

**“ A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND
PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY ”**

Dissertation submitted to

THE TAMILNADU DR M.G.R MEDICAL UNIVERSITY

In partial fulfilment of the regulations for the award of the

M.S.DEGREE EXAMINATION

BRANCH – I

GENERAL SURGERY



STANLEY MEDICAL COLLEGE

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

CHENNAI

CERTIFICATE

This is to certify that this dissertation on “ **A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY** ” is a bonafide work done by **Dr.M.S.VASANTH** Post graduate student (2017- 2020) in the **Department of General Surgery, Government Stanley Medical College & Hospital, Chennai** under my direct guidance and supervision, in partial fulfilment of the regulations of the TheTamilnadu Dr.M.G.R. Medical University, Chennai for the award of **M.S., Degree (General Surgery) Branch-I**, examination to be held in May 2020.

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I, Dr **M.S.VASANTH**, solemnly declare that this dissertation titled “**A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY**”, is a bonafide work done by me, in the Department of General Surgery , Government Stanley Medical College & Hospital- Chennai, under the guidance and supervision of my unit chief **PROF. Dr.C.BALAMURUGAN M.S.**,

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ACKNOWLEDGEMENT

I sincerely thank with gratitude **The Dean, Prof .Dr.R.SHANTHI MALAR M.D.,D.A** Govt. Stanley Medical College, Chennai for having permitted me to carry out this study at Government Stanley Hospital, Chennai.

My special thanks goes to **Prof. Dr.T.SIVAKUMAR.M.S.**, Professor and Head, Department of Surgery, Stanley Medical College, Chennai for his guidance throughout the period of my study.

I am greatly indebted **Prof. Dr. C. BALAMURUGAN M.S.**, my unit chief, who had been a constant source of encouragement and inspiration for the smooth completion of my study.

I express my deepest sense of thankfulness to my assistant professors **.,Dr.D.PRINCESS BUELAH M.S , Dr.M.VIGNESH.M.S., Dr. VINOTH.M.S., Dr.DHANRAJ.M.S** for their immense help and guidance through out my study.

I cannot forget the co-operation of my friends *Dr.Lalith kumar, Dr.Zothanpari Ralte* in completing my study. I am also thankful to my seniors *Dr.Anu, Dr.sahulthan,Dr.Sivagovindan, Dr. Kamalakannan , Dr. Aravind Ram, Dr.Chethan,* for their valuable support in this study.I could not forget to thank my juniors, *Drharshini, DrGokulram, DrGiridharan Dr karupisivan Dr seethe Dr puruthaamman Dr Hari narayan Dr kishore raja* without whom accomplishing this task would have been impossible.

I express my sincere thanks to all patients ,who inspite of their physical and mental sufferings have co-operated and obliged to my request,without whom my study would not be possible.

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INTRODUCTION

The majority of women diagnosed with breast cancer undergo some kind of breast surgery as part of their treatment. Up to 55% of these women experience pain after their surgery, pain which in some cases persists for months to years . The purposes of this study is to identify the different kinds of pain experienced by women after breast cancer surgery, to explore the current literature addressing its nature and incidence, and to discuss the implications of this information for treating the women with breast cancer,

Two pain syndromes that commonly follow breast surgery, post axillary dissection pain and phantom breast pain, will be discussed.Strategies for pain management, including educational intervention and treatment approaches, will also be addressed.

PAIN AS A RESULT OF SURGERY

Pain is defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" and is usually classified as either acute or chronic. Acute pain is described as being brief in duration, lasting <6 months, and usually resolving as healing takes place. Chronic pain is described as prolonged, lasting >6 months. It may be a constant uncomfortable state or episodes of acute pain that recur over a prolonged period of time .

Pain as a result of breast surgery may fall into either of these categories. Post mastectomy pain syndrome has been defined as "chronic pain commencing immediately or soon after mastectomy or removal of a lump, affecting the anterior thorax, axilla, and/or medial upper arm' .

Symptoms experienced by women who have had lumpectomy should be included in reports of post mastectomy pain, despite the fact that they have retained an intact breast

POST AXILLARY DISSECTION PAIN

Pain after dissection of the axillary nodes affects the arm, hand, chest wall, and shoulder on the surgical side. This pain is described as aching or burning with stabs of shooting pain, pins and needles, that begin in the inner posterior aspect of the upper arm and run down the arm to the fingers . The axillary dissection pain as being caused by disruption of the intercostobrachial nerve, occasionally with neuroma development .Other causes suggested are tumor involvement or

radiation fibrosis at the brachial plexus . Post axillary dissection pain has been reported as mild to intense, beginning hours after surgery, often lasting for several years after surgery.

PHANTOM BREAST PAIN (PBP)

Phantom breast sensations described by women after breast surgery are similar to phantom-related phenomena -reported after amputation of a limb. Women report, sensations of the breast still being a present and intact part of their body, despite having had a mastectomy. In some cases, women have reported very disturbing, Painful sensations in particular areas, such as the nipple or scar or over the entire *breast*. *Phantom pain is related differentiation of neurons and their spontaneous and evoked hyper excitability .*

AIM OF THE STUDY

The objectives are

To find out the incidence of post mastectomy pain syndrome and phantom breast syndrome in patients undergoing simple mastectomy or modified radical mastectomy for carcinoma breast.

INTRODUCTOIN

Breast cancer is the most common cancer diagnosed and the second leading cause of cancer mortality in women. Major advances in recent years, including hormonal and monoclonal antibody therapy, have greatly improved outcomes in breast cancer patients

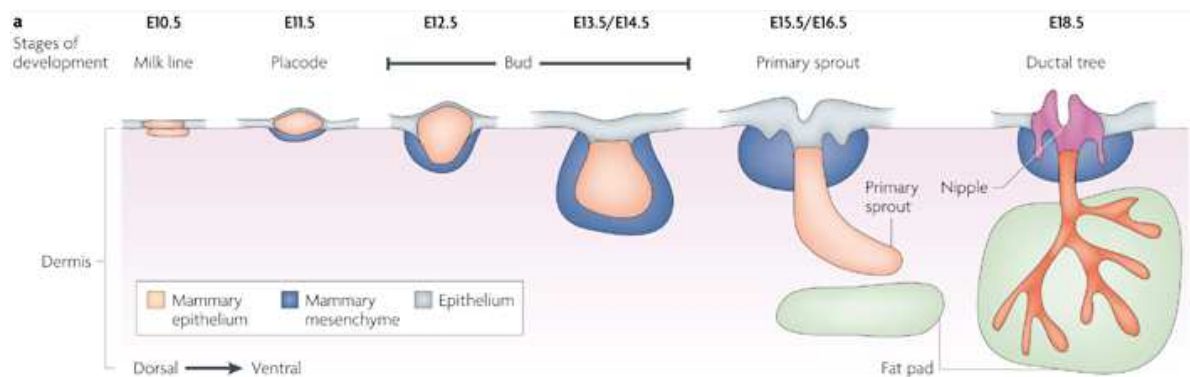
EMBRYOLOGY OF BREAST

The mammary glands are modified and highly specialized sweat glands and therefore develop from the surface ectoderm.

The development occurs as follows:

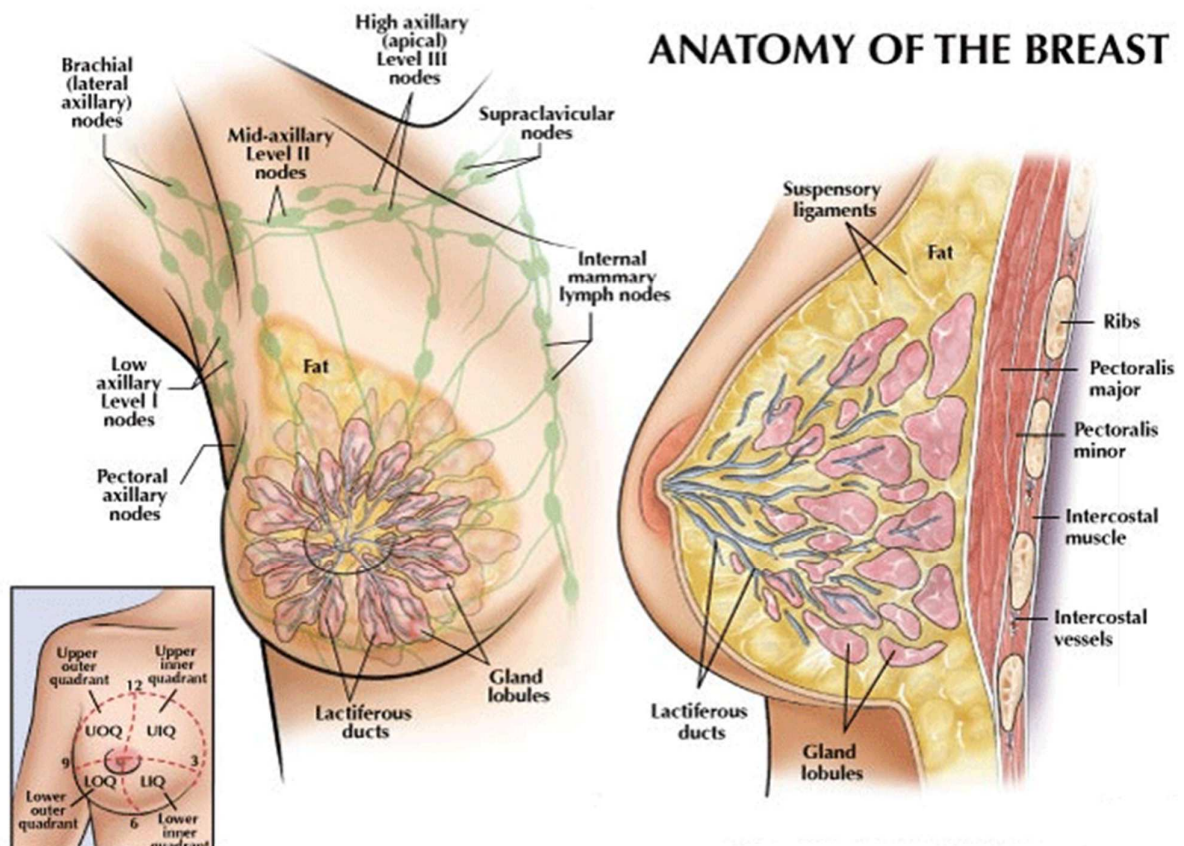
- In the fourth week, the surface ectoderm thickens on either side of the ventral aspect of trunk of embryo along the line extending from the axilla to the inguinal region to form mammary ridge or line.
- About 15–20 mammary buds develop as solid down growths of the epidermis into the underlying mesenchyme along the mammary ridge on each side.
- Normally mammary ridge and mammary buds disappear, except in the pectoral region.
- In the pectoral region, the mammary bud presents a surface depression called mammary pit.
- About 15–20 epithelial cords grow inwards from the bottom of the pit into the underlying dermis. The epithelial cords are primordia of lactiferous ducts.
- The deeper ends of the epithelial cords subdivide further and terminate as ampullated ends—the primordia of ductules and alveoli.

- At the end of fetal life, the epithelial cords and their branches are canalized and form lactiferous ducts.
- Initially the lactiferous ducts open into the bottom of the mammary pit.
- Shortly before birth the pit is evaginated by the growth of underlying mesoderm and form the nipple.
- The rudimentary mammary glands of new born males and females are similar. This condition persists throughout life in males. In females, however, infantile form of mammary gland grows in size at puberty under the influence of sex hormones and assumes a hemispherical outline. The full development of breast occurs at about 19 years of age.

