"SCRUTINY OF EXTENT OF AXILLARY NODE DISSECTION FOR PATIENTS WITH PRIMARY BREAST CANCER"

A 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

DEPARTMENT OF GENERAL SURGERY

STANLEY MEDICAL COLLEGE AND HOSPITAL

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

MAY 2018

CERTIFICATE

This is to certify that the dissertation titled ***"SCRUTINY OF EXTENT OF AXILLARY NODE DISSECTION FOR PATIENTS WITH PRIMARY BREAST CANCER"*** is a bonafide work done by ***Dr. M. MATHEWS,*** Post Graduate student (2016 – 2018) in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under my direct guidance and supervision, in partial fulfilment of the regulations of The Tamil Nadu Dr. M.G.R Medical University, Chennai for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in May 2018.

Prof. DR.C.BALAMURUGAN,M.S.,
Dissertation Guide
Professor of Surgery,
Dept. of General Surgery,
Stanley Medical College,
Chennai-600001.

Prof.DR.A.K.RAJENDRAN,M.S.,
Professor and Head of the Department,
Dept. of General Surgery,
Stanley Medical College,
Chennai-600001.

PROF. DR. S. PONNAMBALANAMASIVAYAM, M.D.,
The Dean,
Stanley Medical College,Chennai-600001

DECLARATION

I, **DR. M. MATHEWS** solemnly declare that this dissertation titled

"SCRUTINY OF EXTENT OF AXILLARY NODE DISSECTION FOR PATIENTS WITH PRIMARY BREAST CANCER"

is a bonafide work done by me in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under the guidance and supervision of my unit chief.

Prof. DR. C. BALAMURUGAN

Professor of Surgery

This dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the university regulations for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in April 2018.

Place: Chennai.

Date: September 2017

DR. M. MATHEWS

ACKNOWLEDGEMENT

My sincere thanks to PROF. DR. S. PONNAMBALANAMASIVAYAM, M.D., The Dean, Govt. Stanley Medical College, Chennai, for permitting me to conduct the study and use the resources of the College.

I consider it a privilege to have done this study under the supervision of my beloved Professor and Head of the Department Prof.Dr.A.K. RAJENDRAN, who has been a source of constant inspiration and encouragement to accomplish this work. I am highly indebted to my guide Prof. Dr. C. BALAMURUGAN, Professor of Surgery for his constant help, inspiration and valuable advice in preparing this dissertation.

I express my sincere gratitude to my guide and mentor Prof.Dr.D.NAGARAJAN, former Head of Department of General Surgery and my former Professor. I express my deepest sense of thankfulness to my Assistant Professors Dr.A.RAJESWARAN and Dr.P.MATHUSOOTHANAN for their valuable inputs and constant encouragement without which this dissertation could not have been completed. I thank them for the constant support, able guidance, inspiring words and valuable help they rendered to me during my course. I would like to thank my former Assistant Professors Dr. MALARVIZHI, Dr. JIM JEBAKUMAR and Dr. PONMUTHU for their valuable suggestions and help in completing this dissertation.

I extend my sincere thanks to the Head of the Department, Professors, Asst. professors and post graduates of Department of Pathology, Govt. Stanley Medical College, Chennai, for extending their help to conduct the study.

I am particularly thankful to my friends Dr. Sreekanth, Dr. Ben Abraham, Dr. Mohan Raj, Dr. Sukumar, Dr. Praveen Jeyakumar, Dr. Vasanth Kumar, Dr. Prasanth, Dr. Ajay Kumar without whom accomplishing this task would have been impossible. I thank my Seniors Dr. Aravind Menon, Dr. Prasanna, Dr. Sakthibalan, Dr. Vinoth, Dr. Sukhdev and Dr. Madhuri for their valuable support in this study.

I am extremely thankful to my patients who consented and participated to make this study possible.

INTRODUCTION

Carcinoma of breast is the most common of non-skin malignancies in women and is second to lung cancer being a cause of cancer deaths. A woman who lives to age 90 has a one in eight chance of developing breast cancer[1]. It is as ironic and tragic that a neoplasm arising in an exposed organ, readily accessible to self-examination and clinical surveillance, continues to exact such a heavy toll.

The treatment of the primary breast cancer relies primarily on surgery. The surgery for breast cancer dates back to first century from when various modification has occurred in its treatment and now being evolved into MODIFIED RADICAL MASTECTOMY (MRM) and Breast conservation surgery which are being performed increasingly over the last 2 decades, and for many surgeons either of these has become the "standard operation" for primary operable breast carcinomas.

The number of positive axillary lymph nodes foresee prognosis and is important in determining adjuvant therapy in breast cancer patients. This study was undertaken to determine if differences in the extent of axillary node dissection would alter the number of reported positive nodes. And there is no authentic evidence that, to which subset of axillary level the interpectoral nodes belong and whether its dissection is essential in routine MRM or not, as this node dissection is a standard procedure in radical mastectomy.

This report is an observational study details from the Department of General Surgery, Govt. Stanley Medical College and Hospital, Chennai, which contains the results of patients undergoing MRM performed between March 2016 to August 2017, in which the each level of axillary node and interpectoral nodes are submitted as a separate sample at the end of the standard MRM procedure for histopathology, and attempts were made to define the incidence of node positivity in various stage of primary breast cancer and evaluate the significance of interpectoral node metastases in patients with primary disease.

REVIEW OF HISTORY

It is remarkable that, the written records and illustrations of carcinoma breast dates back to relic as the location of the organ permitted easy identification. Edwin Smith Surgical Papyrus, dates back to 3,000–2,500 B.C., and is attributable to Imhotep (the Egyptian physician-architect), which provides credible accounts of breast cancer. A case was suspected to be incurable when the disease was "cool to touch, bulging and spread all over the breast"[2]. In ancient Greece, for relief from breast maladies a divinity was incited to offer, which was evidenced by votive offerings in shape of breasts in Greek temples which had Asclepius, who is the god of medicine. Carcinoma (karkinoma), scirrhous (hard, Greek skirros) and cacoethes (malignant disease, Greek kakoethes) in the medical eloquence owe their origins to Hellenistic writings. In 400 B.C. Hippocrates' theory of the imbalance about humours (blood, phlegm, and yellow and black bile) caused disease. He has described the progressive stages of carcinoma breast which represents early axiom about the cause of carcinoma[3].

In 1st century A.D., Leonides of Alexandria followed the traditions of Greek. He detailed about incision and cautery in his approach[4]. His requirement of leaving a wide margin of excision and only removing tumours of limited extent, prefigures the oncological principles of contemporary surgical practice. Galen, explained breast cancer in 200 A.D. as pile of black bile in the blood, wind up that it was a systemic disease. These ancient physicians

presuppose that the cessation of menstruation was linked to carcinoma; it was probably due to the association of carcinoma with old age. Along this theory, Galen made surgical wounds to bleed openly to get rid of the black bile and he dismayed the use of ligatures. He coined the word ‘crab’ for cancer to exemplify the dilated veins radiating from the tumour[5].

But during the Middle Ages there was surgical stagnation in treatment of Breast cancer. From 476 to 1,500 A.D. the religious philosophies unavoidably intertwined medical progress. Early Christian conviction was more towards faith that heals and was doing marvels over surgery, which was felt as barbaric. Islamic evolution made meticulous translations of Greek medicine and saved medical knowledge. In 10th century, Avicenna and Albucasis and in 12th century Maimonides (Spain) were Arab physicians of fame, spread the medical values to all the countries which ever they conquered. Cautery in Surgery was strongly recommended by Albucasis in surgery[6]. They used caustic pastes to bring down the size of the tumor and make it operable, is the same logic for using chemotherapy for large breast cancers nowadays. Albucasis, Henri de Mondeville who is the ‘father’ of French surgery in 13th century and Guy de Chauliac from France, 14th century introduced unique instrument for rapid removal of breast tumors.

The period of Renaissance with celebration of arts and the emergence of surgery, dates back for 16th to 18th centuries, was the age of artistic creativity and was the golden age for emergence of surgery. Andreas Vesalius in 16th

century in Belgium gave a strong anatomical exploration of human body following which refinement of surgery was done. The identification of Cooper's eponymous ligaments of the breast and Sappey's subareolar plexus of lymphatics in 18th century in England and France made clear about the origins and spread of breast cancer[7,8]. In 18th century, John Hunter who was called the Scottish 'father' of investigative surgery made efforts to replace the term 'black bile' to lymph as the cause of breast cancer. There are many theories ranging from inspissated milk, trauma, personality type, exposure to air and infection that were mounted for carcinogenesis. The observation of the disease within families was naturally attributed to infection. While there was an extreme search for the correct treatment of Carcinoma breast surgeries like simple lumpectomies amounting to radical removal of the pectoralis, recreated medical records. These procedures were tremendously appreciated because, the absence of anaesthesia warranted exclusive skill and speed of the surgeon to operate. It is also a grim reminder that surgery was the solitary modality of hope for relief with anecdotal incidences of cure. Use of ligatures or lead plates to strangulate the tumours were the more conservative approaches, preferring them to the horrors of breast amputation.

It was the Nineteenth Century, which is deemed as the golden era of surgery. The surgical exercise improved during this period where there were multiple discoveries in the supporting fields making surgery easy. The first landmark events were invention of Disinfection, sterilisation and use of sterile

gloves. Introduction of General anaesthesia revolutionised surgeon's ease (and indeed the patient's too!). In 1818 James Blundell made an attempt of blood transfusion for treating postpartum haemorrhage, but the safe transfusions were achieved only at the starting of the 20th century, when Karl Landsteiner discovered blood groups. Along with these discoveries, other contributions to cancer came from the identification of normal cells through microscope and their cancerous outrage all the way from Hooke in 17th century to Müller and Virchow in 19th century. Müller was the one who discouraged the humoral theory for origin of cancer, declaring that cancers were composed of living cells and he only suggested that metastasis was due to spread of these living cells. Basis of variety of excision techniques for treatment was framed after the demonstration of breast cancer spread through the lymphatics to corresponding axillary nodes. Unique forms of spread that caused the clinical appearance of carcinoma en cuirasse or peau d'orange and Paget's disease made to think of alternative ways of approaching treatment.

The middle years of 19th century were renowned because of the newly acquired surgical freedom with bold and radical surgeries. The en bloc resections by Charles Moore in London, and Kuster and Volkmann in Germany ran a parallel course[10]. In 1882, William Banks in Liverpool performed Axillary lymph node dissections as part of the philosophy of extermination [11]. It may appear particularly mutilating today, but they provided a unique opportunity to study the spread disease. At the turn of century Breast cancer

surgery came to be synonymous with the name of Sir William S. Halstead, who was the Professor of Surgery at John Hopkins hospital in Baltimore, USA. He was the one who performed first radical mastectomy which was reported in 1894 with the emphasis on removing tissues as a single piece so as to prevent spread and removal of the pectoralis major muscle to prevent recurrence. This method became the accepted way that generations of surgeons trod with diligence [12]. This view of removing the tissue as a single piece is based on the belief that the wound will become infected once there is division of tissues which are invaded by the disease or lymphatic vessels containing the cancer cells, and because shreds or pieces of cancerous tissue may be overlooked in the piecemeal extirpation [13]."

As there were strict rules for non-violation of tumour area, a preoperative biopsy to confirm whether the patient had a cancer or not, was needed. So during olden days the strength of a skilled clinical diagnosis was excellent to do surgery without preoperative biopsy. There was another age old practice of leaving the excised surgical wounds open so that it would granulate. The use of ligatures was not allowed for better wound healing through low infection rates.

At Twentieth Century, the Surgery reinvented itself. The hormone dependency of breast cancer was first thought to be hypothetical, then as the the disease was more aggressive in younger women it was proved to be true. During 1906 Beatson enlightened the era of endocrine surgery [14]—even before the discovery of estrogen receptors by Jensen in 1967[15] along with oopherectomy

and adrenalectomy (to achieve castration) which came as a standard procedure. These methods of surgery were gradually replaced by the use of estrogen receptor modulators, luteinising hormone-releasing agonists and aromatase inhibitors.

Margottini and Veronesi in Milan preserved the legacy of Halsteadian surgery, who removed internal mammary nodes in addition to the procedure and extended the scope of 'radicality' by removing the supraclavicular and mediastinal nodes. However, during the period of late 19th and early 20th centuries there was a common thinking that: big surgeons make big incisions (and hence it is better to perform big surgeries). Patey and Handley from London and Auchincloss Jr. of New York made little changes to the procedure that 'modified' the radical mastectomy and preserved the pectoralis major.[16] following the inventions of radiation as means of destroying the cancer cells and various forms of chemotherapeutic agents were doing the same. Also the invention of medical castration or targeted mutated tumour receptors, insisted the surgeons to revise the cancer management strategies. These discoveries and inventions were coupled with increase in knowledge of the biological behaviour of breast cancer and that made everyone to rethink treatment of the Breast cancer. Mammography made it possible of early cancer detection of smaller lesions that added a new dimension to surgical management.

The surgical fraternity reoriented itself for the reduced morbid surgeries after invention and discovery of all these. Bernard Fisher, Professor of Surgery from the University of Pittsburgh, imposed the belief of Galen that breast cancer was systemic disease. This was proved by large randomised controlled clinical trials which includes the National Surgical Adjuvant Breast and Bowel Project (NSABP), which was published in 1989.[17] Veronesi from Italy and many others were toward the thought that the limited surgery was enough when complemented by adjuvants.[18]

With all these theories and beliefs Surgery rejuvenated itself by joining hands with the other modalities. At the end of the 20th century breast conservation and breast reconstruction were combined with sentinel node dissection[19]. The removal of only selected ‘sentinel’ nodes (those to which the tumour had spread) would reduce the incidence of swollen lymphoedematous arm, which is a distressing manifestation of axillary lymph node dissections.

When the theory of reducing the surgical burden was coming into existence, In 1887, Verneuil, a French surgeon transferred autologous tissue from the normal breast to the diseased one.[20] This method increased the novel ideas for variety of innovative synthetic and autologous materials that offered a restored shape that could match to do nature’s original creation. Natural choices were muscle, myocutaneous flaps, lipomas and omentum. In 1979 Holmstrom introduced the transverse rectus abdominis myocutaneous flap (TRAM) that has

stood the test of time and it has undergone several modifications during the process of evolution[21]. Along with the natural materials Prosthetic and synthetic options were brought into industry like petroleum jelly, glass balls, ivory, rubber, polyvinyl alcohol sponge and silicone.

Ever since the first recorded medical literature, the surgical domination was over the other methods in treatment of breast cancer. But At last, surgery remains as the heart of management in a multimodality setting. It balances cure and cosmesis to breast cancer survivor by providing succour instead of annihilation.

INFERENCES FROM THE HISTORY

The major lessons to be gained from the history of surgery are as follows.

- First, overlooking into history is very important to rediscover the buried insights: Galen's perceptive assessment was, breast cancer is a systemic disease which was rediscovered after two millennia later in 20th century by Fisher's observations.
- Second, the evolution of therapeutic methods has increased the fortunes of medical disciplines (like antisepsis and anaesthesia did for surgery) and has minimised their supremacy as stand-alone choices for treatment or cure.
- Third, adaptation is the best method for survival in contemporary medical practice. Surgery has won the day by adapting and playing a complementary role in modern cancer management as a patient-friendly, scientific and stylised craft.
- Finally any procedure by oncological principle needs complete removal of the cancer affected tissues that needs radicality of removing the affected tissues.

ANATOMY

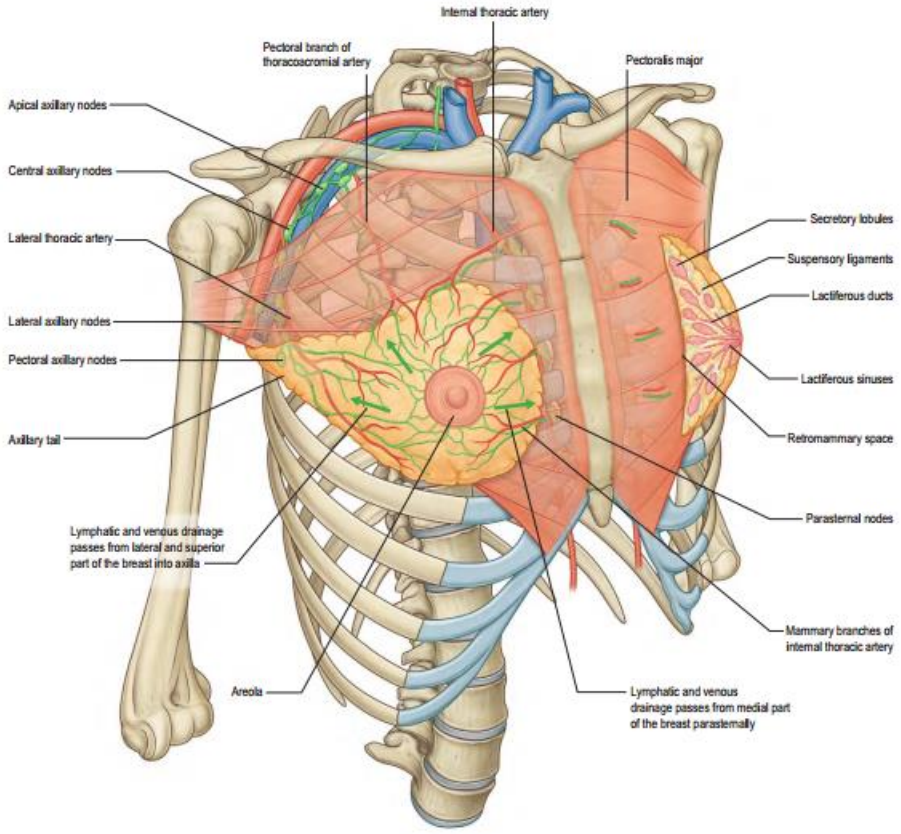
The breasts form the secondary sexual feature of females and are the source of nutrition for neonate. They are present in a rudimentary form in males. The breasts are the site of malignant change in as many as one in ten women. In young adult females, each breast is a rounded eminence that lies within the superficial fascia, largely anterior to upper thorax but spreading laterally to a variable extent. Breast shape and size depends upon genetic, racial and dietary factors, and the age, parity and menopausal status of individual. Breasts may be hemispherical, conical, variably pendulous, piriform or thin and flattened. In an adult female, the base of the breast, i.e. its attached surface, extends vertically from the second or third to the sixth rib, and in transverse plane from the sternal edge medially almost to the mid axillary line laterally. The superolateral quadrant is prolonged towards the axilla along the inferolateral edge of pectoralis major, from where it projects a little, and may extend through the deep fascia up to apex of the axilla (the axillary tail of Spence)[22].

