



# **Assessment of Surgical Margins in Lumpectomy Sample: *Geography versus Biology***

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Breast Disease Centers  
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# The Plan

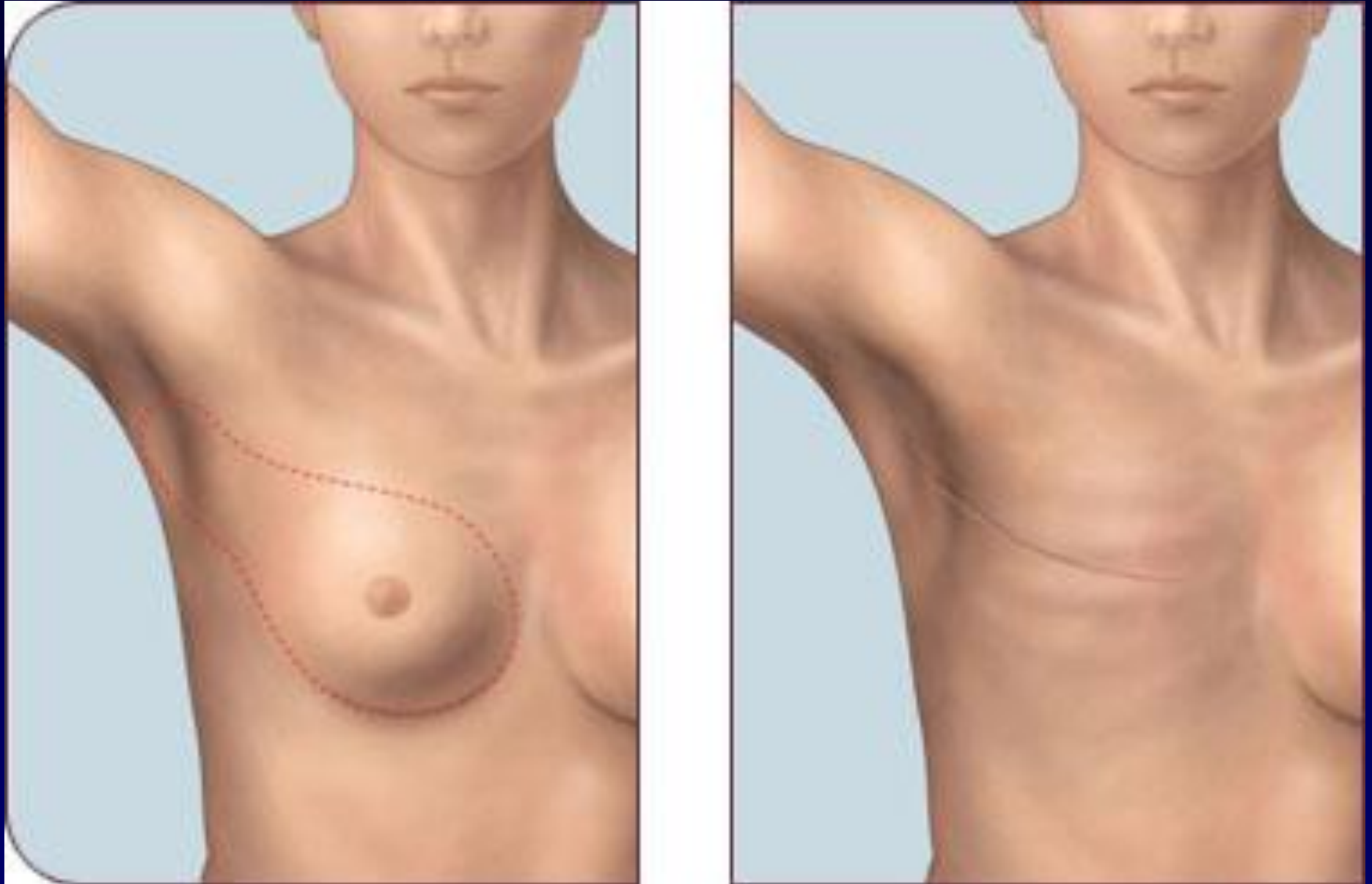
- To provide an overview of the challenges associated with assessment of lumpectomy surgical margins
- To highlight risk factors that contribute to increased rate of local recurrence

# Breast Cancer

## Advances

- Introduction of minimally invasive diagnostic and therapeutic procedures
  - Fine needle aspiration biopsy and core needle biopsy versus open surgical excision
  - Conservation therapy versus mastectomy
  - Sentinel lymph node biopsy versus axillary dissection

