THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

DIAGNOSTIC APPROACH TO PALPABLE BREAST LUMPS-

THE MODIFIED TRIPLE TEST

DISSERTATION SUBMITTED FOR

BRANCH – I.M.S. (GENERAL SURGERY)

SEPTEMBER – 2006

ACKNOWLEDGEMENT

DECLARATION

This is consolidated report on " DIAGNOSTIC APPROACH TO PALPABLE BREAST LUMPS THE MODIFIED TRIPLE TEST", a study conducted at Department of General Surgery, Govt. Rajaji Hospital Madurai, during the period July 2003 to Jan 2006.

This is submitted to TN Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the MS Degree Examination in General Surgery.

Govt. Rajaji Hospital   Dr. M.Lakshmi Narayanan

Madurai.

CONTENTS

INTRODUCTION

Until a few years ago, it was generally believed that breast tumor should be excised and histologically examined to determine its nature with certainty – because the preoperative physical assessment alone was associated with too much uncertainty.

Eventually, with the advent of mammography, a radiological tool became available to the surgeons to make a pre-operative diagnosis of the breast with a reasonable degree of accuracy. However, it was the introduction of FNAC that changed the entire outlook to the matter. The combination of Physical examination, Mammography and FNAC came to be called upon as the "Triple Test" for assessment of breast lumps and has now become the gold standard in the work-up of the same.

Breast Ultrasound has now become available at higher resolutions, and is proving to be a highly useful adjunct to mammography. The wide acceptance of ultrasound as a diagnostic modality has been documented extensively in literature. However, opinions vary about the usefulness of USG breast in the evaluation of masses, and, surgeons are cautioned to be aware of its attributes as well as its deficiencies.

The *'Modified Triple Test'* utilizes-Physical Examination, Ultrasonography of the breast as the radiological method, and FNAC for the diagnosis of palpable breast lumps; and it is gaining acceptance with the recent advances in technology and refinements in the interpretative criteria of sonographically characterized masses.

Today, the studies concentrate on whether a benign result of the tests mentioned above makes excision biopsy unnecessary. Most often, this question arises in connection with localized changes in breasts with Fibrocystic diseases. For these tests to be adopted they must however, have the same degree of accuracy as excisional biopsy – because, non-excision of a malignant tumor is unacceptable.

REVIEW OF LITERATURE

Medical literature abounds with studies of evaluation of breast lumps that emphasizes that the statement "every palpable mass must be assessed and clarified".

Hermansen C. et.al4 in 1987 prospectively studied 650 breast tumors and applied the term *'Triple test'* to the traid of physical examination; mammography and FNAC used to diagnose them. He concluded that the diagnostic accuracy of the triple test is comparable to that of histological examination. Hardy JR. et. Al6. assessed 143 patients with palpable breast modules with clinical examination; FNAC mammography; ultrasonography and magnetic resonance imaging (MRI) and concluded that the combination of cytology and ultrasound was best at correctly diagnosing malignancy.

Lawrence N Bassett et. Al.7 assessed the usefulness of mammography and sonography in women less than 35years of age (1016 women) during a 8 year period. This study found that mammography was not useful in women less than 35 years. However sonography was useful in avoiding unnecessary biopsies and for this reason was the intial examination in younger women. But it was not useful in detecting nonpalpable carcinomas or in differentiating benign from malignant solid masses.

Vetto JJ et al in 1996 studied 55 women below the recommended age of screening mammography with the 3 elements of *'Modified Triple Test'*

(C/E, Usg; FNAC/CNB). The test had a specificity and negative predictive value of 100% for malignancy. They concluded that use of MTT for diagnosis of palpable breast lesions in younger women yields high diagnostic accuracy without the need for routine open biopsy, resulting in overall reduction patient charges.

Purasri P et. al3. retrospectively assessed 603 patients with breast lumps using the *'Quadruple test'* – C/E/USG/Mammography/FNAC. A stepwise logistic discriminant analysis was used to derive a

novel diagnostic index. This predicted the diagnosis in 98% of women <35 years correctly.

Hatada T et. al5. retrospectively studied 114 lesions and compared diagnoses obtained by standard FNAC and that of ultrasound guided FNAC with surgical findings and found the accuracy to be 65% and 86% respectively. They concluded that Usg-guided FNAC improves the preoperative diagnosis especially in patients with tumor less than 2 cm.

Heiken TT et al conducted a prospective analysis of office-bases breast ultrasound, on 660 breast lesions and found that suspicious lesions determined by USG had a 75% chance of being malignant; however 5% of lesions characteristic of fibroadenoma turned out to be malignancies.

Jill S Montrey8 attempted to determine the usefulness of ultrasound as a screening tool for breast cancer in women <35 years, with indeterminate mammography, persistent symptoms and high risk history.

Literary review of Breast Usg for screening :-

Carcinoma detected

Frazier et al	1982 (3)	3/135 (2.2%)
Kopens et al	1985 (2)	3/127 (2.4%)
Basset et al	1987 (1)	1/612 (0.2%)
Frazier et al	1985 (4)	36/600 (6%)

Thus breast ultrasonography when used correctly can be effective, but is not fool proof, especially in lesion <1cm.

DISCUSSION

Breast lumps are an enormous source of anxiety to patients and a stratified approach has to be adopted to properly (chart I) evaluate and treat them. Though benign breast diseases are more common; there is a preoccuption with malignancy (undue but understandable) amongst the patients and physicians alike.

The ultimate diagnosis and treatment of a patient with a dominant breast mass rests with the clinician. A dominant breast mass is defined as a solid or cystic lump that persists throughout the menstrual cycle.

The pre op assessment of a breast mass begins with a through history and systematic physical examination. However it is generally accepted that this alone can be inadequate for an accurate diagnosis. The breast is naturally multiondular and hence the difficulty in appreciating small nodules amidst the normal lumpiness is apparent. Apart from this is the varied expertise of the examiner in breast palpation. Thus imaging of the breast using various physical imaging modalities is important.

The earlist recorded case of breast imaging is that of SALOMON, a German pathologist who in 1913 reported the use of the recently developed X-ray to visualize breast structure in amputated breasts. He demonstrated the irregular mass density and microcalcification which are still in use as the most important benchmarks to identify possible breast malignancy. Even today mammography remains the method of choice for detecting the occult,

CHART – 1

COMMON BREAST SYMPTOMS

LUMP   NIPPLE DISCHARGE   PAIN

NODULATIRY   LUMP   CYCLICAL ONCYCLICAL

DIFFUSE   >30YEARS

SYMMETRICAL LOCALIZED

                    ASSYMETRICAL

REASSURE

&   TRIPLE TEST

DISCHARGE

PHYSICAL   IMAGING   TISSUE

EXAMINATION   DIAGNOSIS

Flow chart show diagnostic protocol for patients with breast complaints

nonpalpable lesion and remains the standard for imaging of breast against which other modalities advocated now are measured.

Other imaging modalities have now been introduced for

- Visualizing lesion missed by mammography
- To replace mammography with another efficient, more economic device that would alsobe used

by non-radiologists.