The trunk superficial fascial system splits and encloses the breast to form the anterior and posterior lamellae. Posterior extensions of superficial fascial system connect the breast to the pectoralis fascia, which is a part of the deep fascial system. The inframammary crease is a zone of adherence of the superficial fascial system to the underlying chest wall at the inferior crescent of the breast. The breast lies upon the deep pectoral fascia, which in turn overlies

pectoralis major and serratus anterior superiorly and external oblique and its aponeurosis (the latter forms the anterior wall of the sheath of rectus abdominis) inferiorly. Between the breast and the deep fascia the loose connective tissue in the ‘submammary space’ allows the breast for some degree of movement on the deep pectoral fascia. Advanced mammary carcinoma may, by invasion, cause tethering or fixation of breast to the underlying musculature.

Occasionally, small projections of glandular tissue may pass through the deep fascia into the underlying muscle in normal subjects. The nipple projects from centre of the breast anteriorly. Its shape and projection varies from cylindrical to round at the top, to hemispherical, to flattened, depending on nervous, hormonal, developmental and other factors. The level of the nipple varies widely from person to person. In females, its site is dependent on the size and shape of the breasts, but it overlies the fourth intercostal space in most young women. In the male, the nipple is usually sited in the fourth intercostal space in the midclavicular line. In the young adult of the either sex, the nipples are usually positioned 20–23 cm from the suprasternal notch in the midclavicular line and 20–23 cm apart in the horizontal plane. With increasing age and parity, female breasts adopt a more ptotic shape and the nipple position drops either to the level of the inframammary crease or it lies below this surface landmark. In the nulliparous, it is pink, light brown or darker, depending on the general melanisation of the body. Occasionally, the nipple may not evert during

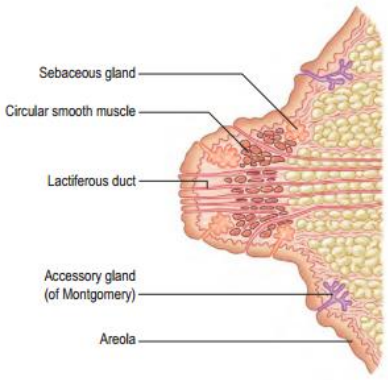
prenatal development, in which case it remains permanently retracted and so it causes difficulty in suckling.



NIPPLE AND AREOLA

The skin that covers the nipple and the surrounding areola (the disc of skin that circles the base of the nipple) has a convoluted surface. It contains numerous sweat and sebaceous glands which open directly onto the skin surface. The oily secretion from these specialized sebaceous glands acts as a protective lubricant and facilitates latching of the neonate during lactation: these glands are often visible in parous women, arranged circumferentially as small

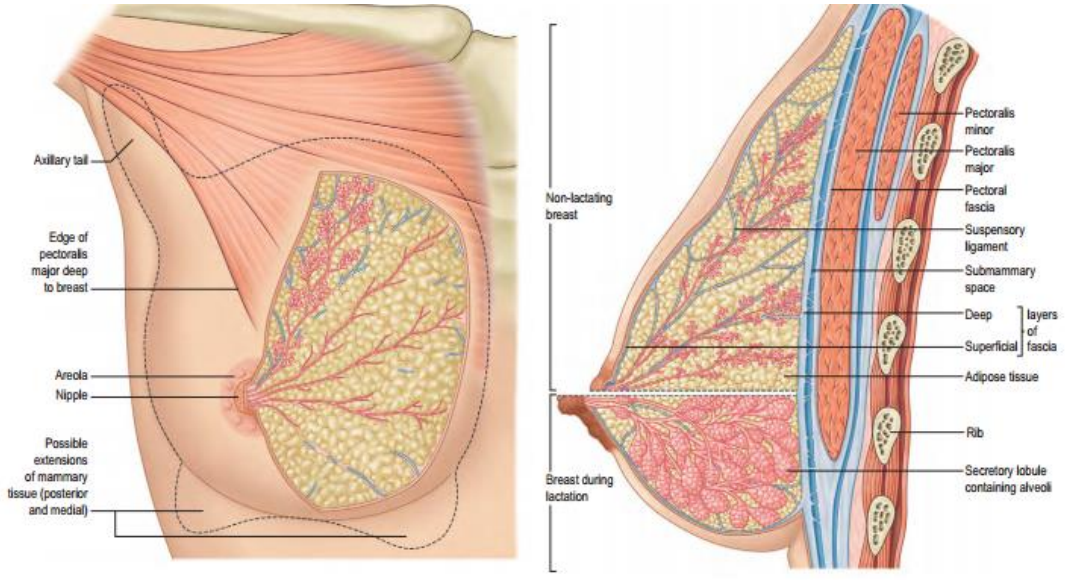
elevations, Montgomery's tubercles, around the areola close to the margin. Other areolar glands, which are intermediate in structure between mammary and sweat glands, become enlarged in pregnancy and lactation as subcutaneous tubercles. The sebaceous glands of the areola usually lack hair follicles. The skin of the nipple and areola is rich in melanocytes and is therefore typically darker than the skin covering the remainder of the breast: further darkening occurs during the second month of pregnancy, which subsequently persists to a variable degree.



SOFT TISSUE

The breast is composed of lobes which contain a network of glandular tissue consisting of branching ducts and terminal secretory lobules in a connective tissue stroma. The terminal duct lobular unit is the functional unit which is the milk secretory component of the breast and pathologically gives rise to primary malignant lesions within the breast. Although the lobes are usually described as discrete territories, they intertwine in three dimensions and

merge at their edges, which cannot be distinguished during surgery. The connective tissue stroma that surrounds the lobules is dense and fibrocollagenous, whereas intralobular connective tissue has a loose texture that allows rapid expansion of secretory tissue during pregnancy. Fibrous strands or the sheets consisting of condensations of connective tissue extend between the layer of deep fascia that covers the muscles of the anterior chest wall and the dermis. These suspensory ligaments (of Astley Cooper) are often well developed in the upper part of the breast that supports the breast tissue and helps to maintain its non-ptotic form. Elsewhere in the normal breast, fibrous tissue surrounds the glandular components and extends to the skin and nipple which assists the mechanical coherence of the gland. The interlobar stroma contains variable amounts of adipose tissue that is responsible for much of the increase in breast size at puberty



VASCULAR SUPPLY

Arteries

The breasts are supplied by branches of the axillary artery, the internal thoracic artery, and some intercostal arteries. The axillary artery supplies blood through the superior thoracic artery, the pectoral branches of the thoracoacromial artery, the lateral thoracic artery (through the branches which curve around the lateral border of pectoralis major that supplies the lateral aspect of the breast) and the subscapular artery. The internal thoracic artery supplies perforating branches to anteromedial part of the breast. The second to fourth anterior intercostal arteries supply perforating branches more laterally in anterior thorax of which the second perforating artery is usually the largest, and supplies the upper region of the breast, and the nipple, areola and adjacent breast tissue.

Veins

Blood drains from the circular venous plexus around the areola and from the glandular tissue of the breast into the axillary, internal thoracic and intercostal veins via veins that accompany the corresponding arteries. Individual variation is common in venous drainage.

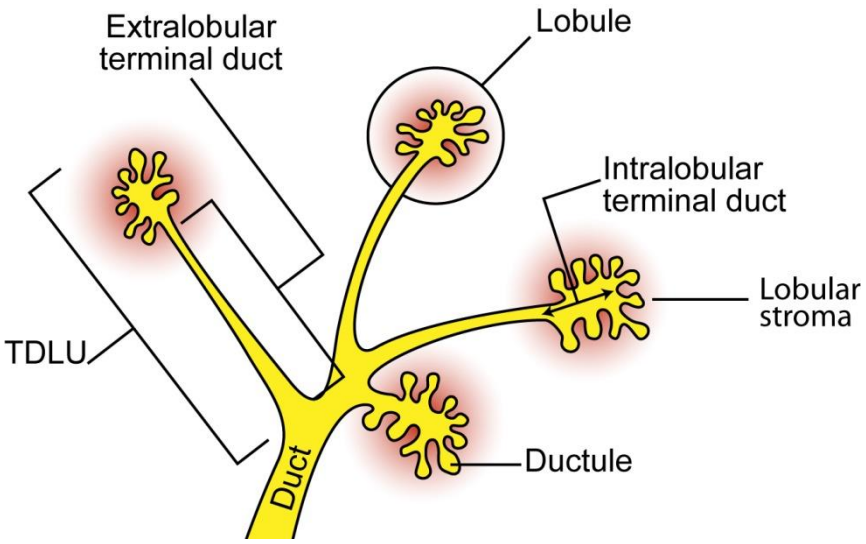
Innervation

The breast is innervated by anterior and lateral branches of fourth to sixth intercostal nerves, which carry sensory and sympathetic efferent fibres. The nipple is supplied from the anterior branch of lateral cutaneous branch of T4 which forms an extensive plexus in the nipple; its sensory fibres terminate close to the epithelium as free endings, Meissner corpuscles and Merkel disc endings. These are essential in signalling pathway during suckling to the central nervous system. Secretory activities of the gland are largely controlled by ovarian and the hypophysial hormones rather than by the efferent motor fibres. The areola has fewer sensory endings.

TERMINAL DUCT LOBULAR COMPLEX

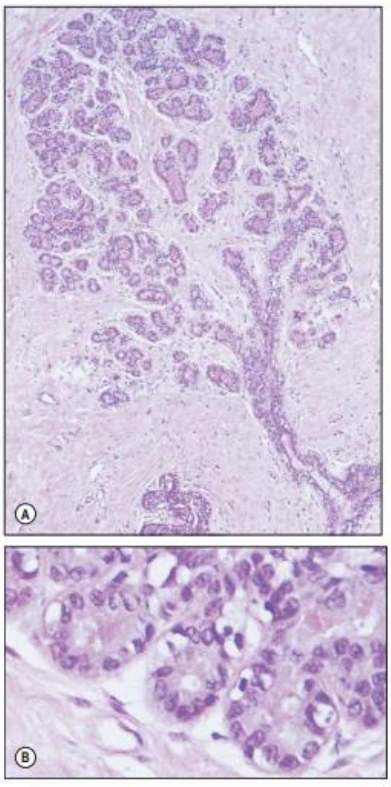
Each breast, contains 15-20 lobes and each lobe is comprised of 20-40 terminal ductal lobular units (TDLU). The TDLU is the functional unit of the breast. TDLUs consists of: Extralobar terminal duct (ETD) which attaches the lobule to the ductal system, Intralobar terminal duct (ITD) that continues the duct system into the lobule clusters of 10-100 sac-like acini that open into the ITD, and the Acini which are the source of milk production. "The epithelium throughout the ductal-lobular system is bilayered, consisting of an inner (luminal) epithelial cell layer and an outer (basal) myoepithelial cell layer" as described above.

Visual, auditory and areola stimulation trigger a neuroendocrine reflex which releases oxytocin from the posterior pituitary. Oxytocin travels in the blood to the mammary gland where it stimulates specific receptors on myoepithelial cells, causing them to contract and expel milk into the ducts and on toward the nipple. Each lobe empties into a lactiferous duct. Lactiferous ducts merge into 5-10 main lactiferous ducts that open at the nipple. The majority of pathologic changes in the breast, including DCIS and invasive carcinomas, are believed to arise from the TDLU.



MICROSTRUCTURE

The microstructure of breast tissue varies with the age, time in the menstrual cycle, pregnancy and lactation. The following description relates to mature, resting breast. For most of their lengths, the ducts are usually lined by columnar epithelium. In case of larger ducts, this is two cells thick, but, in the smaller ones, it is only a single layer of columnar or cuboidal cells. The bases of these cells are in close contact with numerous myoepithelial cells which are ectodermal in origin, similar to those of certain other glandular epithelia. Myoepithelial cells are so numerous that they form a distinct layer around the ducts and the presumptive alveoli and give the epithelium a bilayered appearance.

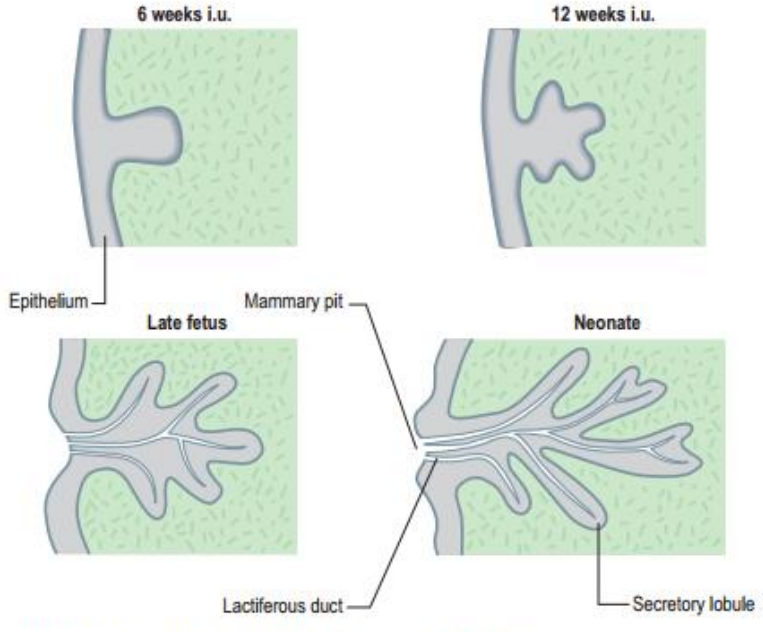


A. A glandular lobule surrounded by collagenous interlobular connective tissue in the mature resting breast. A terminal duct (bottom right) branches extensively to terminate in rudimentary acini, which are shown at higher magnification in the lower panel (**B**). (By permission from Young B, Heath JW 2000 Wheater's Functional Histology. Edinburgh: Churchill Livingstone.)

DEVELOPMENT

The epithelial/mesenchymal interactions gives rise to the glandular tissue of the breast, in both sexes, which can first be seen at about the fifth or sixth week, when two ventral bands of thickened ectoderm, the mammary ridges or milk lines, extend from the axilla to inguinal region. Usually, invagination of the thoracic mammary bud occurs by day 49, and the remaining mammary line involutes. The thoracic ectodermal ingrowths branch into 15–20 solid buds of ectoderm that will become the lactiferous ducts and their associated lobes of alveoli in the fully formed gland. They are surrounded by somatopleuric mesenchyme that forms the connective tissue, fat and vasculature which is invaded by the mammary nerves. Continued cell proliferation, elongation and further branching produce the alveoli and define the duct system. Nipple formation begins at day 56, primitive ducts (mammary sprouts) develop at 84 days and canalization occurs at about the 150th day. During the last 2 months of gestation the ducts become canalized; the epidermis at the point of original development of the gland forms a small mammary pit, into which the lactiferous tubules open. Perinatally the nipple is formed by mesenchymal proliferation. Should this process fail, the ducts open into shallow pits. Rarely, the nipple may not develop (athelia), a phenomenon that occurs more commonly in accessory breast tissue.[22]

At birth the breasts have reached a similar developmental stage in both sexes: the combination of fetal prolactin and the maternal oestrogen which may give rise to transient hyperplasia and secretion of ‘witch’s milk’. In males, the breasts normally remain undeveloped, whereas in females at puberty, in late pregnancy and during the period of lactation, they undergo further, hormone-dependent, developmental changes. The female breast is a unique organ and it remains in a rudimentary (i.e. fetal) form until puberty, at which time its development continues under the influence of sex hormones. The adult form is reached in late adolescence, i.e. the breast is then able to function as a milk-producing organ. At the time of menopause, the breast involutes into a predominantly fatty organ with minimal glandular parenchyma.



Early development of breast epithelium.

CONTROVERSIES IN LITERATURE REGARDING LYMPHATICS

On looking back into the literatures, the standard texts sometimes fail to define the levels of axillary nodes. The levels have been designated mainly based on the fact that the lymph flow from breast form a chain of contiguous spread and so it may be used to prognosticate the disease morbidity if correctly analysed. Let us see some of the discrepancies in the description of anatomy

Gray's anatomy – the anatomical basis of clinical practice 40th edition states that, “The breast lymphatics branch extensively and do not contain valves: lymphatic blockage through tumour occlusion may therefore result in reverse blood flow through the lymphatic channels. The direction of lymphatic flow within the breast parallels major venous tributaries and enters the regional lymph nodes through the extensive periductal and perilobular network of lymphatic channels. Most of these lymphatics drain into axillary group of regional lymph nodes either directly or through the retroareolar lymphatic plexus. Dermal lymphatics also penetrate pectoralis major to join these channels that drain the deeper parenchymal tissues, and follow the vascular channels to terminate in the subclavicular lymph nodes.