# Breast Cancer



# Breast Cancer

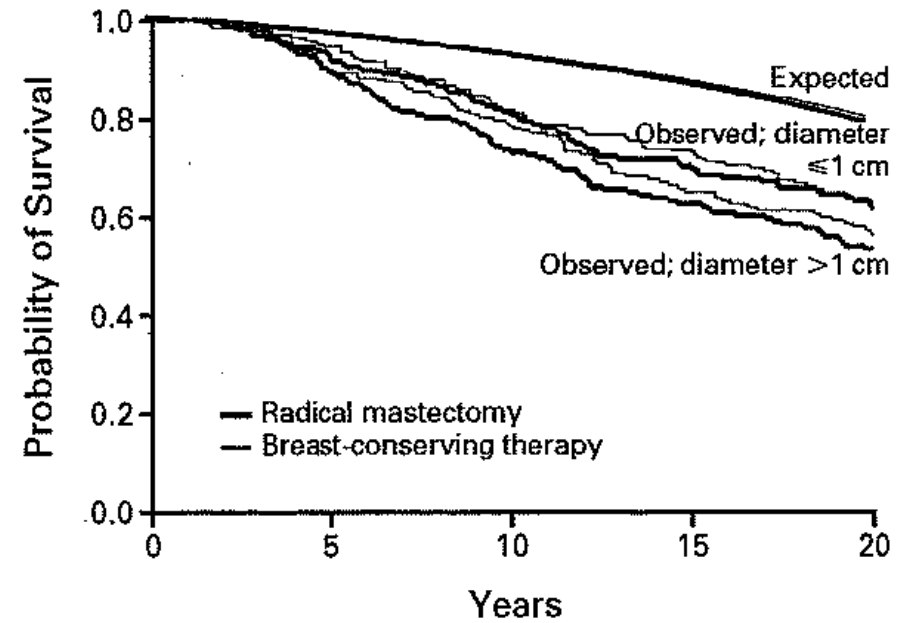
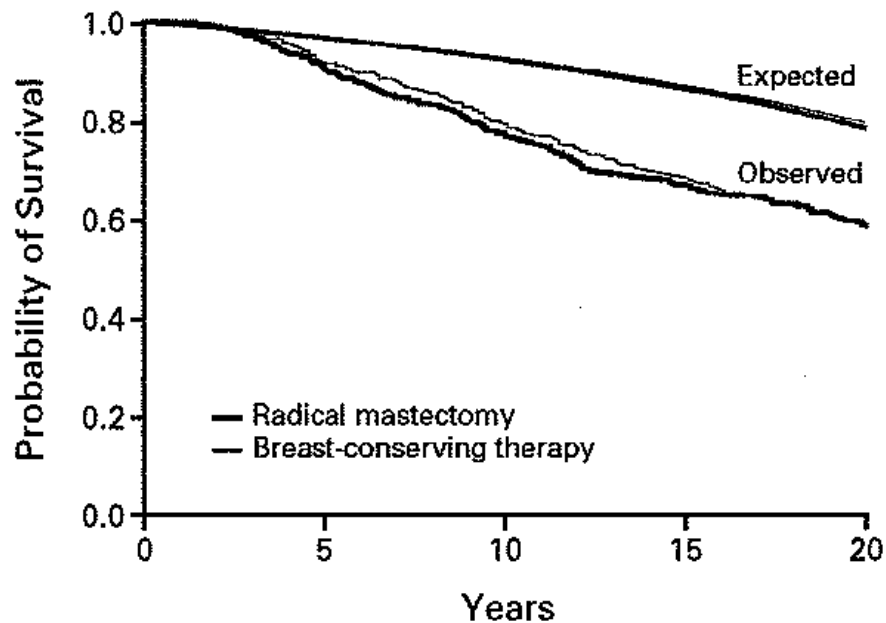
## Definition of Conservation Therapy

**Excision of the primary breast tumor with a rim of adjacent normal breast tissue sufficient to achieve negative resection margins followed by irradiation.**



# Breast Cancer

## BREAST-CONSERVING SURGERY VERSUS RADICAL MASTECTOMY



Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year followup of a randomized Study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002; 347:1227–31.

Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; 347:1233–41.



# Breast Cancer

## Current Trend

- Breast conservation therapy has become the preferred surgical intervention for breast cancer therapy
- The major challenge is the unpredictability of the chances of local recurrence



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You do not have to lose your breast to breast cancer.  
There are alternatives.

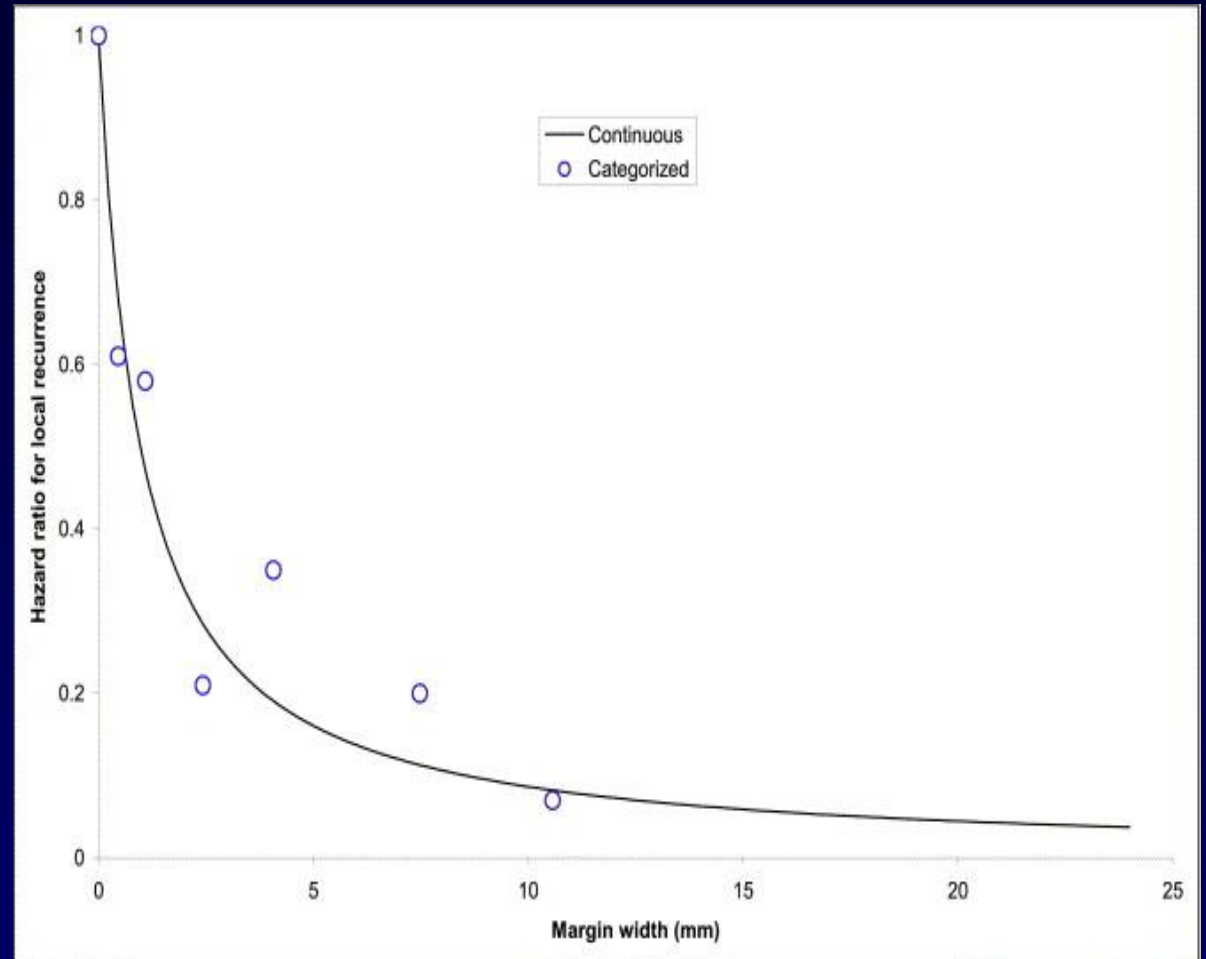
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# Breast Cancer

