which arise from the ducts and which invade the surrounding nipple epithelium. In the absence of an underlying mass, this lesion is usually due to an intraductal carcinoma.

Ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) are confined to the ducts and acini, respectively without breaching the basement membrane and therefore have not invaded the stroma. LCIS is much less common than DCIS and it accounts for about 6% of all cases of breast carcinoma (Stevens and Lowe, 2000). There are four subtypes of DCIS: comedocarcinoma, micropapillary carcinoma, cribriform carcinoma and solid carcinoma. Among these subtypes, comedocarcinoma is the most aggressive. Most or all in situ ductal carcinomas are believed to progress to invasive disease. However, most in situ lobular carcinoma do not become infiltrating (Grainger *et al.*, 2001).

2.3 Breast imaging modalities

2.3.1 Mammography

Mammography has been the basic imaging method in breast diagnostics, and the only tool suitable for screening breast cancer. In screening, its sensitivity and specificity are 90–93% and 93–97%, respectively (Tabár *et al.*, 2000). The aim of interpreting mammograms is to find asymmetric densities, mostly circular or stellate lesions;

parenchymal contour changes; architectural distortion and microcalcifications with or without associated tumor, which may indicate breast malignancy (Tabar, 1998).

Mammography has some recognized limitations and disadvantages. The sensitivity and specificity are highly dependent on the composition of the breast parenchyma, which for its part is influenced by age, hormonal status and possible previous interventions. In young women, the usefulness of mammography is restricted by high prevalence of dense fibroglandular tissue, which impairs both the detection and the differentiation of the lesion. With increasing age, the breast parenchyma usually shows fatty replacement, which makes abnormalities more easily detectable.

Hormone replacement therapy may decrease the sensitivity of mammography by increasing the breast density and enlarging benign masses, such as cysts and fibroadenomas. After breast surgery, mass-like scars and areas of distortion may mimic a tumor or hide subtle signs of malignancy. Radiation after surgical treatment of breast carcinoma leads to skin thickening and increased focal or diffuse density of the breast due to edematous changes. Cysts and solid tumors cannot always be definitely differentiated at mammography. Some carcinomas may have a benign appearance, and some fibroadenomas may be irregular and difficult to differentiate from a malignant tumor. A palpable mass may be partially or completely obscured by adjacent fibroglandular tissue. Even the spiculations within the fibrous tissue surrounding a cancer may be inconspicuous at mammography, because both the spiculation and the adjacent fibrous tissue are of the same density (Stavros *et al.*, 1995).