Lymphatics from the left breast ultimately terminate in the thoracic duct and subsequently the left subclavian vein. On the right, the lymphatics ultimately drain into the right subclavian vein near its junction with the internal jugular vein. Part of medial side of the right breast drains towards the internal thoracic group of lymph nodes. The internal thoracic chain may drain inferiorly

via the superior and inferior epigastric lymphatic routes to the groin. Connecting lymphatics across the midline may provide access of lymphatic flow to the opposite axilla. Axillary nodes receive more than 75% of the lymph from the breast. There are 20–40 nodes, grouped artificially as pectoral (anterior), subscapular (posterior), central and apical. Surgically, these nodes are described in relation to pectoralis minor[23].

Those lying below pectoralis minor are the low nodes (level 1), those behind the muscle are the middle group (level 2), while the nodes between the upper border of pectoralis minor and the lower border of the clavicle are the upper or apical nodes (level 3). There may be one or two other nodes between pectoralis minor and major; this interpectoral group of nodes are also known as Rotter's nodes[25].

Efferent vessels directly from the breast pass round the anterior axillary border through the axillary fascia to the pectoral lymph nodes; some may pass directly to the subscapular nodes. A few vessels pass from the superior part of the breast to the apical axillary nodes, sometimes interrupted by the infraclavicular nodes or by small, inconstant, interpectoral nodes. Most of the remainder drains to parasternal nodes from the medial and lateral parts of the breast; they accompany perforating branches of the internal thoracic artery. Lymphatic vessels occasionally follow lateral cutaneous branches of the posterior intercostal arteries to the intercostal nodes."

However MOORE - CLINICALLY ORIENTED ANATOMY 7TH ED does not include interpectoral nodes in axillary group as it says “The lymphatic drainage of the breast is important because of its role in the metastasis of cancer cells. Lymph passes from the nipple, areola, and lobules of the gland to the subareolar lymphatic plexus. From this plexus: Most lymph (>75%), especially from the lateral breast quadrants, drains to the axillary lymph nodes, initially to the anterior or pectoral nodes for the most part. However, some lymph may drain directly to other axillary nodes or even to interpectoral, deltopectoral, supraclavicular, or inferior deep cervical nodes.”

While LAST’S ANATOMY 12th EDITION says “some lymph from the breast may drain into one or two infraclavicular nodes in the deltopectoral groove or into small inconstant interpectoral nodes between pectoralis major and minor.

Schwartzs - principles of surgery, 10th edition describes, “The boundaries for lymph drainage of the axilla are not well demarcated. The six axillary lymph node groups recognized by surgeons are:

(a) The axillary vein group (lateral), which consists of four to six lymph nodes that lie medial or posterior to the vein and receive most of the lymph drainage from the upper extremity;

(b) the external mammary group (anterior or pectoral group), which consists of five to six lymph nodes that lie along the lower border of the pectoralis minor muscle contiguous with the lateral thoracic vessels and receive most of the lymph drainage from the lateral aspect of the breast;

(c) the scapular group (posterior or subscapular), which consists of five to seven lymph nodes that lie along the posterior wall of the axilla at the lateral border of the scapula contiguous with the subscapular vessels and receive lymph drainage principally from the lower posterior neck, the posterior trunk, and the posterior shoulder;

(d) the central group, which consists of three or four sets of lymph nodes that are embedded in the fat of the axilla lying immediately posterior to the pectoralis minor muscle and receive lymph drainage both from the axillary vein, external mammary, and scapular groups of lymph nodes, and directly from the breast;

(e) the subclavicular group (apical), which consists of six to twelve sets of lymph nodes that lie posterior and superior to the upper border of the pectoralis minor muscle and receive lymph drainage from all of the other groups of axillary lymph nodes; and

(f) the interpectoral group (Rotter's lymph nodes), which consists of one to four lymph nodes that are interposed between the pectoralis major and pectoralis minor muscles and receive lymph drainage directly from the breast. The lymph

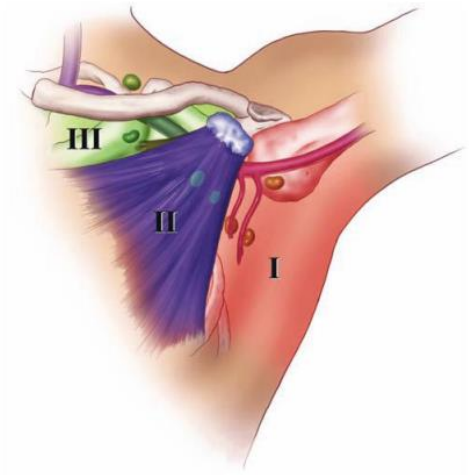
fluid that passes through the interpectoral group of lymph nodes passes directly into the central and subclavicular groups.

The lymph node groups are assigned levels according to their anatomic relationship to the pectoralis minor muscle.

- Lymph nodes located lateral to or below the lower border of the pectoralis minor muscle are referred to as level I lymph nodes, which include the axillary vein, external mammary, and scapular groups.
- Lymph nodes located superficial or deep to the pectoralis minor muscle are referred to as level II lymph nodes, which include the central and interpectoral groups.
- Lymph nodes located medial to or above the upper border of the pectoralis minor muscle are referred to as level III lymph nodes, which consist of the subclavicular group.

The plexus of lymph vessels in the breast arises in the interlobular connective tissue and in the walls of the lactiferous ducts and communicates with the subareolar plexus of lymph vessels. Efferent lymph vessels from the breast pass around the lateral edge of the pectoralis major muscle and pierce the clavipectoral fascia, ending in the external mammary (anterior, pectoral) group of lymph nodes. Some lymph vessels may travel directly to the subscapular (posterior, scapular) group of lymph nodes. From the upper part of the breast, a few lymph vessels pass directly to the subclavicular (apical) group of lymph nodes.

The axillary lymph nodes usually receive >75% of the lymph drainage from the breast. The rest is derived primarily from the medial aspect of the breast, flows through the lymph vessels that accompany the perforating branches of the internal mammary artery, and enters the parasternal (internal mammary) group of lymph nodes."

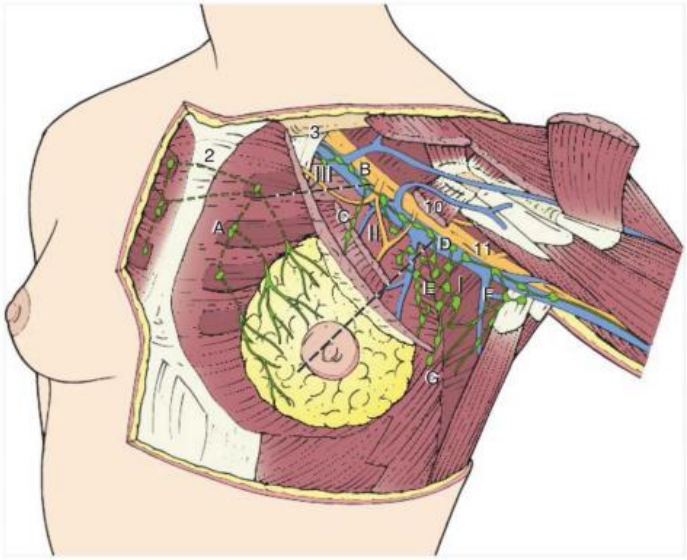


Axillary lymph node groups. Level I includes lymph nodes located lateral to the pectoralis minor muscle; level II includes lymph nodes located deep to the pectoralis minor; and level III includes lymph nodes located medial to the pectoralis minor. The axillary vein with its major tributaries and the supraclavicular lymph node group are also illustrated. (Visual Art: © 2012.The University of Texas MD Anderson Cancer Center.)

Sabiston textbook of surgery - the biological basis of modern surgical practice, 20e says "Level I nodes are located lateral to the lateral border of the pectoralis minor muscle. Level II nodes are located posterior to the pectoralis minor muscle. Level III nodes are located medial to the pectoralis minor muscle and include the subclavicular nodes. Level III nodes are easier to visualize and remove when the pectoralis minor muscle is divided. The apex of the axilla is defied by the costoclavicular ligament (Halsted's ligament), at which point the axillary vein passes into the thorax and becomes the subclavian vein. Lymph

nodes in the space between the pectoralis major and minor muscles are termed the interpectoral group or Rotter's nodes, as described by Grossman and Rotter. Unless these nodes are specifically exposed, they are not encompassed in surgical procedures that preserve the pectoral muscles." Here the author does not include the rotters node in any level of axillary nodes.

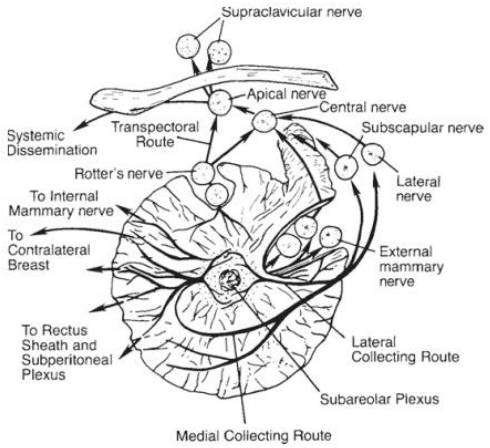
DEVITA, HELLMAN & ROSENBERG'S CANCER - PRINCIPLES AND PRACTICE OF ONCOLOGY 9TH ED



Lymphatic drainage of the breast showing lymph node groups and levels. 1, Internal mammary artery and vein; 2, substernal cross-drainage to contralateral internal mammary lymphatic chain; 3, subclavius muscle and Halsted ligament; 4, lateral pectoral nerve (from the lateral cord); 5, pectoral branch from thoracoacromial vein; 6, pectoralis minor muscle; 7, pectoralis major muscle; 8, lateral thoracic vein; 9, medial pectoral nerve (from the medial cord); 10, pectoralis minor muscle; 11, median nerve; 12, subscapular vein; 13, thoracodorsal vein. Internal mammary lymph nodes (**A**); apical lymph nodes (**B**); interpectoral (Rotter) lymph nodes (**C**); axillary vein lymph nodes (**D**); central lymph nodes (**E**); scapular lymph nodes (**F**); external mammary lymph nodes (**G**). Level I lymph nodes: lateral to lateral border of pectoralis minor muscle; level II lymph nodes: behind pectoralis minor muscle; level III lymph nodes: medial to medial border of pectoralis minor muscle.

FISCHER'S MASTERY OF SURGERY 6E says “Axillary lymphatics are also divided according to their lateral and medial (surgical) anatomic relationships with the pectoralis minor muscle into three distinct levels and are identified as levels I through III.

- Level I nodes are located lateral to or below the inferior border of the pectoralis minor; this level includes the extremal mammary, the lateral axillary vein and the scapular lymph node groups.
- Level II nodes are located deep in or behind the pectoralis minor and include the central lymph node group and possibly some of the subclavicular lymph node group.
- Level III nodes are located superomedial to the upper margin of the pectoralis minor and include the subclavicular (apical) lymph node group.



Schematic drawing of the breast identifying the position of lymph nodes relative to the breast and illustrating routes of lymphatic drainage. The clavicle is indicated as a reference point. See the text and Figure 8 to identify the group or level to which the lymph nodes belong. Level I lymph nodes include the external mammary (or anterior), axillary vein (or lateral), and scapular (or posterior) groups; level II, the central group; and level III, the subclavicular (or apical). The arrows indicate the routes of lymphatic drainage (see text). (From Romrell LJ, Bland KI. Anatomy of the breast, axilla, chest wall, and related metastatic sites. In: Bland KI, Copeland EM III, eds. *The breast: comprehensive management of benign and malignant diseases*, 4th ed. Philadelphia, PA: Saunders Elsevier, 2009:21–38.)

WASHINGTON MANUAL OF SURGERY - 6E describes as “The borders of the axilla are defined as the axillary vein superiorly, latissimus dorsi laterally, and the serratus anterior muscle medially.

A. Axillary lymph nodes are classified according to their anatomic location relative to the pectoralis minor muscle.

1. Level I nodes. Lateral to the pectoralis minor muscle.

2. Level II nodes. Posterior to the pectoralis minor muscle.

3. Level III nodes. Medial to the pectoralis minor muscle and most accessible with division of the muscle.

4. Rotter’s nodes. Between the pectoralis major and the minor muscles.”

Thus there are various controversies in assigning the level of lymph node groups by various authors which elicits the need of interpectoral node dissection in proposed surgery.

AIMS AND OBJECTIVE

1. To determine, if differences in the extent of axillary node dissection would alter the number of reported positive nodes.
2. To examine the pattern of lymph node metastases in the axilla, and evaluate the merits of a level III axillary dissection.
3. To emphasize the presence and importance of dissecting the interpectoral node (Rotter's Node) in Modified Radical Mastectomy.

MATERIALS AND METHODS

SOURCE OF DATA:

- This study is conducted in the Department of General Surgery, Government Stanley Medical College, Chennai.

PERIOD OF STUDY:

- March 2016 to Aug 2017 (18 months)

INCLUSION CRITERIA:

- Patients with primary breast cancer whose clinical stage of Stage I, II A, II B and IIIA (staged as per NCCN guidelines) were included.

EXCLUSION CRITERIA

- Patients undergoing Breast conservation surgery
- Patients who received Neoadjuvant chemotherapy for Stage III A
- Stage III B and IV
- Metastatic Carcinoma breast.
- Recurrent Carcinoma Breast

METHODOLOGY

- Patients were evaluated according to NCCN guidelines and were subjected to Modified Radical Mastectomy for whomsoever it was needed.
- 32 cases underwent Modified Radical Mastectomy with complete axillary dissection (level I/II/III and interpectoral node) according to identical procedure. The dissection was carried out in all patients, irrespective of whether they had palpable nodes or not clinically.
- Level I/II, Level III and interpectoral lymph nodes were sent separately for routine pathological examination.
- Observations were tabulated according to the pre-designed proforma.
- The results are analyzed using Microsoft Excel for tabular transformation and graphical representation.

INVASIVE BREAST CARCINOMA

Invasive breast cancers have been described as lobular or ductal in origin. Early classifications used the term lobular to describe invasive cancers that were associated with LCIS, whereas all other invasive cancers were referred to as ductal[28-31]. Current histologic classifications recognize special types of breast cancers (10% of total cases), which are defined by specific histologic features.[23] To qualify as a special-type cancer, at least 90% of the cancer must contain the defining histologic features. About 80% of invasive breast cancers are described as invasive ductal carcinoma of no special type (NST). These cancers generally have a worse prognosis than special-type cancers. Foote and Stewart originally proposed the following classification for invasive breast cancer[32]:

1. Paget's disease of the nipple
2. Invasive ductal carcinoma—Adenocarcinoma with productive fibrosis (scirrhous, simplex, NST), 80%
3. Medullary carcinoma, 4%
4. Mucinous (colloid) carcinoma, 2%
5. Papillary carcinoma, 2%
6. Tubular carcinoma, 2%
7. Invasive lobular carcinoma, 10%
8. Rare cancers (adenoid cystic, squamous cell, apocrine)

Paget's disease of the nipple was described in 1874. It frequently presents as a chronic, eczematous eruption of the nipple, which may be subtle but may progress to an ulcerated, weeping lesion. Paget's disease usually is associated with extensive DCIS and may be associated with an invasive cancer. A palpable mass may or may not be present. A nipple biopsy specimen will show a population of cells that are identical to the underlying DCIS cells (pagetoid features or pagetoid change). Pathognomonic of this cancer is the presence of large, pale, vacuolated cells (Paget cells) in the rete pegs of the epithelium. Paget's disease may be confused with superficial spreading melanoma. Differentiation from pagetoid intraepithelial melanoma is based on the presence of S-100 antigen immunostaining in melanoma and carcinoembryonic antigen immunostaining in Paget's disease. Surgical therapy for Paget's disease may involve lumpectomy or mastectomy, depending on the extent of involvement of the nipple-areolar complex and the presence of DCIS or invasive cancer in the underlying breast parenchyma.

Invasive ductal carcinoma of the breast with productive fibrosis (scirrhous, simplex, NST) accounts for 80% of breast cancers and presents with macroscopic or microscopic axillary lymph node metastases in up to 25% of screen-detected cases and up to 60% of symptomatic cases. This cancer occurs most frequently in perimenopausal or postmenopausal women in the fifth to sixth decades of life as a solitary, firm mass. It has poorly defined margins and its cut surfaces show a central stellate configuration with chalky white or yellow

streaks extending into surrounding breast tissues. The cancer cells often are arranged in small clusters, and there is a broad spectrum of histologic types with variable cellular and nuclear grades. In a large patient series from the SEER database, 75% of ductal cancers showed estrogen receptor expression[33].

Medullary carcinoma is a special-type breast cancer; it accounts for 4% of all invasive breast cancers and is a frequent phenotype of BRCA1 hereditary breast cancer. Grossly, the cancer is soft and hemorrhagic. A rapid increase in size may occur secondary to necrosis and hemorrhage. On physical examination, it is bulky and often positioned deep within the breast. Bilaterality is reported in 20% of cases.

