

Evolution in Breast Cancer Surgical Management

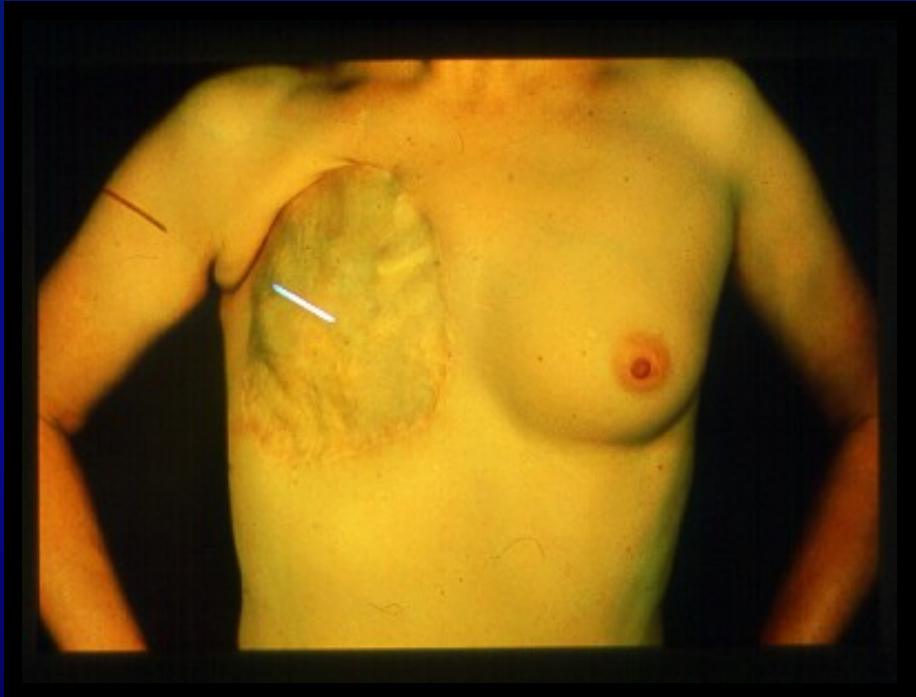
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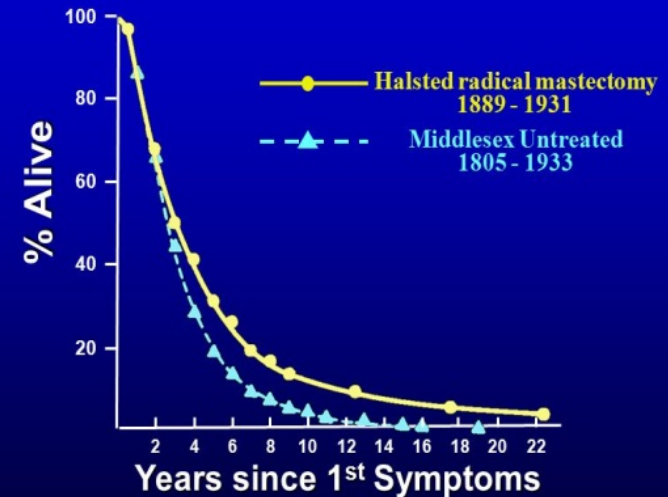
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A Century-Long Unified Paradigm for BC Therapy



Untreated vs. Halsted Patients



Henderson & Canellos, NEJM 1980

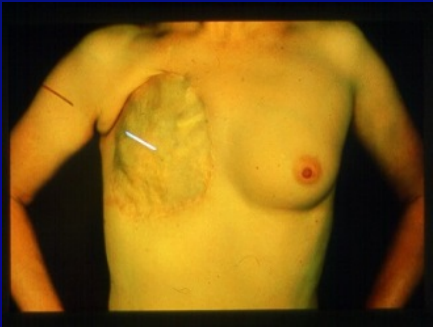
- No adjuvant systemic therapy
- XRT for more advanced presentation

Evolution in Breast Cancer Management

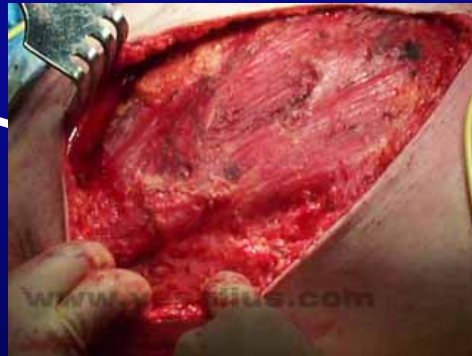
- Changes in the biologic understanding of breast cancer spread and dissemination in the 1960s led to the development of two testable clinical hypotheses regarding early breast cancer management:
 - **De-escalation of surgical therapy** would not affect long-term outcomes
 - **Development and escalation of adjuvant systemic therapy** would improve long-term outcomes