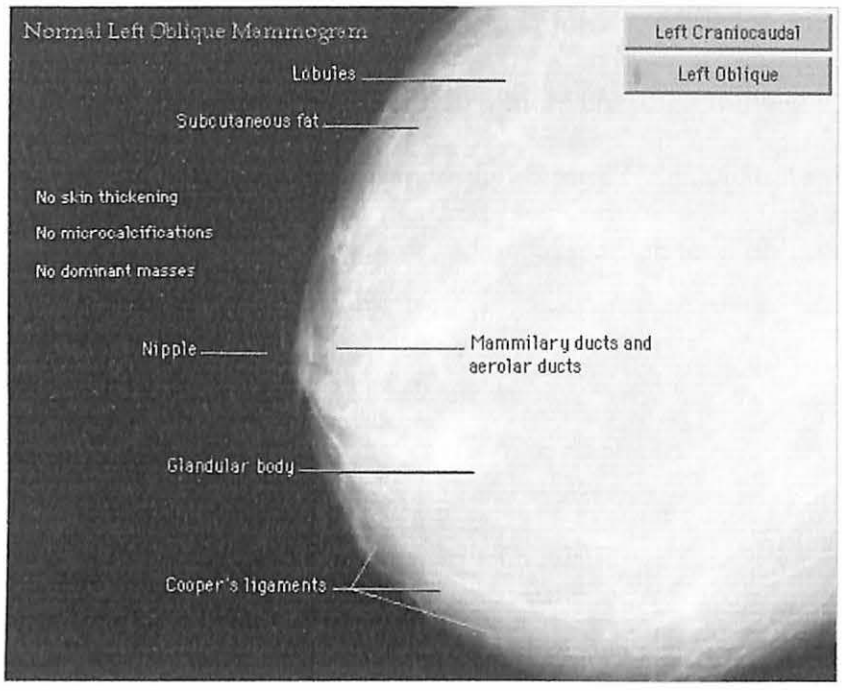

Figure 5: Normal mammogram in mediolateral oblique view

(Adapted from Anonymous **info.med.yale.edu/. ../oblique.html)**

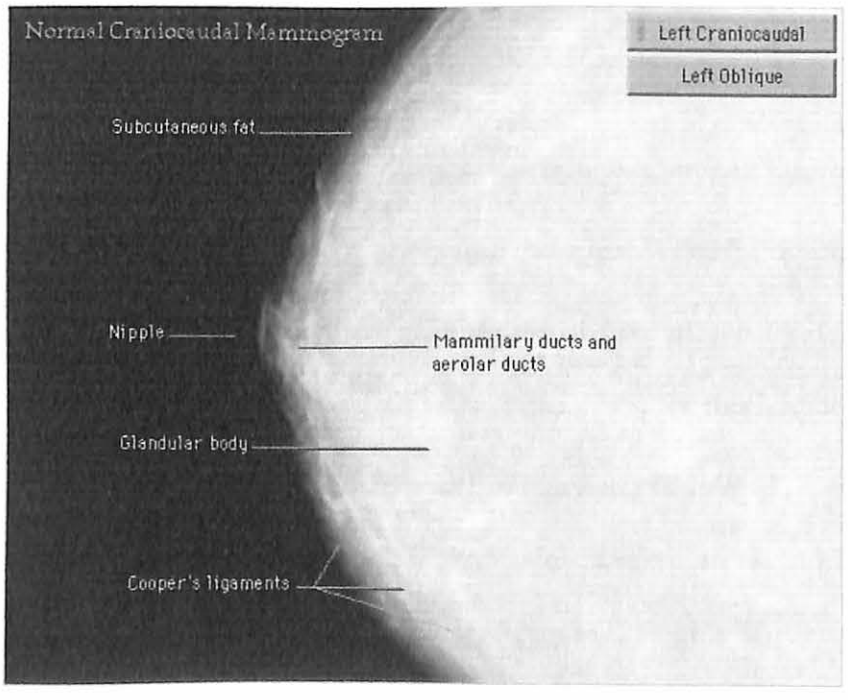

Figure 6: Normal mammogram in craniocaudal view

(Adapted from Anonymous **info.med.yale.edu/. ../oblique.html)**

A negative mammogram, even with tailored additional views, does not exclude the presence of breast cancer. Adjunctive tools are often indicated both for the detection and analysis of breast lesions. Figure 5 and Figure 6 demonstrate normal mammogram in the routine views namely the craniocaudal and mediolateral oblique views.

2.3.2 Ultrasonography

2.3.2 (a) B-mode ultrasonography

Since US introduction in the 1960s, its historical role as an adjunct modality to mammography in differentiating cystic from solid lesions has been widely expanded. Breast ultrasound has evolved from static B-scanners, through water-path immersion scanners, to real-time hand-held scanning, first at 5 MHz, then 7.5 MHz, and now at 10 MHz and above.

In the last few years, differentiation between benign and malignant solid breast lesions by means of US has gained increased interest. The following **Figure 8** to **Figure 12** demonstrate the different characteristics of benign and malignant lesion. The individual characteristics classified by Stavros *et al* (1995) for malignant lesions include spiculation, angular margins, marked hypoechogenicity, shadowing, calcification, duct extension, branch pattern, vertical ("taller than wide") orientation and microlobulation. If a single malignant feature is found, the lesion cannot be considered benign. Intense hyperechogenicity, ellipsoid shape, gentle bi- or trilobulations, thin, echogenic pseudocapsule and lack of malignant findings are considered benign features (Stavros *et al*, 1995).