Medullary carcinoma is characterized microscopically by:

(a) a dense lympho reticular infiltrate composed predominantly of lymphocytes and plasma cells;

(b) large pleomorphic nuclei that are poorly differentiated and show active mitosis;

(c) a sheet-like growth pattern with minimal or absent ductal or alveolar differentiation.

Approximately 50% of these cancers are associated with DCIS, which characteristically is present at the periphery of the cancer, and <10% demonstrate hormone receptors. In rare circumstances, mesenchymal metaplasia or anaplasia is noted. Because of the intense lymphocyte response associated

with the cancer, benign or hyperplastic enlargement of the lymph nodes of the axilla may contribute to erroneous clinical staging.

Women with this cancer have a better 5-year survival rate than those with NST or invasive lobular carcinoma. Mucinous carcinoma (colloid carcinoma), another special type breast cancer, accounts for 2% of all invasive breast cancers and typically presents in the elderly population as a bulky tumor. This cancer is defined by extracellular pools of mucin, which surround aggregates of low-grade cancer cells. The cut surface of this cancer is glistening and gelatinous in quality. Fibrosis is variable, and when abundant it imparts a firm consistency to the cancer. Over 90% of mucinous carcinomas display hormone receptors. Lymph node metastases occur in 33% of cases, and 5- and 10-year survival rates are 73% and 59%, respectively. Because of the mucinous component, cancer cells may not be evident in all microscopic sections, and analysis of multiple sections is essential to confirm the diagnosis of a mucinous carcinoma.

Papillary carcinoma is a special-type cancer of the breast that accounts for 2% of all invasive breast cancers. It generally presents in the seventh decade of life and occurs in a disproportionate number of non white women. Typically, papillary carcinomas are small and rarely attain a size of 3 cm in diameter. These cancers are defined by papillae with fibrovascular stalks and multilayered epithelium. In a large series from the SEER database 87% of papillary cancers have been reported to express estrogen receptor. McDivitt and colleagues noted

that these tumors showed a low frequency of axillary lymph node metastases and had 5- and 10-year survival rates similar to those for mucinous and tubular carcinoma[34].

Tubular carcinoma is another special-type breast cancer and accounts for 2% of all invasive breast cancers. It is reported in as many as 20% of women whose cancers are diagnosed by mammographic screening and usually is diagnosed in the perimenopausal or early menopausal periods. Under low-power magnification, a haphazard array of small, randomly arranged tubular elements is seen. In a large SEER database 94% of tubular cancers were reported to express estrogen receptor. Approximately 10% of women with tubular carcinoma or with invasive cribriform carcinoma, a special-type cancer closely related to tubular carcinoma, will develop axillary lymph node metastases. However, the presence of metastatic disease in one or two axillary lymph nodes does not adversely affect survival. Distant metastases are rare in tubular carcinoma and invasive cribriform carcinoma[35]. Long-term survival approaches 100%. Invasive lobular carcinoma accounts for 10% of breast cancers. The histopathologic features of this cancer include small cells with rounded nuclei, inconspicuous nucleoli, and scant cytoplasm. Special stains may confirm the presence of intracytoplasmic mucin, which may displace the nucleus (signet-ring cell carcinoma). At presentation, invasive lobular carcinoma varies from clinically inapparent carcinomas to those that replace the entire breast with a poorly defined mass. It is frequently multifocal,

multicentric, and bilateral. Because of its insidious growth pattern and subtle mammographic features, invasive lobular carcinoma may be difficult to detect. Over 90% of lobular cancers express estrogen receptor.

Axillary Lymph Node Metastases.

As the size of the primary breast cancer increases, some cancer cells are shed into cellular spaces and transported via the lymphatic network of the breast to the regional lymph nodes, especially the axillary lymph nodes. Lymph nodes that contain metastatic cancer are at first ill-defined and soft but become firm or hard with continued growth of the metastatic cancer. Eventually the lymph nodes adhere to each other and form a conglomerate mass. Cancer cells may grow through the lymph node capsule and fix to contiguous structures in the axilla, including the chest wall.[37] Typically, axillary lymph nodes are involved sequentially from the low (level I) to the central (level II) to the apical (level III) lymph node groups.

Approximately 95% of the women who die of breast cancer have distant metastases, and traditionally the most important prognostic correlate of disease-free and overall survival was axillary lymph node status. Women with node-negative disease had less than a 30% risk of recurrence, compared with as much as a 75% risk for women with node-positive disease.

Distant Metastases.

At approximately the twentieth cell doubling, breast cancers acquire their own blood supply (neovascularization). Thereafter, cancer cells may be shed directly into the systemic venous blood to seed the pulmonary circulation via the axillary and intercostal veins or the vertebral column via Batson's plexus of veins, which courses the length of the vertebral column. These cells are scavenged by natural killer lymphocytes and macrophages. Successful implantation of metastatic foci from breast cancer predictably occurs after the primary cancer exceeds 0.5 cm in diameter, which corresponds to the twenty-seventh cell doubling. For 10 years after initial treatment, distant metastases are the most common cause of death in breast cancer patients. For this reason, conclusive results cannot be derived from breast cancer trials until at least 5 to 10 years have elapsed. Although 60% of the women who develop distant metastases will do so within 60 months of treatment, metastases may become evident as late as 20 to 30 years after treatment of the primary cancer.118 Patients with estrogen receptor negative breast cancers are proportionately more likely to develop immunohistochemical score (IHC4) and two gene expression profile tests (Recurrence Score and PAM50).120 Common sites of involvement, in order of frequency, are bone, lung, pleura, soft tissues, and liver. Brain metastases are less frequent overall although with the advent of adjuvant systemic therapies it has been reported that CNS disease may be seen earlier. There are also reports of factors which are associated with the risk of

developing brain metastases. For example, they are more likely to be seen in patients with triple receptor negative breast cancer (ER-negative, PR-negative and HER2-negative) or patients with HER2-positive breast cancer who have received chemotherapy and HER2-directed therapies.[39-41]

WORK UP

For INVASIVE BREAST CANCER of stage I, II a, II b, or III a (T3, N1, M0) The recommended workup includes: history and physical exam; bilateral diagnostic mammography; breast ultrasonography, if necessary; determination of tumor hormone receptor status(ER and PR determinations); determination of HER-2 receptor status; and pathology review. Complete blood count (CBC) and liver function tests (LFTs) have no added benefit in the detection of underlying metastatic disease in asymptomatic early-stage breast cancer patients. In addition, monitoring of disease relapse with any tumor markers is not recommended.

Use of MRI is optional and is not universally recommended by experts in the field. Breast MRI advocates note its high sensitivity for evaluation of extent of disease, particularly for invasive cancer and in dense breasts where mammographically occult disease is more likely to elude preoperative detection. MRI detractors note that MRI has a high percentage of false-positive findings resulting in further diagnostic workup in many circumstances including MRI-

guided biopsy. MRI findings tend to overestimate extent of disease resulting in increase in frequency of mastectomies.

MRI findings alone are insufficient to determine whether breast conservation therapy is optimal as additional tissue sampling is needed to verify true malignant disease warranting excision. MRI use may increase mastectomy rates by identifying mammographically occult disease satellites that would have been adequately treated with post-lumpectomy radiation had the disease remained undiscovered without MRI.[52]

Two prospective randomized studies have examined the utility of preoperative MRI in determining disease extent, and neither demonstrated improvement in rates of post-lumpectomy re-excision. Retrospective review of utility MRI showed conflicting outcome results, one with benefit and another without. One systematic review documented that breast MRI staging altered surgical treatment in 7.8% to 33.3% of women, however no differences in local recurrence or survival have yet been demonstrated. In addition, there is no evidence that use of breast MRI increases rates of margin-negative resection.

If breast MRI imaging is performed, a dedicated breast coil, an imaging team experienced with breast MRI guided biopsy, and multidisciplinary treatment team are the standard of care. Clinically positive axillary nodes and occult primary breast cancer or paget's disease of the nipple with breast primary not identified on mammography, ultrasound, or physical examination are specific indications for breast MRI imaging. MRI may also be useful for the evaluation

of breast cancer response to preoperative systemic therapy and to assess the potential for breast-conserving therapy.[42]

PATHOLOGY ASSESSMENT

Full knowledge of extent of disease and biologic features is central to the treatment of breast cancer. Several factors contribute to the determination of the disease staging, recurrence risk assessment, and predictive response (ie,ER,PR,HER2).the excised tissue detailing the written pathology report details these key factors. The accuracy of pathology reporting requires communication between the clinician and the pathologist relating pertinent patient history, prior breast biopsies, prior chest irradiation, pregnancy status, biopsy characteristics (i.e., palpable, mammographically detected microcalcifications), clinical state of lymph nodes, presence of inflammatory change or other skin abnormality, and prior treatment administered (i.e., chemotherapy, radiation therapy).

The specimens should be oriented for the pathologist, and specific requests for determination of biomarkers should be stated (e.g., ER, PR, and HER2 status). Data from both national and local surveys show that as many as 50% of pathology reports for breast cancer are missing some elements critical to patient management. Significant omissions include failure to orient and report surgical margins and failure to report tumor grade consistently. CAP has developed pathology reporting protocols to promote complete and standardized reporting of malignant specimens. The NCCN breast cancer panel endorses the

use of the CAP protocols for reporting the pathologic analysis of all breast cancer specimens.

Genetic counselling:

For patients considered to be at high risk for hereditary breast cancer as defined by the NCCN Guidelines for Genetic/Familial High Risk Assessment Breast and ovarian, genetic counselling is recommended

Distress assessment:

Levels of distress may vary in patients and should be addressed individually. Psychological distress can be impacted by body image and other factors. Younger women have higher rates of psychological distress than women diagnosed at older ages. The NCCN Breast cancer panel recommends accessing for distress in patients newly diagnosed with breast cancer.

Fertility counselling:

Numerous epidemiologic studies have demonstrated that child-bearing after treatment for invasive breast cancer does not increase rates of recurrence or death from breast cancer. The offspring of pregnancies after treatment for breast cancer do not have an increased rate of birth defects or other serious childhood illness. However, treatment of breast cancer, especially with cytotoxic agents, may impair fertility.

Many women, especially those younger than age 35, regain menstrual function within two years of completing chemotherapy. Resumption of menses does not necessarily correlate with fertility, and fertility may be preserved

without menses. All premenopausal patients should be informed about the potential impact of chemotherapy on fertility and asked about their desire for potential future pregnancies

A decision for fertility preservation should include multiple factors such as patient preference, tumor stage and biology, age of the patient, risk of premature ovarian failure based on anticipated type and duration of chemotherapy and/or endocrine therapy, as well as the timing and duration allowed for fertility preservation.

Several studies report lower rates of fertility discussion among female patients with cancer despite the updated ASCO guidelines stating that patients should not be excluded from consideration for discussion of fertility preservation for any reason, including parity, prognosis, age, and socioeconomic status. The NCCN panel recommends that all women of childbearing potential should have a discussion with their treating physicians. Patient who desire to bear children after systemic therapy should be referred to a fertility specialist prior to initiating systemic (chemotherapy and endocrine) therapy.

Randomized trials have demonstrated that GnRH agonists (such as goserelin) administered prior to initiating chemotherapy and then administered concurrently with adjuvant chemotherapy protect against ovarian failure and reduce the risk of early menopause. In one trial goserelin improved the probability of pregnancy from 11% to 21% in patients with hormone receptor-

negative early-stage breast cancer. Smaller historical experiences in patients with hormone receptor-positive disease have conflicting results with respect to the protective effects of GnRH agonists in fertility preservation.

Patients should be informed of all the various modalities available to minimize gonadal damage and preserve ovarian function and future fertility. The fertility specialist should discuss specifics of fertility preservation options inclusive of types of hormonal interventions and risk involved with ovarian stimulation, embryo or oocyte cryopreservation, and other investigational options, as well as the probability of successful gestation and childbirth.

Combining the various modalities for a specific patient may increase the odds of preservation of future fertility.it is important for fetal safety that women actively avoid becoming pregnant during breast cancer treatment.

Additional workup

The panel has re-iterated that routine systemic imaging is not indicated for patients with early breast cancer in the absence of signs/symptoms of metastatic disease. These recommendations are based on studies showing no additional value of these tests in patients with early-stage disease.

For patients presenting with disease confined to the breast (stage I to II) the NCCN panel does not recommend routine systemic imaging in the absence of signs or symptoms suspicious for metastatic disease. According to the panel, additional tests may be considered in patients who present with locally

advanced (T3 N1-3 M0) disease and in those with signs or symptoms suspicious for metastatic disease.

CBCs and LFTs may be considered if the patient is a candidate for preoperative systemic therapy, or if otherwise clinically indicated. Additional tests may be considered only based on the signs and symptoms.

A chest diagnostic CT is indicated only if pulmonary symptoms (i.e., cough or hemoptysis) are present. Likewise, abdominal imaging using diagnostic CT or MRI is indicated if the patient has elevated alkaline phosphatase, abnormal results on LFTs, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis.

A bone scan is indicated in patients presenting with localized bone pain or elevated alkaline phosphatase. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III (T3 N1) breast cancer. The recommendation against the use of PET scanning is supported by the high false-negative rate in the detection of lesions that are small(<1 cm) and/or low grade, the low sensitivity for detection of axillary nodal metastases, the low prior probability of these patients having detectable metastatic disease, and the high rate of false-positive scans.

FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.

STAGING

All patients with breast cancer should be assigned a clinical stage of disease, and, if appropriate evaluation is available, a pathological stage of disease. The routine use of staging allows for efficient identification of local treatment options, assists in identifying systemic treatment options, allows for the comparison of outcome results across institutions and clinical trials, and provides baseline prognostic information. Effective January 2010, the AJCC implemented a revision of 7th edition of the AJCC cancer staging manual containing important changes and additions to TNM staging system for breast cancer. This revision differs from the 2003 edition of AJCC staging manual by providing more direction relating to specific methods of clinical and pathologic tumor measurement; recommending that all invasive cancers should be assigned a combined histologic tumor grade using Elston-Ellis modification of the Scarff-Bloom-Richardson grading system; providing clarification of classification of isolated tumor cells in axillary lymph node staging; subdividing stage I into stage IA and IB based upon the presence or absence of nodal micro metastasis (N0 versus N0mi+); and defining a new category of M0(I+) disease referring to tumor cells microscopically detectable in bone marrow or circulating blood or found incidentally in other tissues not exceeding 0.2 mm in patients who have no signs or symptoms of metastasis. This version of the AJCC staging manual also recommends the collection of biomarkers such as hormone receptor status (estrogen receptor ER and progestron receptor PR)

and human epidermal growth factor receptor 2 HER2 status, although these characteristics do not specifically influence assigned stage of disease.

T STAGING

The T classification of the primary tumor is the same regardless of whether it is based on clinical or pathologic criteria, or both. Size should be measured to the nearest millimeter. If the tumor size is slightly less than or greater than a cut off for a given T classification, it is recommended that the size be rounded to the millimeter reading that is closest to the cutoff. For example, a reported size of 1.1 mm is reported as 1 mm, or a size of 2.01 cm is reported as 2.0 cm. Designation should be made with the subscript “c” or “p” modifier to indicate whether the T classification was determined by clinical (physical examination or radiologic) or pathologic measurements, respectively. In general, pathologic determination should take precedence over clinical determination of T size.

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ

Tis (DCIS) Ductal carcinoma in situ

Tis (LCIS) Lobular carcinoma in situ

Tis (Paget’s) Paget’s disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with

Paget's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted

T1 Tumor ≤20 mm in greatest dimension

T1mi Tumor ≤1 mm in greatest dimension

T1a Tumor >1 mm but ≤5 mm in greatest dimension

T1b Tumor >5 mm but ≤10 mm in greatest dimension

T1c Tumor >10 mm but ≤20 mm in greatest dimension

T2 Tumor >20 mm but ≤5 cm in greatest dimension

T3 Tumor >50 mm in greatest dimension

T4 Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)*

T4a Extension to chest wall, not including only pectoralis muscle adherence/invasion

T4b Ulceration and/or ipsilateral satellite nodules and/or edema (including peaud'orange) of the skin, which do not meet the criteria for inflammatory carcinoma

T4c Both T4a and T4b

T4d Inflammatory carcinoma**

*Note: Invasion of the dermis alone does not qualify as T4

**Note: Inflammatory carcinoma is restricted to cases with typical skin changes involving a third or more of the skin of the breast. While the histologic presence

of invasive carcinoma invading dermal lymphatics is supportive of the diagnosis, it is not required, nor is dermal lymphatic invasion without typical clinical findings sufficient for a diagnosis of inflammatory breast cancer.

Regional lymph nodes — Clinical(N)

NX Regional lymph nodes cannot be assessed (e.g., previously removed)

N0 No regional lymph node metastases

N1 Metastases to movable ipsilateral level I, II axillary lymph node(s)

N2 Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases

N2a Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures

N2b Metastases only in clinically detected* ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases

N3 Metastasis in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

N3a Metastasis in ipsilateral infraclavicular lymph node(s)

N3b Metastasis in ipsilateral internal mammary lymph nodes(s) and axillary lymph node(s)

N3c Metastasis in ipsilateral supraclavicular lymph node(s)

*Notes: “Clinically detected” is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with an (f) suffix, e.g., cN3a(f). Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, e.g., cN1. Information regarding the confirmation of the nodal status will be designated in site-specific factors as clinical, fine needle aspiration, core biopsy, or sentinel lymph node biopsy. Pathologic classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathologic T assignment.