De-escalation of Surgical Therapy

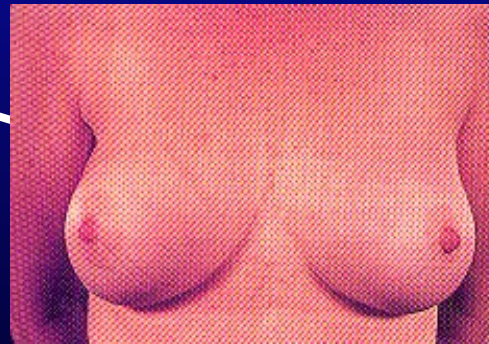
RM



MRM



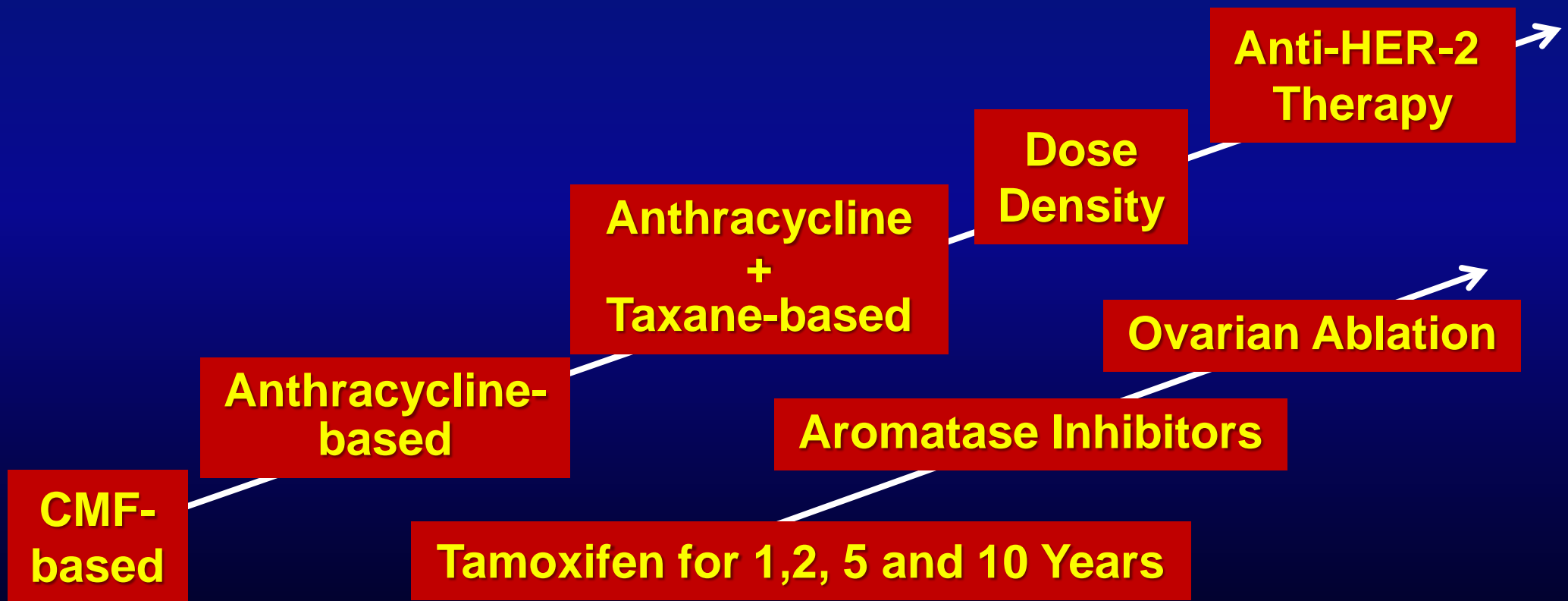
BCT



SLNB



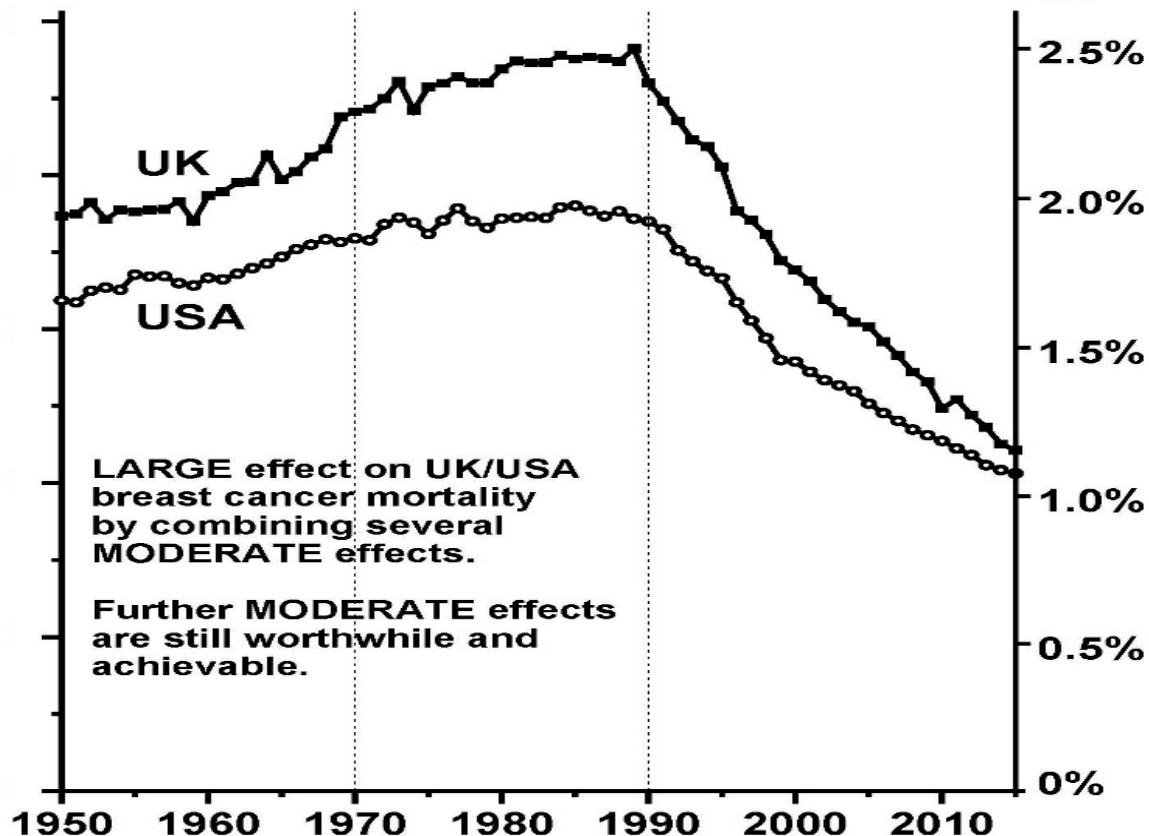
Establishment and Escalation of Adjuvant Systemic Therapy



Breast Cancer Mortality in US and UK

UK & USA BC Mortality 1950-2015

Risk at age 35 of dying from breast cancer <70



Outline

- **Breast cancer diagnosis: core needle biopsy**
- **Breast MRI and axillary ultrasound for preoperative local staging**
- **Surgical management of the primary breast tumor**
- **Surgical management of the axilla: sentinel lymph node biopsy**
- **Surgical management of patients receiving (preoperative) neoadjuvant chemotherapy**

Breast Cancer Diagnosis: Core Needle Biopsy

Core Needle Biopsy

- **Advantages:**

- Differentiates between **invasive and non-invasive** cancer
- **One-stage surgical procedures** (including SLNB before lumpectomy)
- **Adequate material for biomarkers** (ER/PR/HER2)
- **Neoadjuvant chemo** can be given with invasive BC on core

- **Limitations:**

- False negative rate **1-2 %**
- With **non-invasive cancer** on core, **invasive cancer** may still be present in **10-25%** of cases
- With **atypical hyperplasia** on core, **invasive or non-invasive cancer** may be present in **15-40 %** of cases and open biopsy should follow

Breast MRI and Axillary Ultrasound for Preoperative Local Staging

MRI in Preoperative Local Staging

- Because of its high sensitivity, MRI is being **increasingly utilized** in the preoperative local staging of BC
- MRI **identifies additional cancer foci**, otherwise undetected by clinical assessment and conventional imaging (in both breasts)
- **No consensus** on whether **MRI improves patient outcomes** in terms of rates of margin positivity, reoperation rates, in-breast recurrence and overall survival
- **MRI can increase unnecessary mastectomy rates**