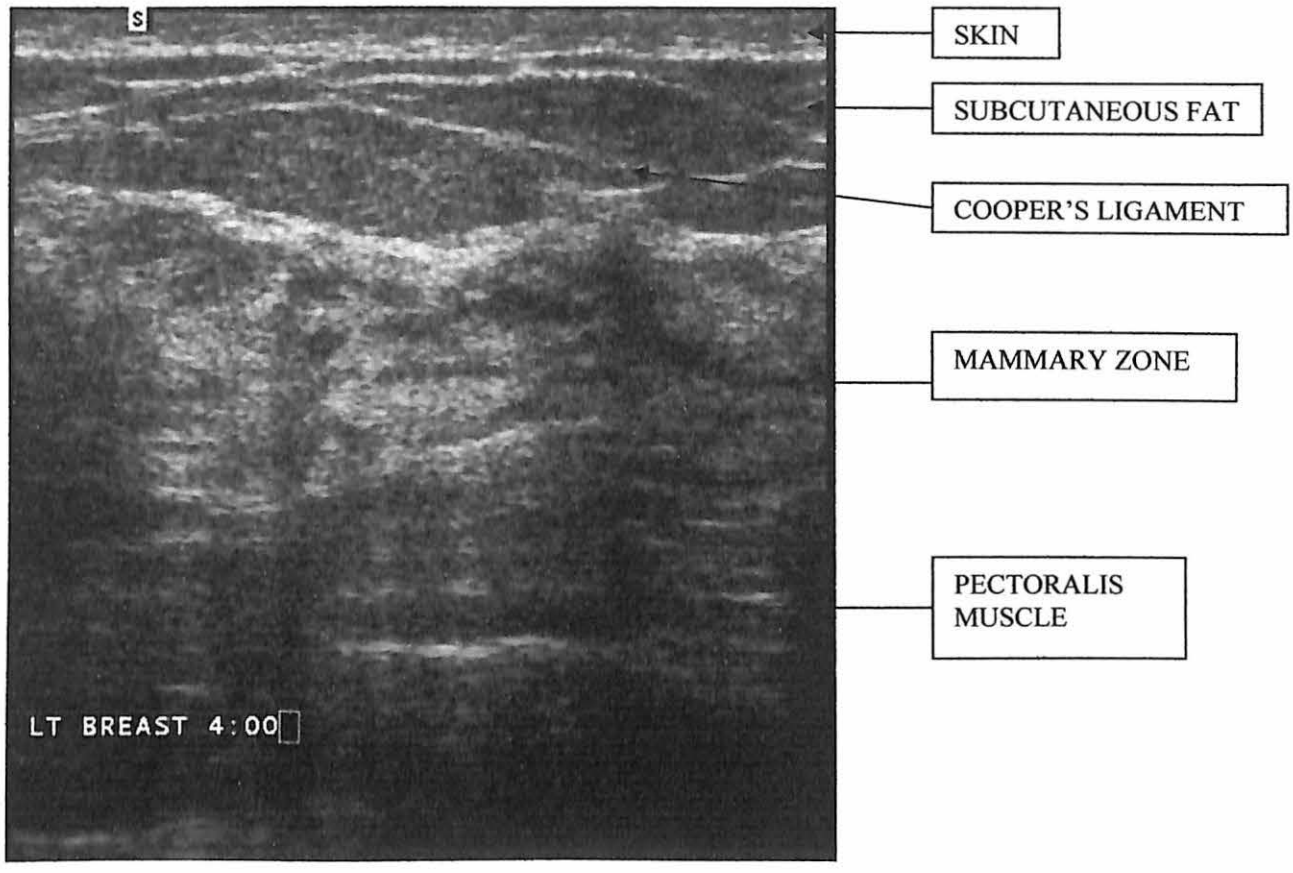

Figure 7: Normal sonographic anatomy of the breast.