Regional lymph nodes—Pathologic (pN)

pNX Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)

pN0b 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 metastasis 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 metastasis histologically, negative molecular findings [reverse-transcriptase polymerase chain reaction (RT-PCR)]

pN0(mol+) Positive molecular findings (RT-PCR)**, but no regional lymph node metastases detected by histology or IHC

pN1 Micrometastases; or metastases in 1-3 axillary lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected***

pN1mi Micrometastases (greater than 0.2 mm and/or more than 200 cells, but none greater than 2.0 mm)

pN1a Metastases in 1-3 axillary lymph nodes, at least one metastasis greater than 2.0 mm

pN1b Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically

detected***

pN1c Metastases in 1-3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected

pN2 Metastases in 4-9 axillary lymph nodes; or in clinically apparent*** internal mammary lymph nodes in the absence of axillary lymph node metastases

pN2a Metastases in 4-9 axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)

pN2b Metastases in clinically detected*** internal mammary lymph nodes in the absence of axillary lymph node metastases pN3Metastases in 10 or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in clinically detected **** ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected***; or in ipsilateral supraclavicular lymph nodes

pN3a Metastases in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes

pN3b Metastases in clinically detected**** ipsilateral internal mammary

lymph nodes in the presence of one or more positive axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected***

pN3c Metastasis in ipsilateral supraclavicular lymph nodes

* Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for "sentinel node," e.g., pN0(sn).

** RT-PCR: reverse transcriptase/polymerase chain reaction.

*** "Not clinically detected" is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.

**** "Clinically detected" is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination.

Distant metastasis (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 non regional 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

STAGING

• Stage I	T1N0M0
• Stage IIa	T0N1M0
	T1 N1M0
	T2N0M0
IIb	T2N1M0
	T3N0M0
• Stage IIIa	T3N1M0
	T0N2M0
	T1 N2M0
	T2N2M0
	T3N2 M0
IIIb	T4N0M0
	T4N1M0
	T4N2M0
IIIc	anyT, N3M0
• Stage IV	anyT, anyN, M1

GRADING

DESCRIPTION STAGE

Stage 0	In Situ Breast Cancer
Stage I, IIA, IIB	Early Invasive Breast Cancer
Stage IIIA or IIIB	Advanced LocoRegional Breast Cancer
Stage IV	Metastatic Breast Cancer

TREATMENT APPROACH

The treatment of breast cancer includes the treatment of the local disease with surgery, radiation therapy, or both and systemic treatment with chemotherapy, endocrine therapy, biologic therapy, or combination of these. The need for and selection of various local or systemic therapies are based on several prognostic and predictive factors. These factors includes tumor histology, clinical and pathologic characteristics of primary tumor, Axillary lymph node status, tumor hormone receptor (ER/PR), tumor HER2 status, mutli-gene testing, presence or absence of detectable metastatic disease, patients co morbid conditions, patient age, and menopausal status. 1% of breast cancer occurs in men and men with breast cancer should be treated similarly to post menopausal woman except that the use of aromatase inhibitors is ineffective without concomitant suppression of testicular steroidogenesis. Patient preference is a major component of the decision making process, especially in

situations in which survival rates equivalent among the available treatment options.

Surgical options for stage I and II breast cancer:

Mastectomy with or without reconstruction.

Radical mastectomy involves total mastectomy, complete Axillary Lymph Node Dissection (ALND) (levels I, II, and III), removal of the pectoralis major and minor muscles, and removal of all overlying skin. This surgical approach is largely historical and is rarely, if ever, performed in modern practice.

Modified radical mastectomy (MRM) involves total mastectomy and ALND. It is indicated for patients with clinically positive lymph nodes or a positive axillary node based on previous SLNB or FNAB.

Total (simple) mastectomy with SLNB is for patients with a clinically negative axilla. A skin-sparing mastectomy (preserves skin envelope and inframammary ridge) may be performed with immediate reconstruction, resulting in improved cosmesis: the nipplearеolar complex, a rim of periareolar breast skin, and any previous excisional biopsy or partial mastectomy scars are excised.

Immediate reconstruction at the time of mastectomy should be offered to eligible patients. Options include latissimus dorsi myocutaneous flaps, transverse rectus abdominis myocutaneous flaps, and inflatable tissue expanders

followed by exchange for saline or silicone implants. Immediate reconstruction has been shown not to affect patient outcome adversely. The detection of recurrence is not delayed, and the onset of chemotherapy is not changed.

Follow-up after mastectomy: physical examination every 3 to 6 months for 3 years, then every 6 to 12 months for the next 2 years, and then annually (J Clin Oncol. 2006;24:5091). Mammography of the contralateral breast should continue yearly. Regular gynecologic follow-up is recommended for all women (tamoxifen increases risk of endometrial cancer).

Breast conservation therapy (BCT): partial mastectomy and SLNB (or ALND) followed by breast irradiation.

Several trials have demonstrated that BCT with adjuvant radiation therapy has similar survival and recurrence rates to those for MRM (J Clin Oncol. 1992;10:976).

Contraindications for BCT: not every patient is a candidate for BCT. Contraindications include patients who may be unreliable with follow-up or radiation therapy (may involve radiation treatment 5 days a week for 5 to 6 weeks); when the extent of disease prevents adequate negative margins; a high tumor-to-breast size ratio, which prevents adequate resection without major deformity; persistently positive margins on re-excision partial mastectomy; and inability to receive adjuvant radiation (e.g., prior radiation to the chest wall; first- and second-trimester pregnancy in which the delay of radiation to the

postpartum state is inappropriate; collagen vascular diseases such as scleroderma).

For patients with large tumors who desire BCT, neoadjuvant chemotherapy or neoadjuvant hormonal therapy may be offered to attempt to reduce the size of the tumor to make BCT attempt possible.

Partial mastectomy incisions should be planned so that they can be incorporated into a mastectomy incision should that prove necessary. Incisions for partial mastectomy and either SLNB or ALND should be separate.

Adjuvant radiotherapy decreases the breast cancer recurrence rate from 30% to less than 7% at 5 years and is a required component of BCT.

Follow-up after BCT.

Physical examinations are the same as those for mastectomy (see earlier discussion). A posttreatment mammogram of the treated breast is performed to establish a new baseline, no earlier than 6 months after completion of radiation therapy. Mammograms are then performed every 6 to 12 months after the new baseline mammogram until the surgical changes stabilize and then annually. Contralateral breast mammography remains on an annual basis. Regular gynecologic follow-up is recommended.[27]

Management of the axilla.

Approximately 30% of patients with clinically negative exams will have positive lymph nodes in an ALND specimen. The presence and number of lymph nodes involved affect staging and thus prognosis. However,

complications are not infrequent. Thus, SLNB was developed to provide sampling of the lymph nodes without needing an ALND.

SLNB has been established as a standard of care for predicting axillary involvement in most patients with breast cancer. The procedure requires a multidisciplinary approach, including nuclear medicine, pathology, and radiology.

(1) It involves injection of blue dye (either Lymphazurin or methylene blue) in the operating room and/or technetium-labelled sulfur colloid (in the nuclear medicine department, radiology suite, or sometimes by the surgeon). The combination of blue dye and radioisotope provides higher node identification rates and increases the sensitivity of the procedure. The goal is to identify the primary draining lymph node(s) in the axillary nodal basin.

(2) A variety of injection techniques are used: intra parenchymal versus intradermal (intradermal methylene blue will cause skin necrosis at the injection site); peritumoral versus periareolar.

(3) The SLN is identified by its blue color, and/or by high activity detected by a handheld gamma probe, or by a blue lymphatic seen to enter a non-blue node. Palpable nodes are also sentinel nodes, even if not blue or radioactive.

(4) Twenty percent to 30% of the time more than one SLN is identified.

(5) Experienced surgeons (those who have performed at least 30 SLNBs, with ALND for confirmation) can identify the SLN in greater than 90% of patients,

accurately predicting the patients' remaining axillary lymph node status in greater than 97% of cases.

(6) If the SLN is positive for metastasis (micrometastasis 0.2 mm or larger, not isolated tumor cells),a standard completion ALND is the current recommendation. A recent randomized trial compared the overall survival and axillary recurrence rates for patients with limited SLN metastatic disease who received breast conservation and systemic therapy and either had ALND versus no further axillary procedures. There was no difference in the two groups, leading many to defer completion ALND for this subgroup of patients. All patients underwent lumpectomy, whole breast radiation, and systemic therapy; thus, the results cannot be generalized to all patients with a positive SLN.

(7) Serial sectioning and immune histochemical staining of SLNB specimens may improve accuracy in detecting micro metastatic disease.

(8) Currently, isolated tumor cells are considered N0 disease, and therapeutic decisions should not be based on finding these.

Axillary Lymph Node Dissection (ALND).

Patients with clinically positive lymph nodes should undergo ALND for local control. ALND involves the following:

(1) Removal of level I and level II nodes and, if grossly involved, possibly level III nodes. Motor and sensory nerves are preserved unless there is direct tumor involvement.

(2) An ALND should remove at least 10 or more nodes. The number of nodes identified is often pathologist dependent.

(3) Patients with 4 or more positive lymph nodes should undergo adjuvant radiation to the axilla. Selective patients with 1 to 3 positive nodes may also benefit from radiation therapy to the axilla.

(4) Intraoperative complications: potential injury to the axillary vessels and neuropathy secondary to injury to the motor nerves of the axilla (the long thoracic, thoracodorsal, and medial pectoral nerves).

(5) Most frequent postoperative complications: wound infections and seromas. Persistent seroma may be treated with repeated aspirations or reinsertion of a drain. Other complications include pain and numbness in the axilla and upper arm, impaired shoulder mobility, and lymphedema. Lymphedema occurs in approximately 10% to 40% of women undergoing axillary dissection; radiation to the axilla increases the risk of this complication. The most effective therapy is early intervention with intense physio massage; graded pneumatic compression devices and a professionally fitted compression sleeve can also provide relief and prevent worsening of lymphedema. Blood draws, blood pressure cuffs, and intravenous lines should be avoided in the affected arm, mainly to avoid infection in it. Infections of the hand or arm should be treated promptly and aggressively with antibiotics and arm elevation because infection can damage lymphatics further and cause irreversible lymphedema. Lymphedema itself increases the risk of developing angiosarcoma.

Adjuvant systemic therapy is given in appropriate patients after completion of surgery.

1. All node-positive patients should receive adjuvant chemotherapy.

Regimens are guided by the tumor biomarkers. Typical regimens comprise four to eight cycles of a combination of cyclophosphamide and an anthracycline, followed by a taxane administered every 2 to 3 weeks.

2. Patients with ER-positive tumors receive adjuvant hormonal therapy for 5 years. Tamoxifen is given to premenopausal women, and aromatase inhibitors are given to postmenopausal women (aromatase inhibitors are not used in premenopausal women because decreased feedback to the hypothalamus and pituitary increases gonadotropin secretion, stimulating the ovary to secrete more substrate).

3. In postmenopausal women older than 70 years, chemotherapy is performed less frequently. In postmenopausal women with tumors with ER or PR positivity, tamoxifen or an aromatase inhibitor is frequently the sole adjuvant medical therapy.

4. In patients with Her2/neu-positive tumors, polychemotherapy is combined with biological therapy targeting theHer2/neu protein: trastuzumab is a recombinant monoclonal antibody that binds toHer2/neu receptor to prevent cell proliferation. The NSABP trial B-31 and the North Central Cancer Treatment Group trial N9831 showed that adding trastuzumab to a chemotherapy regiment of doxorubicin, cyclophosphamide, and paclitaxel was associated with an

increase in the disease-free survival by 12% and a 33% reduction in the risk of death at 3 years. It is usually administered intravenously monthly for 12 months. The most serious toxicity with the regiment was cardiac failure (N Engl J Med. 2005;353:1673).

5. Node-negative patients may have increased disease-free survival from adjuvant chemotherapy and/or hormonal therapy. An individualized approach is crucial and requires thorough discussion with the patient regarding the risks of recurrence without adjuvant therapy, the cost and toxicities treatment, and the expected benefit in risk reduction and survival.

Up to 30% of node-negative women die of breast cancer within 10 years if treated with surgery alone.

Node-negative patients who are at high risk and benefit the most from adjuvant chemotherapy include those with tumors greater than 1 cm, higher tumor grade,Her2/neu expression, aneuploidy, Ki-67 expression, increased percentage in S phase, lymphovascular invasion, and ER/PR-negative tumors.

The NSABP B-20 trial and the International Breast Cancer Study Group trial IX showed that polychemotherapy in combination with tamoxifen was superior to tamoxifen alone in increasing disease-free and overall survival, especially in ER-negative patients, regardless of tumor size.

The St. Gallen Consensus Panel in 1998 suggested that patients who have node-negative disease and whose tumors are 1 cm or less and ER-positive may

be spared adjuvant chemotherapy but still may benefi t from adjuvant endocrine therapy.

The Web site http://www.adjuvantonline.com provides an online tool for physicians to use to calculate the added benefit of hormonal and chemotherapeutic therapies.

Adjuvant radiation

1. Indications for adjuvant radiation to the chest wall and axilla after mastectomy include T3 and T4 tumors, attachment to the pectoral fascia, positive surgical margins, skin involvement, involved internal mammary nodes, inadequate or no axillary dissection, four or more positive lymph nodes, and residual tumor on the axillary vein. Presence of one to three positive axillary nodes is a relative indication.

2. Randomized, prospective trials have shown a significantly decreased recurrence and improved survival in premenopausal women with these indications treated with chemotherapy and radiation therapy (N Engl J Med. 1997;337:949).

3. Adjuvant whole-breast radiationafter BCT decreases the breast cancer recurrence rate from 30% to less than 7% at 5 years.

4. Complications. Radiation to the chest wall can cause skin changes. Infrequent complications include interstitial pneumonitis, spontaneous rib fracture, breast fibrosis, pericarditis, pleural effusion, and chest wall myositis.

Radiation to the axilla can increase the incidence of lymphedema and axillary fibrosis. Angiosarcoma can occur as a late complication.

E. Locally advance breast cancer (LABC) comprises T3 or T4, N1 or greater, and M0 cancers (stages IIIA and IIIB).

1. Staging in LABC. Because of the frequency of distant metastasis at the time of presentation, all patients should receive complete blood cell count, complete metabolic panel, bone scan, and CT scan of chest and abdomen before treatment.

2. Non inflammatory LABC (chest wall or skin involvement, skin satellites, ulceration, fixed axillary nodes)

Patients should receive neoadjuvant chemotherapy (often cyclophosphamide combined with an anthracycline and taxane), followed by surgery and radiation. The high response rates seen with this regimen for stage IIIB allow MRM to be carried out, with primary skin closure. Neoadjuvant chemotherapy also provides information regarding tumor response to treatment that may aid to guide further adjuvant therapy. Adjuvant radiation to the chest wall and regional nodes chemotherapy follow surgery; additional adjuvant chemotherapy is also necessary in select cases. SLNB may be used in selected patients with a clinically negative axilla.

Patients with stage IIIA disease receiving neoadjuvant chemotherapy who can be converted to BCT candidates have no difference in overall survival outcome.

Approximately 20% of patients with stage III disease present with distant metastases after appropriate staging has been performed.

3. Inflammatory LABC (T4d)

This is characterized by erythema, warmth, tenderness, and edema (peau d'orange). It represents 1% to 6% of all breast cancers. An underlying mass is present in 70% of cases. Associated axillary adenopathy occurs in 50% of cases. It is often misdiagnosed initially as mastitis. Skin punch biopsy confirms the diagnosis: in two third of cases, tumor emboli are seen in dermal lymphatics. Approximately 30% of patients have distant metastasis at the time of diagnosis. Inflammatory breast cancer requires aggressive multimodal therapy because median survival is approximately 2 years, with a 5-year survival of only 5%.

Follow-up.

Because of higher risk for local and distant recurrence, patients should be examined every 3 months by all specialists involved in their care.

Locoregional recurrence.

Patients with locoregional recurrence should have a metastatic workup to exclude visceral or bony disease and should be considered for systemic chemotherapy or hormonal therapy.

1. Recurrence in the breast after BCT requires total (simple) mastectomy. Provided margins are negative, survival is similar to that for patients who received mastectomy initially.

2. Recurrence in the axilla requires surgical resection followed by radiation to the axilla and systemic therapy.

3. Recurrence in the chest wall after mastectomy occurs in 4% to 5% of patients. One third of these patients have distant metastases at the time of recurrence, and greater than 50% will have distant disease within 2 years. Multimodal therapy is essential. For an isolated local recurrence, excision followed by radiotherapy results in excellent local control. Rarely, patients require radical chest resection with myocutaneous flap closure.

SURGICAL TECHNIQUE

- A *skin-sparing mastectomy* removes all breast tissue, the nipple-areola complex, and only 1 cm of skin around excised scars. There is a recurrence rate of less than 2% when skin sparing mastectomy is used for T1 to T3 cancers.
- A *total (simple) mastectomy* removes all breast tissue, the nipple areola complex, and necessary skin.
- An *extended simple mastectomy* removes all breast tissue, the nipple-areola complex, necessary skin, and the level I axillary lymph nodes.
- A modified radical mastectomy removes all breast tissue, the nipple-areola complex, necessary skin, and the level I and II axillary lymph nodes.