MRI in Preoperative Local Staging

Potential Candidates

- **Not necessary for all patients who undergo BCS**
- **Can be helpful in:**
 - **Patients with mammographically dense breasts and ill-defined tumors**
 - **Patients with invasive lobular carcinoma**
 - **Patients with multi-centric disease**
 - **Patients who are candidates for neoadjuvant chemotherapy**
- **MRI is essential in patients who present with axillary adenopathy and clinically and radiographically occult breast lesions**

Axillary Ultrasound for Preoperative Local Staging

- **Ultrasound of the axilla with FNA/core bx of indeterminate/suspicious nodes:**
 - **Simple, minimally invasive**
 - **Can provide useful clinical information (avoid SNB, demonstrate direct chemosensitivity to preoperative (neoadjuvant) chemotherapy and mark involved lymph nodes for future resection)**

Surgical Management of the Primary Breast Tumor

Considerable Evolution in Surgical Management of the Primary Breast Tumor

- Evolution in the paradigm of surgical management over the past 30 years
- In the 1980's and 1990's the trend was towards increasing use of breast conserving procedures without compromising patient outcome
- Breast conserving surgery became the **preferred** surgical treatment for the majority of early-stage BC patients

Invasive Breast Cancer

Breast Conserving Surgery vs. Mastectomy

- From 1973-1989, six randomized trials
- Two overview analyses
- Compared mastectomy to BCS \pm XRT
- Maximum tumor size for entry: 2-5 cm
- **No differences in overall survival**
- **XRT significantly reduced the rates of IBTR**

Optimal Lumpectomy Candidates

- Tumors < 5 cm in diameter
- Limited to one quadrant
- Breast size/tumor size ratio permitting lumpectomy with acceptable cosmetic result
- Patient is desirous of breast preservation
- Negative margins following resection
- No contraindications to breast XRT

