MANAGEMENT OF EARLY BREAST CARCINOMA

ESSAY

SUBMITTED FOR PARTIAL FULFILMENT OF MASTER DEGREE IN GENERAL SURGERY

By

Tarek Salah Yousief

(M.B.B.Ch)

SUPERVISED BY

Professor Doctor \ Khaled Zaky Mansour

Professor of General Surgery

Faculty of Medicine

Ain Shams University

Doctor \ Amr Ahmed Abd Elaal

Assisstant Professor of General Surgery

Faculty of Medicine

Ain Shams University

Doctor \ Hany Rafik Halim

Lecturer of General Surgery

Faculty of Medicine

Ain Shams University

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

2009

Acknowledgement

First and for most, I feel indebted to **ALLAH,** most graceful, who gave me the strength to complete this work.

I would like to express my deepest gratitude and appreciation to my principal supervisor, **Prof. Dr. Khalid Zaky Mansour,** Professor of general surgery, Faculty of Medicine, Ain Shams University, for his generous support, encouragement, helpful suggestions and continuous supervision throughout the research, and for his precious time and effort that made this essay possible.

I am particularly grateful to **Prof. Dr. Amr Ahmed Abd Elaal,** Assistant Professor of general surgery, Faculty of Medicine, Ain Shams University, for his valuable foresight and meticulous supervision of this work.

Words are few and do fail to express my deepest gratitude to **Dr. Hany Rafik Halim**, Lecturer of general surgery, Faculty of Medicine, Ain Shams University, for his continuous encouragement, and close supervision throughout the course of this work.

Contents

	Page
ACKNOWLEDGEMENT	i
INTRODUCTION	1
AIM OF THE WORK	3
REVIEW OF LITERATURE	
Anatomy of the breast.	4
Pathology and staging of carcinoma of the breast.	19
Risk factors for development of carcinoma of the breast.	48
Breast cancer screening.	58
Diagnosis of early carcinoma of the breast.	65
Treatment of early carcinoma of the breast .	100
SUMMARY and CONCLUSION	160
REFERENCES	165
ARABIC SUMMARY	

Abbreviations

ACRIN	American College Of Radiologists Imaging Network.
ACS	American Cancer Society.
AIS	Aromatase inhibitors.
AJCC	American Joint Committee On Cancer.
ALND	Axillary lymph node dissection.
APBI	Accelerated partial breast irradiation.
AT	Ataxia-telangiectasia.
ATAC	Arimidex, Tamoxifen, Alone or in combination.
BCDDP	Breast cancer detection demonstration project.
BCT	Breast conservation therapy.
BIG	Breast international group.
BSE	Breast self-examination.
CBE	Clinical breast examination.
CEF	Cyclophosphamide epirubicin and 5-fluorouracil.
DCIS	Ductal carcinoma in situ..
EBCTCG	Early breast cancer trialists collaborative group.
ER	Estrogen receptor.
FFTP	First-full-term pregnancy.
FUS	Focused US.
HR+	Hormone receptor postive.
ILC	Invasive lobular carcinoma.
LCIS	Lobular carcinoma in situ.
LHRH	Luteinizing hormone-releasing hormone.
MC	Medullary carcinoma.
mCi	milliCurie.
NCI	National cancer institute.
NOS	Not otherwise specified.
NST	No special type.
PR	Progesterone receptor.
RFA	Radiofrequency ablation.
RR	Reported relative risk.
TDLU	Terminal duct lobular unit.
WBI	Whole breast irradiation.

