

# Local Recurrence after Conservative Breast Surgery

Essay

*Submitted for Partial Fulfillment  
of Master Degree in General Surgery*

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## List of Abbreviations

<b>ABBI</b>	<i>Advanced Breast Biopsy Instrumentation</i>
<b>ADH</b>	<i>Atypical Ductal Hyperplasia</i>
<b>AJCC</b>	<i>American Joint Committee on Cancer</i>
<b>ALH</b>	<i>Atypical Lobular Hyperplasia</i>
<b>ASCO</b>	<i>American Society of Clinical Oncology</i>
<b>BCS</b>	<i>Breast Conserving Surgery</i>
<b>BCT</b>	<i>Breast Conserving Therapy</i>
<b>BIRADS</b>	<i>Breast Imaging Reporting And Data System</i>
<b>CDK</b>	<i>Cyclin Dependent Kinase</i>
<b>CIS</b>	<i>Carcinoma In Situ</i>
<b>DCIS</b>	<i>Carcinoma In Situ</i>
<b>DVAB</b>	<i>Directional Vacuum Assisted Breast Biopsy</i>
<b>EGFR</b>	<i>Epidermal Growth Factor Receptor</i>
<b>EIC</b>	<i>Extensive Intraductal Component</i>
<b>ELUCA</b>	<i>Enlarged Lobular Unit with Columnar Alteration</i>
<b>ER</b>	<i>Estrogen Receptor</i>
<b>FDG</b>	<i>Fluoro-Deoxy Glucose</i>
<b>FNA</b>	<i>Fine Needle Aspiration</i>
<b>HELU</b>	<i>Hyperplasic Enlarged Lobular Unit</i>
<b>IBTR</b>	<i>Ipsilateral Breast Tumor Recurrence</i>
<b>IDC</b>	<i>Invasive Ductal Carcinoma</i>
<b>ILC</b>	<i>Invasive Lobular Carcinoma</i>
<b>LCIS</b>	<i>Lobular Carcinoma In Situ</i>
<b>LRR</b>	<i>Loco Regional Recurrence</i>
<b>NSABP</b>	<i>National Surgical Adjuvant Breast and Bowel Project</i>
<b>NSM</b>	<i>Nipple Sparing Mastectomy</i>

<b><i>NST</i></b>	<i>Non Special Type</i>
<b><i>OS</i></b>	<i>Overall Survival</i>
<b><i>PCNA</i></b>	<i>Proliferating Cell Nuclear Antigen</i>
<b><i>PET</i></b>	<i>Positron Emitted Tomography</i>
<b><i>PgR</i></b>	<i>Progesterone Receptor</i>
<b><i>SEER</i></b>	<i>Surveillance Epidemiology And End Result</i>
<b><i>SLNB</i></b>	<i>Sentinel Lymph Node Biopsy</i>
<b><i>SMM</i></b>	<i>Scintimammography</i>
<b><i>SSCP</i></b>	<i>Single Stranded Conformational Pleomorphism</i>
<b><i>TGF Beta</i></b>	<i>Transforming Growth Factor Beta</i>
<b><i>TNM</i></b>	<i>Tumor Node Metastases</i>
<b><i>UICC</i></b>	<i>International Union Against Cancer</i>
<b><i>VEGF</i></b>	<i>Vascular Endothelial Growth Factor</i>
<b><i>XRT</i></b>	<i>Radiotherapy</i>
<b><i>YB-1</i></b>	<i>Y-Box binding protein</i>

## INTRODUCTION

The diagnosis of breast cancer in young women presents particular challenges in surgical decision making and treatment. These challenges arise from concurrent genetic or other risk factors, potentially more aggressive tumor biology, larger tumor size, and psychosocial factors unique to young women (*Smith and Black, 2006*).

Options for surgical management of the primary tumor include breast-conserving surgery plus radiation therapy, mastectomy plus reconstruction, and mastectomy alone. Surgical staging of the axilla should also be performed (*Fisher et al., 2002*).