There is a direct relationship between positive surgical margins and increased rate of local recurrence



*H.R. MacDonald et al: The American Journal of Surgery 190:521-525, 2005*



# Studies Reporting on Local Recurrences in Patients Receiving Conventional Histologic Evaluation on Lumpectomy Margins

Investigators	No. of Patients	Follow-up (mo)	Local recurrence with negative margins (%)	Local recurrence with positive margins (%)
Pierce et al.	396	60	3	13
Van Dongen et al.	431	96	9	20
Heimann et al.	869	60	2	11
Burke et al.	306	60	2	15
Fourquet et al.	518	103	8	29
Clarke et al.	436	120	4	10
Mansfield et al.	704	120	8	16
Slotman et al.	514	68	3	10
Veronesi et al.	289	79	9	17
DiBiase et al.	453	120	13	31

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## Summary of Current Status

- **Currently there is a relatively high rate of positive resection margin together with a clear impact on local recurrence and cosmetic results**
- **Positive surgical margins range from 20% to 40% of patients who undergo breast conservation therapy**
- **Risk factors associated with positive margins are predominantly related to tumor biology, patients characteristics, surgical skills and assessment of surgical lumpectomy margins**

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## Current Challenges

- **Optimal initial surgical excision**
- **Appropriate intraoperative assessment of lumpectomy surgical margins**
- **Recognition of the impact of individualized patient characteristics and tumor biology**

# Breast Cancer

## Optimal Initial Surgical Excision

### ○ Clinical presentation

- Palpation of tumor is limited by

- Multicentric disease

- Dense breasts in young women

### ○ Preoperative mammography

- 94% sensitive, 61% specific

### ○ Preoperative ultrasonography

- More accurate for assessment of tumor size and growth pattern

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## Optimal Initial Surgical Excision

### ○ Preoperative MRI

- Detects additional disease in 16% of breast cancer patients
- Contributes to increased number of mastectomies
- Limited value to improve preoperative margin assessment

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## Suggested Modalities of Surgical Approach to Conservation Therapy

- Wire-guided localization
- Ultrasound-guided resection
- Radiofrequency-based intraoperative margin assessment device
- Intraoperative specimen radiography
- Cryoprobe-assisted localization



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## Suggested Modalities of Surgical Approach to Conservation Therapy

- Emerging

- Positron emission tomography imaging

- Radio-guided occult lesion localization

- Near-infrared fluorescence optical imaging

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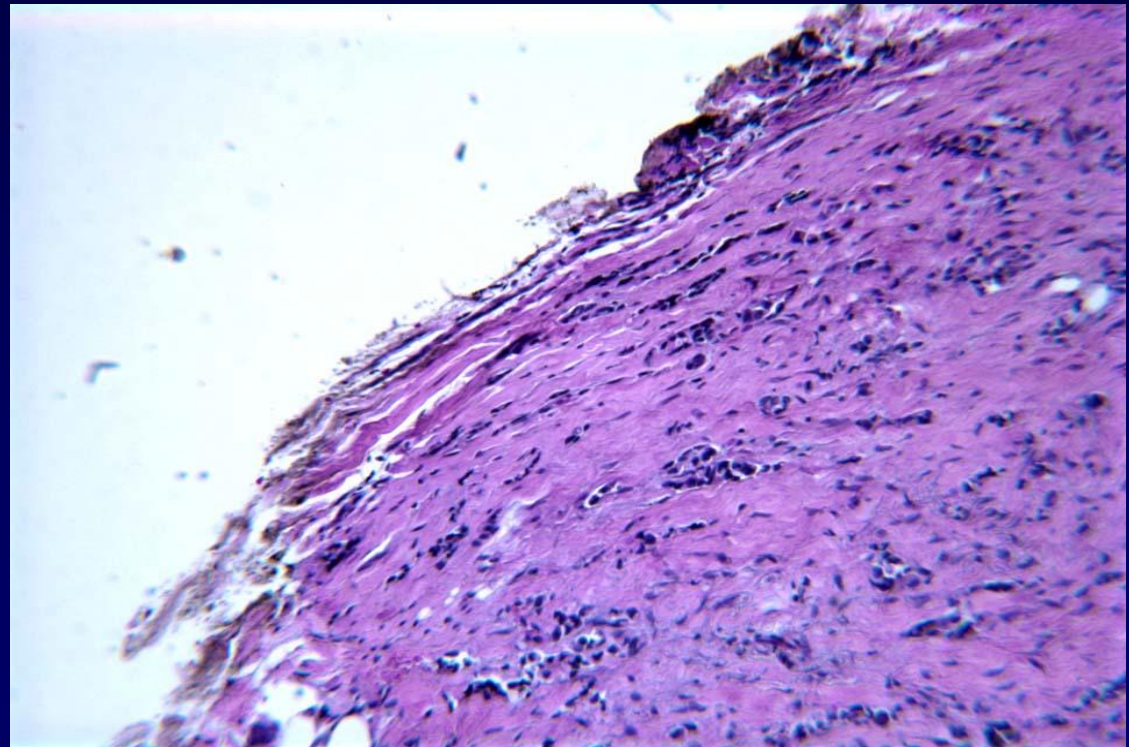
## Current Changes