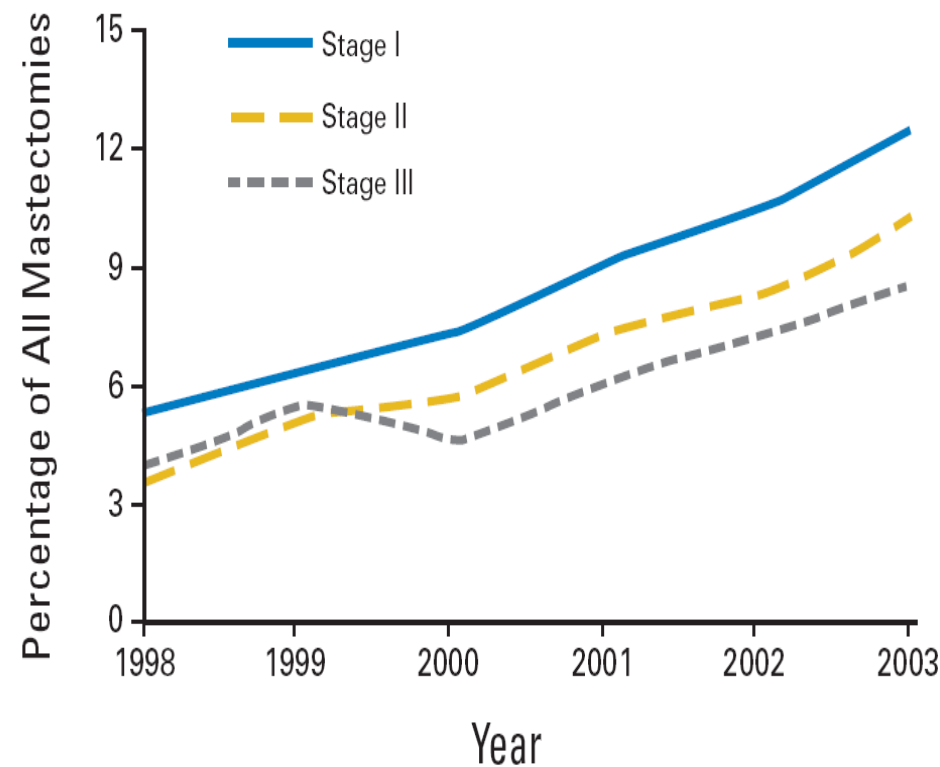
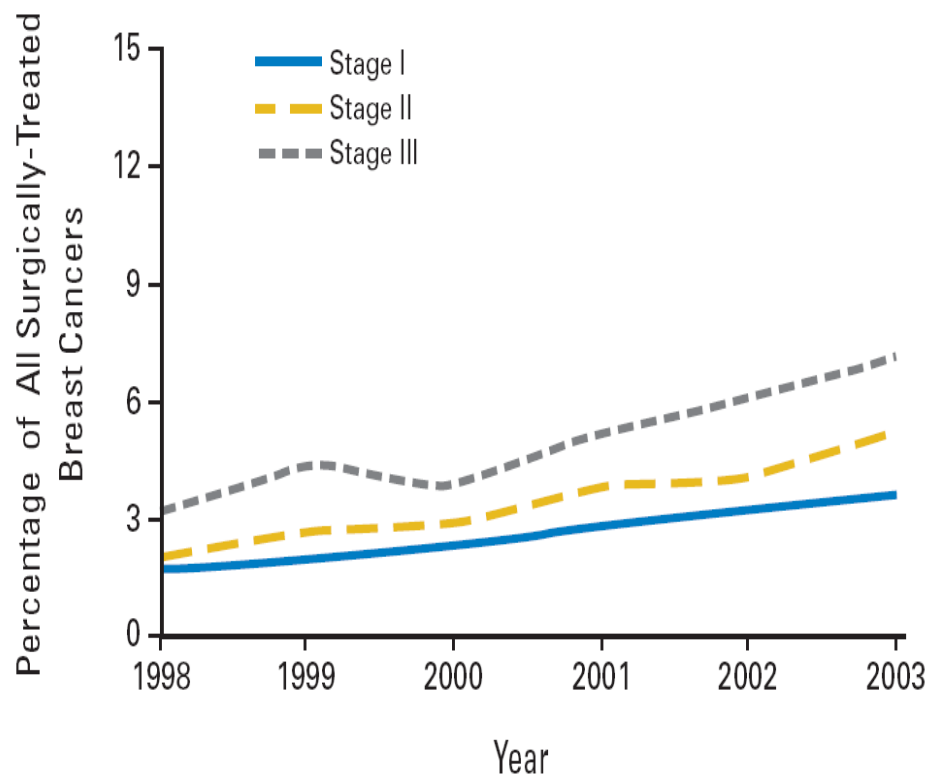
SSO/ASTRO/ASCO: Invasive BC Margins Consensus Guideline

- Use of **no ink on tumor** as the **standard for an adequate margin** in IBC in the era of multidisciplinary Rx results in **low rates of IBTR**
- This approach has the potential to **decrease re-excision rates, improve cosmetic outcomes, and decrease healthcare costs**