- The Patey modification of the modified radical mastectomy also removes the pectoralis minor muscle, which permits complete dissection of the apical (level III) axillary lymph nodes.
- *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 retracted to dissect level III lymph nodes—commonly done now.
- The Halstead radical mastectomy removes all breast tissue, the nipple areolar complex, necessary skin, the pectoralis major and pectoralis minor muscles, and the level I, II, and III axillary lymph nodes.

Currently, chemotherapy, hormone therapy, and radiation therapy for breast cancer have nearly eliminated the need for a Halstead radical mastectomy.

The patient is positioned on the operating table in the supine position for induction of general endotracheal anesthesia. A rolled sheet provides modest elevation of the ipsilateral hemithorax and shoulder so that shoulder movement is not limited. Positioning the patient at the edge of the operating table affords the surgeon and the surgical assistant ample access to the breast

and axilla and avoids undue retraction on the pectoralis muscle groups or the brachial plexus. The ipsilateral breast, neck, shoulder, and hemithorax are prepped down to the operating table and across the midline of the chest. Folded towels are used to expose the prepped operative field, which includes the shoulder, lower neck, sternum, and upper abdominal musculature. The towels are secured in place with towel clips or surgical staples. In addition, the ipsilateral axilla, arm, and hand are fully prepared within the operative field and the arm is positioned on an arm board that is placed perpendicular to the operating field. While alternative methods exist for including the arm and hand in the operative field, isolation of the hand and forearm with an occlusive cotton dressing (stockinette) is preferred. The stockinette is secured in place by applying an elastic or cotton bandage distal to the ipsilateral elbow, thereby ensuring free mobility of the ipsilateral elbow, arm, and shoulder.

Preparation the patient for MRM

At the commencement of a modified radical mastectomy, the first surgical assistant is positioned over the shoulder of the ipsilateral breast, cephalad to the arm board. This position permits the assistant to position the arm and shoulder and retract the pectoral muscles appropriately at the time of the axillary dissection. In an obese patient with large breasts, a second surgical assistant can be positioned on the contralateral side of the operating table to

assist with exposure of the axilla during axillary dissection. Positioning of the surgical team The elliptical incision of the breast skin incorporates the nipple-areola complex and skin overlying the breast cancer en bloc with skin margins that lie 1 to 2 cm from the cephalad and caudal extents of the cancer. Skin flaps are developed using cautery or scalpel and extend to the boundaries of dissection for the modified radical mastectomy, which are (a) the anterior margin of the latissimus dorsi muscle laterally, (b) the midline of the sternum medially, (c) the subclavius muscle superiorly, and (d) the caudal extension of the breast, which is 3 to 4 cm inferior to the inframammary fold, inferiorly. The skin edges are elevated at a right angle to the chest wall to adequately expose the superficial fascia. Skin flaps include the skin and tela subcutanea and vary in thickness depending on body habitus. The appropriate dissection plane for skin flap elevation is deep to the subcutaneous vasculature and superficial to the vessels of the breast parenchyma. The classic Stewart Elliptical Incision The surgeon elevates the skin flap with consistent thickness to avoid creation of devascularized subcutaneous tissues, which can contribute to wound seroma, skin necrosis, and flap retraction. Once the skin flaps are developed, the breast parenchyma and pectoralis major fascia are elevated from the underlying pectoralis major muscle in a plane parallel with the muscle bundles as they course from their medial origin (ribs 2 to 6) to their lateral insertion on the humerus.

Perforating vessels from the lateral thoracic or anterior intercostal arteries, which are end arteries that supply the pectoralis major and minor muscles and breast parenchyme, are regularly encountered during elevation of the breast parenchyme and pectoralis major fascia. These vessels are individually identified and secured with 2-0 or 3-0 nonabsorbable sutures. Elevation of the breast parenchyme and pectoralis major fascia is continued laterally until the lateral edge of the pectoralis major muscle and the underlying pectoralis minor muscle are exposed. The surgeon is aware of the anatomic location of the lateral neurovascular bundle in which the medial pectoral nerve (laterally placed with origin from the medial cord) courses to innervate the pectoralis major and minor muscles. If possible, this nerve is preserved to prevent atrophy of the lateral head of the pectoralis major, a significant cosmetic and functional defect. Once elevation of the breast parenchyme and pectoralis major muscle fascia from the underlying pectoralis major muscle is completed, an incontinuity axillary lymph node dissection is performed. Exposure of the pectoralis minor muscle and incision of the investing fascia of the axilla. Upward retraction of the pectoralis major muscle reveals the underlying pectoralis minor muscle and an intervening compartment {Rotter's space), which contains lymph nodes {Rotter's nodes). After incision of the investing fascia of the axillary space the tendinous portion of the pectoralis minor muscle and underlying structures {axillary artery and vein, brachial plexus) are readily identified. Digital protection of the brachial plexus for division of the insertion of the pectoralis

minor muscle on the coracoid process if needed. All loose areolar and lymphatic tissues are swept en bloc with the axillary contents. Dissection commences superior to inferior with complete visualization of the anterior and ventral aspects of the axillary vein.

Dissection cranial to the axillary vein is inadvisable, for fear of damage the brachial plexus and the infrequent observation of gross nodal tissue cephalic to the vein. lnvesting fascial dissection of the vein is best completed with the cold scalpel following exposure, ligation, and division of all venous tributaries on the anterior and ventral surfaces. Caudal to the vein, loose areolar tissue at the junction of the vein with the anterior margin of latissimus is swept lnferomedially inclusive of the lateral (axillary) nodal group (level l). Care is taken to preserve the neuro vascular thoraco dorsal artery, vein, and nerve in the deep & axillary space. The thoracodorsal nerve is traced to its innervation of the latissimus dorsi muscle laterally. Lateral and axillary nodal groups are retracted inferomedially and anterior to this bundle for dissection en bloc with the subclavicular (level 3) group. The superomedial most extent of the dissection is the clavipectoral fascia (Halsted's ligament). This level of dissection with this technique allows the surgeon to mark with metallic clip or suture, the superior most extent of dissection. All loose areolar tissue just inferior to the apical nodal group is swept of the chest wall leaving the fascia of the serratus anterior intact.

With dissection parallel to the long thoracic nerve (respiratory nerve of Bell), the deep investing serratus fascia is incised. This nerve is closely applied

to the investing fascial compartment of the chest wall and must be dissected in its entirety cephalic to caudal, to ensure innervation of the serratus anterior and avoidance of the “winged scapula” disability.

Axillary lymph node dissection.

The loose areolar tissue of the axillary space is elevated and the investing layer of the axillary vein is dissected sharply with dissection continuing to allow complete visualization of the anterior and ventral surfaces of the vein, as well as ligation and division of intervening venous tributaries. The loose areolar tissue at the juncture of the axillary vein with the anterior margin of the latissimus dorsi muscle laterally is swept inferomedially to include the lateral group of axillary lymph nodes (level I). The thoracodorsal artery and vein, which are located deep in the axillary space and are invested with loose areolar tissue and the axillary lymph nodes of the lateral and subscapular groups, are preserved. The lateral axillary lymph node group is retracted inferomedially and anterior to the thoracodorsal neurovascular bundle and dissected en bloc with the subscapular group of axillary lymph nodes (level I), which is located medially between the thoracodorsal nerve and the lateral chest wall. Dissection then proceeds medially with extirpation of the central axillary lymph node groups {level II}. The long thoracic nerve (Bell's respiratory nerve), which is constant in its location anterior to the subscapularis muscle, and is closely applied to the investing fascial compartment of the chest wall is identified and preserved. The

axillary contents anterior and medial to the long thoracic nerve are then swept infero medially with the dissection specimen. When level III lymphadenopathy is present, a Auchincloss modification of the axillary dissection is performed which involves retraction of the pectoralis minor muscle. This modification provides exposure for dissection of the apical axillary lymphnodes (level III).

COMPLICATIONS

Anatomic Complications of the Modified Radical Mastectomy

Vascular Injury

- The first and second perforating vessels are too large for cautery.
- They are ligated.
- The axillary vein, if torn, is repaired. Ligation may cause chronic edema.

Nerve Injury

- Intercosto brachial nerve: When cut, circumscribed numbness of the medial aspect of the ipsilateral upper arm results.
- Long thoracic nerve: If cut, a winged scapula deformity results.
- Medial and lateral thoracic nerves: If cut, the pectoralis muscles atrophy.
- Thoracodorsal nerve: If cut, internal rotation and abduction of the shoulder are weakened.

PATHOLOGY ASSESMENT

A central component of the treatment of breast cancer is full knowledge of extent of the disease and biologic features. These factors contribute to the determination of the stage of disease, assist in the estimation of the risk that the cancer will recur, and provide information that predicts response to therapy (eg: ER, PR, HER2). These factors are determined by examination of excised tissue and are provided in a written pathology report. Accurate pathology reporting requires communication between the clinician and the pathologist relating to relevant patient history, prior breast biopsies, prior irradiation to the chest, pregnancy status, characteristics of the abnormality biopsied (eg: palpable, mamographically detected micro calcification), clinical state of lymph nodes, presence of inflammatory change or other skin abnormality, and any prior treatment administered (eg: chemotherapy, radiation therapy). The specimen should be oriented for the pathologist, and specific requests for the determination of biomarkers should be stated (eg: ER, PR, HER2 status). The use of consistent unambiguous standards for reporting is strongly encouraged. Data from both national and local surveys show that as many as 50% of the pathology reports for breast cancer missing some element critical to patient management. Significant omissions include failure to orient and report surgical margins and failure to report tumor grade consistently.

The College of American Pathologists (CAP) has developed pathology reporting protocols to promote complete and standardised reporting of

malignant specimens. CAP provides a protocol for each disease site. That includes cancer case summaries (check lists along with background documentation). These check lists form the basis for a synoptic, standardised reporting of pathologic findings. Consistent, unambiguous, and complete pathology reporting is a corner stone of quality breast cancer care, and the NCCN breast cancer panel endorses the use of the CAP protocol for reporting the pathologic analysis of all breast cancer specimens.

CAP GUIDELINES for pathology reporting

SPECIMEN IDENTIFICATION

The following 4 elements identifying the specimen may be listed separately or on 1 line:

Procedure

- Excision without image-guided localization
- Excision with image-guided localization
- Total mastectomy (including nipple and skin)
- Other (specify): _____
- Not specified

Lymph Node Sampling (select all that apply) (required only if lymph nodes are present in the specimen)

- Sentinel lymph node(s)
- Axillary dissection (partial or complete dissection)

- Lymph nodes present within the breast specimen
- Other lymph nodes (eg, supraclavicular or location not identified)
- Specify location, if provided: _____

Specimen Laterality

- Right
- Left
- Not specified

Tumor Site: Invasive Carcinoma

- Upper outer quadrant
- Lower outer quadrant
- Upper inner quadrant
- Lower inner quadrant
- Retro Areolar
- Nipple

Tumor Size: Size of Largest Invasive Carcinoma

- Microinvasion only (≤1 mm)
- Greatest dimension of largest focus of invasion >1 mm: ___ mm
- Additional dimensions: ___ x ___ mm
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy

- Cannot be determined (explain): _____

Note: The size of the invasive carcinoma should take into consideration the gross findings correlated with the microscopic examination. In some cases, it may be helpful to use information about tumor size from imaging studies. If multiple foci of invasion are present, the size listed is the size of the largest contiguous area of invasion. The size of multiple invasive carcinomas should not be added together. The size does not include adjacent ductal carcinoma in situ (DCIS).

If there has been a prior core needle biopsy or incisional biopsy showing a larger area of invasion than in the excisional specimen, the largest dimension of the invasive carcinoma in the prior specimen should be used for T classification, if known.

If there has been prior neoadjuvant treatment and no invasive carcinoma is present, the cancer is classified as yTis if there is residual DCIS and yPT0 if there is no remaining carcinoma. A protocol is not required if no cancer is present in the specimen

Histologic Type

- Invasive mammary carcinoma of no special type (ductal, not otherwise specified)
- Micro-invasive mammary carcinoma
- Invasive mammary carcinoma with extensive intraductal component
- Invasive mammary carcinoma with matrix production

- Invasive lobular carcinoma
- Invasive mammary carcinoma, no special type, with lobular features
- Invasive lobular carcinoma with pleomorphic features
- Invasive lobular carcinoma, alveolar variant
- Invasive carcinoma with ductal and lobular features (“mixed type carcinoma”)
- Mucinous carcinoma
- Invasive mammary carcinoma with mucinous features
- Tubular carcinoma
- Invasive mammary carcinoma with tubular features
- Invasive mammary carcinoma, tubulo-lobular variant
- Invasive cribriform carcinoma
- Invasive mammary carcinoma with cribriform features
- Invasive micropapillary carcinoma
- Invasive carcinoma with micropapillary features
- Invasive mammary carcinoma associated with encysted papillary carcinoma
- Invasive papillary carcinoma
- Invasive solid papillary carcinoma
- Encapsulated papillary carcinoma
- Medullary carcinoma
- Invasive mammary carcinoma with medullary features

- Metaplastic carcinoma
- Metaplastic carcinoma with squamous features
- Low grade adenosquamous carcinoma
- Metaplastic carcinoma with low-grade adenosquamous features
- Low-grade fibromatosis-like metaplastic carcinoma
- Metaplastic carcinoma, spindle cell type
- Metaplastic carcinoma, mixed epithelial and mesenchymal type
- Invasive carcinoma with metaplastic features
- Carcinosarcoma
- Adenoid cystic carcinoma
- Invasive mammary carcinoma with apocrine features
- Invasive carcinoma with clear cell (glycogen rich) features
- Invasive mammary carcinoma with neuroendocrine features
- Invasive carcinoma, with signet-ring cell features
- Secretory carcinoma
- Invasive carcinoma, type cannot be determined
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Other(s) (specify): _____

Note: The histologic type corresponds to the largest carcinoma. If there are smaller carcinomas of a different type, this information should be included under “Additional Pathologic Findings.”

Inflammatory carcinoma requires the presence of clinical findings of erythema and edema involving at least one-third or more of the skin of the breast (see explanation under “Pathologic Staging”).

Special type carcinomas should consist of at least 90% pure pattern.

Histologic Grade (Nottingham Histologic Score)

- Glandular (Acinar)/Tubular Differentiation
- Score 1 (>75% of tumor area forming glandular/tubular structures)
- Score 2 (10% to 75% of tumor area forming glandular/tubular structures)
- Score 3 (<10% of tumor area forming glandular/tubular structures)
- Only microinvasion present (not graded)
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Score cannot be determined

Nuclear Pleomorphism

- Score 1 (nuclei small with little increase in size in comparison with normal breast epithelial cells, regular outlines, uniform nuclear chromatin, little variation in size)
- Score 2 (cells larger than normal with open vesicular nuclei, visible nucleoli, and moderate variability in both size and shape)
- Score 3 (vesicular nuclei, often with prominent nucleoli, exhibiting marked variation in size and shape, occasionally with very large and bizarre forms)

- Only microinvasion present (not graded)
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Score cannot be determined

Mitotic Rate

- Score 1 (≤3 mitoses per mm2)
- Score 2 (4-7 mitoses per mm2)
- Score 3 (≥8 mitoses per mm2)
- Only microinvasion present (not graded)
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Score cannot be determined
- Number of mitoses per 10 high-power fields: ___
- Diameter of microscope field: ___ mm

Overall Grade

- Grade 1 (scores of 3, 4, or 5)
- Grade 2 (scores of 6 or 7)
- Grade 3 (scores of 8 or 9)
- Only microinvasion present (not graded)
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Score cannot be determined

Note: The grade corresponds to the largest area of invasion. If there are smaller foci of invasion of a different grade, this information should be included under "Additional Pathologic Findings."

Tumor Focality (required only if more than 1 focus of invasive carcinoma is present)

- Single focus of invasive carcinoma
- Multiple foci of invasive carcinoma
    - Number of foci: ____
    - Sizes of individual foci: ____
- No residual invasive carcinoma after presurgical (neoadjuvant) therapy
- Cannot be determined

OBSERVATION AND RESULTS

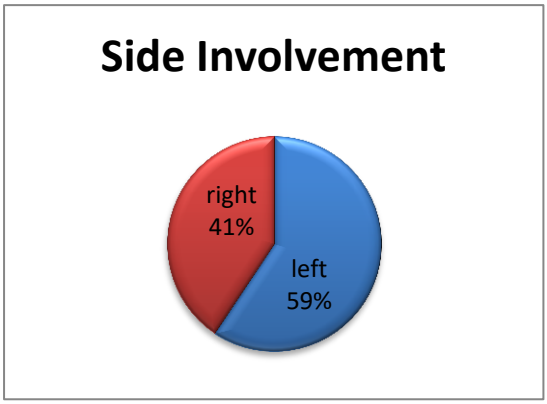
This study was conducted in Department of General Surgery, Govt. Stanley Medical College, Chennai, for a period of 18 months

The total number of patients enrolled for the study: 32

For all the patients Total Mastectomy with Axillary lymph Node dissection was done by giving clearance including Level I, II, III and interpectoral nodes which were sent for analysis. The histopathology reports were obtained according to CAP protocol and the results were analysed. All the patients enrolled in the study were females.