Today, the majority of small invasive and noninvasive breast cancers are treated with breast conservation therapy (BCT). The incidence of local-regional recurrence (LRR) after BCT for stage 0, I, and II patients ranges between 5% and 22% (*Huston et al., 2005*).

To tailor local treatment in breast cancer patients there is a need for predicting ipsilateral recurrences after breast-conserving therapy. After adequate treatment (excision with free margins and radiotherapy), young age and incompletely excised extensive intraductal component are predictors for local recurrence, but many local recurrences can still not be predicted (*Nuyten et al., 2006*).

Beyond established risk factors, genetic testing allows identification of high-risk patients (BRCA mutation carriers) who may benefit from bilateral mastectomy rather than BCS. Human genetic variation (SNPs/CNVs) and DNA methylation may be relevant for local failures assessment (*Ziogas and Roukos, 2009*).



## THE AIM OF THE WORK

To spot light on factors affecting local recurrence of  
after Conservative breast surgery.

## PATHOLOGY OF FEMALE BREAST CANCER

**B**reast cancer is the most common cancer in women in Developed western countries and is becoming even more significant in many developing countries. In Egypt, breast cancer is the most common cancer among women, representing 18.9% of total cancer cases with an age-adjusted rate of 49.6 per 100,000 populations (*Shoma et al., 2009*).

Histogenetically, breast cancer, ductal or lobular type, arises from the terminal duct-lobular unit. atypical duct hyperplasia (epitheliosis) and atypical lobular hyperplasia are the only two lesions of fibroadenosis that are considered precancerous (8% risk in 10 years).breast carcinoma begins as carcinoma insitu (CIS) either lobular (LCIS) or ductal (DCIS) then invades the basement membrane and reaches the stroma where it becomes vascularized and is capable of producing metastases (*Hoda and Rosen, 2002*).

### **Histological classification of female breast cancer**

#### ***I- Noninvasive (5%)***

DCIS 4%

LCIS 1%

#### ***II- Invasive (95%)***

- ***Duct carcinoma (85 %):***

- Non Special Type (NST) 70%.
- Special types 14%.
- Rare unfavorable 1%.

- ***Lobular carcinoma (10%).***

*(Hoda and Rosen, 2002)*

## **Carcinoma in situ (CIS)**

The enthusiasm for screening has led to the increasing detection of breast cancer at early carcinoma in situ (CIS) stage. Before mammography the incidence of non invasive carcinoma was only 5% but increased to 15% and more in screening series. By definition, the carcinoma is confined by the basement membrane within the duct or lobule, and it is classified into ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) with an incidence ratio of 4:1 respectively (*Fisher et al., 2001*).

## **Ductal Carcinoma in situ**

DCIS is divided into comedo and noncomedo type with marked biologic difference. Comedo carcinoma shows solid tumor in the ducts with central necrosis. Noncomedo group includes 5 subtypes: solid, cribriform, micro papillary, papillary and clining. The comedo type is the most common (about 40% of CIS) and most aggressive. The solid type may precede the comedo variant and is

biologically similar. The micropapillary type is most likely to be multicentric (*DeBock et al., 2004*).

### **Lobular carcinoma in situ**

LCIS is an incidental and uncommon lesion (1% of breast biopsies). It is often multicentric (50%) and bilateral. Histologically, the acini of the lobular unit are distended by uniform cells with obliteration of the lumen. LCIS has low risk to progress into an invasive carcinoma with an annual cumulative risk of 1% only. The developing invasive tumors are commonly ductal rather than lobular carcinomas (*DeBock et al., 2004*).

### **Invasive carcinomas**

The invasive breast carcinomas consist of several histologic subtypes; the estimated percentage are from contemporary population-based series of 135,157 women with breast cancer reported to the Surveillance Epidemiology and End Result (SEER) database of the National Cancer Institute between 1992 and 2001:

- Infiltrating ductal-76%
- Invasive lobular-8%
- Ductal/lobular-7%
- Mucinous (colloid)-2.4%
- Tubular-1.5%

- Medullary-1.2%
- Comedocarcinoma-1.6%
- Papillary-1%

*(Li et al., 2005)*

Other subtypes, including Paget's disease, metaplastic breast cancer, and invasive micropapillary breast cancer all account for fewer than 5% of cases (*Schnitt et al., 2004*).