SSO/ASTRO/ASCO: DCIS Margins Consensus Guideline

- Use of a **2-mm margin** as the standard for an adequate margin in DCIS treated with **whole-breast irradiation** is associated with **lower rates of IBTR** and has the potential to **decrease re-excision rates**, **improve cosmetic outcomes**, and **decrease health care costs**
- **Clinical judgment** should be used in determining the **need for further surgery** in patients with **negative margins narrower than 2 mm**

A Recently Observed Trend: Increase in the Incidence of Contralateral Prophylactic Mastectomy



Nipple-Sparing Mastectomy

Rationale

- In more recent mastectomy series nipple involvement is seen in 6-11%
- Several series have demonstrated the feasibility of NSM but long term FU is needed
- **Main advantages:** cosmesis and preservation of nipple sensation (variable)
- **Potential concerns:** nipple necrosis, long-term oncologic safety

Nipple-Sparing Mastectomy

Appropriate Candidates

- **Tumor size 3 cm or less**
- **Tumor location at least 2 cm from the nipple-areola complex**
- **Absence of multicentricity**
- **Absence of segmental malignant calcifications extending to the nipple-areola complex**
- **Clinically negative nodes**
- **Negative intraoperative biopsy of nipple-areola complex**

Surgical Management of the Axilla: Sentinel Lymph Node Biopsy

Surgical Management of the Axilla

Sentinel Lymph Node Biopsy

- **About 75% of patients with operable breast cancer have negative axillary nodes upon dissection**
- **There is still significant morbidity from the procedure**
- **An alternative method for identifying histologically node-positive patients is desirable**

Sentinel Node Concept

- Metastasis to regional lymphnodes is **not a random event** but instead there is **orderly progression** of tumor cells within the lymphatic system
- Primary draining or **sentinel node** is the first to contain metastases
- Biopsy of this **sentinel node** can accurately predict axillary involvement



Lymphatic Mapping and SN Identification Technique

Lymphoscintigraphy



Gamma-Probe

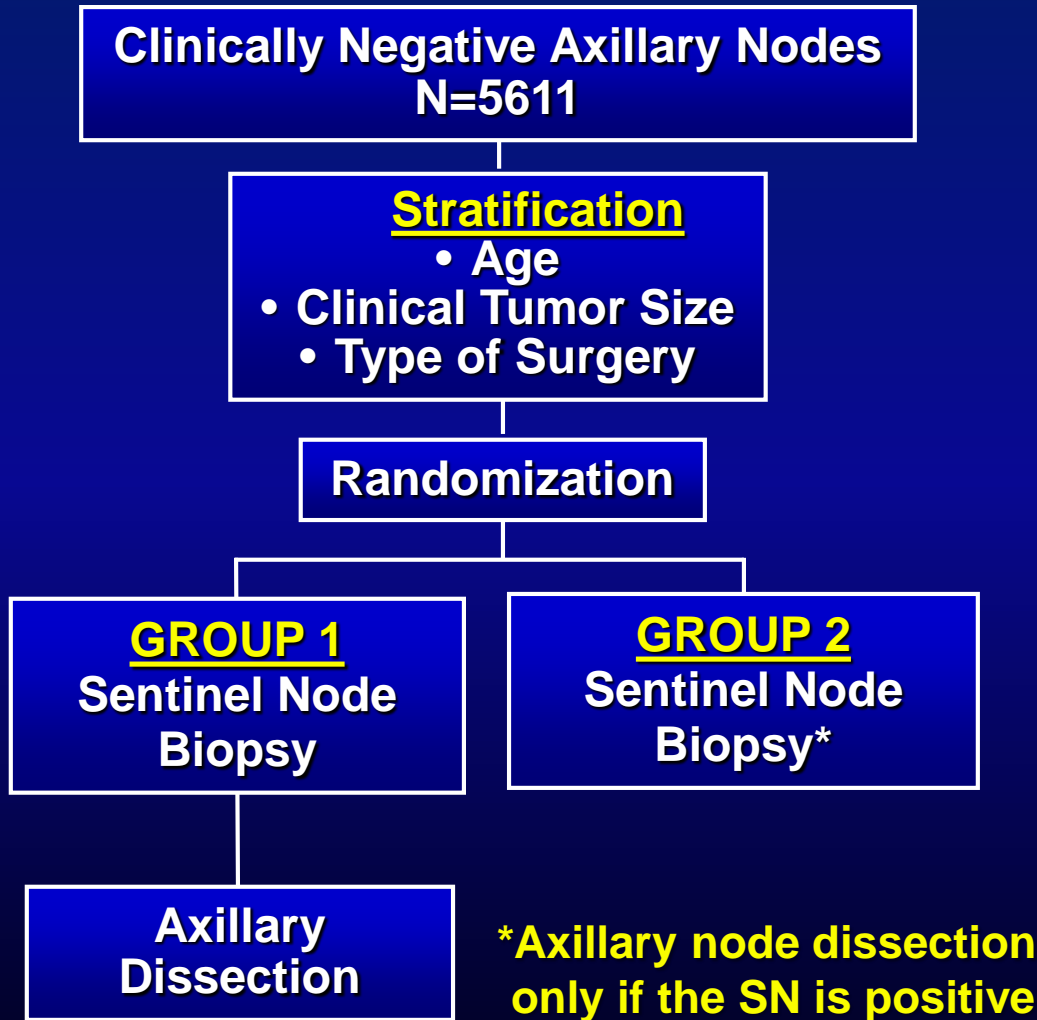


Blue-Dye Injection



Management of the Axilla in Patients With Negative Sentinel Node(s)