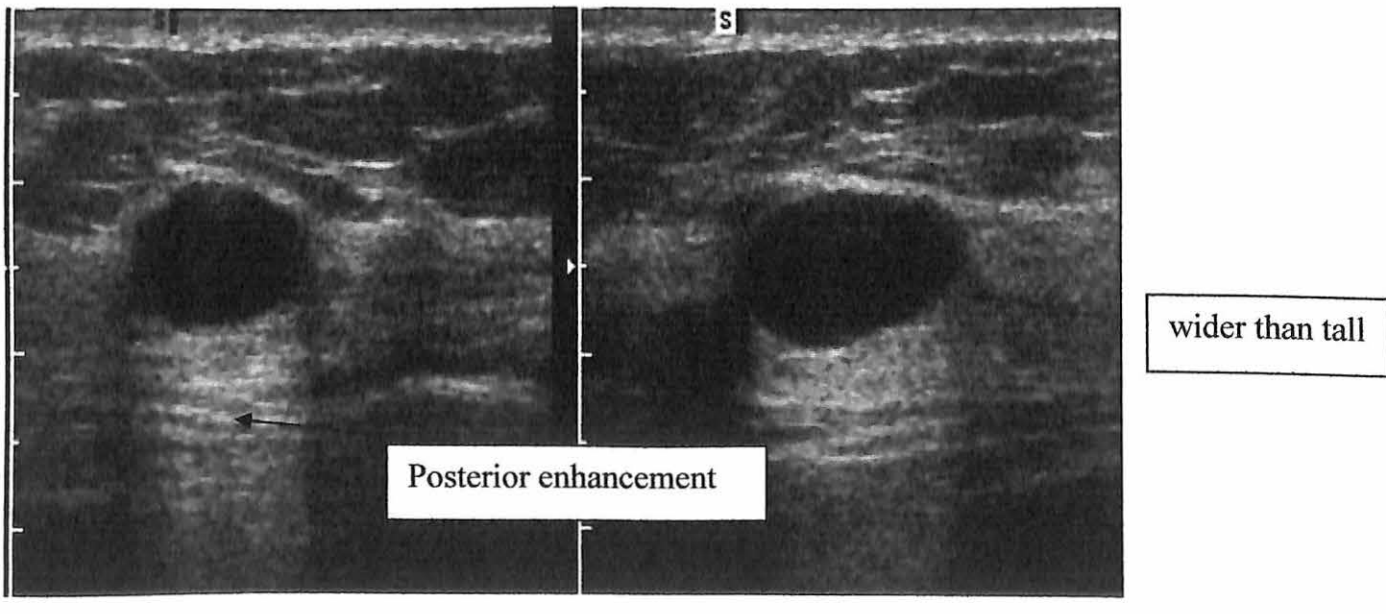

Figure 8: B-mode US of benign breast lesion with posterior shadowing (cyst).

A well defined elliptical mass with posterior enhancement. B-mode ultrasound image showing a well defined elliptical mass which is suggestive of a benign lesion. Note the posterior enhancement