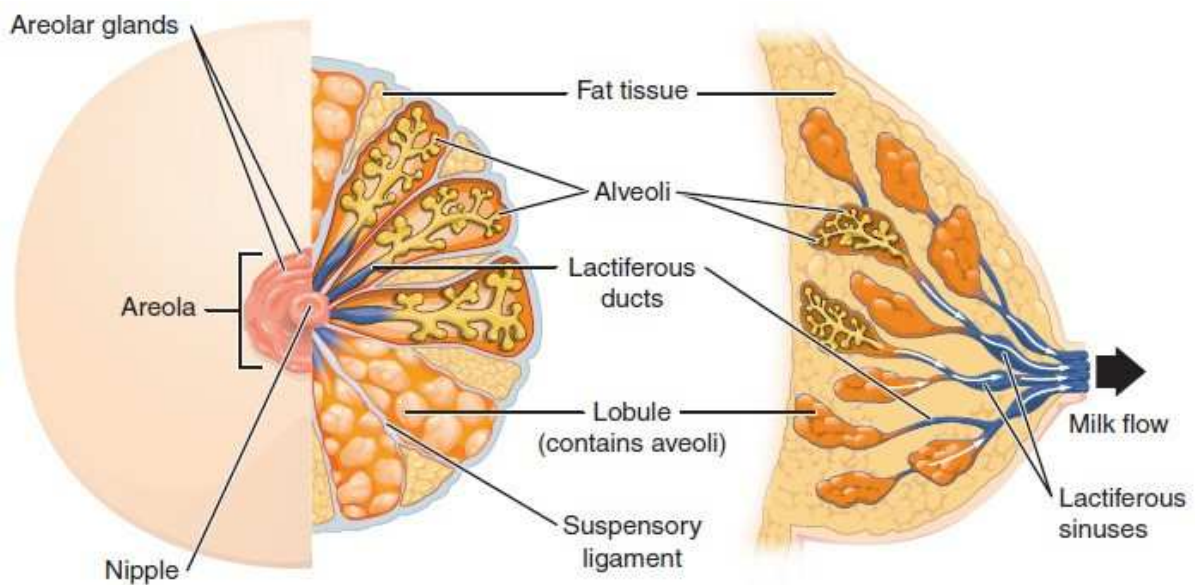


SURGICAL ANATOMY OF BREAST

The adult female breast or mammary gland lies in the subcutaneous tissue (superficial fascia) of the anterior thoracic wall. Despite individual variations, the extent of the base of the breast is almost constant, from the sternal edge to the midaxillary line, and from the second to sixth ribs. It overlies pectoralis major, overlapping onto serratus anterior and a small part of the rectus sheath and external oblique muscle.



A small part of the upper outer quadrant may be prolonged towards the axilla. This extension (the axillary tail) usually lies in the subcutaneous fat; rarely it may penetrate the deep fascia of the axillary floor and lie adjacent to axillary lymph nodes. Some 15–20 lactiferous ducts, each draining a lobe of the breast, converge in a radial direction to open individually on the tip of the nipple, the projection just below the centre of the breast which is surrounded by an area of pigmented skin, the areola. Each lactiferous duct has a dilated sinus at its terminal portion in the nipple.



Smooth muscle cells are present in the nipple and their contraction causes erection of the nipple. Large sebaceous glands, sweat glands and other areolar glands are present in the skin of the areola. The areolar glands form small elevations (tubercles of Montgomery), particularly when they enlarge during pregnancy.

Behind the breast the superficial fascia (the upward continuation of the membranous layer of superficial abdominal fascia of Scarpa) is condensed to form a posterior capsule. Strands of fibrous tissue (forming the suspensory ligaments of Cooper) connect the dermis of the overlying skin to the ducts of the breast and to this fascia. Between the capsule and the fascia over pectoralis major is the loose connective tissue of the retromammary space.

BLOOD SUPPLY

The blood supply of breast is from internal thoracic artery, a branch of 1st part of subclavian artery which supplies medial aspect of breast.

Lateral part receives blood supply from pectoral branches of thoraco acromial artery, lateral thoracic artery, branch of axillary artery.

Lateral perforator branches of posterior intercostal artery (2nd, 3rd, 4th) & few unnamed branches from anterior intercostal artery.

VENOUS DRAINAGE:

- Internal mammary vein
- Lateral thoracic vein which drains into axillary vein
- Lateral perforator branch which drains into intercostal veins, in turn to vertebral vein & plexus – BATESON'S PLEXUS, the main route of bone metastasis.

LYMPHATIC DRAINAGE

- Sub areolar plexus of lymphatics communicates with lymphatics within the breast.
- Around 75% of the lymphatic drainage of the breast passes to axillary lymph nodes, mainly to the
 - Anterior nodes – along lateral thoracic vein
 - Posterior nodes – posterior axillary fold along subscapular vessels
 - Lateral nodes – upper part of humerus along axillary vein.
 - central nodes – upper part of axillary pad of fat.
 - Apical – superior to central group of nodes.
- Much of the rest of the lymphatic drainage, originating particularly from the medial part of the breasts, is to internal mammary nodes along the internal thoracic artery.

The superficial lymphatics of the breast have connections with those of the opposite breast and the anterior abdominal wall, from the extra peritoneal tissues of which there is drainage through the diaphragm to posterior mediastinal nodes. Direct drainage from the breast to inferior deep cervical (supraclavicular) nodes is possible. These minor pathways tend to convey lymph from the breast only when the major channels are obstructed by malignant disease

NORMAL DEVELOPMENT AND PHYSIOLOGY

In the United States, puberty, as measured by breast development and the growth of pubic hair, begins between the ages of 9 and 12 years, and menarche (onset of menstrual cycles) begins at approximately 12 to 13 years of age. These events are initiated by low-amplitude pulses of pituitary gonadotropins, which increase serum estradiol concentrations.

In the breast, this hormone-dependent maturation (thelarche) entails increased deposition of fat, the formation of new ducts by branching and elongation, and the first appearance of lobular units. This process of growth and cell division is under the control of estrogen, progesterone, adrenal hormones, pituitary hormones, and the trophic effects of insulin and thyroid hormone.

The post pubertal mature or resting breast contains fat, stroma, lactiferous ducts, and lobular units. During phases of the menstrual cycle or in response to exogenous hormones, the breast epithelium and lobular stroma undergo cyclic stimulation. The dominant process appears to be hypertrophy and alteration of morphology rather than hyperplasia. In the late luteal (premenstrual) phase, there is an accumulation of fluid and intralobular edema.

With pregnancy, there is diminution of the fibrous stroma and the formation of new acini or lobules, termed adenosis of pregnancy. After birth, there is a sudden loss of

placental hormones, which, combined with continued high levels of prolactin, is the principal trigger for lactation.

The actual expulsion of milk is under hormonal control and is caused by contraction of the myoepithelial cells that surround the breast ducts and terminal ductules. There is no evidence for innervation of these myoepithelial cells; their contraction appears to occur in response to the pituitary-derived peptide oxytocin.

Stimulation of the nipple appears to be the physiologic signal for continued pituitary secretion of prolactin and acute release of oxytocin. When breastfeeding ceases, the prolactin level decreases and there is no stimulus for release of oxytocin. The breast returns to a resting state and to the cyclic changes induced when menstruation resumes.

Coursing close to the chest wall on the medial side of the axilla is the long thoracic nerve, or the external respiratory nerve of Bell, which innervates the serratus anterior muscle. This muscle is important for fixing the scapula to the chest wall during adduction of the shoulder and extension of the arm, and division of the nerve may result in the winged scapula deformity. For this reason the long thoracic nerve is preserved during standard axillary dissection. The second major nerve trunk encountered during axillary dissection is the thoracodorsal nerve to the latissimus dorsi muscle at the lateral border of the axilla. This nerve arises from the posterior cord of the brachial plexus and enters the axillary space under the axillary vein, close to the entrance of the long thoracic nerve. It then crosses the axilla to the medial surface of the latissimus dorsi muscle. The thoracodorsal nerve is usually preserved during dissection of the axillary nodes. The medial pectoral nerves innervate the pectoralis major muscle and are in a neurovascular bundle that wraps around the lateral border of the pectoralis minor muscle. The pectoral neurovascular bundle is a good landmark in that it indicates the position of the axillary vein just above and deep (superior and Posterior) to the bundle. This neurovascular bundle needs to be preserved during standard axillary dissection.

The large sensory intercostal 3rachial or brachial cutaneous nerves span the axillary space and supply sensation to the under surface of the upper part of the arm and skin of the chest wall along the posterior margin of the (Alia. Cutting these nerves causes cutaneous anaesthesia in these areas, which is described to patients before

axillary dissection. Denervation of the areas supplied by these sensory nerves can cause chronic and uncomfortable pain syndromes in a small percentage of patients. Preservation of the superior-most nerve leaves sensation to the posterior aspect of the upper part of the arm intact without compromising the axillary dissection in most patients.

Aetiology

- Carcinoma breast is more common in developed, western countries.
- It is second most common carcinoma in females. Incidence is 19-34%. Median age is 47 years

Risk factors:

1. Genetic factors:

- BRCA 1 & BRCA 2 gene mutation
- Cowdens syndrome
- Li- Fraumeni syndrome
- BRCA 3 & p53 mutation
- Ataxia telangiectasia

2. Obesity

3 . Family history of breast cancer, uterine/ovarian/colonic cancers.

4. Previous therapeutic radiation (thoracic)

5 . Diet low with phytoestrogens and high alcohol intake have high-risk of breast cancer. Vitamin C reduces the risk.

6. Benign breast diseases with atypia, hyperplasia and epitheliosis has got higher risk in a patient with family history. RR in nonproliferative fibrocystic disease is 1.0; proliferative without atypia is 1.5; proliferative with atypia is 4.0 (with family history 6.5, premenopausal 6.0)

Hormonal factors:

- Increased estrogen exposure - nulliparous woman, early menarche, late menopause
- Late first child birth after 35 yrs.
- Hormone replacement therapy > 5 yrs

Incidences in carcinoma breast

- 30% of all female cancers
- 20% of cancer related deaths in females
- 2-4% bilateral 2-5% hereditary
- Lump in the breast—most common presentation (75%)
- 10% presents with pain
- 35-45% with mutation of BRCA1 gene
- 70% blood spread occurs to bones

Risk factors classification

Slight to moderate risk

- Florid hyperplasia
- Solid duct papilloma
- Obesity, alcohol, HRT
- Nulliparity
- Early menarche, late menopause

Moderate to high-risk

- Age > 60 years
- ATD / ALS/ LCIS
- History of DCIS
- Cancer on one side breast

Very high-risk

- Therapeutic radiation
- Family history of breast cancer in two 1st degree relatives
- Family history of breast and ovarian cancer
- BRCA1 and BRCA2 mutation carrier or 1st degree relative with mutation

CLASSIFICATION OF PRIMARY BREAST CANCER

Carcinoma in situ

LCIS(Lobular carcinoma in situ)

DCIS (Ductal carcinoma in situ)

Invasive carcinoma

- **Paget's disease of the nipple**
- **Invasive ductal carcinoma**
 - Invasive ductal with NST (no special type) -70%
 - Medullary carcinoma – 4%
 - Tubular carcinoma—2%

- mucinous —2%
- Invasive cribriform—2%
- Invasive papillary—1%

Mixed connective tissue and epithelial

- Phyllodes,
- angiosarcoma,
- carcinosarcoma

DCIS (DUCTAL CARCINOMA IN SITU)

It is intraductal proliferation of malignant mammary ductal epithelial cells without any invasion into the basement membrane.