NSABP B-32 Schema



- ID Rate: **97%**
- FN Rate: **9.7%**
- No differences in disease-free survival and overall survival
- Axillary recurrence with SLNB alone: **0.5%**
- **Significant reduction in arm morbidity:**
 - Range of motion
 - Arm numbness/tingling
 - Lymphedema

Management of the Axilla in Patients With Positive Sentinel Node(s)

ACOSOG Z0011

**Clinically Negative Patients
1-2 Positive SNs by H & E**

**Target Accrual: 1900 pts (500 deaths)
Actual Accrual: 991 pts (94 deaths)**

**Lumpectomy +
Breast XRT**

Randomization

**Completion
ALND
(n=445)**

**No Further
Surgery
(n=446)**

N=420

N=436

Included in Primary Analysis

Endpoint	SLNB Alone	SLNB + ALND	P value
3 or More Positive Nodes	5%	17.6%	<0.001
Additional Positive Nodes on ALND	N/A ??	27.3% 97 pts	
5-Year In-Breast Recurrence	2.1%	3.7%	0.16
5-Year Axillary Nodal Recurrence	1.3%	0.6%	0.44
5-Year Overall Survival	92.5% (90-95.1)	91.8% (89.1-94.5)	HR: 0.87 0.25
5-Year DFS	83.9% (80.2- 87.9)	82.2% (78.3-86.3)	HR: 0.88 0.14

IBCSG 23-01 Trial

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- Tumor Size ≤ 5 cm
- Clinically Node Negative
- ≥ 1 Micrometastases in the Sentinel Node

Randomize
N=934

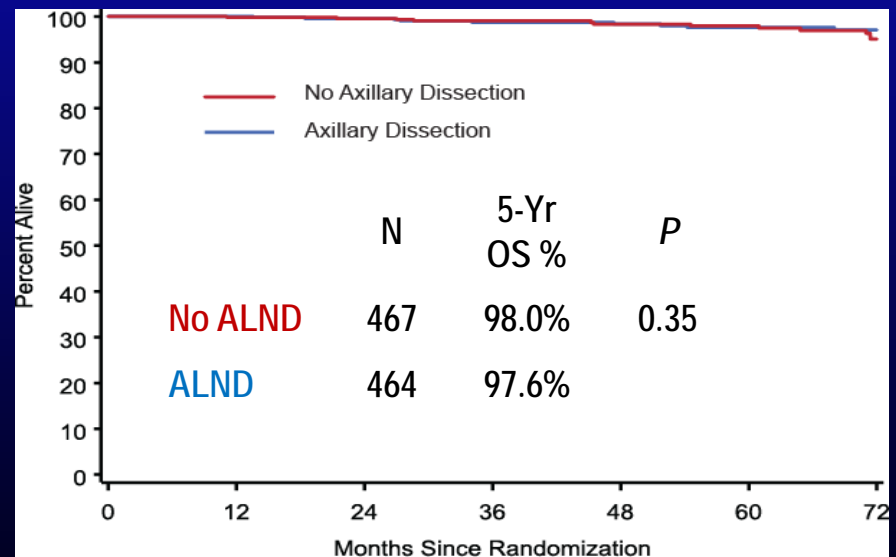
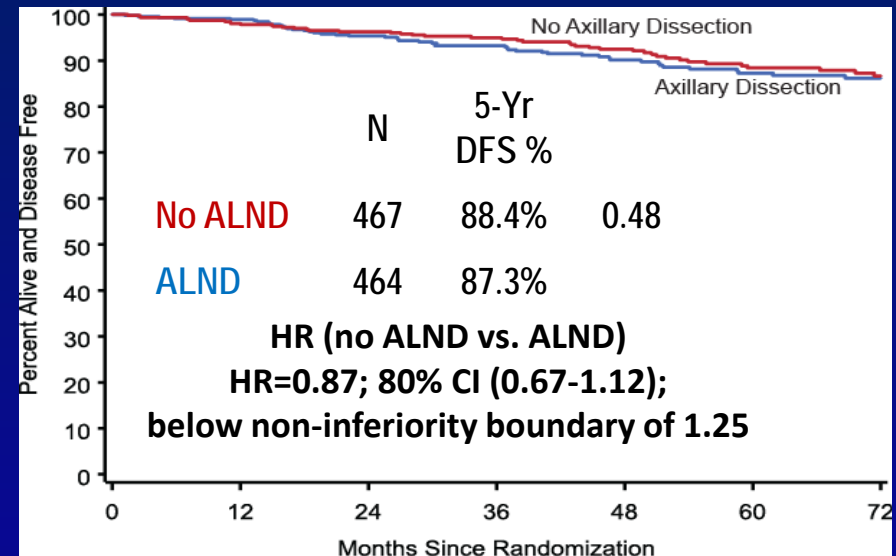
ALND