LIST OF FIGURES

		Page
Fig. 1	Normal development of the breast.	4
Fig. 2	The adult female breast.	5
Fig. 3	Arterial supply of the breast.	8
Fig. 4	Lymphatic drainage of the breast.	13
Fig. 5	Walls and contents of axilla	16
Fig. 6	Breast examination.	68
Fig. 7	Classification of Mme Le Gal for clustered microcalcifications.	73
Fig. 8	Full-field digital mammograms.	75
Fig. 9	Ultrasound findings of malignant lesion.	78
Fig. 10	MRI demonstrated a speculated mass (arrow) with adjacent satellite lesions	80
Fig. 11	PET scan showing locally advanced right breast cancer with axillary metastasis.	87
Fig. 12	Ductoscopy and ductal lavage in the case of nipple discharge.	92
Fig. 13	Ultrasound-guided biopsy.	96
Fig. 14	Stereotactic mamographic devices.	97
Fig. 15	Breast-conserving surgery.	106
Fig. 16	Recommended locations of incisions for performing breast biopsy.	107

Fig. 17	Tumor removal during breast conserving surgery.	108
Fig. 18	Cosmetic outcome after breast-conserving therapy.	111
Fig. 19	Purse-String Technique in centrally located breast tumors.	112
Fig. 20	Wedge Resection in centrally located breast tumors.	113
Fig. 21	Batwing Technique in centrally located breast tumors.	114
Fig. 22	Hall-Findlay Technique in centrally located breast tumors.	115
Fig. 23	Technique of excising nonpalable cancers.	116
Fig. 24	Incision placement for modified radical mastectomy.	118
Fig. 25	Technique of RFA.	127
Fig. 26	Intraoperative breast ultrasound.	128
Fig. 27	Ultrasound of tumor with cryoablation needle centered in tumor before ablation.	132
Fig. 28	Cryotherapy ablation of a breast cancer.	134
Fig. 29	Interstitial catheter-based brachytherapy.	141
Fig. 30	Balloon-based intracavitary brachytherapy	142

LIST OF TABLES

		Page
Table 1	Classification of primary breast cancer.	19
Table 2	Contrasting features of cancerization of lobules by ductal carcinoma in situ and lobular carcinoma in situ.	25
Table 3	Manchester staging system.	41
Table 4	Columbia staging system.	42
Table 5	American Joint Committee on Cancer Staging System for Breast Cancer, 2002.	44
Table 6	Stage Groupings for patients with breast cancer according to the TNM Classification.	46
Table 7	Histopathological tumor grade.	47
Table 8	Breast cancer susceptibility genes.	50
Table 9	Diagnosis: medical history of a breast problem.	66
Table 10	Breast Imaging Reporting And Data System classification: final assessment categories.	71
Table 11	Nodal status and 10 year survival.	156
Table 12	Relationship between tumor size and axillary node status.	157

Introduction

Breast cancer ranks first among cancers affecting women throughout the world and its marked impact is not restricted to western industrialized societies (**Ibrahim et al., 2007**).

Latest estimates suggest that more than 1,050,000 new breast cancer cases occur worldwide annually, with nearly 580,000 cases occurring in developed countries and the remainder in developing countries **(Benard and Paul, 2003)**.

Breast cancer is a progressive disease, and small tumors are more likely to be at an early stage, have a better prognosis, and more successfully treated **(Matthew, 2006).**

In any patient who presents with a breast lump or other symptoms suspicious of carcinoma, the diagnosis should be made by a combination of clinical assessment, radiological imaging and a tissue sample taken for either cytological or histological analysis; the so-called triple combination should exceed 99.9% **(Sainsbury, 2004)**.

Mammography has long been used for early detection of and screening for breast cancers. With optimal technique and patient conditions, it has a reported sensitivity between 69% and 90%. Ultrasound has been used as an adjunct to mammography, with particular value in differentiating cystic from solid lesions and in facilitating guided biopsy of suspicious areas. The utility of MRI in breast imaging has undergone much advancement in the last 25 years. It shows promise in many areas, including staging of breast cancers,

determination of tumor size and spread, and may be a valuable screening tool for those patients with a high risk of breast cancer. It may also be of value in those patients whose breasts that are too dense for mammography **(Shah et al., 2005).**