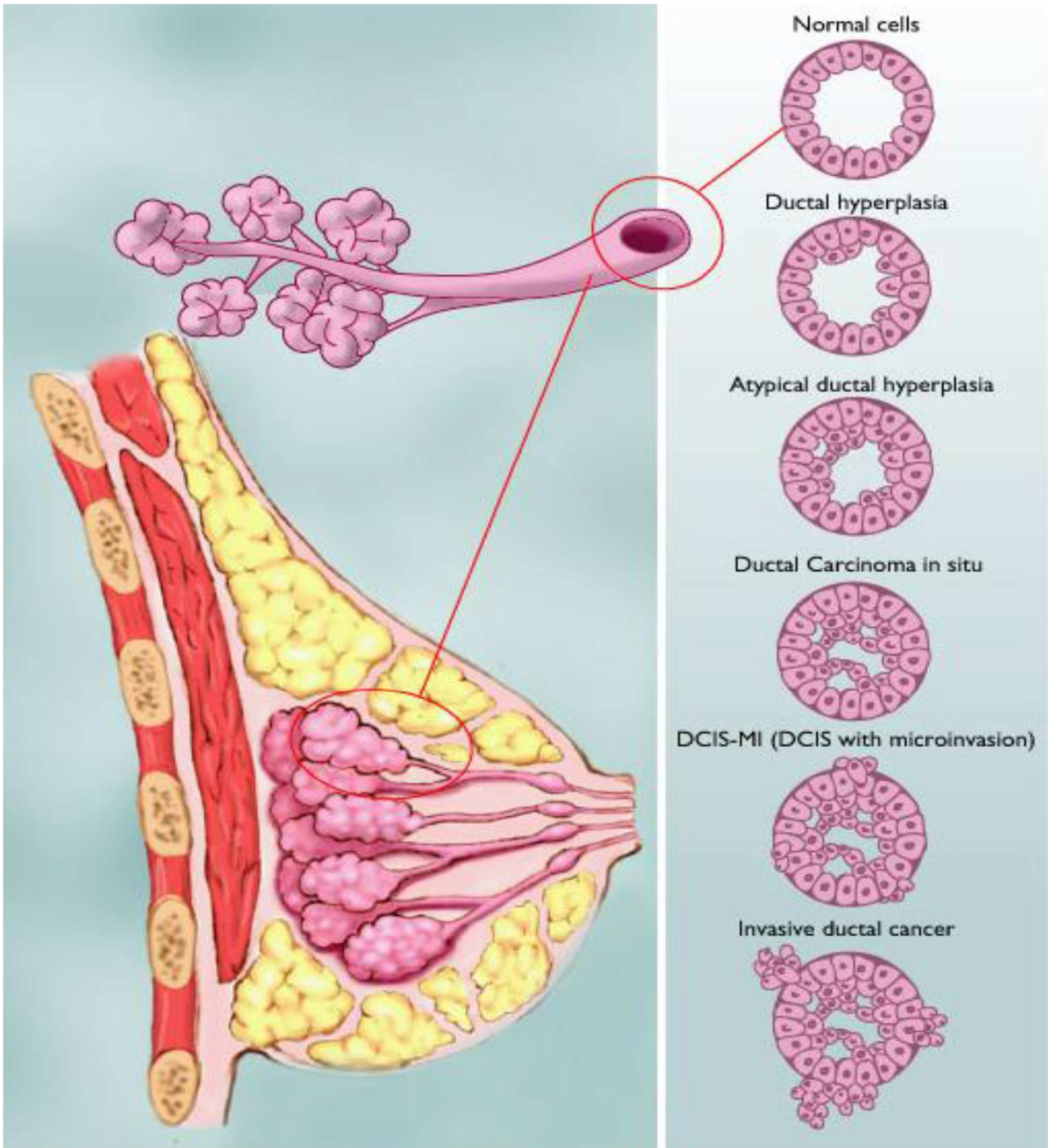
It can be:

- Solid& comedo (high grade)
- Cribriform& papillary (low grade)
- Micropapillary.

It is associated with high expression of C – erb2 gene (80%).

In 20% of cases synchronous invasive carcinoma in duct is seen.

Untreated DCIS becomes invasive in > 50% cases (5 fold).



NOTTINGHAM PROGNOSTIC INDEX (NPI):

$(0.2 \times \text{Tumour size in cm}) + \text{Lymph node stage} + \text{Tumour grade}$

NPI score—< 3.4 Good prognosis with 80% survival (15 years)

NPI score—3.4 –5.4 Moderate prognosis with 40% survival

NPI score—> 5.4 Poor prognosis with 15% survival

TYPES OF CARCINOMA BREAST

1. Scirrhou carcinoma:

- ❖ 60% .
- ❖ hard, whitish, or whitish yellow, noncapsulated, irregular, with cartilaginous consistency.

2. Medullary carcinoma (5%):

- ❖ Also called as ‘encephaloid type’ because of its brain like consistency.
- ❖ It contains malignant cells with dispersed lymphocytes

3. Inflammatory carcinoma/Lactating carcinoma/Mastitis carcinomatosis:

- ❖ Most aggressive type of carcinoma breast.
- ❖ It is 2% common.
- ❖ common in pregnancy & lactation.
- ❖ mimics acute mastitis
- ❖ rapidly progressive tumour
- ❖ Treatment includes external radiotherapy and chemotherapy.
- ❖ Salvage surgery whenever possible. worst prognosis.

4. Colloid carcinoma:

It produces abundant mucin, both intraandextracellularly carrying better prognosis.

5. Paget's disease of the nipple

- ❖ It is superficial manifestation of an intraductal carcinoma.
- ❖ The malignancy spreads within the duct up to the skin of the nipple and down into the sub stance of the breast.
- ❖ It mimics eczema of nipple and areola.

6. Tubular, papillary, cribriform are other types of duct carcinomas.

7. Atrophic scirrhous carcinoma.

8. Lobular carcinoma in situ:

- ❖ It originates in terminal duct lobular unit .
- ❖ It is multifocal, bilateral (50%). It is an incidental pathological entity.
- ❖ Classical type carries better prognosis; pleomorphic type does not so; occasionally mixed ductal and lobular in situ may be seen. Immunohistochemistry using e-cadherin antibody shows positive reaction in lobular carcinoma.

9. Disease of Reclus:

- ❖ It is a rare intracysticapilliferous carcinoma of breast presenting as a cystic swelling with bloody discharge from the nipple.

GRADING OF THE TUMOUR

It can be

Grade-1 well-differentiated

Grade -2 moderately differentiated and

Grade -3 poorly differentiated .

ELSTON-ELLIS MODIFIED BLOOM-RICHARDSON GRADING SYSTEM

Parameters used :

1) Nuclear pleomorphism:

Score 1—relatively small uniform nuclei;

score 2—intermediate pleomorphic nucleoli;

score 3—relatively large prominent nucleoli

2) Mitotic count:

Score 1—< 10% mitoses in 10 HPF;

score 2—10-20% mitoses;

score 3—>20% mitoses

3) Tubule formation:

Score 1—>75% cells in tubule forms;

score 2—10-75% cells in tubule forms;

score 3—< 10% cells in tubule forms

GRADE	SCORE
Favourable	1
Unfavourable	Up to 3
Grade I	3-5
Grade II	6-7
Grade III	8-9

Well differentiated low grade -grade 3, 4, 5

Moderately differentiated intermediate grade-grade 6, 7

Poorly differentiated high grade-8, 9

BIOLOGICAL BEHAVIOUR AND CLINICAL FEATURES OF CARCINOMA

BREAST

- ✓ clinically palpable breast lump- commonly in upper outer quadrant
- ✓ nipple retraction & discharge
- ✓ skin changes(tethering,puckering,dimpling,retraction of nipple)
- ✓ peau d'orange,skin ulceration & nodules
- ✓ fixity to underlying muscle & chest wall
- ✓ enlargement of lymph nodes

- ✓ distant spread
 - Chest pain and haemoptysis
 - Bone pain, tenderness, and pathological fracture
 - Pleural effusion, ascites
 - Liver secondaries, secondary ovarian tumour

CAUSES OF LYMPHATIC BLOCK IN CARCINOMA BREAST

- ✚ Involvement and fixation of the axillary nodes level I, II and III
- ✚ After levels I, II and III dissection
- ✚ After radiotherapy to axilla
- ✚ Inoperable fixed nodes in axilla
- ✚ Recurrent axillary disease
- ✚ associated with cancer-en-cuirasse
- ✚ Secondary infection Effects of lymphatic obstruction
- ✚ Peaud'orange • Brawny oedema of arm- indurated, painful, nonpitting-occurs in fixed nodes in axilla
- ✚ Elephantiasis chirurgens- after radical mastectomy or radiotherapy to axilla
- ✚ Cancer-en-cuirasse- seen in locally advanced carcinoma of breast. Skin of chest wall is studded with hard fixed nodules like armour coat (of soldiers)
- ✚ Lymphangiosarcoma after radical mastectomy or MRM (Stewart-Treves's)

HAEMATOGENOUS SPREAD

Common sites of distant spread in carcinoma breast

- Bones—70% (lumbar vertebrae, pelvic bones, long bones)
- Lungs and pleura—20-30%
- Soft tissues—5-15%
- Liver—10-12%
- Brain—2-5%
- Adrenals—2-5%

Transcoelomic Spread Through mediastinal lymph nodes, it may spread into peritoneal cavity causing secondaries in liver, peritoneum, ovary (Krukenbergsecondaries—occurs in menstruating age groups. During ovulation, cells get attached over the ovarian capsule).

STAGING

TNM STAGING

TUMOUR:	
<u>Tx</u>	Cannot be assessed
<u>T0</u>	No evidence of primary
<u>Tis</u>	Carcinoma <u>insitu</u> (DCIS or LCIS)
<u>Tis paget's</u>	<u>Pagets</u> disease of nipple with no <u>tumour</u>
<u>T1mic</u>	<u>Microinvasion</u> <0.1cm
<u>T1</u>	<u>Tumour</u> size <2cm in greatest diameter(T1a-0.1-0.5cm; T1b-0.5-1.0cm;T1c-1-2cm)
<u>T2</u>	Size 2-5cm
<u>T3</u>	Size >5cm
<u>T4</u>	<u>Tumour</u> fixed to chest wall or skin (T4a-fixed to chest wall not including pectoral muscle;T4b-fixed to skin;T4c-T4a+T4b;T4d-inflammatory carcinoma breast)

NODE	
<u>Nx</u>	Cannot be assessed
<u>N0</u>	No nodes
<u>N1 mic</u>	Node with <u>micrometastasis</u>
<u>N1</u>	<u>Axillary</u> nodes- <u>ipsilateral</u> mobile discrete
<u>N2</u>	
<u>N2a</u>	Fixed /matted <u>ipsilateral</u> axillary nodes
<u>N2b</u>	<u>Ipsilateral</u> internal mammary nodes in the absence of clinically <u>axillary</u> nodes
<u>N3</u>	
<u>N3a</u>	Spread to <u>ipsilateral infraclavicular</u> lymph nodes with or without <u>axillary</u> nodes
<u>N3b</u>	Spread to <u>ipsilateral internal mammary</u> nodes and <u>axillary</u> nodes
<u>N3c</u>	Spread to <u>ipsilateral supraclavicular</u> lymph node with/without <u>axillary</u> or internal mammary nodes.