No ALND

9% had mastectomy

13% +NSNs

Median FU 57 months



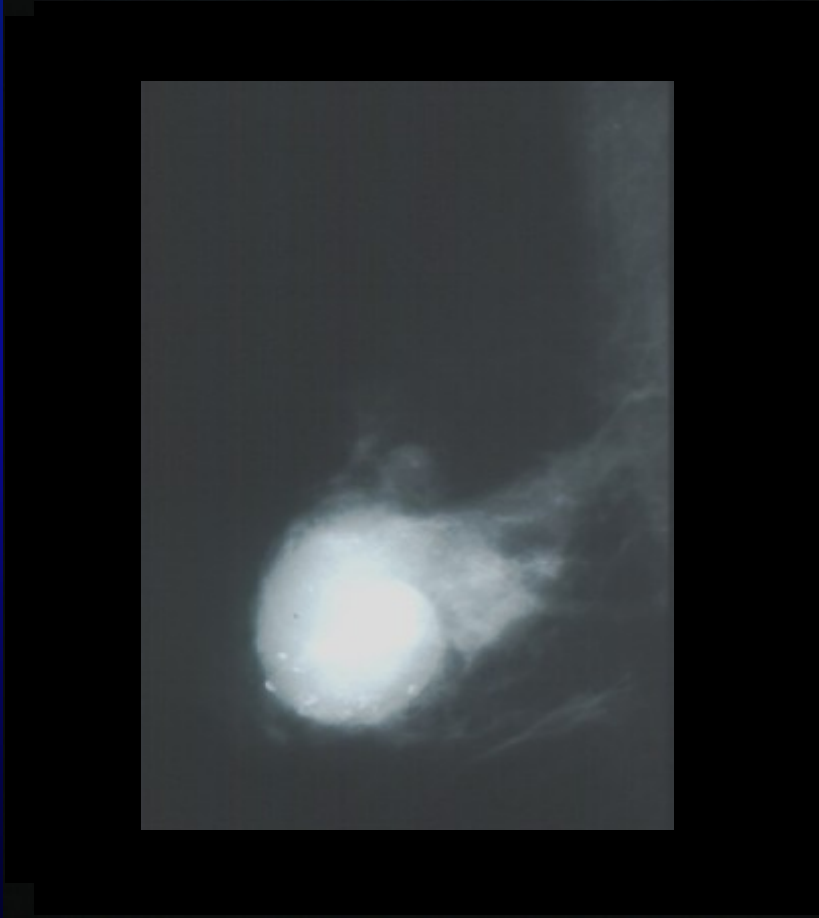
How Do We Incorporate the Recent SNB Data into Clinical Practice?

- For lumpectomy patients (who meet Z11 criteria) intraoperative assessment on the SN(s) can be omitted
 - If 1-2 SN(s) are positive consider no further surgery vs. axillary XRT
- For mastectomy patients, and patients who do not meet Z11 criteria, intraoperative assessment could be helpful
 - If the SNs are positive, consider completion ALND vs. axillary XRT

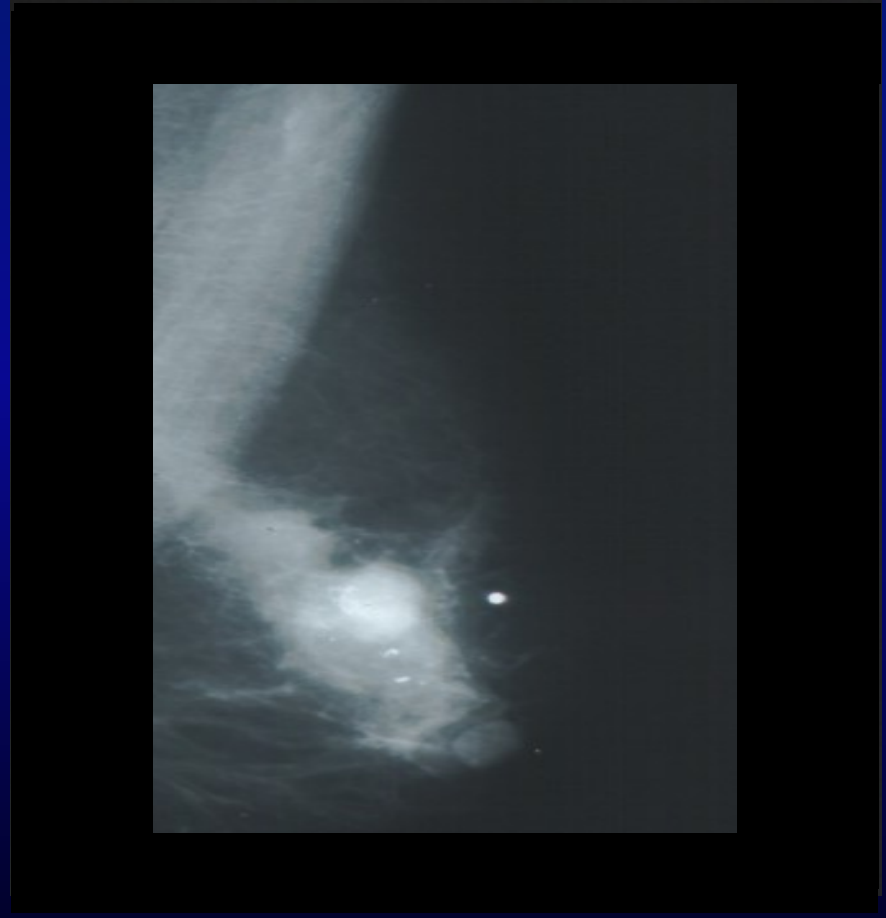
**Surgical Management of
Patients Receiving
Preoperative (Neoadjuvant)
Chemotherapy**