Breast cancer management has been evolving toward minimally invasive approaches. Image-guided percutaneous biopsy techniques provide accurate histological diagnosis without the need for surgical biopsy. Breast conservation therapy has become the treatment standard for early stage breast cancer. Sentinel lymph node biopsy is a new procedure that can predict axillary lymph node status without the need of axillary lymph node dissection. The next challenge is to treat primary tumours without surgery. For this purpose, several new minimally invasive procedures, including radiofrequency ablation, interstitial laser ablation, focused ultrasound ablation, and cryotherapy, are currently under development and may offer effective tumor management and provide treatment options that are psychologically and cosmetically more acceptable to the patients **(George and Helena, 2007).**

Several randomized trials with very long follow-ups have established that breast-conserving therapy and mastectomy share equivalent outcomes in terms of overall survival. Breast-conserving surgery followed by a course of postoperative radiotherapy is now considered to be the current standard of care for patients with early operable breast cancer **(Alain et al., 2007).**

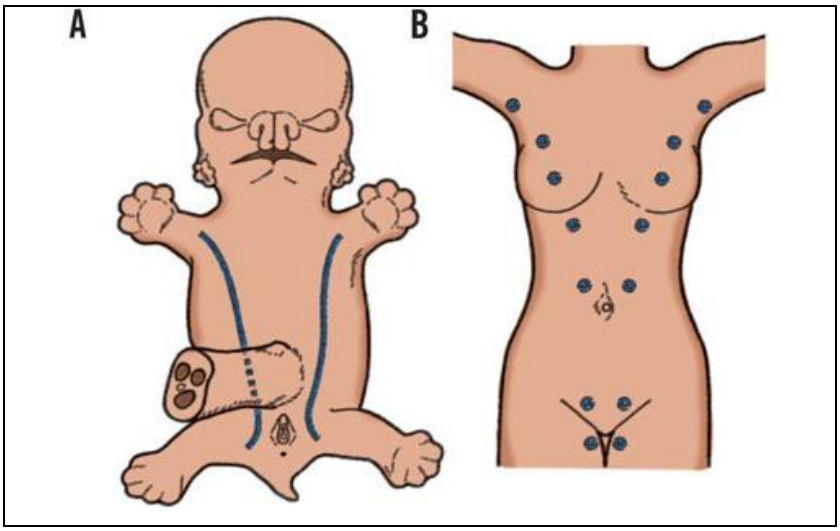
Aim of the work

The aim of this work is to discuss the different methods used for diagnosis and treatment of early breast carcinoma.

Anatomy of The Breast

Normal development:

In the young embryo a linear thickening of ectoderm appears called the milk ridge, which extends from the axilla obliquely to the inguinal region (fig.1). In animals, several mammary glands are formed along this ridge. In the human, the ridge disappears except for a small part in the pectoral region. This localized area thickens, becomes slightly depressed, and sends off 15 to 20 solid cords, which grow into the underlying mesenchyme. Meanwhile, the underlying mesenchyme proliferates and the depressed ectodermal thickening becomes used to form the nipple. At the 5th month, the areola is recognized as a circular pigmented area of skin around the future nipple **(Snell, 2004).**



(Fig.1)**A.** The milk lines in a generalized mammalian embryo. Mammary glands form along these lines. **B.** Common sites of formation of supernumerary nipples or mammary glands along the course of the milk lines in the human **(Skandalakis et al., 2006).**

Gross anatomy:

Each breast (right or left) is a rounded elevation present on the front of the upper part of the thorax, over the pectoral region. Over the centre of the breast the skin shows a dark circular area which is called the areola. In the centre of the areola there is a conical projection called the nipple **(Singh, 2002).**