The diagnostic utility of ultrasonogram was documented in 1950s; but it was only with the development of "grey scaling" by Korsakoff and associates in Sweden years later that better issue representation was obtained. Recent technical advances in ultrasonography have expanded the potential utility of this modality in the evaluation of breast lesions far beyond distinguishing solid abnormalities from cystic ones.

Tissue diagnosis remains the most reliable confirmatory tool for breast lumps. In 1912, Ward used fine needle aspiration (FNAC) Cytology to examine lymph nodes for lymphoma. Eventually the procedure was attempted on patients with breast lumps in 1962 by Martin and Ellis at New York. Cytological interpretation requires skill particularly in view of cell types and pathologies encountered, but high levels of accuracy can be obtained with experience.

CLINICAL EXAMINATION

A palpable breast mass may be identified when it becomes it becomes sufficiently large to be differentiated from surrounding breast tissue physically by an examiner – usually the patient or the physician; or is perceived on an imaging examination. Determining by physical examination whether a mass is present can be difficult, as, all breasts are variable in the combination of glandular tissue, fibrosis and fat. True masses are generally asymmetric in relation to the other breast; distinct from the surrounding tissue and three dimensional.

The underlying cause of complaints about the breast proves to be benign in the overwhelming majority of cases. Breast symptoms, however, induce such a great anxiety in the patient that malignancy needs to be excluded as speedily as possible.

The first steps in this are the classic ones of history and physical examination.

Essential points in the history include :

- ◄ Age

- ◄ Menstrual status

- ◄ Family and reproductive history

- ◄ Lactational history

- ◄ Radiation to the chest

- ◄ H/o benign breast disease

In physical examination of patients with a breast with a breast complaint-seclusion, warmth and privacy are particularly important in the examination of the breast. This avoids discomfort and embarrassment to the patient. Good lighting enables detection of minor abnormalities. The patient sits stripped to the waist. Attention is paid to

GENERAL APPEARANCE :

Nourishment, colour, mucous membranes, palms.

Inspection from bed end :

1.   Arms by side

2.   Arms elevated. Looked for

Symmetry of nipples and breasts.

a.   Niple abnormalities

b.   Vascularity

c.   Indrawing and prominence of skin

d.   Tethering

e.   Peau d' orange

f.   Skin nodules

g.   Ulceration

Palpation :

1. Supraclavicular fossae

2. Breasts :

   a. Lightly

   b. Deeply systematically from the areola concentrically outwards including the axillary tail.

3. Axillae :

   1. Taking the weight of the patient's forearm on the examiner's.

   2. Both axilae simultaneously from behind the patient.

3. Abdomen for ascites, hepatomegaly or abnormal masses.

Particularly valuable in practice are

   a) inspection with arms firstly dependent, then elevated.

   b) Intial light touch over the breats prior to systematic deepar palpation in concentric circles, working outwards.

   c) Simulatancous examination of the axillae performed from behind the patient.

Atypical cancer may be firm and have indistinct borders and attachments to the skin or fascia with dimpling or nipple retraction. Benign lesions typically have discrete borders, well defind margins and are mobile. Cysts can be differentiated from solid lesions by palpation.

Rosner et al reported that physical examination can correctly identify only 58% of 66 patients with cysts. Significant discordance among experienced examiners may occur. In one study, surgeons performed physical examination independently and agreed on the need for biopsy in only 73% of 15 masses subsequently proved malignant. (Boyd et al).

Somers et al studied certain palpable abnormalities defined as areas of thickening, predominence of tenderness without an associated dominant mass on physical examination; no

suspicious mammographic lesion; and rubbery, firm, cystic soft mass, needle sensation by FNA. The incidence of malignancy in these 'suspicious' group was less than 1% (1/06), leading to the conclusion that this subset of patients with palpable abnormalities did not require surgical biopsy.

Nevertheless, the physical findings or benign disease and malignancy in its earliest stages may overlap; and without the use of FNA and/or breast imaging, some palpable malignant lesions may be followed up inappropriately; leading to serious consequences for both the patient and the physician.

Although some masses exhibit distinct physical findings, an imaging evaluation is required in almost all cases to characterize the palpable lesion, search for ipsilateral multifocal or multicentric carinoma, and screen the contralateral breast. A negative imaging evaluation, however, should never over rule a strongly suspiscious finding on physical examination or vice versa.

****

ULTRASOUND OF THE BREST

Although diagnostic ultrasound equipment has been available since the 1950s. it is only in relatively recent years that the widespread use of this technique has been accepted by radiologists and then by surgeons. A lot of this has related to difficulties with earlier machines.

HISTORY

The transducers that produce the ultrasonic signal were initially quite crude devices that operated with low frequencies. Although penetration of the signal is better at these frequencies, resolution of tissue abnormalities is not as good. It was not until the development of 'gray scaling' by Korsakoff and associates in Sydney that better tissue representation was obtained. As the name of the technique implies, the images now obtained were in shapes of gray and this shading was corresponding to tissue changes and particularly to areas of localized pathology. Improvements in transducer design followed, allowing various frequencies to be used, with the higher frequencies used in areas such as the breast, thyroid and testis.

Even with all the advances, it must be stated and emphasized that the use of USG equipment is very operator dependant and interpretation of the images requires a large amount of practical training. Skilled interpreters of ultrasonic images, do, however, follow 3 golden rules –

1. Never make an interpretation on a single image, superimpose the ultrasonic images mentally to formulate a 3 dimensional image of the scanned tissues and to ensure that the displayed feature is consistent with the 3D image.

2. Because a feature is displayed it is not necessarily real – always rule out artifacts.

3. Because a feature is not displayed it is not necessarily not there.

The original use of USG was to determine whether a breast mass was a cyst or solid lesion. Advances in technology and refinements in interpretative criteria have expanded the role of USG in characterizing masses as having benign, malignant or equivocal features.

BREST ULTRASOUND TECHNIQUE :

≺ Confirm the location of the mass noted on physical examination; a diagram from the referring physicians to demonstrate the lesions' position.

◄ A high-resolution small parts transducer 7.5 – 10 mhz is used.

◄ Evaluate the Region of Interest (ROI) to assess whether the clinical abnormality is corresponding to the ultrasound findings.

◄ Patient positioning: The patient is positioned in an oblique manner with a pillow placed under the shoulder of the breast to be examined.

The degree of obliquity is determined by the position of the breast – aiming to have the breast spread evenly over the wall, with the nipple pointing to the ceiling. The arm should be elevated over the patient's head to facilitate even distribution of the breast tissue, but should not be so elevated that the breast is retracted superiorly. A little care exercised in positioning makes the USG localization of the lesion less of a problem.

　　a.　　Lumps felt better in the upright position may be scanned in that position.

　　b.　　Fluid in cystic masses may be confirmed by changing to upright/decubits position.

◄ Region of interest is trapped with the examining finger and the transducer is placed directly over the abnormality.

◄ Examine in overlapping radial/antiradial planes – to determine relation of lesion to ducts and avoid errors as mistaking fat islands for solid masses.