- Appropriate intraoperative assessment of lumpectomy surgical margins

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## Definition of the positive surgical margin

- Closest microscopic distance between the inked lumpectomy tissue edge and the tumor



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**There is no universally accepted definition for the optimal tumor-free margin**

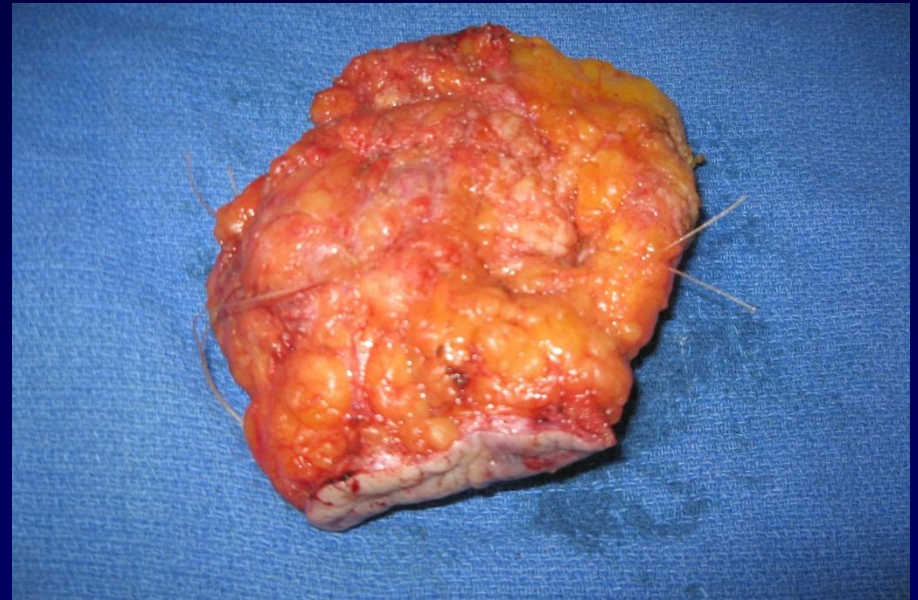
## **o The Choices**

- No tumor at inked surgical margins**
- No tumor within 1.0-5.0 mm of inked surgical margin**
- No tumor within 10 mm of inked surgical margin**

# Breast Cancer

## What Does A Pathologist Need From a Surgeon?

- Proper orientation of the original biopsy specimen (for example, short suture in the superior margin, long suture in the lateral margin) will allow identification of the individual margin surfaces involved with tumor.
- Submission of the specimen as a single intact tissue fragment without surface defects or incisions



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## Pathologic Assessment of Lumpectomy Surgical Margins

### Intraoperative Consultation

- Gross inspection
- Frozen section
- Imprint cytology



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## Pathologic Assessment of Lumpectomy Surgical Margins

### Frozen Section: The Challenges

- Labor intensive
- Technically difficult to freeze and cut adipose tissue
- Time consuming and expensive
- Tissue loss during the procedure

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## Pathologic Assessment of Lumpectomy Surgical Margins

### Imprint Cytology: The Procedure

- After specimen orientation, different margins are identified
- Labeled glass slides are prepared corresponding to six different margins
- Imprints are made from each site by pressing the glass slide to the margin of interest
- Slides are air dried, fixed , stained and immediately examined