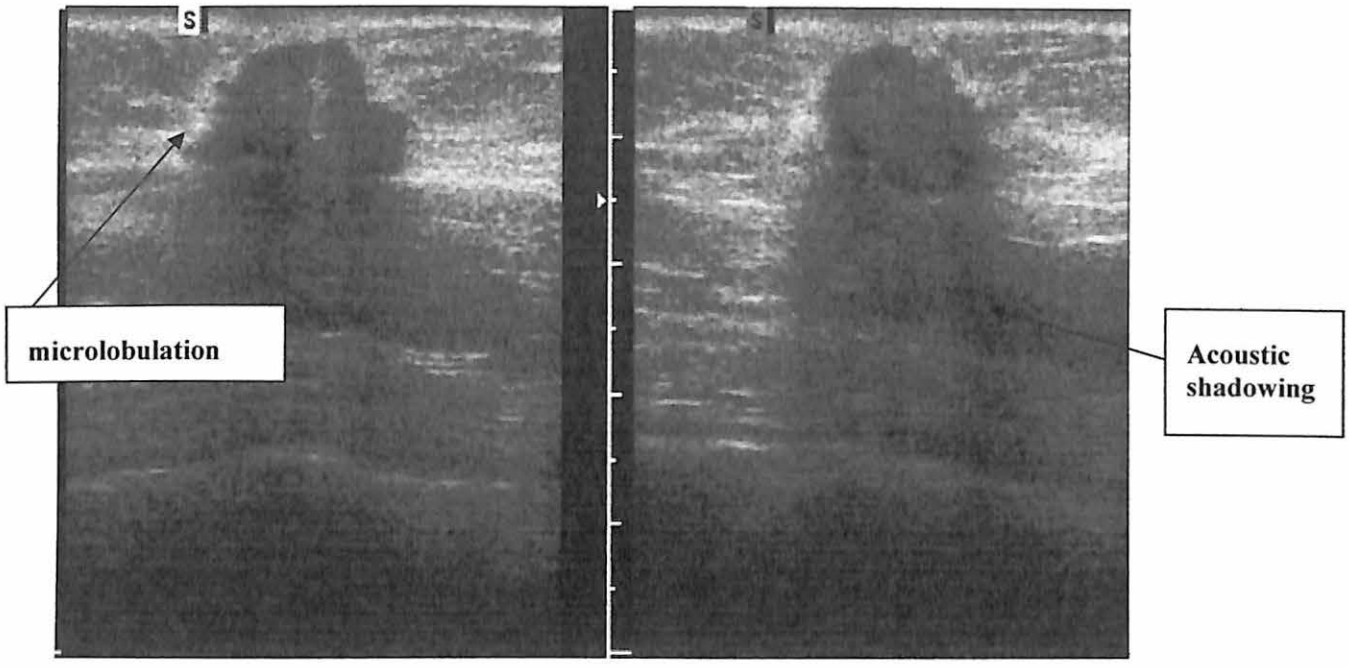

Figure 9:B-mode US of malignant lesion with microlobulation (infiltrating ductal carcinoma).

Microlobulation with irregular shape, posterior acoustic shadowing and microlobulation in a malignant lesion.

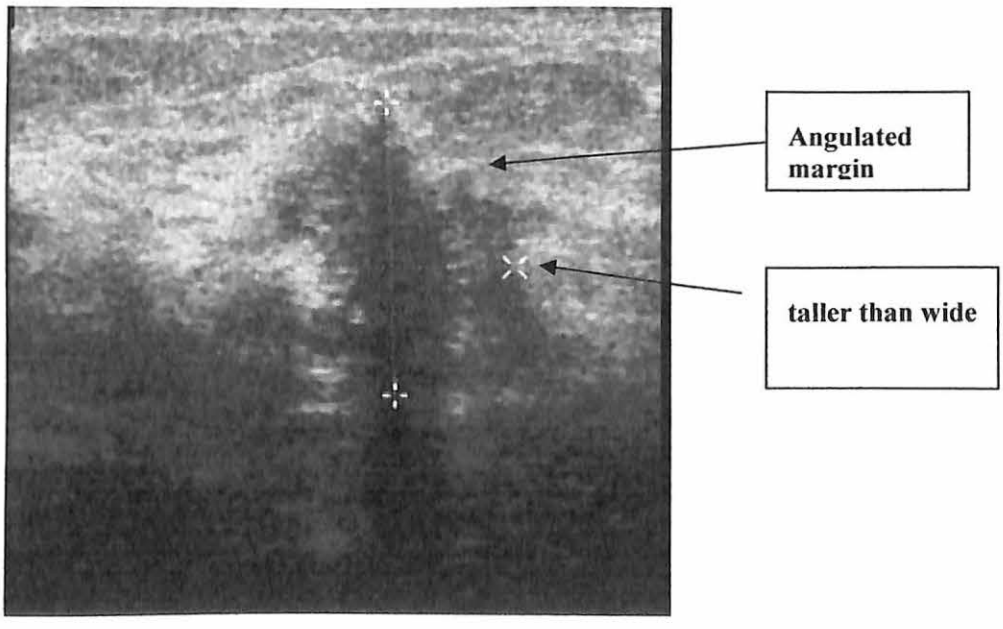

Figure 10: B-mode US of a malignant lesion with angulated margin and taller than wide.

Irregular shape, angular margins and spiculations of a malignant lesion. Note that the lesion is taller than wide.