◄ The entire periphery of the lesion must be evaluated in multiple planes through a 180 degree are to determine the nature of margins, its shape and appearance of surrounding tissue.

◄ Compression of tissue with the transducer is helpful in spreading apart breast tissues, flattening

islands of fatty tissue, and eliminating artifictual shadowing.

◄ The rest of the breast tissue is systematically imaged from periphery to the nipple.

◄ The retroareolar area can be evaluated with the transducer angled into the area in multiple planes.

LABELING OF LESIONS :

◄ The lesion is labelled on a clock face.

◄ Its distance form nipple is given in centimeters.

◄ The greatest diameter should be measured.

◄ The height (AP diameter) is determined to obtain a height/width ratio.

NORMAL APPEARANCE OF THE BREAST :

Knowledge of normal variations of breast architecture is essential for the detection and accurate diagnosis of abnormalities.

SKIN :

The skin is imaged as an echogenic layer of approximately 3mm or less in thickness, often a hypoechnoic central line. Large areas of skin thickening are difficult to recognize without comparing the ROI to the opposite breast or to a normal area within the same breast. A stand-off pad may be used to detect subtle abnormalities.

SUBCUTANEOUS TISSUE :

The subcutaneous fat layer is a hypoechoic layer situated between the skin line and the breast parenchyma. Cooper's ligaments are imaged as curvilinear lines extending from the breast tissue to the superficial fasical layer-producing a scalloped appearance.

Breast cancer does not arise in the subcutaneous but may involve it by direct extension.

Focal increased echotexture: Malignancy, inflammatory lesions, edema, fat necrosis, or biopsy scar.

Diffuse increased reflectivity : edema of any cause (e.g., Heart failure), diffuse from of breast cancer, inflammatory breast cancer, inflammatory mastitis, or radiation therapy.

Lesions indigenious to this plane are sebaceous cysts, epidermoid inclusion cysts, hemangiomas, and rarely smooth muscle and fibrous tissue tumors.

NIPPLE AND AREOLA :

This is difficult area to visualize because of difficulties with transducer contact by nipple protrusion or inversion, producing air trapping which is a source of shadowing. Compression of the nipple and imaging with multiple planes angled toward the subareolar region can be of help. Ducts can be visualized and traced upon the breast tissue, echogenic areas within the ducts usually represent debris. Visualization of a mass within a dilated duct may indicate a papilloma, carcinoma or other lesion.

BREAST PARENCHYMAL LAYER :

The breast tissue is more dense and uniform in the younger patient, age and parity however, are not good predictors for the USG appearance for any one individual.

The breast parenchyma consists of ductal, lobular and fibrous tissue in varying proportions. The normal appearance of the breast can range form almost completely fatty with only a few echogenic fibroglandular tissue with little or no fat.

Whatever the relative composition of fibroglandular tissue and fat, the fibroglandular tissue should have a regular appearance of echogenic structures arranged in multiple layers parallel to the chest wall without distortion or swirled or pulled appearance.

Most benign and malignant lesions are imaged as nodules hypoechoic relative to paraenchyma and are seen most easily in homogenously echogenic breasts, which do not deform with compression. However, the most useful maneuver is imaging in multiple planes, which will demonstrate the continuity of fat island with other areas of fat.

RETROMAMMARY AREA :

It is a hypoechoic fat plane, deep to the superficial fascia, pectoralis. Usually well demonstated deep to the echogenic glandular tissue.

LYMPHNODES, ARTERIES, AND VEINS

Lymphonods are frequently imaged within the breast and axilla as oval nodules with an eccentric hyperechoic hilum a surrounding less echogenic rim of tissue.

Benign nodes – large in size but maintain their morphology.

Malignant nodes – only gross abnormalities can be detected., when they appear as lobulated hypoechoiec nodules.

Arteries and veins are visualized as tubular anechoic structures within the breast. Pulsation will confirm the arterial nature of a vassel. Color Doppler can be used to demonstrate vascular structure within the breast and tumors.

****

CHARACTERIZATION OF BREAST MASSES

CYSTS :

The first step in characterizing breast masses is cyst/solid differentiation. When the breast masses meet all of the diagnostic criteria for cysts the USG accuracy approaches 100%.

The criteria include :

1.   Round, oval lobulated shape.

2.   Anechoic

3.   Well-defined posterior border

4.   Increased through and through transmission

5. No alteration of surrounding parenchyma.

Unfortunately, not all cysts display these criteria. The resolution of USG for cystic lesions is up to 5mm with 100% accuracy.

The presence of internal echoes is the most common diagnostic difficulty in cyst/solid differentiation. Cysts have internal echoes due to

- Presence of cholesterol or calcium

- Hemorrhage

- Infection

FOLLOW UP OF CYSTIC LESIONS

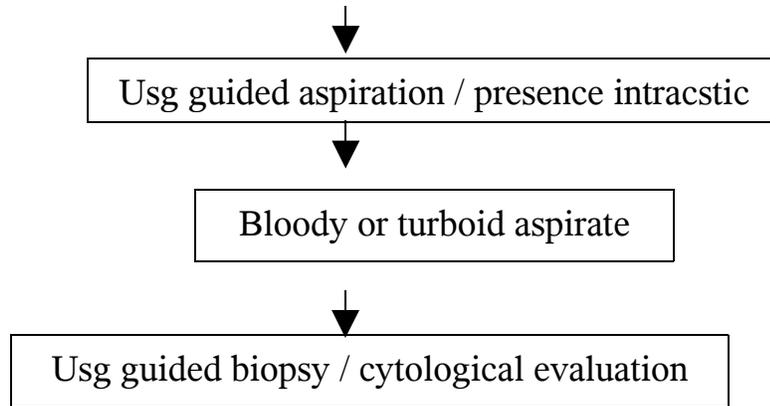Chart – (2)

SIMPLE CYST

| Confirm benign nature and observe |

⇩

| Follow-up Usg at 4-6 months |

⇩

| No malignant or indeterminate features |

⇩

| Observe |
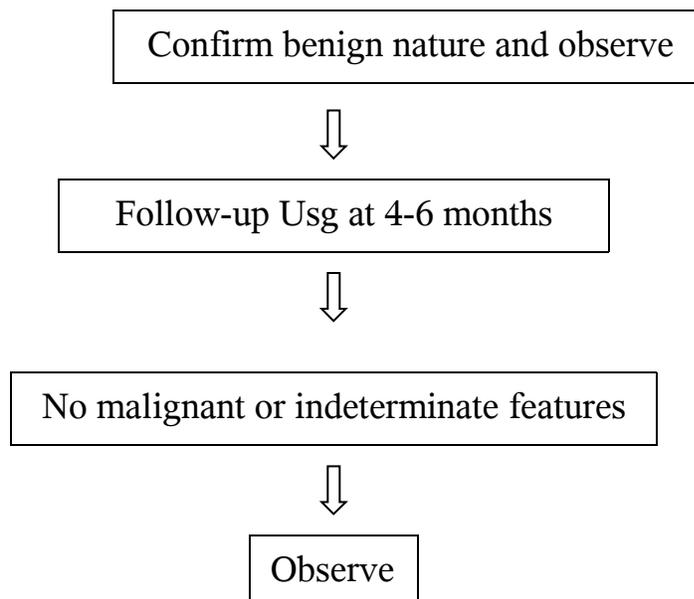
COMPLEX CYST

| Large complex/indeterminate cysts |

```
          ↓
┌─────────────────────────────────────────┐
│  Usg guided aspiration / presence intracstic  │
└─────────────────────────────────────────┘
                    ↓
        ┌───────────────────────────┐
        │  Bloody or turboid aspirate  │
        └───────────────────────────┘
                    ↓
    ┌─────────────────────────────────────┐
    │  Usg guided biopsy / cytological evaluation  │
    └─────────────────────────────────────┘
```

SOLID MASSES :

Ultrasound features of a solid included –

- ◄ Primary signs – changes produced by the mass itself.