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PATHOLOGY DEPT  
*Anterior*

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*posterior*

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*Superior*

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*Inferior*

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*lateral*

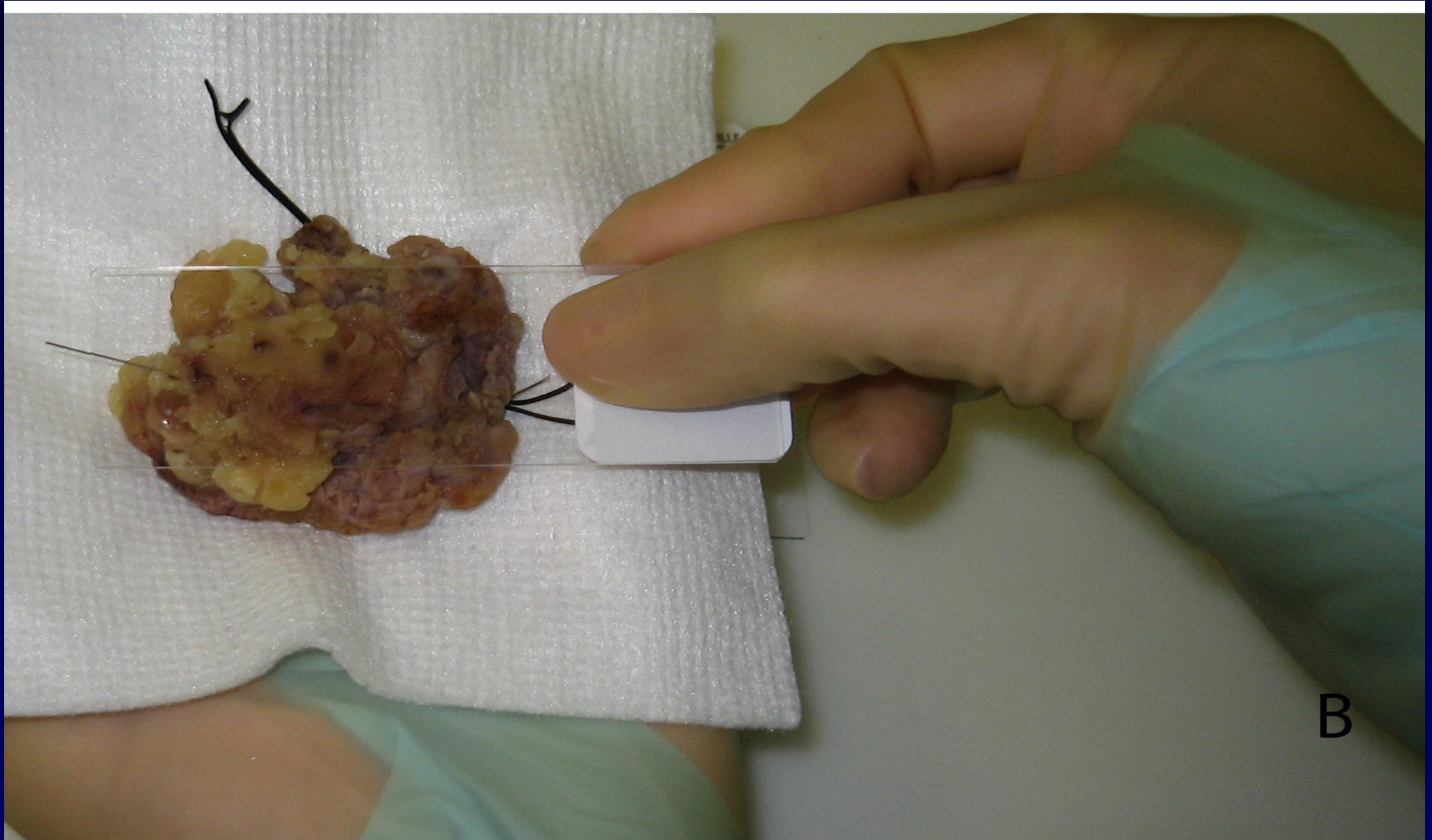
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*Medial*



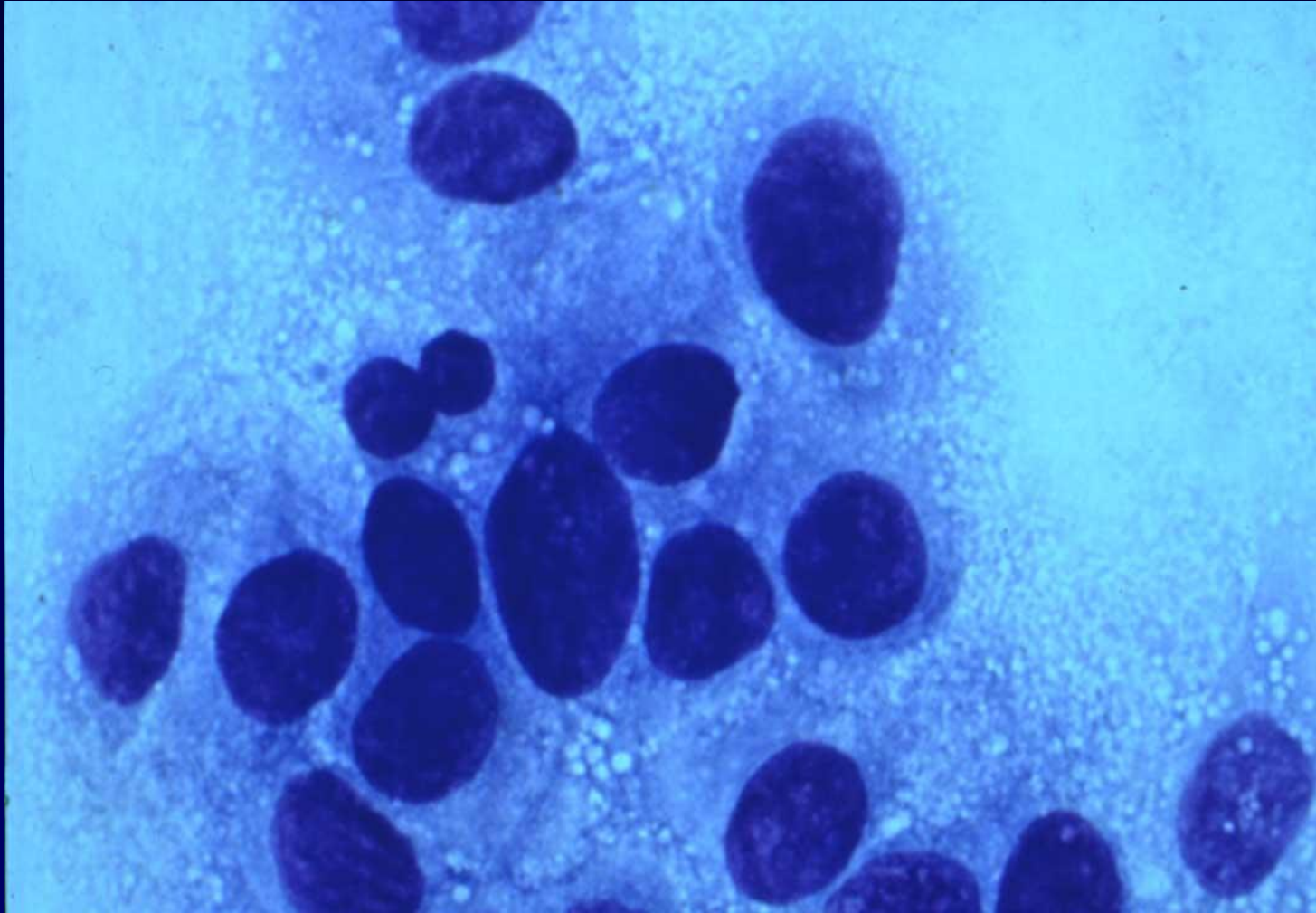
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# Breast Cancer