The adult female breast is located within the superficial fascia of the anterior chest wall. The base of the breast extends from the second rib above to the sixth or seventh rib below, and from the sternal border medially to the midaxillary line laterally. Two-thirds of the base of the breast lies anterior to the pectoralis major muscle; the remainder lies anterior to the serratus anterior muscle (fig.2). A small part may lie over the aponeurosis of the external oblique muscle **(Skandalakis et al., 2006).**

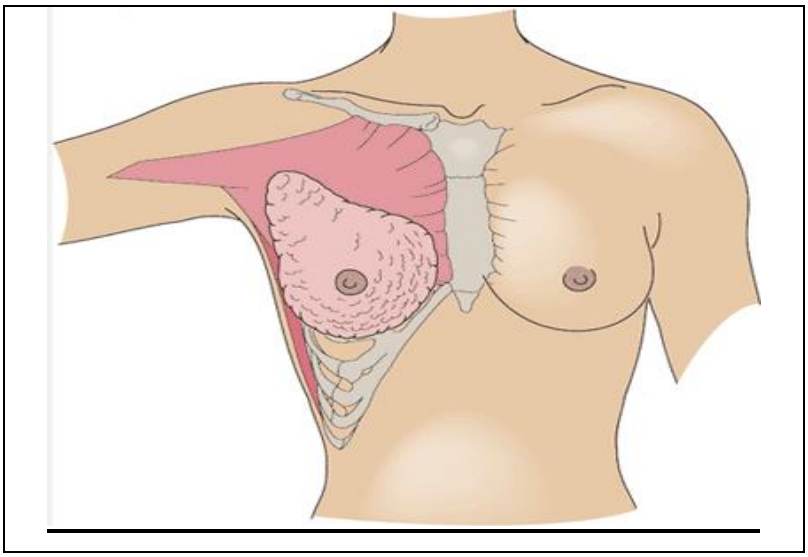


Fig.2 The adult female breast. The upper and medial portions of the breast rest on the pectoralis major muscle, and the inferolateral portion rests on the serratus anterior **(Morrow and Khan, 2006).**

From the upper lateral part of the gland an extension of glandular tissue passes through an aperture in the deep fascia over the axilla to enter the latter (The aperture is the foramen of Langer). This extension is called the axillary tail **(Singh, 2002).**

The lobule is the basic structural unit of the mammary gland. The number and size of the lobule vary enormously: they are most numerous in young women. From ten to over 100 lobules empty via ductules into a lactiferous duct, of which there are 15-20.each lactiferous duct is lined with a spiral arrangement of contractile myoepithelial cells and is provided with a terminal ampulla, a reservoir for milk or abnormal discharges **(Sainsbury, 2004).**

The ligaments of Cooper are hollow conical projections of fibrous tissue filled with breast tissue, the apices of the cones being attached firmly to the superficial fascia and thereby to the skin overlying the breast. These ligaments account for the dimpling of the skin overlying a carcinoma **(Sainsbury, 2004).**

The areola contains involuntary muscle arranged in concentric rings as well as radially in the subcutaneous tissue. The areolar epithelium contains numerous sweat glands and sebaceous glands, the latter of which enlarge during pregnancy and serve to lubricate the nipple during lactation (Montgomery's tubercles) **(Sainsbury, 2004).**

The nipple is covered by thick skin with corrugations. Near its apex lie the orifices of the lactiferous ducts. The nipple contains smooth muscle fibers arranged concentrically and longitudinally; thus, is an erectile structure which points outwards **(Sainsbury, 2004).**

A distinct space, the retromammary bursa, can be identified anatomically on the posterior aspect of the breast and resides between the deep layer of the superficial fascia and the deep investing fascia of the pectoralis major and the contiguous muscles of the thoracic wall. The retromammary bursa contributes to the mobility of the breast on the chest wall **(Bland, 2007).**

Small branching lymphatic and blood vessels course through the retromammary space between the posterior surface of the breast parenchyma and the fascia of the pectoralis major muscle; therefore the correct plane of dissection in a total mastectomy is beneath deep fascia of pectoralis muscle **(pass, 2001).**