REGIONAL LYMPH NODES (N)

PATHOLOGIC (PN)*

- pNX** Regional lymph nodes cannot be assessed (for example, previously removed, or not removed for pathologic study)
- pN0** No regional lymph node metastasis identified histologically
Note: Isolated tumor cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm, or single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.
- pN0(i-)** No regional lymph node metastases histologically, negative IHC
- pN0(i+)** Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
- pN0(mol-)** No regional lymph node metastases histologically, negative molecular findings (RT-PCR)
- pN0(mol+)** Positive molecular findings (RT-PCR)**, but no regional lymph node metastases detected by histology or IHC

DISTANT METASTASIS(M)

Distant Metastases (M)

- M0** No clinical or radiographic evidence of distant metastases
- cM0(i+)** No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases
- M1** Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

pT		pN		pTNM-Stage	
Tis	DCIS LCIS Paget nipple	pN1mi	Micrometastasis > 0,2 mm to 2 mm	0	DCIS
		pN1a	1-3 axillary nodes		
T1 mic	≤ 0,1 cm	pN1b	Internal mammary nodes with microscopic/macrosopic metastasis by sentinel node biopsy but not clinically detected	IA	T1No
T1a	≤ 0,5 cm			IB	To-1N1mi
T1b	> 0,5 - 1 cm				
T1c	> 1 cm - 2 cm	pN1c	1-3 axillary nodes and internal mammary nodes and internal mammary nodes with microscopic/ macrosopic metastasis by sentinel node biopsy but not clinically detected	IIA	To-1N1 T2No
T2	> 2 cm - 5 cm			IIB	T2N1 T3No
T3	> 5 cm				
T4a	Extension to chest wall (does not include pectoralis muscle invasion only)	pN2a	4-9 axillary nodes	IIIA	To-2N2 T3N1-2
		pN2b	Internal mammary nodes, clinically detected, without axillary nodes		
T4b	Ulceration, ipsilateral satellite skin nodules, or skin oedema - including peau d'orange.	pN3a	≥ 10 axillary nodes or infraclavicular	IIIA	T4No-2 T3N1-2
		pN3b	Internal mammary nodes, clinically detected, with axillary node(s) or > 3 axillary nodes and internal axillary mammary nodes with microscopic metastasis by sentinel node biopsy but not clinically detected		
T4c	a+b	pN3c	Supra-clavicular	IIIC	anyT N3
T4d	Inflammatory ca			IV	systemic

SELECTION OF SURGICAL THERAPY

Mastectomy and breast-conserving therapy have been shown to be equivalent in terms of patient survival, and the choice of surgical treatment is individualized. Patients who desire breast conserving surgery must be willing to attend postoperative radiation therapy sessions and to undergo postoperative surveillance of the treated breast..

In patients with large tumours for whom adjuvant (postoperative) systemic chemotherapy will likely be recommended, the use of preoperative chemotherapy may be considered. Chemotherapy administered before surgery

may decrease the tumour size sufficiently to permit breast-conserving surgery in patients who would not otherwise appear to be good candidates.

Another strategy is to consider local tissue rearrangement or pedicled myocutaneous flaps (latissimus dorsi) to fill the defect resulting from breast-conserving surgery. Patients with multicentric tumors are usually served best by mastectomy because it is difficult to perform more than one breast-conserving surgery in the same breast with acceptable cosmesis. Although high nuclear grade, presence of lymphovascular invasion, and negative steroid hormone receptor status all have been linked to increased local recurrence rates, none of these factors are considered contraindications to breast conservation.

Surgeries for Carcinoma Breast

Total (simple) mastectomy: The breast tissue, tumour, fat along with pectoral fascia removed without axillary clearance.

Total mastectomy with axillary clearance: Total mastectomy is done along with removal of axillary Level I and II nodes.

Modified radical mastectomy [MRM]:

Patey's operation: It is total mastectomy with clearance of all levels of axillary nodes and removal of pectoralis minor muscle.

Nerve to serratus anterior, nerve to latissimus dorsi, intercostobrachial nerve, axillary vein, cephalic vein and pectoralis major muscle are preserved. Wound is closed with a suction drain.

Scanlon's operation: Is a modified Patey's operation wherein instead of removing pectoralis minor, it is incised to approach the affected level III lymph nodes.

Auchincloss modified radical mastectomy: Here pectoralis minor muscle is left intact and level III lymph nodes are not removed—commonly done now.

Halsted Radical Mastectomy (Complete Halsted): Structures removed are:

- Tumour.
- Entire breast, nipple, areola, skin over the tumour with margin.
- Pectoralis major and minor muscles.
- Fat, fascia, lymph nodes of axilla.
- Few digitations of serratus anterior.

Structures retained are (ABC)

- Axillary vein
- Bells nerve (nerve to serratus anterior)
- Cephalic vein

CONSERVATIVE BREAST SURGERIES:

Wide local excision: Tumour is removed along with one cm clearance.

Pectoral fascia is usually not opened in wide local excision unlike in total mastectomy. And axillary dissection is carried out through separate incision.

The specimen is marked after placing in orientation grid and mammography of the specimen is done followed by frozen section biopsy to look for clearance.

At least 1 mm clearance is needed for adequacy. Margins where clearance is less than 1 mm need re-excision at that particular margin.

Quadrantectomy: It is removal of entire segment/ quadrant with ductal system with 2-3 cm normal breast tissue clearance along with axillary dissection (level I and II) through separate incision and RT to breast area.

Toilet mastectomy: In locally advanced tumour, tumour with breast tissue and whatever possible is removed to prevent further fungation. But its use and significance is under question. It is often done after giving chemotherapy.

Extended radical mastectomies: It includes radical mastectomy + removal of internal mammary lymph nodes of same side with or without opposite side. It is not done at present.

Skin sparing mastectomy (SSM/Key hole mastectomy) is becoming popular with different approaches.

Complications of MRM/mastectomy

- Injury/thrombosis of axillary vein
- Seroma—50-70% Shoulder dysfunction 10%
- Pain (30%) and numbness (70%)
- Flap necrosis/infection

- Lymphoedema (15%) and its problems
- Axillary hyperaesthesia (0.5-1%)
- Winged scapula
- Occasionally if on table injury occurs to axillary vein, it should be repaired by vascular suturing using 5 zero polypropylene
- Numbness over the medial upper part of the arm can occur due to intercostobrachial nerve injury
- Pectoral muscles atrophy if medial and lateral pectoral nerves are injured
Weakening of internal rotation and abduction of shoulder occurs due to injury to thoracodorsal nerve

Lymphangiosarcoma (Stewart-Treves's syndrome) of upper limb can develop in patients who have developed lymphoedema after mastectomy with axillary clearance. Usually it occurs 3-5 years after development of lymphoedema. Such patient may require fore-quarter amputation. It has got poor prognosis. It presents as multiple

Radiotherapy in Carcinoma Breast

Indications: Patient who undergo conservative breast surgery, breast is irradiated after surgery.

Radiotherapy in carcinoma breast

To chest wall

- T3 tumour >5 cm
- Residual disease-LABC
- Positive margin/close surgical margin of < 2 cm
- After conservative surgery
- Higher risk group
- Inflammatory carcinoma

To axilla

- 4 or more nodes positive
- Extranodal spread
- Axillary status not known/not assessed
- RT is a must after conservation of breast
- Local as well as to axilla
- Tangential fields 50 Gy/25 fractions/5 weeks
- Another 10 Gy to tumour bed
- Internal mammary and supraclavicular area may be included in radiation field

- External radiotherapy is given over the breast area, axilla (in selected patients like if axillary dissection is not done or more than 4 positive axillary nodes), internal mammary and supraclavicular area
- Total dosage 5000 cGY units
- 200-cGY units daily 5 days a week for 6 weeks

HORMONE THERAPY IN CARCINOMA BREAST

Principles: It is used in ER/PR positive patients in all age group.

- i. Hormone therapy reduces the recurrence rate and so probably improves the life span and quality of life, which includes,
 - ii. Oestrogen receptor antagonists—tamoxifen.
 - iii. Ovarian ablation by surgery (Bilateral oophorectomy) or by radiation.
 - iv. LHRH agonists (Medical oophorectomy).
 - v. Oral aromatase inhibitors for postmenopausal women.
 - vi. Adrenalectomy or pituitary ablation.
 - vii. Progesterone receptor antagonist.
 - viii. Androgens—Inj testosterone propionate 100 mg IM three times a week.
 - ix. Aminoglutethimide—blocks the synthesis of steroids by inhibiting conversion of cholesterol to pregnenolone— medical adrenalectomy.
 - x. Progestogens, e.g. medroxyprogesterone acetate.

Tamoxifen

- It is an antioestrogen. It blocks cytosolic oestrogen receptors.
- Dose is 10 mg BID or 20 mg OD for 5 years.
- Half life of tamoxifen is 7 days; it takes 4 weeks to show its benefits. It reduces the cholesterol and also cardiovascular morbidity.
- Adverse effects: are flushing, tachycardia, sweating, genital itching, vaginal atrophy and dryness (premenopausal), vaginal discharge (postmenopausal), fluid retention, weight gain.
- It increases the incidence of endometrial cancer.
- DVT (3%), pulmonary embolism, CVA, TIA, cataract, fractures. Side effects and endometrial cancer are less in selective drugs like raloxifene. Advantages:

Selective oestrogen antagonists

- Do not cause endometrial hyperplasia or endometrial carcinoma.
- Drugs include droloxifen, toremifen, raloxifene

Letrozole

- It is a nonsteroidal competitive inhibitor of the enzyme 'aromatase'. This enzyme converts adrenal androgens to oestrogen (aromatization). So it is an aromatase inhibitor.
- Other aromatase inhibitors are anastrozole and exemestane (in postmenopausal). It is expensive but more effective than tamoxifen. It is also used in recurrent disease.

- Letrozole is used as an adjuvant endocrine therapy in postmenopausal women with hormone sensitive breast

Transtuzumab

It is a monoclonal antibody that blocks HER-2/Neu receptors thereby preventing growth of cancer cells. It is a new drug. It is presently marketed as herceptin. It is c-ErbB2 (growth factor receptor) inhibitor. It is a newer biological agent. Her 2/Neu receptor is tyrosine kinase receptor.

Chemotherapy in Carcinoma Breast

- ❖ Adjuvant chemotherapy
- ❖ Neoadjuvant chemotherapy

REGIMENS

CMF regime	CAF regime	MMM regime
Cyclophosphamide	Cyclophosphamide	Methotrexate
Methotrexate	Adriamycin	Mitomycin-C
5-Fluorouracil	5-Fluorouracil	Mitozantrone

- ❖ Toxic effects are: Alopecia, bone marrow sup pression, cystitis, megaloblastic anaemia, GIT disturbances, nephritis.
- ❖ CMF and CAF are commonly used with monthly/3 weeks cycles for 6 months.
- ❖ Other anthracyclines like doxorubicin or epirubicin should be used often for better result.

- ❖ Taxanes: They are newer chemotherapeutic drugs which act by G2/M phase of cell cycle. It is commonly used in metastatic carcinoma of breast. Drugs are paclitaxel and docetaxel. Taxanes have no cross-resistance with anthracyclines and so can be used sequentially or concurrently with anthracyclines.
- ❖ Gemcitabine is also used often in selected cases for better results.

The majority of women diagnosed with breast cancer undergo some kind of breast surgery as part of their treatment. Up to 55% of these women experience pain after their surgery, pain which in some cases persists for months to years. Women with breast cancer frequently turn to their nurse for comfort, information, and assistance in coping with effects of their disease and treatment. The purposes of this study is to identify the different kinds of pain experienced by women after breast cancer surgery, to explore the current literature addressing its nature and incidence, and to discuss the implications of this information for interventions in caring for women with breast cancer. Two pain syndromes that commonly follow breast surgery, postaxillary dissection pain and phantom breast pain, will be discussed. Strategies for pain management, including educational intervention and treatment approaches, will also be addressed. This information valuable as they help women adjust after surgery and offer guidance in seeking management of postmastectomy pain. For many years, the prevalence of phantom pain had been underestimated. Poor understanding of how pain could be perceived in an absent body part led many physicians to believe that such pain was a psychological phenomenon and led many patients to believe that reporting such pain would Make their physicians think they were mentally It is now realized

that phantom sensation is ubiquitous, and the prevalence of phantom pain is as high as 85%. Rehabilitation professionals have a heightened awareness of phantom pain after limb amputation because of its disabling nature and potential effect on function. However, many are less aware that phantom-pain can occur after amputation of other body parts such as the breast. Phantom breast pain can also be disabling and have an effect on functional status, particularly in those with a preexisting disability

The clinical course of postmastectomy pain can be quite variable. For some, the pain can be intermittent, whereas for others, it can be continuous. Typically, it begins in the immediate postoperative period but can begin at >6 months after surgery. The most common exacerbating factor in postmastectomy pain is movement of the arm or shoulder on the affected side, and consequently, PMP can significantly interfere with daily activities. Walking, running, and aerobic exercise have also been reported to make postmastectomy pain worse. The most striking risk factor for postmastectomy pain is age, with a decreasing occurrence in older women. Increased body mass index and increased height are also associated with increased frequency of postmastectomy pain. Pain syndromes similar to postmastectomy pain have also been reported with varying prevalence after breast augmentation and reduction surgeries. As is typical of neuropathic pain, postmastectomy pain does not respond well to opioids.