- ◄ Secondary signs – changes produced in the tissues surrounding a mass.

<u>BENIGN CHARTERISTICS OF SOLID MASSES</u> – The diagnosis of a benign nodule based on USG findings is rarely specific. The appearance of fibro adenomas, focal fibrocystic changes, tubular adenomas and other benign solid nodules overlap. Characteristic of benign solid lesions include.

1. Shape-oval, round with few lobulations

2. Margins that are sharply demarcated with a thin echogenic pseudocapsule.

3. A depth/width ratio of <1

4. No disruption of surrounding tissues

5. Absence of malignant characteristics

6.   Homogenous low level internal echoes are usually present.

FIBROADENOMAS :

They are most common benign solid nodules. They are most commonly detected in the younger age group. The USG appearance is determined by the relative amounts of fibrous and epithelial tissue.

c.   Enhanced through and through transmission

d.   Posterior attenuation in relation to the fibrous component

e.   Coarse calcifications in degenerating fibroadenomas producing shadowing.

f.   Tubular structures seen with lactating and juvenile types.

g.   Different from fat lobules by their non compressible characteristics.

LIPMAS AND FIBROADENOMYOLIPOMA :

1.   Lobulated masses that do not distort surrounding tissues.

2.   Presence of internal due to fat

FAT NECECROSIS :

1.   Focal hyperechoic nodule with a central lucency.

MALIGNANT CHARTISTICS OF BREAST LESIONS

16. Stellate masses

17. Circumscribed masses

18. Diffuse edema changes

19. Calcifications

Stellate masses : Desmoplastic reaction produces contraction of the breast tissue towards the mass, disrupting the normal parallel soft tissue planes.

- These masses have an irregular hypoechoic lesion with distortion of the surrounding breast tissue.
- Disruption of normal trabecular structures.
- Extension along the plane of the ducts.
- Posterior acoustic shadowing.
- Increased reflectivity of the subcutaneous tissue.

DD of stellate lesions :

- Carcinoma (most common)
- Radial scar
- Sclerosing adenosis
- Post surgical scarring

Circumscribed masses : Breast cancer also commonly presents as hypoechoic masses that appear to displace breast tissue.

- Oval, round

- Multilobulated
- Height / width ratio > 1
- >3 lobulations
- reactive halo surrounding the mass

DD of circumscribed masses :

- Carnioma – Usually the high grade NOS variety of ductal carcinoma & medullary, colloid, and papillary ca.,
- Metastatic lesions – from lymphona, melanoma, leukemia, sarcoma, adencarcinoma from other sites.
- Inflammation and abscesses.
- Hematoma.
- Phylloides tumour
- Fibroadenoma.

Diffuse edema changes : A difficult type of carcinoma to distinguish is one that does not produce a mass but only diffuse changes in echotexture and parenchymal pattern.

- Subtle increased reflectivity of parenchyma and subcutaneous fat.
- Loss of normal orientation of tissue planes.
- Poor differentiation in the fat-parenchyma interface.

DD of diffuse edema :

- Lobular and ductal carcinoma, inflammatory carcinoma.
- Breast contusion.

- Congestive cardiac failure (usually bilateral).
- Breast / chest wall irradiation.
- Superior vena cava obstruction.
- Axillary Lymphatic obstruction.

Calcifications : Breast carcinoma may produce calcification both with and without mass. Calcification of sufficient size and clustered variety in a homogenous tissue can be picked up by USG.

Intracystic carcinomas : Rare lesions, usually papillary carcinoma that has obstructed a duct and bleed producing a blood filled cyst.

DD of intracystic mass :

- Papillary carcinoma
- Necrotic solid tumor
- Cysts containing hemorrhage, debirs
- Abscess
- Hematoma

With tha aid of the above criteria USG can come to a reliable diagnosis of breast lumps, depending upon the size of the lesions. The minimum size of cystic lesions picked up by USG are 2-3 mm. Solid lesions > 0.5 cm are usually categorized with accuracy, 80% of solid lesions >2 cms and, 20% of lumps> 1-2cms 5% of lumps <1cm is the diagnostic accuracy of USG.

*****

INDICATIONS FOR BREAST ULTRASOUND

From the above discussion we can summarise the now standardized indications for Breast Ultrasound as follows :

1. Evaluation of a palpable lump or mammographic abnormality.
2. To confirm the existence of a lesion and its nature.
3. Single imaging modality in our patients or in pregnant or lactating patients who present with symptoms.
4. To differentiate solid from cystic lesions.
5. For pathological examination of indeterminate lesions-guided FNA/CNB can be carried out.
6. Pre operative localization of lesions with needle placements, documentation of lesion removal by Usg of biopsy specimen.
7. Follow up of surgically altered breast – by tracing it through the breast and subcutaneous layer to the biopsy scar on skin, as well as for guidance for FNA/ CNB.
8. Follow up after augmentation mammoplasty to detect extracapsular rupture / contour abnormalities of the prosthesis.
9. Follow up of probably benign lesions that have not been biopsied.
10. Adjunctive to mammography as a screening tool for Carcinoma breast.

*****

ADVANTAGES OF USG OVER BREST MAMMOGRAPHY

1. No risk of radiation and its inherent consequences.

2. Can quality a lesion-as size, shape, echogenicity and relation to surrounding tissues as against a mammographic report of a 'density' which is less specific.

3. Sonographically guided biopsies are more accurate than streotactic biopsies as the needle can be visualized in real time throughout the entire procedure. This adds confidence that the biopsy sample was obtained from the lesion.

4. Mammographic positioning for pre-operative localization of the masses is cumbersome and time consuming and less accurate. Hence USG is the modality of choice for guidance.

5. Surgically altered breast has confusing findings and is non-informative on mammography.

6. Palpable lumps following extracapsular rupture of a prosthesis may be impossible to image by mammography.

7. Long term follow-up of benign nodules not excised is associated with risk of radiation on mammography and hence best performed by USG.