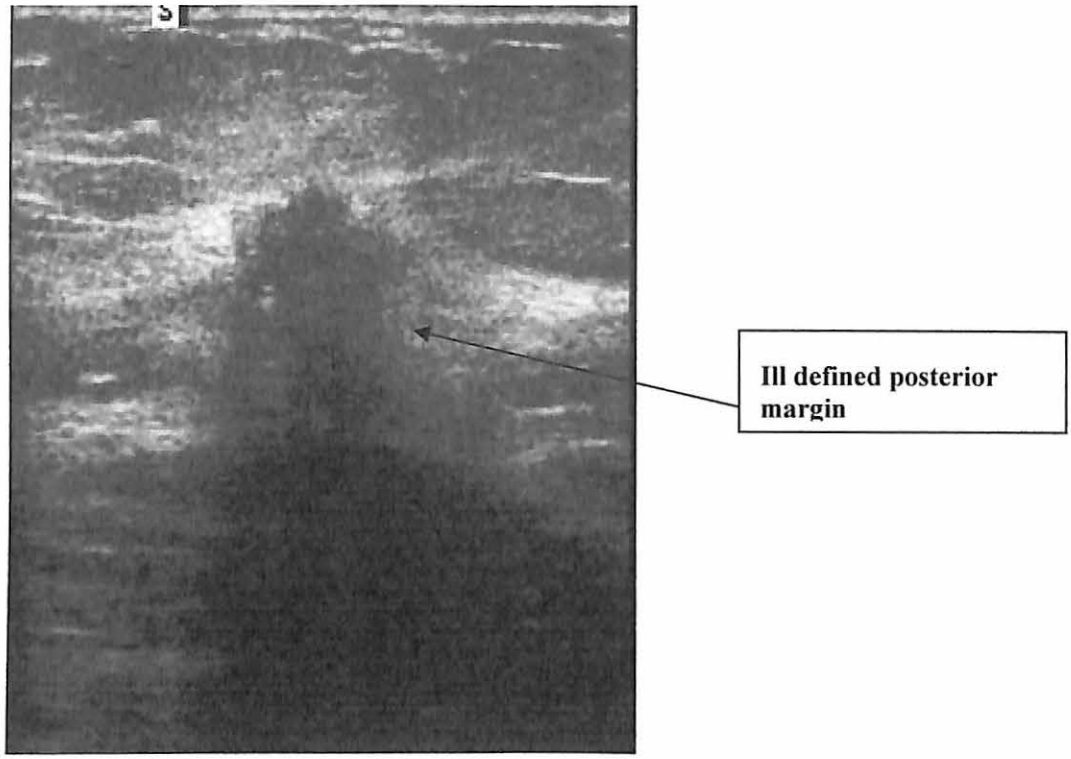

Figure 11:B-mode US of a malignant lesion (infiltrating ductal carcinoma).

Ill defined posterior margin in a malignant lesion.

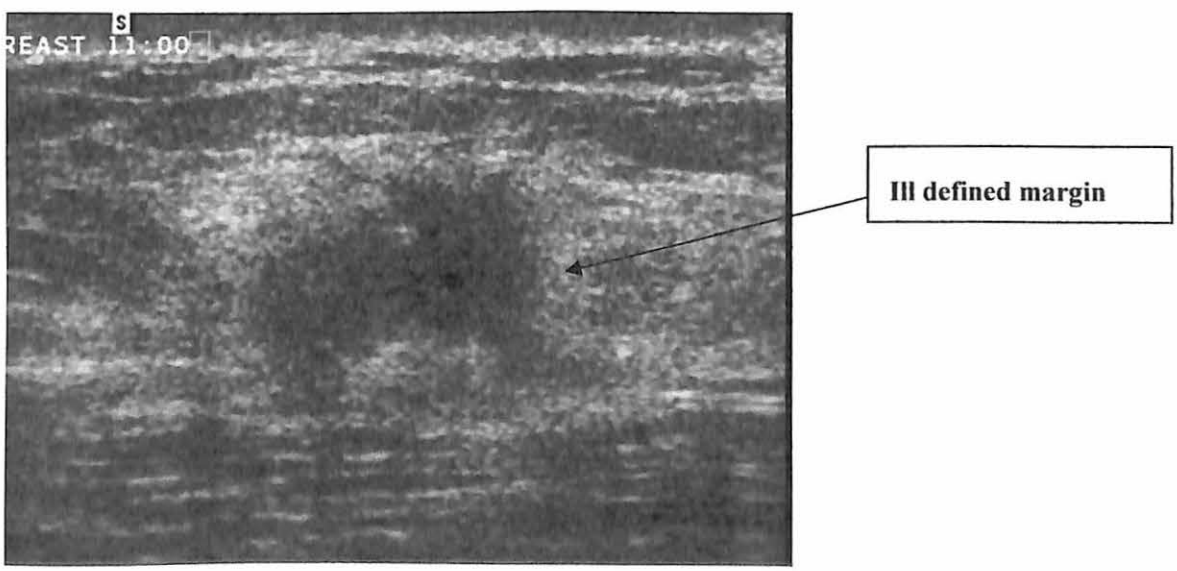

Figure 12: B-mode US featuring a malignant feature (ill defined margin).