In many reports, pain relief described by women is suboptimal, and in addition to medications, numerous nonpharmacologic treatments such as heat, ice, elevation, and massage are frequently implemented. In a double-blind, placebo-controlled, crossover

study, amitriptyline has been shown to improve symptoms in women with postmastectomy pain. Unfortunately, the side effects precluded many from continuing treatment. Two studies have also demonstrated the usefulness of topical capsaicin in the treatment of postmastectomy pain. postaxillary dissection pain. Nine studies were and in which researchers evaluated postaxillary dissection pain.

Phantom breast pain:

Phantom breast syndrome is a separate and distinct clinical entity seen after mastectomy. It is defined as sensation, painful or painless, referred to the amputated breast. Phantom breast pain is distinguished from PMP in that it represents painful sensations in the amputated breast and not the anterior chest wall, axilla, or upper arm, as seen in PMP. Phantom breast pain occurs in 12-55% of women who undergo mastectomy. Phantom breast pain generally begins within the first three postoperative months although it has been reported to begin >1 yr after surgery. Described as sharp, burning, shooting, stabbing, lancinating, aching, crushing, and pressing, phantom breast pain typically begins in the nipple area and becomes more diffuse over time. Exacerbation of pain can occur with emotional distress, exercise, touch, and movement of the arm on the affected side. There seems to be no association between phantom breast pain and breast tumor type, postoperative sequelae, adjunctive radiation or chemotherapy, or side of mastectomy. An association between pre-mastectomy pain and phantom breast pain and an occurrence of phantom breast pain in younger women has been reported. Neither the prevalence nor the intensity of phantom breast pain seems to decline over time; consequently, phantom breast pain

can remain a significant problem for years. Although similar in some respects, there seems to be significant differences between phantom limb pain and phantom breast pain. The prevalence of phantom breast pain is less than phantom limb pain, possibly because of the smaller central sensory area represented by the breast and the fact that the breast does not provide kinesthetic input as is seen in the limbs. In many cases of phantom breast pain, the pain begins localized around the nipple and becomes more generalized over time, with no diminution of prevalence or intensity. The opposite seems to occur in phantom limb pain, which typically begins more diffuse or generalized and, over time, becomes more localized and, in many cases, decreases in intensity, frequency, and duration.^{1,7} There has been little written about the treatment of phantom breast pain, and it would seem logical to apply treatment modalities utilized in the treatment of phantom limb pain. Temporary relief of phantom pain is often experienced with the use of physical agents such as transcutaneous nerve stimulations, ultrasound, acupuncture, and vibration.¹ Medical management, however, may be the most common form of treatment, and in general, it is believed that neurogenic pain such as phantom pain is unresponsive to opioids. Anticonvulsants such as carbamazepine and sodium valproate have been used and are reported to control the lancinating or stabbing component of pain. Proposed treatment for the constant burning pain include antidepressants such as amitriptyline and imipramine and the sodium channel blocker mexiletine. Other medical options include beta-blockers, calcitonin, capsaicin, and local anesthetics. In our patient, gabapentin at a relatively low dose provided significant relief of symptoms.

Amputation will frequently result in a change in body image and can be associated with such emotions as anger and grief. A number of psychological interventions have been used to deal with these emotions and to help individuals adapt to chronic pain and changes in body image. Biofeedback, hypnosis, support groups, and cognitive and behavioral therapies are examples of such interventions.]. Reports of phantom breast pain frequently cite emotional distress as a provoking factor, and one report found a correlation between phantom breast syndrome and patients who reported a lower evaluation of their relationship with their husbands and perceived less emotional support from their surgeons. This leads one to believe these psychological modalities may be beneficial in some cases of phantom breast pain. Finally, reamputation treatment of pain and educational efforts directed at change in body image and potential complications, including the possibility of phantom breast pain, may be helpful in preventing phantom breast pain. 1. Four studies were found in which researchers addressed the incidence, nature, and temporal course of PBP

The incidence of phantom breast pain is thought to be underestimated, because women may hesitate to report it to their health care provider unless specifically questioned. Intermittent pains may be viewed as nonthreatening, something that needs to be tolerated. Some women have expressed the fear that they will be thought crazy for having pain in an area of their body that is surgically absent among the samples studied, incidences of PBP ranged from 12.7 to 55%. This large range could be explained by the method used to evaluate PBP, because the higher incidence was reported with the use of a very detailed, forced-choice questionnaire. The nature of

the pain is similar in all reports. it is usually described as sharp and shooting, lasting from a few seconds to a few minutes at a time. They also noted that pain was initially localized in the nipple but became diffuse over time, involving the entire breast.

Temporal course of PBP was evaluated in two of the studies by either stratifying patients according to length of time since surgery or by following subjects prospectively over time. Onset was noted within the first 3 months postsurgery . Prevalence remained relatively constant in ail studies, with no relation to length of time since surgery . Unlike phantom limb pain, which tends to diminish over time, phantom breast pain may remain a significant and disturbing problem for years . Despite limitations, these studies serve to document the existence of PBP as a consequence of breast surgery, draw attention to the need for patient education before surgery, and indicate the need for intervention to eliminate pain after surgery.

REVIEW OF LITERATURE

Lierman reported that subjects in her study primarily complained of burning, aching pain located in the upper arm, and sharp, shooting pains in the chest area. All the descriptors noted in these reports are commonly associated with pain due to nerve injury, in these cases, the intercostobrachial nerve.

Patients in our study also majority of them experienced pricking type of pain

Study	Incidence	Nature of pain
Assa (1974)	100% in traditional	Pricking throbbing
Lierman et al (1988)	Arm pain - 65%, chest pain -45%,	Sharp shooting pinpricks
Vecht et al (1989)	18%	Aching ,burning, stabbing
Gerber et al (1992)	MRM - 23%, lumpectomy - 52%	Chest wall tenderness with palpation
Hiadiuk et al (1992)	16%	
Ivens et al (1992)	33%	-

From the above post axillary dissection pain among the MRM pts in our study is around 39%

With 26% of them having it in the chest and 135 of them in the arm .majority of the patients described the pain as pricking type

Study (phantom pain)	No of Pts	Nature of surgery
Slaps et al (1985)	89	MRM
Karydas et al (1986))	132	MRM or lumpectomy
Kroner et al (1989)	120	MRM
Kroner et al (1992)	69	MRM

In our study totally 17 pts experienced phantom breast syndrome which in our population presented as disabled feeling ,phantom pain and sensation of these 83% of them were in the age group of 20 - 40 years with 3 of them presenting were beyond 40 yrs .hence in our population the occurrence of phantom breast syndrome was mainly in age group below 40 yrs and pts in their period of reproductive age group.

Study (phantom pain)	Incidence
Stops et al (1985)	33%
Karydas et al (1986))	55%- MRM, 61%- simple mastectomy
Kroner et a) (1989)	13%
Kroner et al (1992)	17%

MATERIALS AND METHODS

Place : Department of surgery

Design : observational Study.

Period : 2018-2019

Sample Size : 100 Patients

Inclusion criteria:

Patients above 18 years

Patients who underwent modified radical mastectomy/simple mastectomy

Pts who were given neoadjuvant or adjuvant chemotherapy

Pts who were given radiotherapy

Exclusion criteria:

Patients less than 18 yrs

Patients with bilateral breast disease

Patients who underwent lumpectomy or quadrantectomy or breast reconstruction

Patients who underwent previous surgery in axilla

Pain associated with upper extremity lymphedema

patients with local recurrence

Methods

Patients were reviewed during follow up approximately 8 —12 weeks after surgery

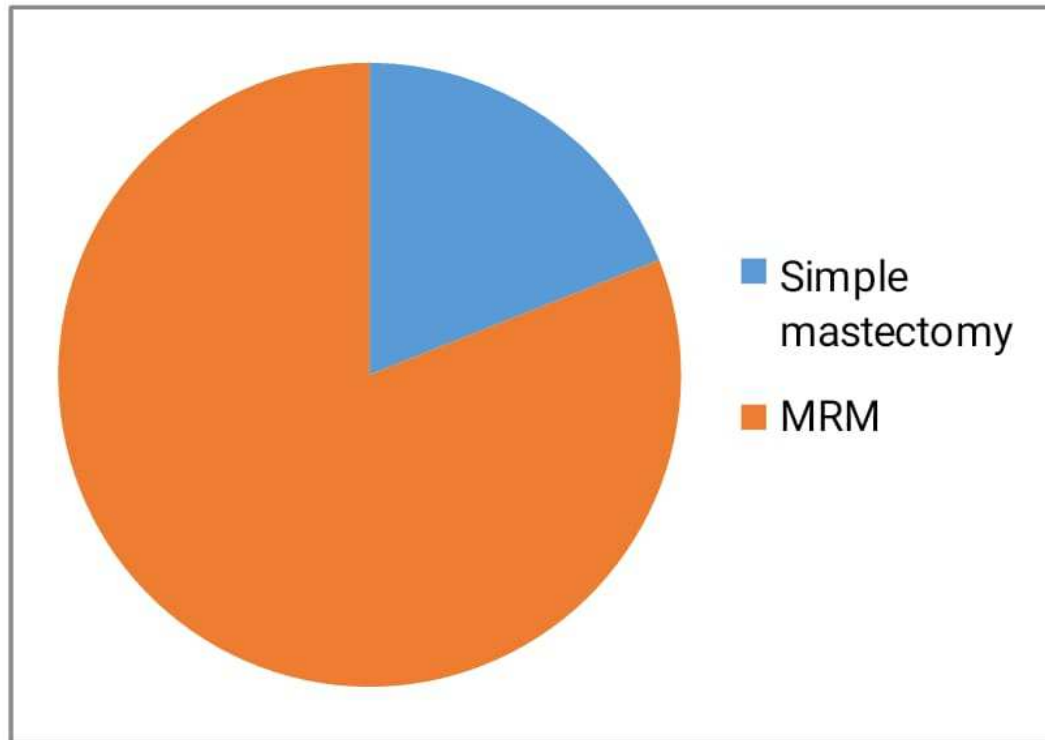
Patients were subjected to thorough physical examination ..