*****

LIMITATIONS OF BREAST ULTRASOUND

Breast ultrasound usage is avoided in certain situations where no efficacy has been documented:

1. Routine evaluation of post operative breast.
2. Cancer Screening – as USG cannot detect all the non-palpable cancers that are also missed on mammography.
3. Cannot detect microcalcification well; small solid lesions in fatty or mixed breast tissue are not sonographically visible.
4. High false negative rate for non palpable cancers, (23%) which are smaller, clinically occult.
5. Substantial false positive rate-sonogram may pick up 'lesions' which are rarely clinically significant.
6. Unreliable in lesions<1 cm.
7. Less accurate in dense breasts.

These data suggest that breast ultrasound can be useful both as a single imaging modality and as a adjunct of mammography in evaluation of patients with breast Jumps. In addition, ultrasound facilitates preoperative needle biopsy of non-palpable abnormalities, permitting timely and cost effective patient care.

*****

FINE NEEDLE ASPIRATION CYTOLOGY

The advent of cytology and availability of experienced cytologists has diminished the diagnostic role of excision biopsy especially with regard to breast lumps.

FNAC can play a significant role in the early diagnosis of breast lumps to rule out malignancy, as an attractive alternative to open biopsy. It is our responsibility to further

the integrity of this important procedure by understanding the merits and pitfalls of breasts FNAC and adhering to the defined guidelines.

HISTORY :

Martin and Ellis in 1926, New York first introduced the concept of FNAC in the midst of controversies regarding the credibility of the procedure. Breast FNAC is a simple complex procedure that is influenced by many variables. Accurate interpretation of breast FNAC requires clear guidelines for specimen acquisition, staining and preparation.

Bamforth in 1966 defined cytology as; "The examination of cells obtained by needle or drill biopsy in solid organs or tissue masses or form cut surface of such materials freshly removed by surgical biopsy:.

Innumerable studies have now shown that cytological examination of cells obtained this way is a rapid and reliable method of diagnosing malignant diseases of the breast.

REQUIRMENTS :

1. Spirit swab to clean the skin.
2. Disposable 10ml or 20ml syringe with fine needle 22G/23G.
3. A number of 76mm x 26mm microscopic Slides.
4. Fixatives like cytofix solution which is a commercial preparation, containing absolute alcohol slides.
5. Transport box for prepared slides.

6.   Complete lab. Request form giving patient's particulats

PROCEDURE :

The Procedure is usually performed without anaesthesia. Very rarely local anaesthesia is used. Local anaesthesia is generally not necessary because it is painful and may obsure the mass.

1.   The skin over the lump is wiped with antiseptic and the lump is fixed between the fingers and the thumb and held steadily for needling. Then needle is guided through the skin into the lesion.

2.   Once the needle is felt to enter the lesion, the plunger is retracted to create vacuum. Should the lesion prove to be cystic the fluid should be aspirated in its entirety and expressed into a universal container and sent for cytological examination.

3.   If the lump is found to be solid, the needle is gently moved back and forth into the substance of the tumor three or four times and is inserted into a different part of the tumor each time to dislodge the cells from the tumor, so that the aspirate will contain the sufficient material for cytological studies.

4.   Throughout the technique a negative pressure must be sustained in the syringe. Only after the tumor has been repeatedly probed, should suction be released and the pressure in the syringe allowed to return gradually to atmospheric pressure and the needle is withdrawn from the breast. The pressure in the syringe must be adjusted in a way, so that the aspirated cells are retained in the lumen of the needle, sustained suction as the needle is withdrawn result in, the cells being withdrawn into the barrel of the syringe rendering them inaccessible for processing.

PREPARATION OF ASPIRATE :

It is possible to make smear directly from the aspirate in the outpatient department. Alternatively, the aspirated cells can be suspended in fixative and transferred to cytologic laboratory for processing.

PREPARATION OF SMEAR :

- After aspiration the needle and syringe are withdrawn from the skin.
- Although nothing is visible in the syringe cells should have collected inside the bore of the needle.
- The needle is disconnected from the barrel, the syringe is filled with air.
- A clean glass slide should be ready and the needle is reconnected to the barrel and the aspirated material is blown out into the slide.
- Any large tissue fragments which do not spread easily should be crushed between the cover slip and the slide.
- The smear is air dried and fixed in cytofix solution. Then the slide is duly labelled.

FINATIVES :

A number of fixatives are used in cytology –
- 95% Ethyl alcohol
- 95% Ethyl Alcohol with 3% glacial acetic acid – to improve the nucleoprotein fixing properties.

STAINING PROCEDURES :

Some cytopathologists prefer to interpret these slides stained

❑ Papanicolaou method – when available this may be preferred in cytology for its superior display of nuclear morphology and clear translucent demonstration of cytoplasm.

❑ Hematoxylin and Eosin method.

*****

NORMAL CYTOLOGY OF THE BREAST

The mammary gland is a compound gland made up of independent units containing their own ducto-alveolar systems.

The alveoli are lined by simple cuboidal or low cuboidal epithelium which may alter in size depending on the secretary status of the breast. The ducts are also similar in lining, becoming pseudostratified along the main lactiferous and stratified as they approach the nipple.

The typical cytological features in different breast condition are given below.

BENIGN :

FYBROADENOMA :

❑ Duct cells are seen in large group and sheets surrounded by "stripped" nucleus.

❑ A small degree of nuclear pleomorphism of duct cells is usually present.

❑ Their high cellularity and moderate pleomorphism can be mistaken for a malignancy.

FIBROCYSTIC DISEASE :

- Numerous small foam cells and large metaplastic apocrine cells with acidophilic cytoplasm.
- Dark pyknotic nuclei,

Sheets and clusters of uniform elongated cell; with transparent cytoplasm and having dendrite process.

PLASMA CELL MASTITIS :

- Foam cells and sheets of depenerate epithelial cells are common.
- Lipid containing macrophages and occasional foreign body giant cells.
- Diagnostic feature is presence of large amounts of plasmacytes, Lymphyocytes and esinophils and few neutrophils.

MALIGNANCY :

There are structured criteria for the diagnosis of malignancy by cytology, which are stratified into :
- Structural alterations in the cells.
- Changes in inter relationship of cells in cell clusters.
- Indirect criteria.

Structural modifications :

- Alterations of nuclear cytoplasmic ratio with disproportionate enlargement of nuclei.
- Hyperchromasia due to increased chromosomal content, aberrant chromatin

pattern.

- ◄ Increased number of nucleoli beyond the normal.
- ◄ Multinucleation with nuclear atypia, abnormal mitotic figures.
- ◄ Marked thickening of nuclear membrane.
- ◄ Cytoplasmic changes enhanced by staining, such as pronounced basophilia/acidophilia.
- ◄ Presence of cytoplasmic inclusions like pigment granules, leukocytes and cellular debris.
- ◄ Atypical vacuolation especially in adenorcarcinoma.

Cell –Cell changes :

- ◄ Enlargement of cells beyond normal shape.
- ◄ Aberrant forms with associated nuclear atypia.
- ◄ Degenerative or necrotic changes.
- ◄ Lack of uniform orientation of cells and nuclei.
- ◄ Anisocytosis/anisokaryosis – with marked variation in size of cells/nuclei within the same cell cluster.
- ◄ Loss of distinct cell boundaries.
- ◄ Dense grouping of and crowding of cells and nuclei.
- ◄ Engulfment of one cell by another.
- ◄ Cells grouping into characteristic patterns.