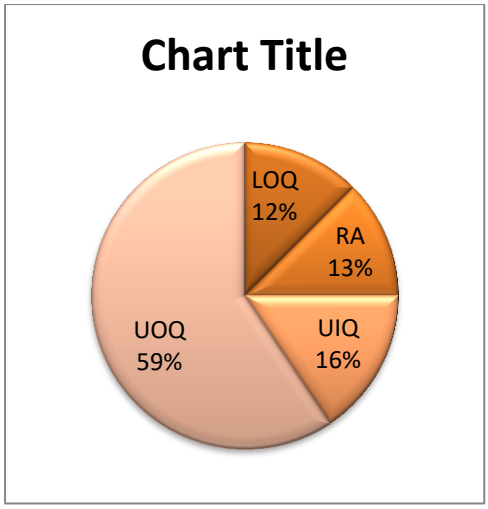
- An average of 13 lymph nodes were examined per case (range: 8−20)
- Axillary lymph node involvement was found in 56% of the cases (18/32).
- Of the 18 cases, 83% (n = 15) had involvement of level I/II nodes only, and 16% (n = 3) had positive ALN in levels III and, or, interpectoral nodes, in addition to level I/II.
- Involvement of lymph nodes in level III and interpectoral nodes without a level I metastasis was not found.

- By the inclusion of level III to a level I/II dissection, two cases (11%) were converted from one to three positive nodes (pN1) to ≥4 positive nodes (pN2). Involvement of lymph nodes in level III was found in 3 cases (16%)
- 10/32 cases (31%) had ≥4 positive nodes who required adjuvant therapy
- Palpability of ALN, pathological tumour size, and lymphovascular invasion, were significantly associated with level III involvement and ≥4 positive nodes
- There was predominance of left side involvement for carcinoma which constitutes 19 patients of 32 enrolled



SIDE	Number of patients	percentage
RIGHT	13	41%
LEFT	19	59%

Of the affected breast the upper outer quadrant involvement is the most prevelant owing to 59%, followed by upper inner quadrant 16%, followed by retroareolar and lower outer quadrant of 12% each and with no involvement of lower inner quadrant.

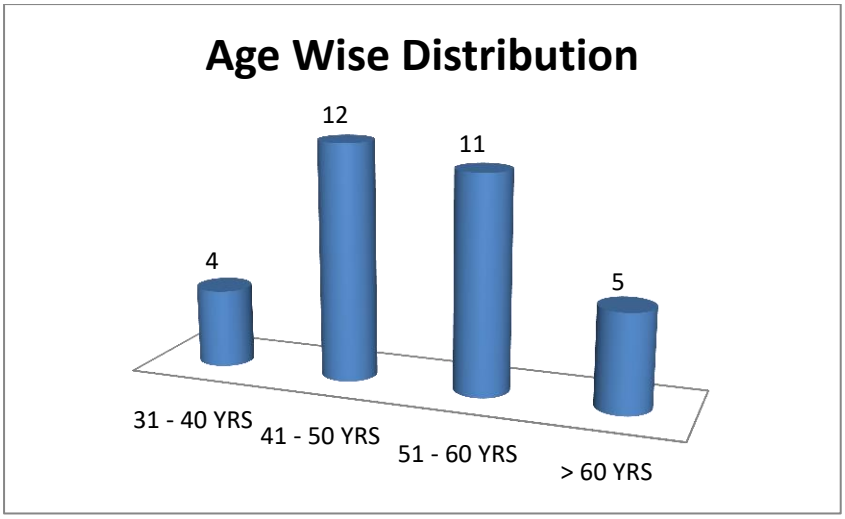


Quadrant involved	number	percentage
RA	4	12%
LOQ	4	13%
UIQ	5	16%
UOQ	19	59%
LIQ	0	0%

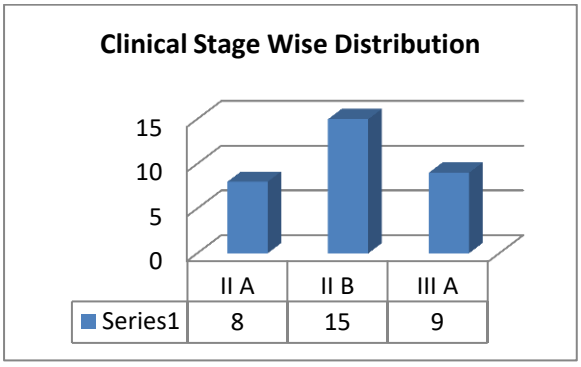
RA - retroareolar; LOQ - lower outer quadrant; UIQ - upper inner quadrant; UOQ - upper outer quadrant; LIQ - lower inner quadrant.

The age wise distribution predominates people of age group from 41 to 50 years which constitutes around 37% followed by 51 to 60 yrs constituting 35%, followed by 31 to 40 years and 61 to 70 years each of 12.5% and more than 70 yrs occupying 3%. This defies that the perimenopausal age group are more susceptible with breast cancer

Age	Number	Percentage
31 to 40 yrs	4	12%
41 to 50 yrs	12	38%
51 to 60 yrs	11	34%
>60 yrs	5	16%



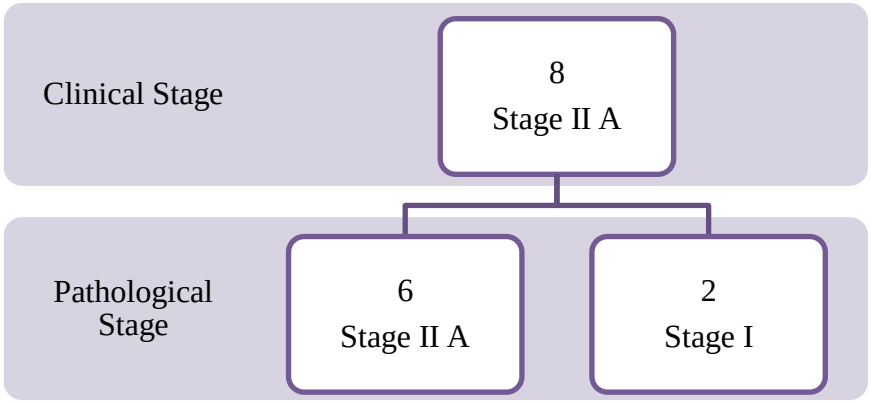
By clinical staging most of the patients belongs to stage II B (47%), followed by stage III A (28%) and stage II A (25%) but the pathological staging of the disease varies after HPE report.



Clinical stage	Number	Percentage
II a	8	25%
II b	15	47%
III a	9	28%

Of the 8 patients in the clinical stage II A disease all were T2N0 disease, post operatively 6 belonged to stage II A itself and 2 were only of stage I with average size of the tumor being 1.82, average number of nodes that could be dissected from the specimen was 12 nodes and all level of nodes including interpectoral nodes were negative for malignancy. This signifies that the clinical

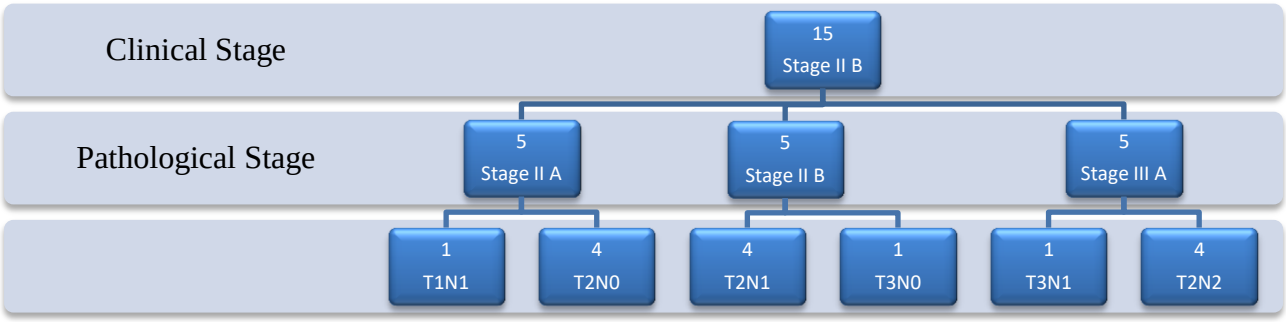
size of mass is a little larger than pathological size and breast conservation surgery can be a good option for these kind of people with T2N0 disease.



Of 15 patients in clinical stage II B, 13 being T2N1 disease and two being T3N0 disease, post operatively 5 belonged to II A, 5 belonged to II B while 5 belonged to III A disease.

- Of the 5 patients with pathologic staging II A all were node negative (pT2N0) except for one (pT1N1), whose single level I/II node positive for malignancy out of 11 nodes dissected. The other 4 patients all the level of lymph nodes were negetive with average number of node dissected being 11. The average size of tumor was 2.3
- Of 5 patients belonging to pathologic stage II B, one was negative for all levels of lymph nodes while 4 were positive for level I/II lymphnodes with negative interpectoral and level III nodes. The average number of node positive being 2 out of 10 nodes dissected. The average size of the tumor being 3.4 cms

- Of 5 patients of pathologic stage III A with clinical stage II B, all were postive for level I/II nodes with an average of 4 nodes positive out of 13 dissected nodes with negative interpectoral nodes and level III nodes. The average size of tumor was 3.5



Of 9 patients in clincal stage III A, two were pathologic stage II B and all others were III A. the average size of the tumor being 5.3 cms.

In this group all the patients were positive for level I/II with an average of 4 nodes out of 14 nodes dissected and two patients were postive for interpectoral and 3 patients for level III nodes.

REVIEW OF LITERATURE

1) Interpectoral nodes in carcinoma of the Breast: Requiem or Resurrection

Authors *(Rajiv Y. Chandawarkar MD, Shashank R. Shinde MD); Journal of SurgicalOncology;10.1002/(SICI)1096-9098(199607)62:3<158::AID-SO2>3.0.CO;2-6*

Fifty-eight consecutive patients undergoing a modified radical mastectomy were subjected to complete dissection and pathological assessment of the interpectoral fascia and the group of lymph nodes it contains. The dissection was carried out in all patients, irrespective of whether they were palpable or not. Interpectoral nodes (IPNs) were anatomically present in 28 patients (48%) and were completely absent in 30 patients (52%). Ten patients were Stage I, 18 were Stage II, and 30 were Stage III. Of the 25% (15/58) of patients with microscopic metastasis, only 12/15 had palpable nodes; 66% (10/15) of patients had axillary and apical nodes positive. Significantly, two patients with negative nodes in the axillary and apical group had metastatic Rotter's nodes. Of the 15 patients with positive IPNs, nine had primary tumors located within the upper quadrants of the breast, whereas only five had tumors in lower quadrants and one had a centrally located tumor. The neurovascular bundle to the pectoralis major could be safely preserved in 93% (54/58) of patients. The incidence of impalpable nodes with microscopic metastasis and the evidence of exclusively metastatic interpectoral nodes with uninvolved axillary and apical nodes prompt the following conclusions: (1) interpectoral

fascia and nodes should be mandatorily dissected in all patients irrespective of the nodes being palpable or not; (2) the dissection is anatomic and is associated with almost no additional morbidity; (3) the group of patients with IPNs positive and the axillary group negative, would benefit maximally from the IPN dissection. Similarly, this dissection in all other groups of patients would enable a more accurate staging and selection of therapeutic strategies. © 1996 Wiley-Liss, Inc.

2. Variation in axillary node dissection influences the degree of nodal involvement in breast cancer patients

Authors Sanjoy Saha MD, William B. Farrar MD, Donn C. Young PhD, John J. Ferrara MD, William E. Burak Jr. M

The study population consisted of 302 patients with invasive breast cancer who underwent complete (level I/II/III) axillary lymph node dissection. Assuming that all patients had undergone a level I/II dissection, it was determined how frequently a patient's nodal category (0, 1–3, 4–9, >10 positive nodes) would have been altered if a level I or level I/II/III dissection were performed. 302 patients had undergone a level I/II dissection, performing only level I dissection would have resulted in a change in nodal category in 15.9% of all patients and 36.1% of patients with positive nodes. The corresponding changes for a level I/II/III dissection would have been 4.3% and 9.5%, respectively.

3) A role of interpectoral (Rotter's) lymph node dissection in modified radical mastectomy for breast cancer. *(PMID:1448050) Yamasaki N , Kodama H, Department of Surgery, Niigata Prefectural Central Hospital, Japan.*

To study the influence of interpectoral lymph node (IPN) dissection on the prognosis of patients who underwent modified radical mastectomy, IPN was carefully dissected and studied pathologically on 168 cases of our breast cancer patients operated with modified radical mastectomy. There were 1.2 lymph nodes on an average in the interpectoral region, and they were almost 1-2mm in diameter. IPN metastases were found in 10 cases. (Tis: 0%, Stage I: 4.9%, Stage II: 5.7%, Stage III: 13%). Tumour's located in outer quadrant in almost all these cases. Positive IPN were found in 6 (16%) of n1 alpha group, 1 (10%) of n1 beta group, and in 3 (50%) of n2 group. All these 3 cases of n2 died of distant metastasis and local recurrence. Two (1.7%) of axillary node (1a, 1b) negative patients had micro involvement of cancer only in IPN, and are currently disease-free. These data suggest that IPN metastasis may occur even in the early breast cancer patients, and that may be controllable by lymph node excision. Therefore, routine and careful dissection of IPN through wide opening of sulcus interpectoralis is necessary for modified radical mastectomy and even for breast preserving operation.

CONCLUSION

On concluding with the observations and results from our study the key points were:

Variations in the level of axillary node dissection for breast cancer which includes the interpectoral and level III nodes can result in significant changes in the number of positive axillary nodes stepping up the pathologic nodal status from pN1 to pN2. This can potentially bias adjuvant therapy recommendations if treatment decisions are based on this prognostic factor.

Involvement of lymph nodes in level III and interpectoral nodes without a level I/II metastasis was not found. Level III axillary dissection is appropriate for patients with palpable ALN, to reduce the risk of axillary recurrence and provide essential adjuvant therapy.

Interpectoral nodes were positive in patients with stage III A that upstages the nodal status of disease for adjuvant therapy, that emphasize the importance of interpectoral node dissection to be included in Modified radical mastectomy procedure as a routine.

Other observations were the patient presents to the doctor with carcinoma breast only when it attains stage II, this shows the lack of awareness of screening procedures in patients which can pick up stage I disease. On observation there was no interconnection between the grade of differentiation and the level of nodal metastasis.

BIBLIOGRAPHY

1. *Benson JR, Jatoi I: The global breast cancer burden. Future Oncol 8:697, 2012. [The incidence of breast cancer is increasing rapidly in developing countries. This review discusses possible etiologic factors and the challenge of diagnosing and treating cancer in areas with limited resources.]*
2. *Breasted JH, editor. The Edwin Smith Surgical papyrus. Chicago, Illinois: The University Chicago Press; 1930. special edition, 1984..*
3. *Homer. Iliad. [Translated by WHD Rouse] New York: A Signet Classic. New American Library; 1966. p. 36.*
4. *Ariel IM. Breast cancer, a historic review: is the past prologue? In: Ariel IM, Cleary JB, editors. Breast Cancer Diagnosis and Treatment. New York: McGraw-Hill; 1987. pp. 3–26.*
5. *Lewison EF. The surgical treatment of breast cancer; an historical and collective review. Surgery. 1953;34:904–53. [PubMed].*
6. *Cooper WA. The history of radical mastectomy. Ann Med Hist. 1941:36–54.*
7. *Cooper AP. The anatomy and diseases of the breast. Philadelphia: Lea and Blanchard; 1845*
8. *Sappey MPC. Anatomie, physiologie, pathologie des vaisseaux lymphatiques considérés chez l'homme et les vertébrés. Paris: A Delahaye and E Lecrosnier; 1874.*

9. *Moore C. On the influence of inadequate operations on the theory of cancer. Royal Medical and Chirurgical Society. London. Med Chir Trans. 1867;32:245–80. [PMC free article] [PubMed]*
10. *Ekmektzoglou KA, Xanthos T, German V, Zografos GC. Breast cancer: From the earliest times through to the end of the 20th century. Eur J Obstet Gynecol Reprod Biol. 2009;145:3–8. doi: 10.1016/j.ejogrb.2009.03.017. [PubMed] [Cross Ref]*
11. *Banks WM. Free removal of mammary cancer with extirpation of the axillary glands as a necessary accompaniment. 1882. Paper read before the British Medical Association at Worcester. [PMC free article] [PubMed]*
12. . *Halsted WS. The results of operations for the cure of cancer of the breast performed at the Johns Hopkins Hospital from June 1889 to January 1894. Johns Hopkins Hospital Reports, Baltimore. 1894–95;4:297–350. [PMC free article] [PubMed]*
13. *Sakorafas GH, Safioleas M. Breast cancer surgery: an historical narrative. Part II. 18th and 19th centuries. Eur J Cancer Care. 2010;19:6–29. doi: 10.1111/j.1365-2354.2008.01060.x. [PubMed] [Cross Ref]*

14. *Twenty years' experience with prophylactic bilateral oophorectomy in the treatment of carcinoma of the breast.HORSLEY JS 3rd, HORSLEY GW Ann Surg. 1962 Jun; 155():935-9. [PubMed]*
15. *Jensen EV, DeSomber ER, Jungblut PW. Estrogen receptors in hormone responsive tissues and tumors. In: Wissler RW, Dao TL, Wood S Jr, editors. International Symposium on Endogenous factors influencing host-tumor balance. Chicago and London: University of Chicago Press; 1967.*
16. *Special Report: Treatment of primary breast cancer. N Engl J Med. 1979;301:340*
17. *Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer.Fisher B, Redmond C, Poisson R, Margolese R, Wolmark N, Wickerham L, Fisher E, Deutsch M, Caplan R, Pilch Y N Engl J Med. 1989 Mar 30; 320(13):822-8.[PubMed]*
18. *Quadrantectomy versus lumpectomy for small size breast cancer.Veronesi U, Volterrani F, Luini A, Saccozzi R, Del Vecchio M, Zucali R, Galimberti V, Rasponi A, Di Re E, Squicciarini P Eur J Cancer. 1990; 26(6):671-3.*
19. *Breast cancer surgery: an historical narrative. Part III. From the sunset of the 19th to the dawn of the 21st century. Sakorafas GH, Safioleas M Eur J Cancer Care (Engl). 2010 Mar; 19(2):145-66. [PubMed]*