Patients were evaluated with a standardized Questionnaire in a language

Acceptable and understandable for them

OBSERVATION AND RESULTS

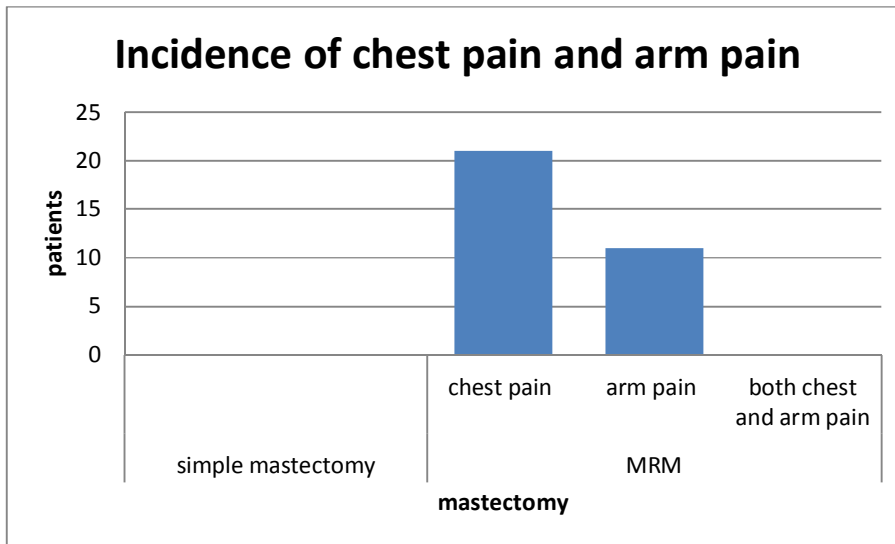
PERCENTAGE OF PATIENTS WHO UNDERWENT SIMPLE AND MODIFIED RADICAL MASTECTOMY



81 of them underwent modified radical mastectomy with axillary lymph node dissection and 19 of them underwent simple mastectomy for locally advanced carcinoma breast as a palliative measure.

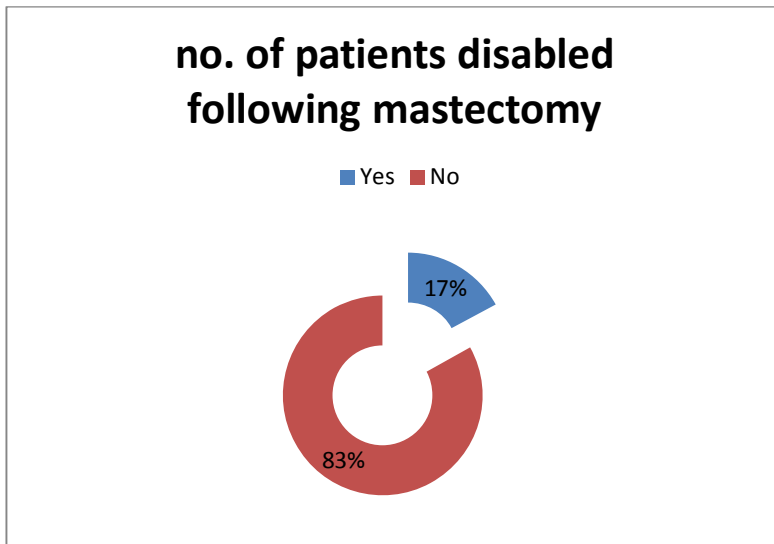
Of these patients post operatively after complete healing of the main wound (> 3 weeks) and following a period of 10 -12 weeks with the help of a questionnaire incidence of post mastectomy pain syndrome presenting with chest wall pain , axillary pain and both were found

INCIDENCE OF CHEST PAIN AND ARM PAIN



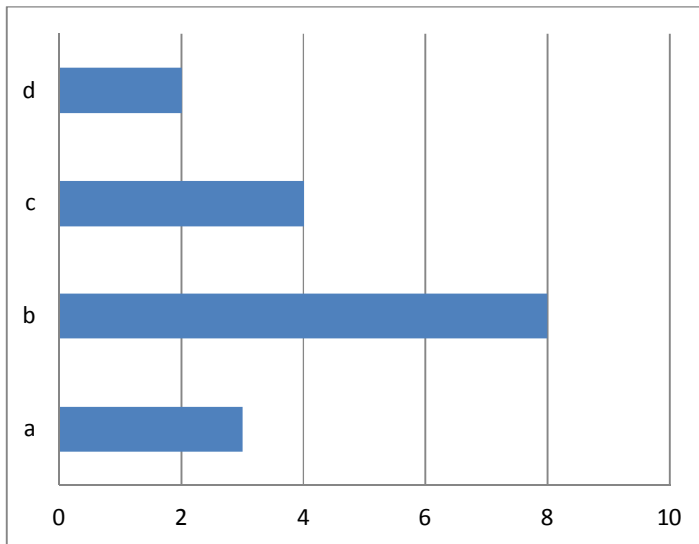
the incidence of pain following simple mastectomy was none and following modified radical mastectomy 21 patients experienced post mastectomy pain over the chest wall with 11 of them having pain in the arm Only.

DISABLED FOLLOWING MASTECTOMY



Patients who felt themselves disabled following mastectomy were picked through questionnaire and was found to be 17 pts among the 100.

IMPACT OF MASTECTOMY AMONG PATIENTS



When asking about how they felt about the loss their responses were categorised into the Following

a was Sad and crying about your loss (3)

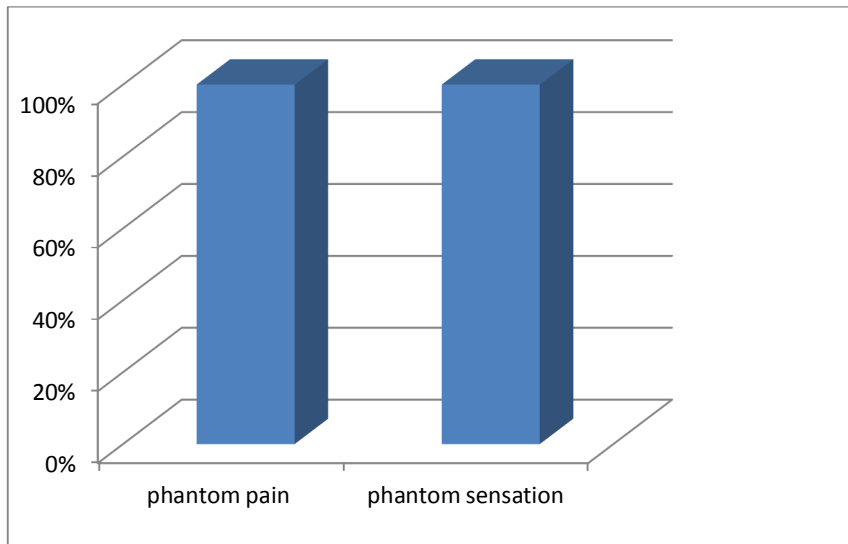
B was not able to move freely as before surgery (8)

C was Sad about affection of sexual life (4)

D was Do you feel like having prosthesis (2)

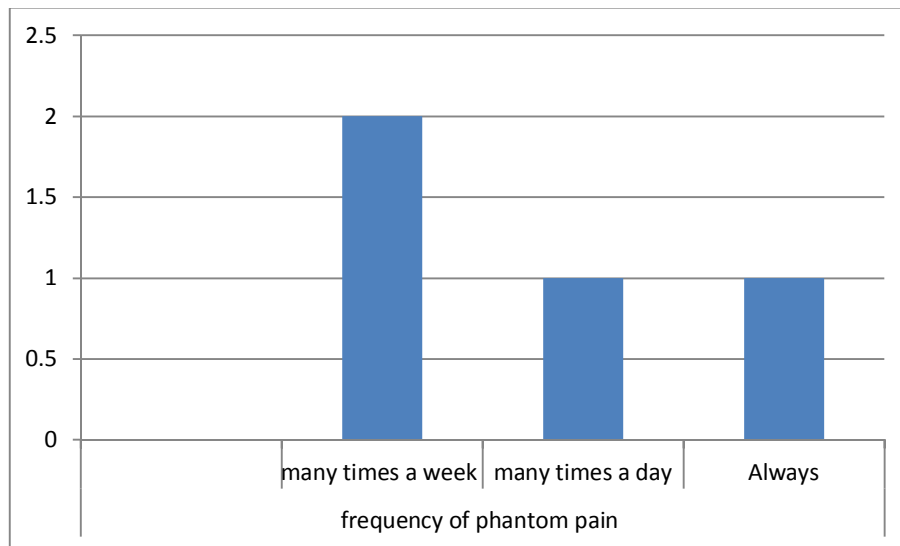
Rest of them had none of these

INCIDENCE OF PHANTOM BREAST SYNDROME



Finally pts with phantom sensation and phantom pain were found with the help of questionnaire and it was around 4 of them experienced phantom pain alone 6 of them experienced phantom sensation in the region of operated breast

FREQUENCY OF PHANTOM PAIN EXPERIENCED



1-Never

2-Monthly

3-weekly

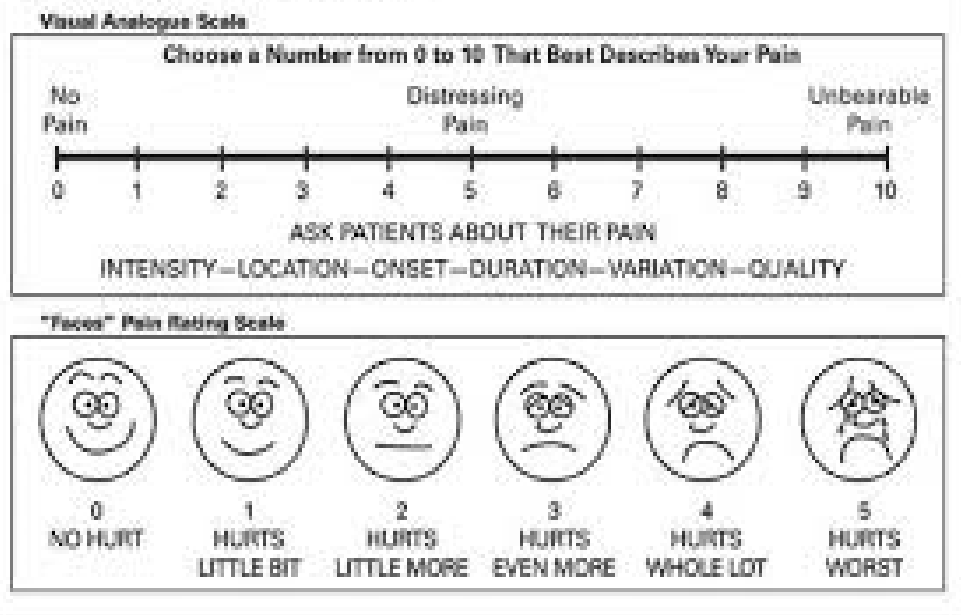
4-Many times a week (2 pts)

5-daily

6-many times a day (1 pt)

7-Always (1 pt)

Figures: Tools Commonly Used to Rate Pain



DISCUSSION

The incidence of phantom breast pain is thought to be underestimated, because women may hesitate to Report it to their health care provider unless specifically questioned. Intermittent pains may be viewed as nonthreatening, something that needs to be tolerated. Some women have expressed the fear that they will be thought crazy for having pain in an area of their body that is surgically absent. The incidence of post axillary dissection pain appears to vary with the type of surgery performed.

No study reported any increased prevalence over time. It is unknown how pain changes ,if at all, after this period Authors in two studies compared the incidence of pain 'after mastectomy to that after lumpectomy and Radiotherapy. Subjects in both groups had full axillary dissection as part of their surgical treatment. No solid conclusion about which treatment type causes less pain can be drawn from these data. However, it is clear that axillary dissection may result in pain regardless of the type of mastectomy, segmental or modified radical, that is performed.

our study is also based on the MRM with Axillary dissection Several authors agreed that pain is particularly a problem when the intercostobrachial nerve is disrupted during surgery . Current treatment practice should employ nerve sparing technique during axillary dissection to ensure a better medical outcome for the patient. The nature of postaxillary dissection pain was addressed by

investigators in three of the studies. Subjects in each study used words such as pricking, sharp, shooting, and stabbing tom. Burning, aching sensations were discussed as part of introductions to all of the studies but only reported by subjects in two .