Indirect Changes :
- ◄ Presence of blood.
- ◄ Increased Lymphocytes.
- ◄ Prominent histiocytes and polymorphonuclear cells.

<center>*****</center>

<u>ADVANTAGES OF FNAC :</u>

1. Does not require anaesthesia.

2. Tolerated by patients as an OP procedure.

3. No secialized equipment required.

4. No damage to breast tissue that may occur with open biopsy.

5. Though small hematomas may be encountered, neither hemorrhage nor sepsis is noted.

6. Remote chances of tumor seeding along needle tract.

7. Lymphatic / vascular dissemination of tumor is virtually unknown.

8. Can easily diagnose cysts / abscesses and treat them.

9. Eliminated need for open biopsy when a diagnosis of carcinoma is made that is the incidence of false positive in malignancy is almost nil.

10. Can be easily repeated.

<u>LIMITATIONS</u>

1. Cannot qualify the type of malignancy.

2. False negative reporting when

    a. Small tumors <1 cm.

    b. Sclerotic lesions.

    c. Deep seated tumors.

    d. Large/pendulous breasts.

    e. Lesions beyond the length of the needle.

<center>*****</center>

CORE NEEDLE BIOPSY (CNB)

Dominant lumps >2 cm in diameter can be approached by a wide bore cutting needle; such as Tru-Cut needle that the advantage of producing a core of tissue which can be paraffin embedded and used as a normal histological speciman with a modern spring loaded device, with a local amaesthesia to the skin; a series of high quality cores can be obtained rapidly and almost painlessly.

ADVANTAGES :

- Ability to obtain a core of tissue that is sufficiently large for HPE
- Providing more details of tumor structure.
- Ability to distinguish between invasive and IDCA.
- Any pathologist can interpret the results obviating the need for special skill of a cytopathologist.
- Large amount of prognostic information can be obtained including.

  - Biological grade
  - Receptor level
  - DNA analysis

DISADVANTAGES :

Risk of seeding the needle tract with tumor cells.

Biopsy should be adjusted to avoid carrying potentially malignant tissue into the chest wall.

False positive incase of radial scars.

False positive incase of hard lesions, deflecting the needle into surrounding fat.

Thus CNB can be adopted as an alternative office biopsy technique to FNAC carrying sensitivity of 89%-100%.

*****

AIM OF STUDY

The study is conducted with the objective of assessing the combined and individual reliablility of the Modified Triple Test in making a pre-procedural diagnosis of palpable breast lumps.

The components of the Modified Triple Test are :

1. Clinical Examination (C/E)
2. Breast Ultrasonogram (USG)
3. Fine Needle Aspiration Cytology/Core Needle Biopsy (FNAC/CNB)

*****

MATERIALS AND METHODS

A prospective cross sectional study of 100 female patients attending the out patient department at the Department of General Surgery, Government Rajaji Hospital, Madurai, with the complaint of a palpable lump/lumps in the breast was undertaken.

Male patients and female patients with advanced Breast Cancer that makes diagnosis obvious were excluded from the study (n=32).

The inclusion criteria were :

1. Female >30 years.
2. C/o breast lump – clinically palpable as a localized lesion differing from the surrounding breast tissue.

Each patient was put through the Modified Triple Test. On the basis of a systematic clinical examination, the lumps were grouped as – Malignant, Benign or inconclusive.

The lesions were classified as Malignant, Benign or lnconclusive based on the following features.

a. Malignant – ill defined, heterogenous mass with sharp angulations; presence of microcalcifications.
b. Benign lesions were either cystic or solid

Cysts – Round, oval, anechoic, well defined with through and through transmission in simple cysts. Abscesses show low level internal echoes.

Solid : 1.   Fibroadenoma   - Round, oval

                                    Bi/Trilobulated

                                    Well defined with pseudocapsule

                                    Homogenous internal echos

       2.   Fibroadenosis   - Generalized increase in the fibroglandular

                                      elements of breast.

                                    Hyperechoeic shadows with cystic areas

                                    No distortion of breast architecture

Ultrasound examination also included the contralateral breast, axillae, internal mammary lymph nodes. For deeply seated lesions Sono-guidance was utilized to aspirate cysts and to take biopsies.

After this, **FNAC/CNB** was performed by the attending surgeon and sent for cytological/Histopathological examination.

CHART – 3

FLOW CHART DEPICTING THE STUDY PROTOCOL
SAMPLE SIZE

N=100

INCLUDED IN STUDY N=68

EXCLUDED FROM STUDY N=32

NO.OF PALPABLE BREASI LUMPS N=73

MODIFIED TRIPLE TEST

C/E	CE	MALIGNANT - 29
USG	USG	BENIGN - 24
FNAC/CNB	FNA/CNB	INCONCLUSIVE – 4

OBSERVATION N=16 (22%)

EXCISION BIOPSY / DEFINITIVE SURGERY N=57

MALIGNANT N=24 SURGERY

BENIGN N=33 SURGERY / FOLLOW UP

FNAC was reported as follows :

a. Insufficient material   Cell content in the aspirate too poor for cytological assessment.

b. Benign cells :   Sufficient material with benign cells indicating Fibroadenoma of Fibrocstic disease.

c. Atypical cells :   Slight atypia; interpreted as benign lesion.

d. Suspicious :   Malignancy – suspect cells; not interpretable

as carcinoma with certainity.

e.   Carcinoma :   Cells indicative of malignancy.

Results were interpreted as follows :

a-repeat FNAC/CNB

b,c-benign

d-inconclusive

c-malignant

The results of the modified Triple Test were then analysed individually and as a combination. Any component indicating a malignant report were taken as malignancy. Inconclusive reports were subject to excision biopsy on an inpatient basis. Patients with malignancy were treated with definitive surgery. The post procedural histopathological reports were compared to the results of the Modified Triple Test.

*****

DATA ANALYSIS

Of the patients randomly referred for the study (n=100), patients not fitting the inclusion criteria were excluded (n=32). Thus 68 patients with 73breast lumps were inducted into the study.

The MTT obviated excision biopsy in 16 patients (22%) and this is the potential advantage of this test. Thus the final study group (n=57) underwent the MTT followed by excision biopsy, the results of which were available for comparison.