# Breast Cancer



# Breast Cancer

## Pathologic Assessment of Lumpectomy Surgical Margins

### Imprint Cytology: The Advantages

- Provides complete microscopic analysis of the entire lumpectomy specimen surface area
- It is rapid, easy to use and cost effective
- Saves tissue for permanent sectioning and rendering an accurate diagnosis



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## Pathologic Assessment of Lumpectomy Surgical Margins

### The Procedure

- Positive imprint cytology results in the re-excision of the correlated margin
- After imprint cytology, the margins are inked and sectioned bread loaf style



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## Pathologic Assessment of Lumpectomy Surgical Margins

Retrospective correlative analysis of 510 imprint  
cytology with the corresponding permanent  
sections

- Sensitivity of 97%
- Specificity of 99%

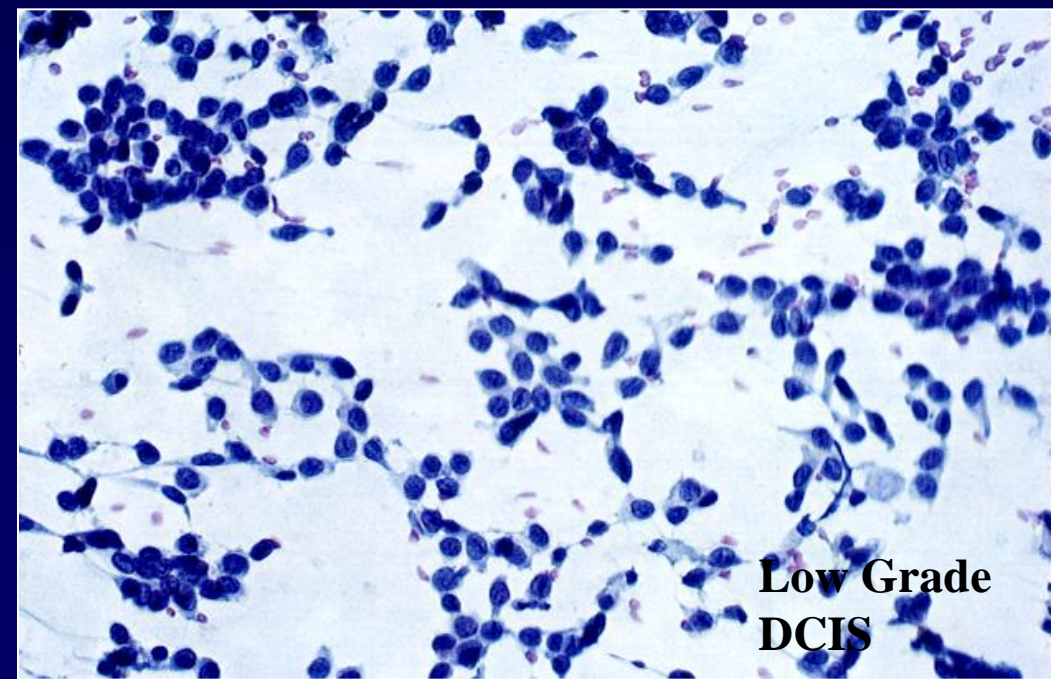
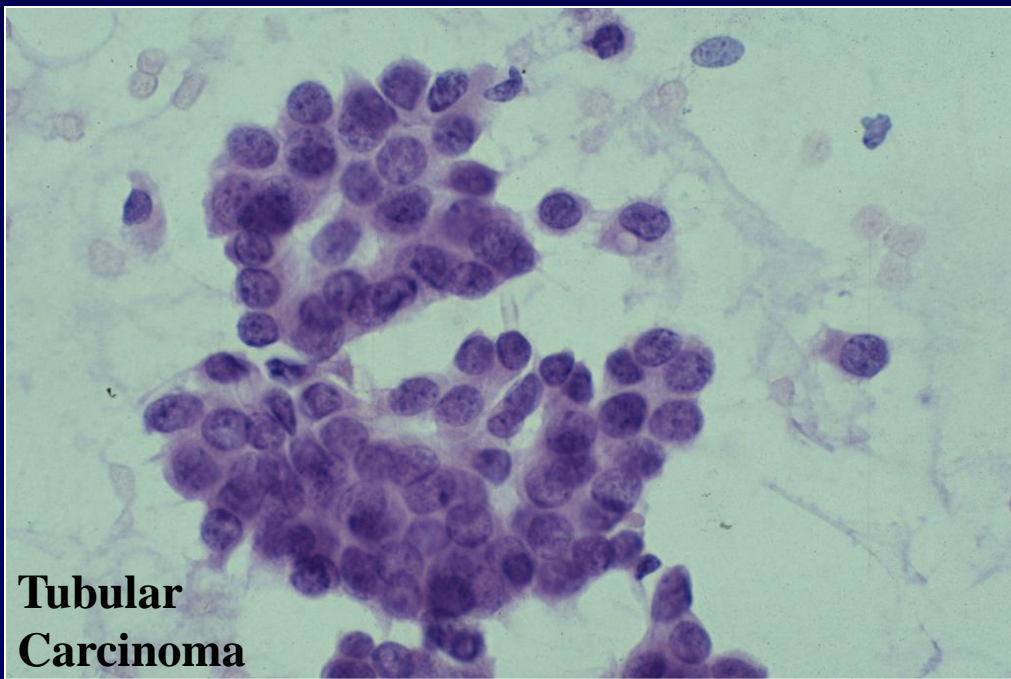
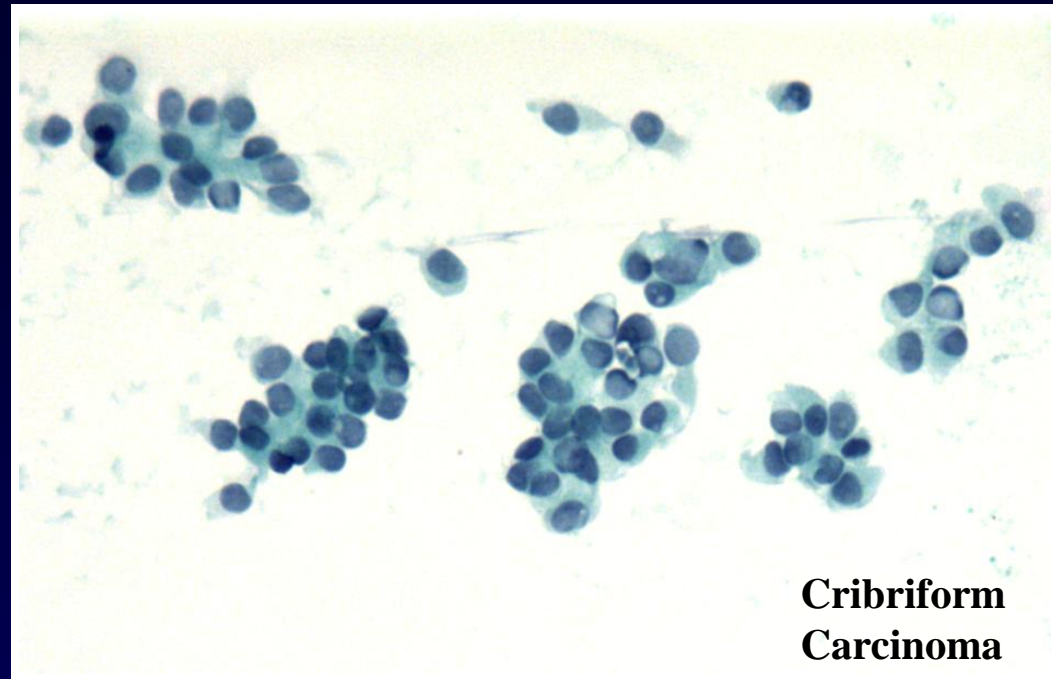
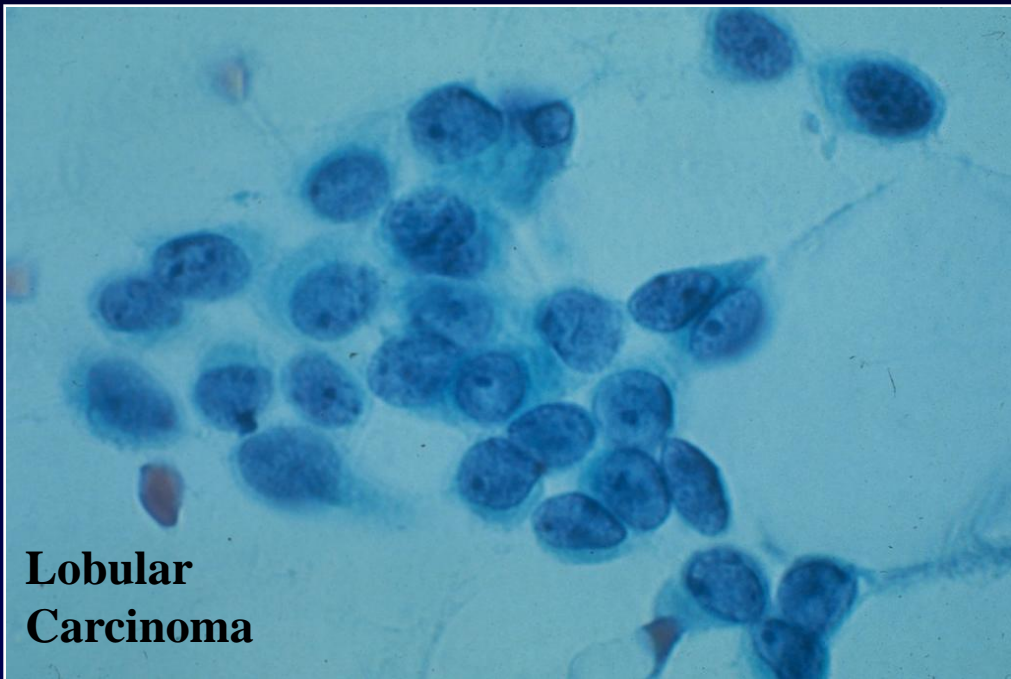
Bakhshandeh M, Masood S et al Diagn Cytopathol 35 (10):656-9,2007.