The observation of the occurrence of phantom breast syndrome in our population was found to be 17% . The unrecognised entity of the phantom Breast syndrome in our population has showed that its all the more common as in western population and it needs to treated for the improved quality of living it is of utmost importance that women undergoing breast surgery be informed about the pain that they may experience as a result of their surgery. Alterations in sensory experiences can cause additional stress, vulnerability, and fear after diagnosis and treatment of breast cancer . Nurses can reduce the distress experienced by women undergoing breast surgery by helping them to understand the pain they may experience, its causes, and by assuring them that pain management is a priority in their care.

Without this information, pain may not be reported by many women because they think it is a normal postoperative symptom they need to tolerate, and that it will, eventually, go away. Unreported pain that goes unrelieved may lead to suffering, anxiety, and depression . As time goes by, women may fear that persistent pain means metastases or recurrent tumor. As the literature has documented, however, pain after breast surgery is a common experience and is

frequently related to the surgery rather than the disease. This pain is often reported persisting over a long period it is important then that nurses assess pain experienced by women after breast surgery, even years after the actual operation. Preparatory information including subjective features such as physical sensations and objective features such as temporal and spatial characteristics have been found to enhance the patient's ability to cope and diminish distress and should, therefore, be included in patient teaching before breast surgery. As we incorporate information about post mastectomy pain into their daily practice, they can make a significant difference in each women's experience with breast cancer surgery and improve her quality of life by assuring that she has accurate expectations for pain after surgery and options for pain management. Risk factors including the type of surgery, nerve sparing techniques, and treatment planned after the surgery, such as radiation to the chest wall, may influence the development of pain after breast surgery. Unfortunately, the literature does not offer a clear answer as to which treatment methods will result in the least pain.

Being aware of the causes of pain can, however, be of benefit in choosing a surgeon through inquiry as to his/her practice with regard to the intercostobrachial nerve. Nurses educating women before breast surgery can empower their patients to discuss with their physician nerve-sparing techniques to be used during surgery. Further investigation is necessary with specific attention to methods used to treat postaxillary dissection and phantom breast pain syndromes. Studies, that assess

efficacy of specific treatment methods are essential. Future studies should investigate health care providers' knowledge of and attitudes toward these pain syndromes; determine whether patients who experience postaxillary dissection pain or PBP report their symptoms to health care providers and whether they are offered treatment; and examine different treatment modalities and assess their efficacy: Pain after breast Surgery continues to be a problem faced by many women with breast cancer. Energy should be focused on finding management techniques that will improve the outcome of the pain experience, move women along the path to recovery, and increase chances for satisfying quality of life after surgery.

CONCLUSION

1. out of 100 patients,81 underwent Modified Radical Mastectomy and the remaining underwent simple Mastectomy.
2. Mean age of patients 47. 21% of patients experienced post mastectomy pain over the chest wall and 11 % of them having pain in the arm.
3. 17% of Patients felt themselves disabled following mastectomy
4. 5.4 % of patients experienced phantom pain alone.
5. 6.6 % of them experienced phantom sensation in the region of operated breast.
6. The occurrence of phantom breast syndrome in our patients was found to be 17%.

Urkund Analysis Result

Analysed Document: Project comp.docx (D57464590)
Submitted: 10/22/2019 4:17:00 PM
Submitted By: msvasanthmbbs@gmail.com
Significance: 8 %

Sources included in the report:

[https://journals.lww.com/ajpmr/Fulltext/2004/08000/
Phantom_Breast_Pain_as_a_Source_of_Functional_Loss.13.aspx](https://journals.lww.com/ajpmr/Fulltext/2004/08000/Phantom_Breast_Pain_as_a_Source_of_Functional_Loss.13.aspx)



GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL, CHENNAI -01
INSTITUTIONAL ETHICS COMMITTEE

TITLE OF THE WORK : A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY.

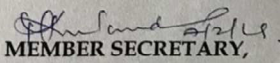
PRINCIPAL INVESTIGATOR : DR. M.S. VASANTH,
DESIGNATION : PG IN MS GENERAL SURGERY,
DEPARTMENT : DEPARTMENT OF GENERAL SURGERY,
GOVT. STANLEY MEDICAL COLLEGE.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.01.2019 at the Council Hall, Stanley Medical College, Chennai-1 at 10am.

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.


MEMBER SECRETARY,
IEC, SMC, CHENNAI

QUESTIONNAIRE

Name: Age: IP/OP No: Date:

1. When was mastectomy done
2. What Was the indication for surgery
3. How did the breast lump present as
 - a. Asymptomatic lump
 - b. Pain with the lump
 - c. Non palpable lesion
 - d. Others.
4. What kind of surgery did you underwent ?
 - Modified radical mastectomy
 - Simple mastectomy
 - Others.
5. Did you experience pain following surgery (<3 weeks)? yes/no
6. If yes whether it was in
 - a. Chest wail
 - b. Axilla
7. Do you think you are disabled following surgery (>3 weeks)

8. If yes then on a scale from 0 -10 how much do you think of yourself as disabled ?

1. 0 (not at all
2. 1-5 (consider disabled often)
3. 5-10 (always consider myself disabled)

9. When you think about your loss which statement best suits your reaction ?

- a. Sad and crying about your loss
- b. Not able to move freely as before surgery
- c. Sad about affection of sexual life
- d. Do you feel like having a prosthesis
- e. None of the above

10. Do you feel any pain in the region of the breast following surgery?

11. If yes is that pain sensation similar to the one felt before surgery?

12. How frequent is the breast pain experienced?

- a. 1- never 4 - many times a week
- b. 2 - monthly 5 - daily
- c. 3 - weekly 6 - many times a day
- d. 7 always

13. if no pain do you have any sensation of breast following surgery?

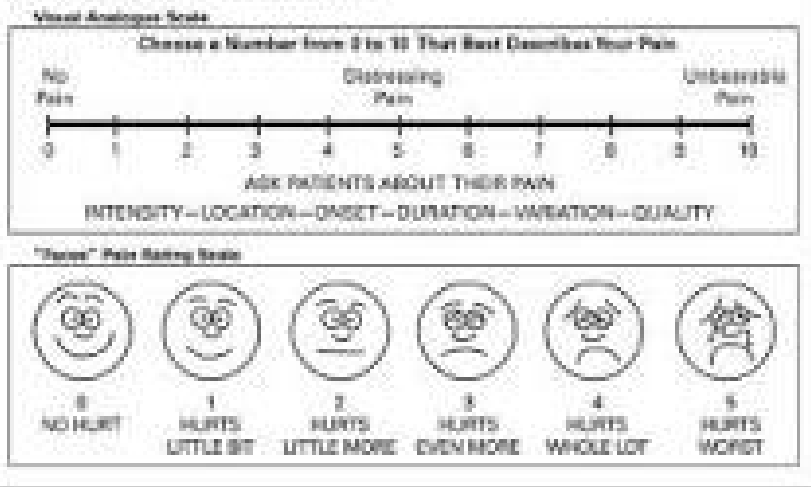
14. On a scale of 1 - 10 how much upsetting is the phantom pain / sensation to you

- i. 0 - not at all
- ii. 5 - quite upsetting
- iii. 10 - extremely upsetting

15. Phantom breast treatment outcome: { treatment ladder)

	reassurance	Placebo	analgesics	antidepressants
After One month				
After month two				
After months three				

Figures: Tools Commonly Used to Rate Pain



INFORMED CONSENT

DISSERTATION TOPIC:

“A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND
PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY

”

PLACE OF STUDY: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI

NAME AND ADDRESS OF PATIENT:

I, _____ have been informed about the details of the study in my
own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I
will continue to receive the medical treatment as usual.

I understand that I will not get any payment for taking part in this study.

I will not object if the results of this study are getting published in any medical
journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full co-operation for this study.

Name and Address of the Volunteer:

Signature/Thumb impression of the Volunteer

Date:

Witnesses:

(Signature, Name & Address)

Date:

Name and signature of investigator:

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001

INFORMED CONSENT

DISSERTATION TOPIC:

“A STUDY ON THE INCIDENCE OF POST MASTECTOMY PAIN AND
PHANTOM BREAST SYNDROME FOLLOWING MASTECTOMY”

PLACE OF STUDY: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI

NAME AND ADDRESS OF PATIENT:

நான், _____

எனது சொந்த மொழியில் ஆய்வு விவரங்களை பற்றி தெரிவிக்கப்பட்டது.

நான் முற்றிலும் ஆய்வு விவரங்களை புரிந்து கொண்டேன்.

ஆய்வு பங்கெடுத்துக் கொண்டுள்ள நான்,

சாத்தியமான அபாயங்கள் மற்றும் பயன்களை அறிந்து இருக்கிறேன்.

நான் எந்த நேரத்திலும் ஆய்வு இருந்து திரும்ப முடியும் மற்றும் அதன்பின்னர்,

நான் வழக்கம் போல் மருத்துவ சிகிச்சை பெற தொடரும் என்று புரிந்து கொள்ள.

நான் இந்த ஆய்வில் பங்கு எடுத்து எந்த பணம் பெற முடியாது என்று புரிந்து.

நான் ஆட்சேபிக்கிறேன் மாட்டேன் இந்த ஆய்வின் முடிவு,

எந்த மருத்துவ இடத்தில் கிடைக்கும் என்றால்,

என்தனிப்பட்ட அடையாள வெளிப்படவில்லை வழங்கப்படும்.

நான்இந்தஆய்வுபகுதியாகஎடுத்துசெய்யவேண்டும்என்றுஎனக்குநான்இந்தஆய்வுஎன்மு
முடித்துழைப்புநீட்டிக்கஎன்றுஉறுதியளிக்கிறேன்.

பெயர்மற்றும்தொண்டர்முகவரி:

தொண்டர்கையொப்பம் / பெருவிரல்ரேகை

நாள்:

சாட்சிகள்:

(கையொப்பம், பெயர்மற்றும்முகவரி)

நாள்:

பெயர்மற்றும்புலன்விசாரணையொப்பம்: (டாக்டர்)

BIBLIOGRAPHY

1. Maunsell E, Brisson J, Deschenes L Arm problems and psychological distress after surgery for breast cancer. *Can J Surg* 1992;36:315-20.
2. International Association for the Study of Pain, Task Force on Taxonomy. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms, 2nd ed. Seattle: IASP Press, 1994
3. McCaffery M, Beebe A. Pain: clinical manual for nursing practice. St. Louis: CV Mosby, 1989.
4. Vecht CI Arm pain in the patient with breast cancer. *J Pain Symptom Management* 1990;5:109-17.
5. Karydas I, Fentiman I, Habib F, Hayward J. Sensory changes after treatment of operable breast cancer. *Breast Cancer Res Treat* 1986;8:55-9
6. Gerber L, Lampert M, Wood C, et al. Comparison of pain, motion, and edema after modified radical mastectomy vs. local excision with axillary dissection and radiation. *Breast Cancer Res Treat* 1992;21:139-45.
7. Wood KM. Intercostobrachial nerve entrapment syndrome. *South Med J* 1978;76:662-3
8. Vecht O, VandeBrand Hi, Wajer OM. Post-axillary dissection pain in breast cancer due to a lesion of the intercostobrachial nerve. *Pain* 1989;38:171-6
9. Assa J. The intercostobrachial nerve in radical mastectomy. *J Surg Oncol* 1974;6:123-6
10. Lierman L. Sensory and physical alterations after mastectomy. *Health Care for Women International* 1988;9:263-79.