The average age of women in this study was 41.84+9.1 The mean shifting to 47 years in patients with malignancy, the youngest patient was 30 years and the oldest was 65 years. This conforms with the suitable age for subjecting patients to screening procedure followed worldwide (i.e.) above 40 years. 9 women were nulliparous of which only 3 had malignant lesions. The rest (n-48) were nulliparous. The results do not point to any positive association between partiy and malignancy (P>0.05). (Table :1)

TABLE : 1

ASSOCIATION BETWEEN PARITY AND BREAST PATHOLOTY

Parity	Malignant	Benign
Nulliparous	3	6
Multipara	21	27

P>0.05

Benign lesions were more common amongst premenopausal women (n=33); though malignancy could not be excluded in this group (n=24). However, all the lesions detected in pecumenopausal (n=5) posmenopausal women were malignant. (N=6) (Table – 2)

TABLE : 2

<u>ASSOCIATION BETWEEN MANSTRUAL STATUS AND MALIGNANCY</u>

Menstrual status	Malignant	Benign
Postmenopausal	6	0
Perimenopausal	5	0
Premenopausal	13	33

P<0.001

On excision biopsy, the 57 lumps were confirmed histopathologically as cither Malignant (n=24) and Benign (n=33).

The pathological reports were :

Total of malignancies	=	24
Intra Ductal Carcinoma	=	20
Lobular Carcinoma	=	1
Medullary Carcinoma	=	1
Carcino Sarcoma	=	1
Malignant cystosarcoma Phylloides	=	1
Total no. of Benign lesions	=	33
Fibroadenoma	=	14
Fibrocystic Disease	=	10
Breast Abscess	=	6
Benign cystosarcoma Phylloides	=	3

The associations between each component of MTT and the combined MTT with the biopsy report were subjected to computer generated analysis.

Clinical examination finding of a hard, irregular lump was more like to be malignant, while a soft or firm mass with regular surface suggested benign lesions ($P>0.001$). Benign lesions most often confused with malignancy were Benign cystosarcoma phylloides & Fibrocystic disease. (Table-3)

Table : 3

Consistency	Malignancy	Benign
Hard	18	3
Firm	5	30
Soft	0	1
Surface		
Irregular	18	6
Regular	6	27

P<0.001

The intial indications of USG in differentiating a solid from cystic lesions may be non benefical in coming to a correct diagnosis. Our study shows no association between character of the lesion and diagnosis (P>0.05)

(Table – 4)

TABLE :4

ULTRASOUND FINDINGS AND HPE

	Malignant	Benign
Cystic	2	6
Solid	22	28

A regular, well defined; hyperechoeic lesion was usually benign. An irregular; ill defined mixed echogenic mass indicated malignancy. Hypoechoeic lesions were not characteristic of either (P=0.05). Echogenicity could not thus be used as a singular feature to rule out malignancy except when they were hyperechoeic. (Table – 5)

TABLE –5

ECHOGENICITY OF LESIONS AND HPE:

Echogenicity	Malignant	Benign
Mixed	10	6
Hypoechoeic	14	23
Hyperchoeic	0	4

$P = 0.05$

Ultrasound detected Axillary nodes in all patients (n=12) found to be clinically node positive; however it could not distinguish whether the node had malignant infiltration or not.

Ultrasound guided FNA/CNB was done in 6 cases; 2 of which were cystic lesions with a residual mass on aspiration of the cysts. Both turned out to malignancies missed on routine FNAC.

Amongst the individual tests; clinical examination was more likely to miss a malignancy (Sensitivity 75%); as against ultrasound (Sensitivity 92%) or FNA / CNB (Sensitivity 100%). FNA/CNB correctly identified malignancy in all 24 cases; while ultrasound misinterpreted 1 case as malignant (a case of Benign cystosarcoma phylloides) with specificities of 100% and 85% respectively.

The MTT was 85% specific with malignant lesions. But 5 cases were misdiagnosed as malignancies and turned out in 3 cases to be Fibrocystic Disease and 2 cases were Benign cystosarcoma phylloides – both benign lesions. Inconclusive results (n=4) on MTT were also confirmed to be benign lesions. Thus MTT, though had false positives with respect to malignancy but no false negatives (i.e.,) a negative predictive value of 100%. These data are comparable to the original triple test with its sensitivity (65%-96%) and specificity (55%-98%) as reported in various studies (Tables – 6-10).

TABLE – 6

ASSOCIATION BETWEEN CLINICAL EXAMINATION AND HISTOPATHOLOGY RESULT

CLINICAL EXAMINATION	HISTOPATHOLOGY	
	Maignant	**Benign**
Malignant	18	1
Benign	1	23
Inconclusive	5	9
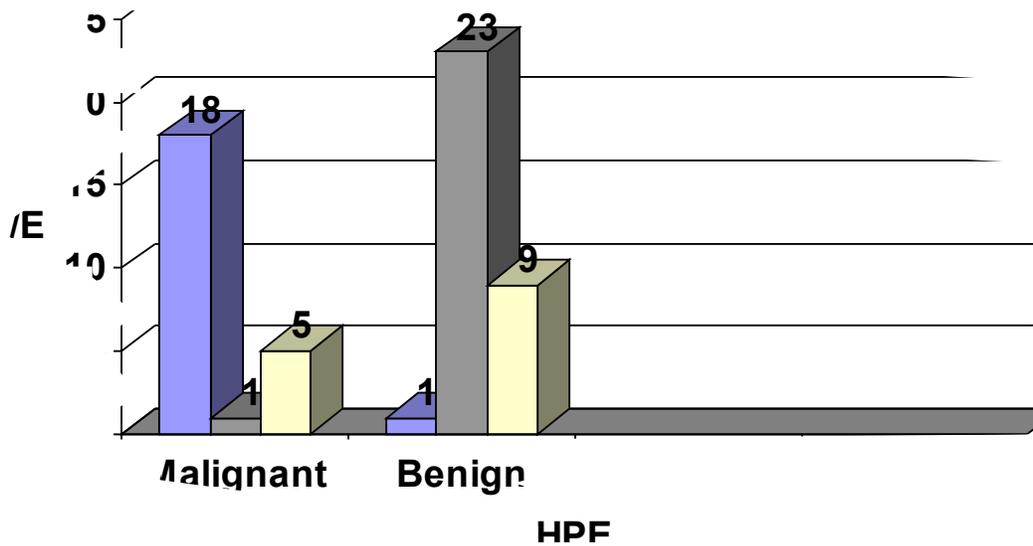
TABLE – 7

ASSOCIATION BETWEEN ULTRASONOGRAM AND HPE

ULTRASONOGRAM	HPE	
	Maignant	Benign
Malignant	22	3
Benign	1	28
Inconclusive	1	2
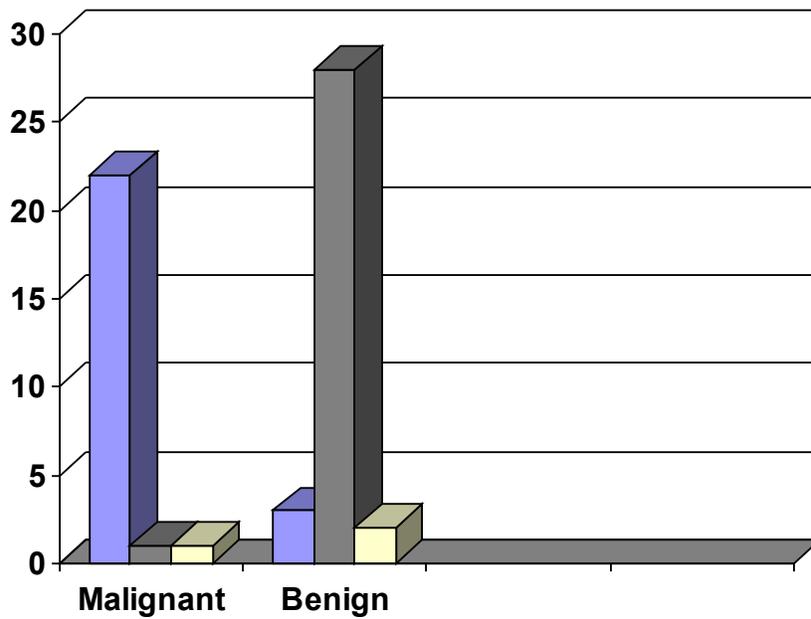
TABLE – 8