20. *Post-mastectomy breast reconstruction: a history in evolution.Rozen WM, Rajkomar AK, Anavekar NS, Ashton MW Clin Breast Cancer. 2009 Aug; 9(3):145-54.[PubMed]*

21. *The free abdominoplasty flap and its use in breast reconstruction. An experimental study and clinical case report. Holmström H Scand J Plast Reconstr Surg. 1979; 13(3):423-27. [PubMed]*

22. *Ellis H, Colborn GL, Skandalakis JE 1993 Surgical embryology and anatomy of the breast and its related anatomic structures. Surg Clin North Am 73: 611–32.*

23. *Fentiman IS 1993 Detection and Treatment of Early Breast Cancer. London:MartinDunitz.Fry WA 2000 Thoracic incisions. In: Shields TW, LoCicero III J, Ponn RB(eds) General Thoracic Surgery, 5 th edn. Philadelphia:LippincottWilliams & Wilkins: 367–74.*

24. *Kurihara Y, Yakushiji YK, Matsumoto J, Ishikawa T, Hirata K 1999 The ribs:anatomic and radiologic considerations. Radiographics 19: 105–19. Includes some chest wall and ribcage abnormalities. Rubio IT, Klimberg S 2001 Techniques of sentinel lymph node biopsy. Semin Surg Oncol 20: 214–23.*

25. *Serletti JM, Moran SL 2000 Microvascular reconstruction of the breast. Semin Surg Oncol 19: 264–71.*

26. *Tanis PJ, Nieweg OE, Valdes Olmos RA, Kroon BB 2001 Anatomy and physiology of lymphatic drainage of the breast from the perspective of sentinel node biopsy. J Am Coll Surg 192: 399–409.*
27. *Yap LH, Whiten SC, Forster A, Stevenson JH 2002 The anatomical and neurophysiological basis of the sensate free TRAM and DIEP fl aps. Br J Plast Surg 55: 35–45.*
28. *Devitt JE, Barr JR. The clinical recognition of cystic carcinoma of the breast. Surg Gynecol Obstet. 1984;159:130-132.*
29. *Gallager HS, Martin JE. The study of mammary carcinoma by mammography and whole organ sectioning. Early observations. Cancer. 1969;23:855-873.*
30. *Seth A, Kitching R, Landberg G, et al. Gene expression profiling of ductal carcinomas in situ and invasive breast tumors. Anticancer Res. 2003; 23:2043-2051.*
31. *Simpson JF, Wilkinson EJ. Malignant neoplasia of the breast: Infiltrating carcinomas. In: Bland KI, Copeland EMI, eds. The Breast: Comprehensive Management of Benign and Malignant Diseases. Philadelphia:WB Saunders; 1998:285.*
32. *Foote FW, Stewart FW. Lobular carcinoma in situ: A rare form of mammary cancer. Am J Pathol. 1941;17:491-496.*

33. *Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. Breast Cancer Res. 2007 9:R6.*

34. *McDivitt RW, Boyce W, Gersell D. Tubular carcinoma of the breast. Clinical and pathological observations concerning 135 cases. Am J Surg Pathol. 1982;6:401-411.*

35. *Jatoi I. Screening clinical breast examination. Surg Clin North Am. 2003;83:789-801.*

36. *Rosato FE, Rosato EL. Examination techniques: Roles of the physician and patient evaluating breast diseases. In: Bland KI, Copeland EMI, eds. The Breast: Comprehensive Management of Benign and Malignant Diseases. Philadelphia:WB Saunders;1998:615.*

37. *Bassett LW. Breast imaging. In: Bland KI, Copeland EMI, eds. Philadelphia: WB Saunders; 1998:648.*

38. *Fletcher SW, Elmore JG. Clinical practice. Mammographic screening for breast cancer. N Engl J Med. 2003;348: 1672-1680.*

39. *Miller AB. Screening and detection. In: Bland KI, Copeland EMI, eds. The Breast: Comprehensive Management of Benign and Malignant Diseases. Philadelphia: WB Saunders; 1998:625.*

40. *Schnall MD. Breast MR imaging. Radiol Clin North Am. 2003;41:43-50.*

41. *Seidman H, Gelb SK, Silverberg E, et al. Survival experience in the Breast Cancer Detection Demonstration Project. CA Cancer J Clin. 1987;37:258-290.*

42. *Pisano ED, Gatsonis C, Hendrick E, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med. 2005;353:1773-1783.*

43. *Ciatto S, Houssami N, Bernardi D, et al. Integration of 3D digital mammography with tomosynthesis for population breastcancer screening (STORM): a prospective comparison study. Lancet Oncol. 2013; 14:70134-70137.*

44. *Krishnamurthy S, Sneige N, Bedi DG, et al. Role of ultrasound-guided fine-needle aspiration of indeterminate and suspicious axillary lymph nodes in the initial staging of breast carcinoma. Cancer. 2002;95:982-988.*

45. *Turnbull L, Brown S, Harvey I, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. Lancet. 2010;375:563-571.*

46. *Houssami N, Turner R, Morrow M. Preoperative magnetic resonance imaging in breast cancer: meta-analysis of surgical outcomes. Ann Surg. 2013; 257:249-255.*

47. *Robinson DS, Sundaram M. Stereotactic imaging and breast biopsy. In: Bland KI, Copeland EMI, eds. The Breast: Comprehensive Management*

of Benign and Malignant Diseases. Philadelphia: WB Saunders; 1998:698.

48. *Wilkinson EJ, Masood S. Cytologic needle samplings of the breast: Techniques and end results. In: Bland KI, Copeland EMI, eds. The Breast: Comprehensive Management of Benign and Malignant Diseases. Philadelphia: WB Saunders; 1998:705.*
49. *Greene FL, Page DL, Fleming ID, eds. Breast. AJCC Cancer Staging Manual 6th ed. New York: Springer-Verlag: 2002.*
50. *Britton PD, Goud A, Godward S, et al. Use of ultrasoundguided axillary node core biopsy in staging of early breast cancer. Eur Radiol. 2009;19:561-569.*
51. *Fisher B, Slack NH. Number of lymph nodes examined and the prognosis of breast carcinoma. Surg Gynecol Obstet. 1970.131:79-88.*
52. *AJCC Cancer Staging Manual 7th ed. Springer:2010.*
53. *Du Toit RS, Locker AP, Ellis IO, et al. Evaluation of the prognostic value of triple node biopsy in early breast cancer. Br J Surg. 77:163-167.*
54. *Dillon DA. Molecular markers in the diagnosis and staging of breast cancer. Semin Radiat Oncol. 2002;12:305-318.*
55. *Esteva FJ, Sahin AA, Cristofanilli M, et al. Molecular prognostic factors for breast cancer metastasis and survival. Semin Radiat Oncol. 2002;12:319-328.*

56. *Haffty BG. Molecular and genetic markers in the localregional management of breast cancer. Semin Radiat Oncol. 2002;12:329-340.*

57. *Morabito A, Magnani E, Gion M, et al. Prognostic and predictive indicators in operable breast cancer. Clin Breast Cancer. 2003; 3:381-390.*

58. *Rogers CE, Loveday RL, Drew PJ, et al. Molecular prognostic indicators in breast cancer. Eur J Surg Oncol. 2002;28: 467-478.*

59. *Rampaul R, Ellis IO, Robertson JFR. Prognostic indices in breast cancer. In: Autier BP, Adebamowo C, Anderson BO, et al, eds. World Breast Cancer Report, iPRI:2012:323-332.*

MASTER CHART

NAME	*AGE*	BIOPSY NUMBER	SIDE	QUADRANT	clinical T	clinical N	stage	T staging	N staging	STAGE	SIZE OF GREATEST DIMENSION (CMS)	GRADE	LEVEL I/II NODE	INTERPECTORAL NODES	LEVEL III NODES	TOTAL	DISSECTED
GANDHIMATHY	50/F	252/17	LEFT	UPPER OUTER QUADRANT	2	0	IIA	1	0	I A	0.4	GRADE III	0	0	0	0	12
RAMZAN BEE	38/F	799/17	LEFT	UPPER OUTER QUADRANT	2	0	IIA	2	0	II A	2	GRADE II	0	0	0	0	12
RAMISHA BAI	39/F	7080/16	RIGHT	UPPER OUTER QUADRANT	2	0	IIA	2	0	II A	2.5	GRADE II	0	0	0	0	13
MURUGESHWARI	41/F	1355/17	RIGHT	UPPER INNER QUADRANT	2	0	IIA	2	0	II A	2.5	GRADE III	0	0	0	0	15
ANJALI	45/F	4812/16	LEFT	UPPER OUTER QUADRANT	2	0	IIA	2	0	II A	2.5	GRADE II	0	0	0	0	13
PANAMNA	48/f	4585/17	LEFT	LOWER OUTER QUADRANT	2	0	IIA	2	0	II A	3	GRADE III	0	0	0	0	10
DHANAM	48/F	577/17	LEFT	UPPER INNER QUADRANT	2	0	IIA	1	0	II A	0.7	GRADE II	0	0	0	0	11
JOTHI	67/F	2912/16	LEFT	UPPER INNER QUADRANT	2	0	IIA	2	0	II A	1	GRADE II	0	0	0	0	10
DEVI	35/F	1847/17	RIGHT	UPPER OUTER QUADRANT	2	1	IIB	2	0	II A	2	GRADE II	0	0	0	0	12
PREMILA	36/F	3638/16	LEFT	LOWER OUTER QUADRANT	2	1	IIB	2	0	II A	2.5	GRADE II	0	0	0	0	10
JARINA	50/F	6895/16	RIGHT	UPPER OUTER QUADRANT	2	1	IIB	1	1	II A	0.5	GRADE II	1	0	0	1	11
SHANTHI	60/F	6793/16	LEFT	UPPER OUTER QUADRANT	2	1	IIB	2	0	II A	4	GRADE II	0	0	0	0	9
JENOVAH MARY	60/F	7354/16	RIGHT	UPPER OUTER QUADRANT	2	1	IIB	2	0	II A	2.5	GRADE II	0	0	0	0	13
SARALA	45/F	1266/17	LEFT	UPPER INNER QUADRANT	2	1	IIB	2	1a	II B	3	GRADE II	3	0	0	3	10
VIJAYALAKHSMI	53/F	1698/17	LEFT	UPPER OUTER QUADRANT	2	1	IIB	2	1a	II B	3	GRADE II	3	0	0	3	14
KANNIAMMAL	55/F	1897/17	LEFT	RETRO AREOLAR	2	1	IIB	2	1a	II B	3	GRADE II	1	0	0	1	8
MANGALAM	60/F	7170/16	RIGHT	UPPER OUTER QUADRANT	2	1	IIB	2	1a	II B	2	GRADE II	1	0	0	1	8
RUKMANIAMMAL	70/F	768/17	RIGHT	UPPER OUTER QUADRANT	3	0	IIB	3	0	II B	6	GRADE II	0	0	0	0	11

SULTHAN BEEVI	46/F	4574/17	RIGHT	UPPER OUTER QUADRANT	3	1	IIIA	3	0	II B	5	GRADE II	0	0	0	0	10
MALLIGA	55/F	5132/16	LEFT	UPPER OUTER QUADRANT	3	1	IIIA	2	1a	II B	3.5	GRADE II	4	0	0	4	20
KAMSALA	45/F	4552/17	LEFT	UPPER OUTER QUADRANT	3	0	IIB	3	1a	III A	6	GRADE II	2	0	0	2	12
NAGAMMAL	45/F	7023/16	RIGHT	UPPER OUTER QUADRANT	2	1	IIB	2	2a	III A	2.5	GRADE II	5	0	0	5	11
NAGARATHINAM	50/f	5289/16	LEFT	UPPER OUTER QUADRANT	2	1	IIB	2	2a	III A	3	GRADE III	4	0	0	4	13
AMUDHA	51/F	1683/17	RIGHT	LOWER OUTER QUADRANT	2	1	IIB	2	2a	III A	3	GRADE III	6	0	0	6	15
SUBHAMMAL	60/F	1648/17	LEFT	UPPER OUTER QUADRANT	2	1	IIB	2	2a	III A	3	GRADE II	4	0	0	4	14
YEGAVALI	50/F	941/17	RIGHT	UPPER INNER QUADRANT	3	1	IIIA	3	2a	III A	6	GRADE II	3	1	1	5	16
NEELA	54/F	1396/17	RIGHT	UPPER OUTER QUADRANT	3	1	IIIA	3	1a	III A	6	GRADE III	3	0	0	3	11
PATCHAIAMMAL	55/F	4201/17	LEFT	RETRO AREOLAR	3	1	IIIA	2	2a	III A	4	GRADE II	4	0	0	4	18
JAYANTHI	60/F	4150/17	LEFT	RETRO AREOLAR	3	1	IIIA	3	1a	III A	6	GRADE II	3	0	0	3	13
RABEKKA	64/F	1155/17	RIGHT	UPPER OUTER QUADRANT	3	1	IIIA	3	2a	III A	7	GRADE II	5	1	1	5	14
NEELAVATHY	70/F	4733/17	LEFT	LOWER OUTER QUADRANT	3	1	IIIA	3	1a	III A	6	GRADE II	3	0	2	5	11
CHINNAPONNU	80/F	1716/17	LEFT	RETRO AREOLAR	3	1	IIIA	2	2a	III A	4.5	GRADE II	5	0	0	5	15

URKUND

Urkund Analysis Result

Analysed Document: document.docx (D31094923)
Submitted: 10/7/2017 8:48:00 AM
Submitted By: mathews.tnj@gmail.com
Significance: 16 %

Sources included in the report:

Thesis copy semifinal.docx (D30605160)
Master Thesis Shad Emin KB5 civ..pdf (D8239782)
Comparitive study of neoadjuvant chemotherapy in hormone receptor positive and negative locally advanced breast carcinoma (Repaired).docx (D31026035)
Comparitive study of neoadjuvant chemotherapy in hormone receptor positive and negative locally advanced breast carcinoma.docx (D30753575)
5 Manish Ujwal.pdf (D17227260)
Rodriguez-Rausis-Kyong-Bok.pdf (D29624045)
THESIS Final sony.docx (D30753015)
Clinicopathological analysis of breast lump in females compiled document.docx (D30583390)
Comparitive study of neoadjuvant chemotherapy in hormone receptor positive and negative locally advanced breast carcinoma.docx (D30755485)

Instances where selected sources appear:

157

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled ***"SCRUTINY OF EXTENT OF AXILLARY NODE DISSECTION FOR PATIENTS WITH PRIMARY BREAST CANCER"*** of the candidate ***DR. M. MATHEWS*** with registration Number ***221511070*** for the award of ***M. S. DEGREE*** in the branch of ***GENERAL SURGERY***. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows ***16*** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

PROFORMA

SL. NO :

NAME : AGE /SEX: IP NO:

ADDRESS

CONTACT NUMBER:

DATE OF ADMISSION: DATE OF DISCHARGE/ DEATH:

HISTORY OF PRESENTING ILLNESS:

H/O lump in breast Onset,site,location

Progression

Associated symptoms

Nipple Discharge

Nipple Retraction

Trauma,Fever

H/o abdominal pain,jaundice

H/o headache,back pain

H/o Loss of Weight,Loss of Appettite

PAST HISTORY:

Whether a known case of DM/hypertension/asthma/TB/epilepsy/cardiac illness

H/o similar episodes of cancer or lump breast in the past, if any:

H/o major illness/ hospital admissions, if any:

H/o drug intake/hormonal manupulation usage,if any:

PERSONAL HISTORY:

Age of menarche Marital status Consanguinity No.of. Children

Breast fed: Yes/No If Yes,Duration of feed: Age of menopause:

FAMILY HISTORY:

H/o similar complaints in mother, grandmother, female siblings, if any

CLINICAL EXAMINATION:

General examination: (after getting consent, with female attender by side)

Local Examination: Breast and Axilla

Arm, Chest wall, Supraclavicular fossa/ infraclavicular fossa

Systemic examination: CVS, RS, CNS, Abdomen, Spine and Cranium

PROVISIONAL DIAGNOSIS:

Staging:

Risk factors:

Comorbid disease:

INVESTIGATIONS:

CBC:	RFT:	HIV:	HBsAg:
Anti-HCV:	Blood Grouping & Typing:		BT/CT:
Chest X-Ray:	ECG:		
USG Breast/Mammogram:		FNAC/Trucut Biopsy:	
USG ABDOMEN:		CT Thorax/Bone scan	

FINAL DIAGNOSIS :

Revised staging :

Histopathological report :

Grade of differentiation :

ER/PR status :

Level I/II node :

Level III node :

Interpectoral node :

GOVT.STANLEY MEDICAL COLLEGE, CHENNAI- 600 001

INFORMED CONSENT

DISSERTATION TOPIC:

"SCRUTINY OF EXTENT OF AXILLARY NODE DISSECTION FOR PATIENTS WITH PRIMARY BREAST CANCER"

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:

(Dr. Mathews. M)