Guita et al (1999) retrospectively investigated the grey-scale US findings of 162 patients with breast tumours, and reported that all tumours that satisfied all of the three following criteria were benign: i) Round or oval in shape; ii) Circumscribed margin; iii) Width to anteroposterior dimension ratio >1.4. Features that characterize masses as malignant included irregular shape, microlobulated or spiculated margins, and width-to–AP dimension ratio of 1.4 or less.

Despite the encouraging results of some studies (Stavros *et al*, 1995), there are still cases with a substantial overlap in sonographic characteristics between benign and malignant tumours. Currently, most solid breast lesions undergo a diagnostic or preoperative needle biopsy (Guita *et al*, 1999).

2.3.2 (b) Doppler ultrasonography

In the Doppler effect, the sound waves reflected from a moving medium undergo a frequency shift, which is used to image red blood cells moving within vessels and to measure their velocity. In medical ultrasonography, a Doppler shift occurs when reflectors move relative to the transducer. The frequency of echo signals from moving reflectors is higher or lower than the frequency transmitted by the transducer, depending on whether the motion is away or towards the transducer (Zwiebel, 2000).

Colour Doppler has already been used to sonographically analyze blood flow in breast tumours but has not gained clinical relevance until recently. In colour Doppler US, the presence of flow, the direction of flow and the existence of focal flow disturbances are

seen. The direction of flow is indicated by the displayed colour in which red encodes flow towards the transducer while blue away from the transducer.

Several investigators have evaluated quantitative colour Doppler US in assessment of vascularity of breast masses. Cosgrove et al (1993) analysed the average number of vessels per square centimeter and average density of colour pixels while using a semiquantitative scoring system. They found that colour signals were present in 98% of the tumours but there was no correlation between colour Doppler US scores with conventional prognostic indicators such as lymph node status or survival. Mc Nicholas et al (1993) studied the number of detectable vessels, the Doppler US spectrum and maximum velocities. They concluded that spectral patterns and maximum velocities were useful indicators of malignancy only when the patient age, lesion size and other US features of the lesion are also considered.

Power Doppler is a different Doppler technique in which colour encodes the energy of the Doppler signal instead of its mean frequency shift. Blood flow is also visualised in superposition to the B-mode scan in real time. Power Doppler US based on total integrated power of the Doppler spectrum is now considered superior to colour Doppler US in the demonstration of vascular flow because of such advantages as high sensitivity to slow flow, no angle dependency and no aliasing. In color Doppler ultrasound, the Doppler signals received from flowing blood are processed and colour-encoded. The velocities are displayed in various colours and brightness levels. The colour-encoded flow information is superimposed onto the B-mode image in real time. The more recent power Doppler gives also color-encoded information, but it analyzes the amplitude of the

reflected signal, not the frequency shift. The amplitude depends on the quantity or density of the blood cells that are detected. The signal-to-noise ratio is better with power Doppler, which enables more accurate detection of the small tumour vessels than conventional colour Doppler.

Raza and Baum (1997) prospectively evaluated solid breast lesions using power Doppler US. They found that the pattern of distribution and morphology of blood vessels in solid breast masses were potentially important features to be considered along with other sonographic criterias to predict the likelihood of malignancy. Out of 25 cancers, 68% (17/25) had penetrating arteries, four had peripheral vessels and four had no vessels. By using penetrating vessels alone to indicate malignancy, sensitivity for power Doppler US was 68%, specificity was 95%, positive predictive value (PPV) was 85% and negative predictive value (NPV) was 88%. Although power Doppler is more sensitive than colour Doppler, neither examination technique nor interpretation of the Doppler images are standardized and the results of the studies vary considerably [Cosgrove *et al* (1993), McNicholas *et al* (1993), Kedar *et al* (1995), Raza and Baum (1997) and Milz *et al* (2001)].

A considerable problem in ultrasonography is that it is equipment and operator dependent. Furthermore, the spatial resolution of Doppler imaging is limited, and only major feeding vessels of the tumors are detectable, not the abnormal complex microvascularity. Most recently, ultrasound contrast agents which employ encapsulated