ASSOCIATION OF FNA/CNB WITH HPE

| CLINICAL | HISTOPATHOLOGY | |
EXAMINATION	Maignant	Benign
Malignant	18	1
Benign	1	23
Inconclusive	5	9
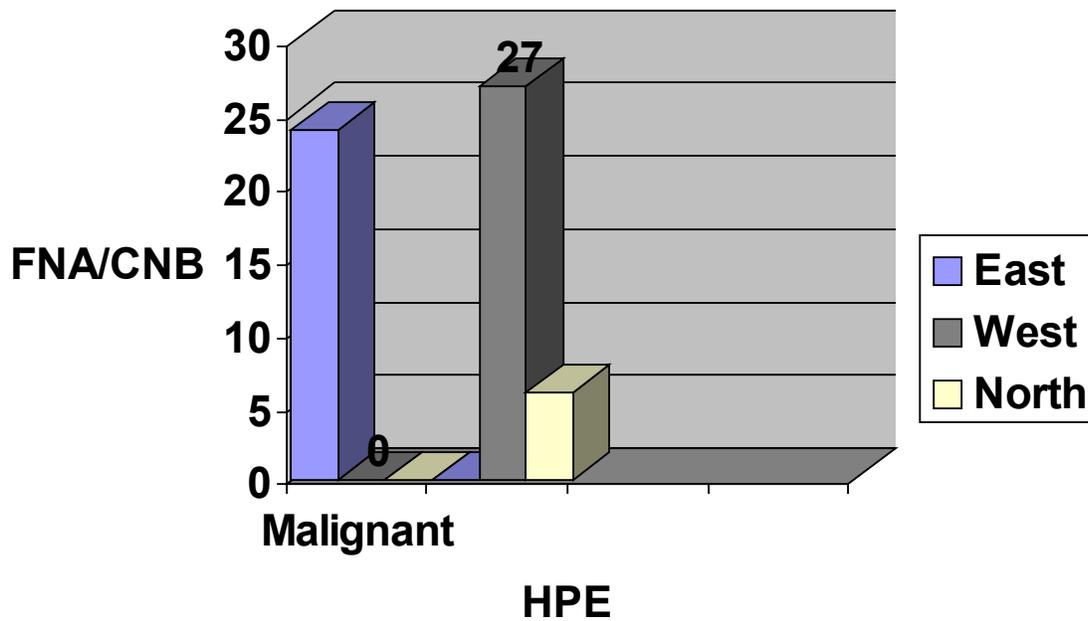
TABLE – 9

ASSOCIATION MODIFIED TRIPLE TESTS WITH HPE

MTT	HPE	
	Maignant	Benign
Malignant	24	5

Benign	0	24
Inconclusive	0	4
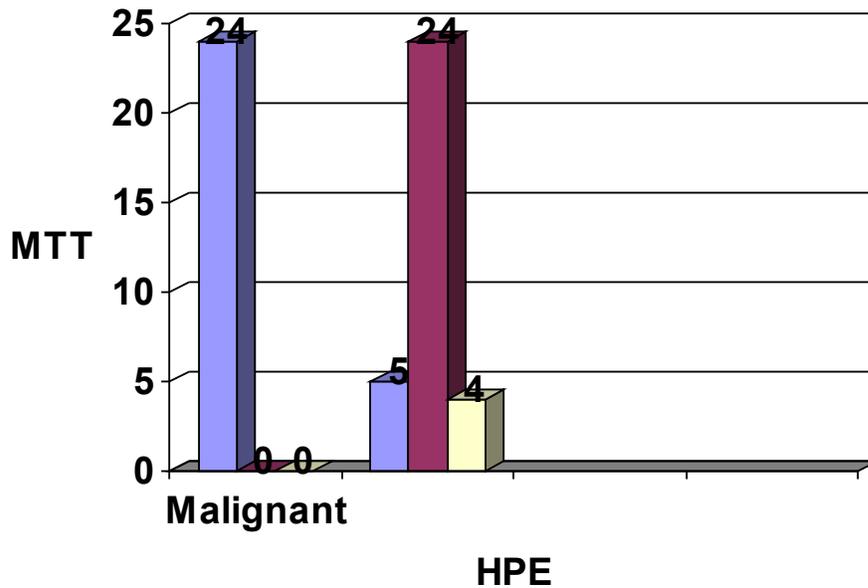
TABLE – 10

STATISTICAL ANALYSIS OF THE STUDY

	C/E	USG	FNA/CNB	MTT
Sensitivity	75%	92%	100%	100%
	(53-80%)	(72-99%)	(83-100%)	(83-100%)
Specificity	97%	85%	100%	85%
	(82-100%)	(67-94%)	(87-100%)	(67-94%)

Positive Predictive Value	95% (70-99%)	81% (61-93%)	100% (83-100%)	83% (64-93%)
Negative Predictive Value	84% (64-90%)	93% (76-99%)	100% (87-100%)	100% (85-100%)
'P' Value	<0.001	<0.001	<0.001	<0.001

FNA / CNB as a single test was a superior diagnostic test than the other two tests, but only when complemented by them could the lesion be characterized in all dimensions for the chosen interventional procedure.

When an inconclusive was reported the likelihood of malignancy increases in ascending order from FNA/CN, USG to C/E (n=o, n=1, n=5) respectively. All 4 cases deemed inconclusive after MTT were later diagnosed as Fibrocystic disease.

CONCLUSION

Detection and management of a breast mass requires an optimal environment for interpretation, relevant use of clinical information, technically excellent imaging procedures, proper interpretation of finding and patient recommendations.

Our results show that the diagnostic accuracy of combined physical examination breast USG and FNA/CNB is comparable to that of histological examination.

A fine collaboration between experienced radiologists, cytologist and the Clinician is required.

Ultrasound when replacing mammography serve as effective an imaging modality in palpable breast lumps and is more comprehensive.

Ultrasound breast aids biopsy techniques by guidance to the representative area than increasing yield.

CNB is a suitable alternative when FNA is inconclusive and may offer additional information.

Thus the use of MTT to complement findings in differential diagnosis of a lesion in a symptomatic women seeking medical care deserves acceptance and further evalution. This may lead to less delay in treatment when malignancy is suspected and to avoidance of surgical exploration when a benign nature of lesion is suspected.