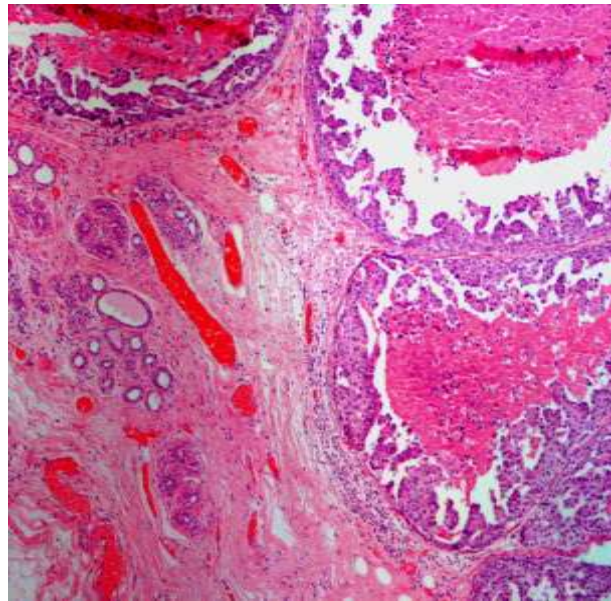
### **Invasive duct carcinoma (IDC)**

This large group of tumor accounts for the majority (85 to 95%) of invasive breast cancer cases and can be broadly divided into those of "no special type" or 'not otherwise specified'(NST, NOS) and "special type" tumors of distinctive appearance and behavior (*Fisher et al., 2001*).

#### **Non special type (NST):**

Various studies place the percentage of NST breast carcinomas at 50 to 75 percent of all invasive breast cancers. It is aggressive tumor. Grossly, it appears as firm (schirrhous) tumor, whitish gray in color with irregular stellate shape. Histologically, composed of pleomorphic cell population with central nuclei and evidence of ductal differentiation. It is usually graded into three grades according to tubule formation, anaplasia and mitosis. The relative frequency of grades is Grade I (18%), Grade II

(37%) and Grade III (45%). Lymphatic invasion by tumor is found in 10% of node negative patients and is a prediction of recurrence and metastatic spread. It is associated with high risk of local recurrence (24% in 5 years) after conservation surgery especially in premenopausal women (*Hoda and Rosen, 2002*).



**Fig. (1):** Breast lump showing infiltrating carcinoma breast with central necrosis (*Hoda and Rosen, 2002*).

### **Special types:**

#### **- *Tubular carcinoma***

A distinctive type of cancer breast characterized by proliferation of angulated tubules, lined by a single layer of flat epithelial cells and separated from each other by reactive fibroblastic stroma. The recognition of tubular carcinoma is important because of its good prognosis and rarity of axillary metastases (*Papadatos et al., 2001*).

**- *Mucinous carcinoma***

In this form the uniform tumor cells are accompanied by large amount of extra-cellular mucin lakes. A pure and mixed variant of mucinous carcinomas have been recognized. The pure typing cells carcinoma is known to have amore favorable prognosis than the mixed type (*Annank et al., 2001*).

**- *Signet ring cell carcinoma***

It is clear now that signet ring is not a variant of mucinous carcinoma because of the different clinical and biological behaviour of the lesion. Signet ring carcinoma may be either ductal or lobular in nature. Carcinoma with prominent signet cell component behaves more aggressively and tends to metastasize to unusual sites (*Omar and Contesso, 2001*).

**- *Medullary carcinoma***

The tumor has fleshy soft consistency, composed of anastmozing cords and sheets of round tumor cells with abundant cytoplasm, round vesicular nuclei with frequent mitotic figures, and separated by loose connective tissue with moderate to pronounced lymphatic infiltration. This lymphatic reaction may be linked to favorable prognosis (*Omar and Contesso, 2001*).

**- *Inflammatory carcinoma***

This type is considered as the most malignant type of breast cancer. It represents 1-2% of breast cancer in western literature. However, in Egypt and in North Africa it is not