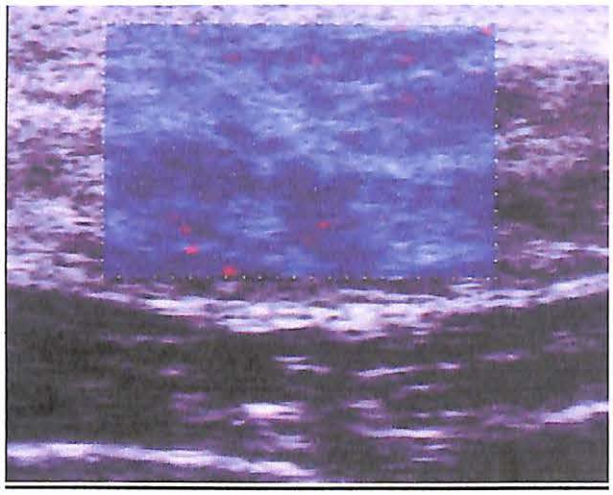

Figure 13: Power Doppler US image showing low flow vessel

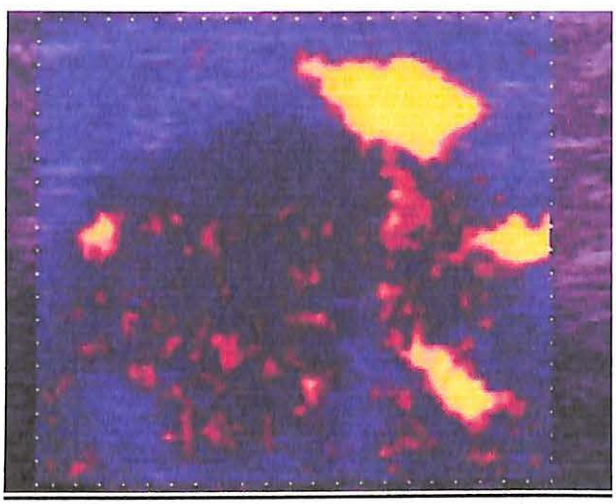

Figure 14: Power Doppler US image of a ductal breast carcinoma with a high flow vessel with irregular flow pattern.

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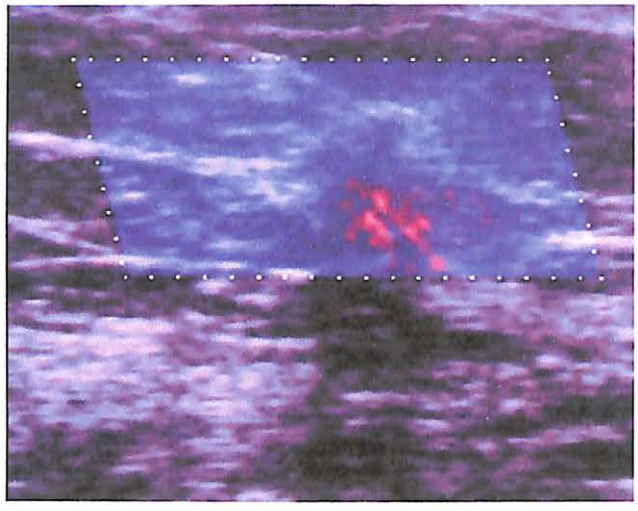

Figure 15: Intermediate flow vessels in a small ductal breast carcinoma.

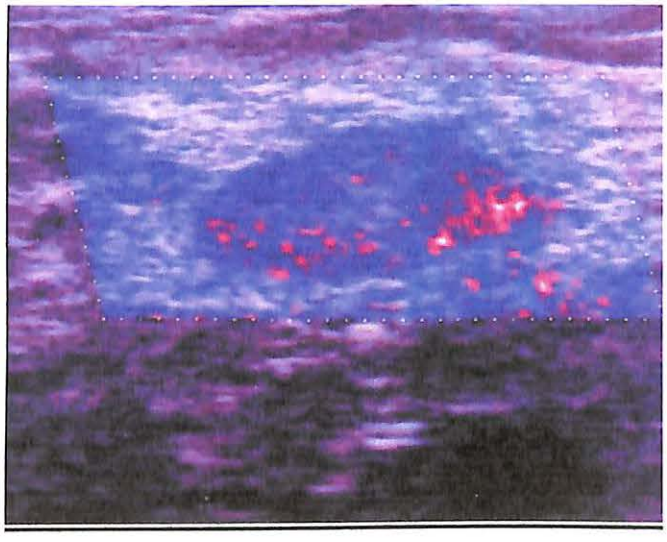

Figure 16: Biopsy proven fibroadenoma with intermediate flow vessels and regular flow pattern.