Blood supply of the breast :

- **Arterial supply:**

It is not derived from a single source. The principle vascular supply of the breast enters the gland from its superolateral and superomedial borders. Only scant vascularity is derived from inferior aspect of the gland **(Lawson, 2002).**

The breasts are supplied by branches of the axillary artery, the internal thoracic artery, and some intercostal arteries. The axillary artery supplies blood from several branches, namely the superior thoracic, the pectoral branches of the thoraco-acromial artery, the lateral thoracic (via branches which curve around the lateral border of pectoralis major to supply the lateral aspect of the breast) and the subscapular artery. The internal thoracic artery supplies perforating branches to the anteromedial part of the breast. The second to fourth anterior intercostal arteries supply perforating branches more laterally in the anterior thorax. The second perforating artery is usually the largest, and supplies the upper region of the breast, and the nipple, areola and adjacent breast tissue (Fig.3) **(Johnson et al., 2008).**

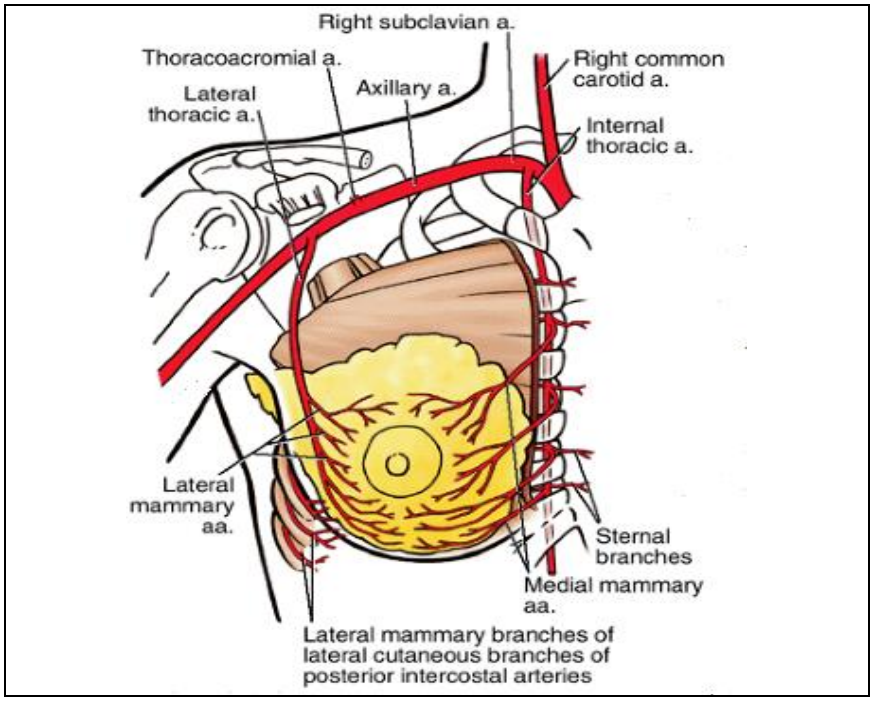


Fig.3 Arterial supply of the breast **(Moore and Agur, 2007).**

- **Venous drainage:**

There is a circular venous plexus around the areola. From this, and from the glandular tissue, blood drains in veins which accompany the corresponding arteries that supply the breast **(Johnson et al., 2008).**

The axillary, internal thoracic, and the third to fifth intercostal veins drain the mammary gland. These veins follow the arteries. The perforating tributaries from the medial half of the breast carry the greater part of the venous drainage. They enter the internal thoracic vein, which joins the brachiocephalic vein. The axillary vein is formed by the junction of the basilic and brachial veins. It lies medial or superficial to the axillary artery and receives one or two pectoral branches from the breast. As it crosses the lateral border of the first rib, the axillary vein becomes the subclavian vein. The intercostal veins communicate posteriorly with the vertebral venous