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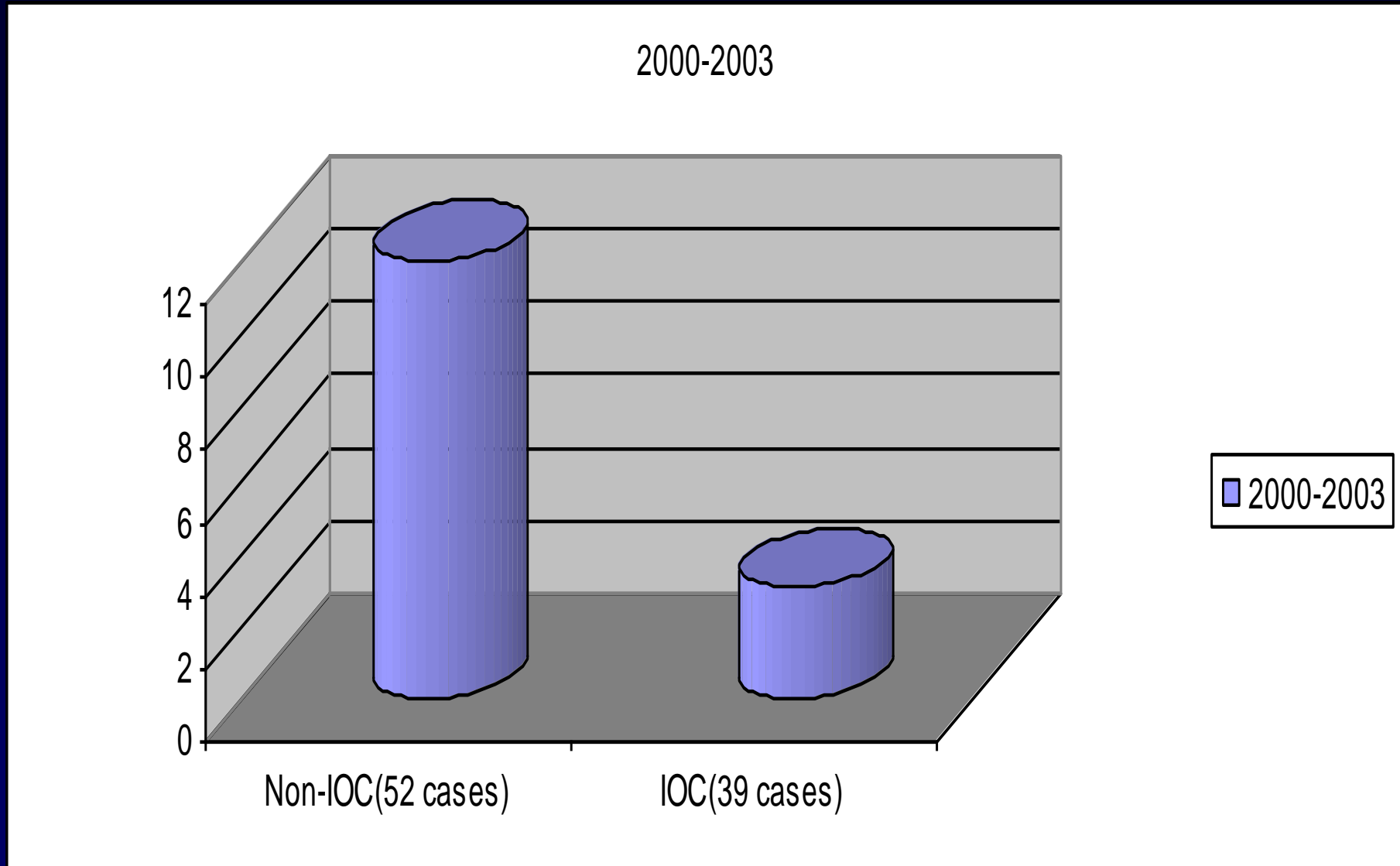
## Pathologic Assessment of Lumpectomy Surgical Margins

- Experience and interest in breast cytopathology
- Familiarity with tumors with morphologic pattern and insignificant atypia
  - Low grade breast carcinoma
  - Infiltrating lobular carcinoma





# Number of Mastectomies



Using Graph Pad InStat statistical analysis software to perform a two tailed unpaired t test the difference in mastectomy and re-excisions rates between the 2 groups was statistically significant ( $p < .0001$ )

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## Current Challenges

- **Recognition of the impact of individualized patient characteristics and tumor biology**

# Breast Cancer

Several independent risk factors for increased local recurrence:

- Age at diagnosis
- High nuclear grade
- Extensive ductal carcinoma-in-situ
- Unfavorable tumor type
- Large tumor size
- Multifocal Disease
- **Positive margin status**

# Breast Cancer

**Several independent risk factors for increased local recurrence:**

- Negative hormone receptor status**
- Positive HER-2/neu oncogene expression/amplification**
- Triple negative breast cancer cases**



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**Risk factors for reduced local recurrence:**

- **Breast cancer patients who receives:**
  - **Chemotherapy**
  - **Hormone Therapy**
  - **Radiation Therapy**

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## Future Directions

- **Realization of the fact that the local presence or absence of tumor cells may no longer be the only critical factor in reducing local recurrence**
- **Looking beyond geography and focusing on tumor biology**

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## Future Directions

- In the United States, a plan is underway to initiate a consensus development process to better define the definition of negative margins
- American College of Surgeons Oncology Group, American Society of Radiation Oncology and College of American Pathology are the three major participants in the process

# Breast Cancer

## Future Directions

- **Multidisciplinary research should focus on techniques that provide the surgeon with effective tools to obtain an optimal balance between safe surgical margins, good cosmetic results and better patient outcome**