11. Hladiuk M, Huchcroft S, Temple W, Schnurr B. Arm function after axillary dissection for breast cancer: a pilot study to provide parameter estimates. *J Surg Oncol* 1992;50:4752
12. Ivens D, Hoe AL, Podd T.J, Hamilton CR, Taylor 1, Royle GT. Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992;66:136-8
13. Keramopoulos A, Tsionou C, Minaretzis D, Michalas S, Aravantinos D. Arm morbidity following treatment of breast cancer with total axillary dissection: a multivariate approach. *Oncology* 1993;50:445-9
14. Kroner K, Knudsen U, Lundby L, Hvid H. Long-term phantom breast syndrome after mastectomy. *Clin J Pain* 1992;8:346-50.
15. Karb VB. Pain. In: *Medical surgical nursing: concepts and clinical practice*, 3rd ed. St. Louis: CV Mosby, 1987
16. Stops T, Hoogenhout J, Wobbes T. Phantom breast sensations following mastectomy. *Cancer* 1985;56:2898-901,
17. Kroner K, Krebs B, Skov J, Jorgensen H. Immediate and longterm phantom breast syndrome after mastectomy: incidence, clinical characteristics and relationship to 7re-mastectomy breast pain. *Pain* 1989;36:327-34.
18. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and longterm phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain* 1985;21:267-78.
19. Agency for Health Care Policy and Research. *Management of cancer pain: clinical practice guideline*. Rockville: AHCPR, U.S. Department of Health and Human Services, Public Health Service, 19

20. World Health Organization. Cancer pain relief and palliative care: report of a WHO expert committee. Geneva, Switzerland World Health Organization, 1990. http://ovidsp.tx.ovid.com/spb/ovidweb.cgi?&S=NBCFFPLODDDDHLBEMCGLDDNKAEKGAA00&Link+Set74.s.h.38.%7c1.%7csl_10-36
21. Watson CP, Evans RJ, Waif VR. The post-mastectomy pain syndrome and the effect of topical capsaicin. *Pain* 1989;51:375-9
22. Dini D, Bertelli G, Gozza A, Forno G. Treatment of postmastectomy pain syndrome with topical capsaicin. *Pain* 1993;54:223-6
23. Watson CP, Evans RJ. The postmastectomy pain syndrome and topical capsaicin: a randomized trial. *Pain* 1992;51:375-9
24. Johnson JE, Lauver DR. Alternative explanations of coping, with stressful experiences associated with physical illness. *Adv Nurs Sci* 1989;11:39-52
25. Bennett S, Kaelin CM: *Benign breast disease*. In: Branch WT, ed.. *Office Practice of Medicine*, 4th ed. Philadelphia: WB Saunders; 2003.
26. Donegan WI, Spratt JS: *Cancer of the Breast*, 5th ed. Philadelphia, WB Saunders, 2002.
27. Haagensen CD: *Diseases of the Breast*, 3rd ed. Philadelphia, WB Saunders, 1986.
28. Rossouw JE, Anderson GL, Prentice RL, et al: Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002; 288:321-333.

29. Lind DS, Smith BL, Souba *WW: 5 Breast Complaints*. In: Souba *WW*, Fink MP, Jurkovich 01, et al ed. *2 Breast, Skin, Soft Tissue, and Neck ACS Surgery Online*, New York: WebMD; 2004.
30. Pisano ED, Gatsonis C, Hendrick E, et al: Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group. Diagnostic performance of digital versus film mammography for breast-cancer screening. *N Engl J Med* 2005; 353:1773-1783.
31. Silverstein MJ, Lagios MD, Recht A, et al: Image-detected breast cancer: State of the art diagnosis and treatment. *J Am Coll Surg* 2005; 201:586-597.
32. Hylton N: Magnetic resonance imaging of the breast: Opportunities to improve breast cancer management. *J Clin Oncol* 2005; 23:1678-1684.
33. Elmore JG, Armstrong K, Lehman CD, Fletcher SW: Screening for breast cancer. *JAMA* 2005; 293:1245-1256.
34. Berry DA, Cronin KA, Plevritis SK, et al: Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005; 353:1784-1792.
35. Meyer JE, Smith DN, Lester SC, et al: Large-core needle biopsy of nonpalpable breast lesions. *JAMA* 1999; 281:1638-1641.
36. Darling ML, Smith DR, Lester SC, et al: Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: Results of surgical excision. *AJR Am J Roentgenol* 2000; 175:1341-1346.
37. Willett WC, Rockhill B, Hankinson SE, et al: *Nongenetic factors in the causation of breast cancer*. In: Harris JR., Lippman ME, Morrow M, Osborne CK, ed.

- Diseases of the Breast*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004:223-276.
38. Rosen PR: *Rosen's Breast Pathology*, 2nd ed. Philadelphia, Lippincott Williams & Wilkins, 2001.
 39. Hartmann LC, Sellers TA, Frost MH, et al: Benign breast disease and the risk of breast cancer. *N Engl J Med* 2005; 353:229-237.
 40. Domchek 5, Weber BL: *Inherited genetic factors and breast cancer*.
in: Harris A, Lippman ME Morrow M, Osborne CK, ed. *Diseases of the Breast*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004:276-313.
 41. Stefanick ML, Anderson GL, Margolis KL, et al: Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *AMA* 2006; 295:1647-1657:
 42. Pawels Ti: Anti-oestrogenic prevention of breast cancer—the make or break point. *Nat Rev Cancer* 2002; 2:187-794.
 43. Hartmann LC, Schaid DJ, Woods JE, et al: Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med* 1999; 340:77-84.
 44. Elston CW, Ellis 10: *Systemic Pathology: the Breast*, 3rd ed. Edinburgh, Churchill Livingstone, 1998.
 45. Rosen PR: *Rosen's Breast Pathology*, 2nd ed. Philadelphia, Lippincott Williams & Wilkins, 2001.
 46. Jemal A, Siegel R, Ward E, et al: Cancer statistics, 2006.- *CA Cancer Clin* 2006; 56:106-:130.

47. Fisher B, Jeong JH, Anderson S, et al: Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. *N Engl J Med* 2002; 347:567-575.
48. Smith BL, Souba WW: In: Wilmore DW, Cheung LY, ed. *Breast Procedures, American College of Surgeons Surgery: Principles and Practice*, New York: WebMD; 2002:606619.
49. Lyman GH, Giuliano AE, Somerfield MR, et al: American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *J Clin Oncol* 2005; 23:7703-7720.
50. Noik AM, Fey J, Gemignani M, et al: The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection: A follow-up study of 4008 procedures. *Ann Surg* 2004; 240:462-468.
51. Fisher B, Dignam J, Wolmark N, et al: Tamoxifen in treatment of Intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. *Lancet* 1999; 353:1993-2000.
52. Fisher B, Dignam J, Wolmark N, et al: Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-17. *J Clin Oncol* 1998; 16:441-452.
53. Wong JS, Koelin CM, Troyan SL, et al: A prospective study of wide excision alone for intraductal carcinoma in situ (DCIS) of the breast. *J Clin Oncol* 2006; 24:1031-1036.

54. Silverstein MJ, Lagios MD, Craig PH, et al: A prognostic index for ductal carcinoma in situ of the breast. *Cancer* 1996; 77:2267-2274.
55. Early Breast Cancer Trialists' Collaborative Group: Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: An overview of the randomised trials *Lancet* 2000; 355:1757-1770.
56. Arthur DW; Vicini FA: Accelerated partial breast irradiation as a part of breast conservation therapy. *J Clin Oncol* 2005; 23:1726-1735.
57. Toghian A, Jeong JH, Mamounas E, et al: Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: Results from five NSABP randomized clinical trials. *J Clin Oncol* 2004; 22:4247-4254.
58. Wolmark N, Wang J, Mamounas E, et al: Preoperative chemotherapy in patients with operable breast cancer: Nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. *J Natl Cancer Inst Monogr* 2001; 30:96-102.
59. Hughes KS, Schnaper L, Berry D, et al: Comparison of lumpectomy plus tamoxifen with and without radiotherapy (rt) in women 70 years of age or older who have clinical stage I, estrogen receptor-positive breast carcinoma. *N Engl J Med* 2004; 351:971-977.

60. Fyies AW, McCready DR, Manchul LA, et al: Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. *N Engl J Med* 2004; 351:963-970.
61. Smith BL: *Advanced Therapy of Breast Disease, Paget Disease*, Hamilton, Ontario, BC Decker, 2000.
62. Giordano SH, Buzdar AU, Hortobagyi GN: Breast cancer in men. *Ann Intern Med* 2002; 137:678-687.
63. Perou CM, Sorlie T, Eisen MB, et al: Molecular portraits of human breast tumors. *Nature* 2000; 406:747-752.
64. Paik S, Tang G, Shak S, et al: Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. *J Clin Oncol* 2006; 24:3726-3734.
65. In: Harris JR, Lippman ME, Morrow M, Osborne CK, ed. *Diseases of the Breast*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004.
66. Early Breast Cancer Trialists' Collaborative Group: Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: An overview of the randomised trials. *Lancet* 2005; 365:1687-1717.
67. Citron ML, Berry DA, Cirincione C, et al: Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as post-operative adjuvant treatment of node-positive primary

breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741.

J Clin Oncol 2003; 21:1431-1439.

68. Romond EH, Perez EA, Bryant J, et al: Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005; 353:1673-1684.
69. Joensuu H, Kellokumpu-Lehtinen P-L, Bono P, et al: Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. *N Engl J Med* 2006; 354:809-820.
70. Goss PE, Strasser K: Aromatase inhibitors in the treatment and prevention of breast cancer. *J Clin Oncol* 2001; 19:881-894.
71. Early Breast Cancer Trialists' Collaborative Group: Tamoxifen for early breast cancer: An overview of the randomised trials. *Lancet* 1998; 351:1451-1467.
72. Mouridsen HT, Robert NJ: The role of aromatase inhibitors as adjuvant therapy for early breast cancer in postmenopausal women. *Eur J Cancer* 2005; 41:1678-1689.
73. Winer EP, Hudis C, Burstein HJ, et al: American Society of Clinical Oncology technology assessment on the use of aromatase inhibitors as adjuvant therapy for women with hormone receptor-positive breast cancer: Status report 2002. *J Clin Oncol* 2002; 20:3317-3327.

74. Goldhirsch A, Glick JH, Gelber RD, et al: Meeting highlights: International expert consensus on the primary therapy of early breast cancer 2005. *Ann Oncol* 2005; 16:1569-1583.
75. Antoniou AC, Easton DF. Models of genetic susceptibility to breast cancer. *Oncogene* 2006;25(431):5898.
76. Wooster R, Weber BL. Breast and ovarian cancer. *N Engl J Med* 2003;348(231):2339.
77. Walsh T, King MC. Ten genes for inherited breast cancer. *Cancer Cell* 2007;11(2):103.
78. Cox A, Dunning AM, Garci -Closas AA. et al. A common coding variant in CASP8 is associated with breast cancer risk. *Nat Genet* 2007;39(3):352,
79. Easton OF, Pooley KA, Dunning AM, at al. Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature* 2007;447(7144):1087.
80. Hunter Di, Kraft P, Jacobs KB, et al. A genome-wide association study identifies alleles in FGFR2 associated with risk of sporadic postmenopausal breast cancer. *Nat Genet* 2007,39(7):870.
81. Pharoah PD, Tyrer J, Dunning AM, Easton OF, Ponder BA, Association between common variation in 120 candidate genes and breast cancer risk. *PLoS Genet* 2007;3:e42.

82. Couch FJ, Weber BL. Breast cancer. In: The genetic basis of human cancer, Vogelstein B, Kinzler KW, eds. New York: McGraw-Hill, NI, 2002;549-581.
83. Parvin JD, Sankaran S. The BRCA1 E3 ubiquitin ligase controls centrosome dynamics. *Cell Cycle* 2006;5(17):1946.