Neoadjuvant Chemotherapy

Before



After



Neoadjuvant Chemotherapy and Surgical Management

- To decrease the extent of surgery in the breast and axillary nodes

Mastectomy



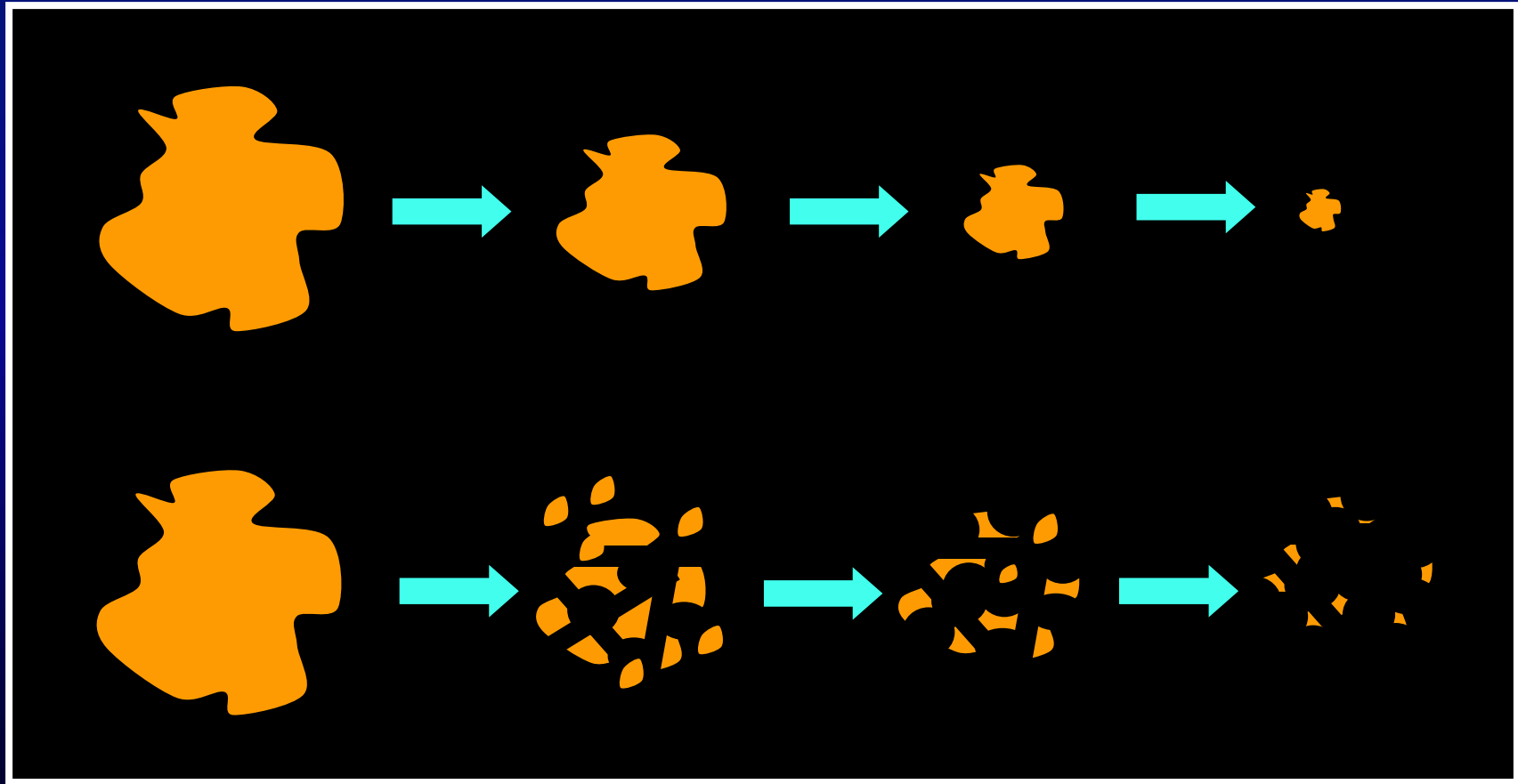
Lumpectomy

Axillary Node Dissection

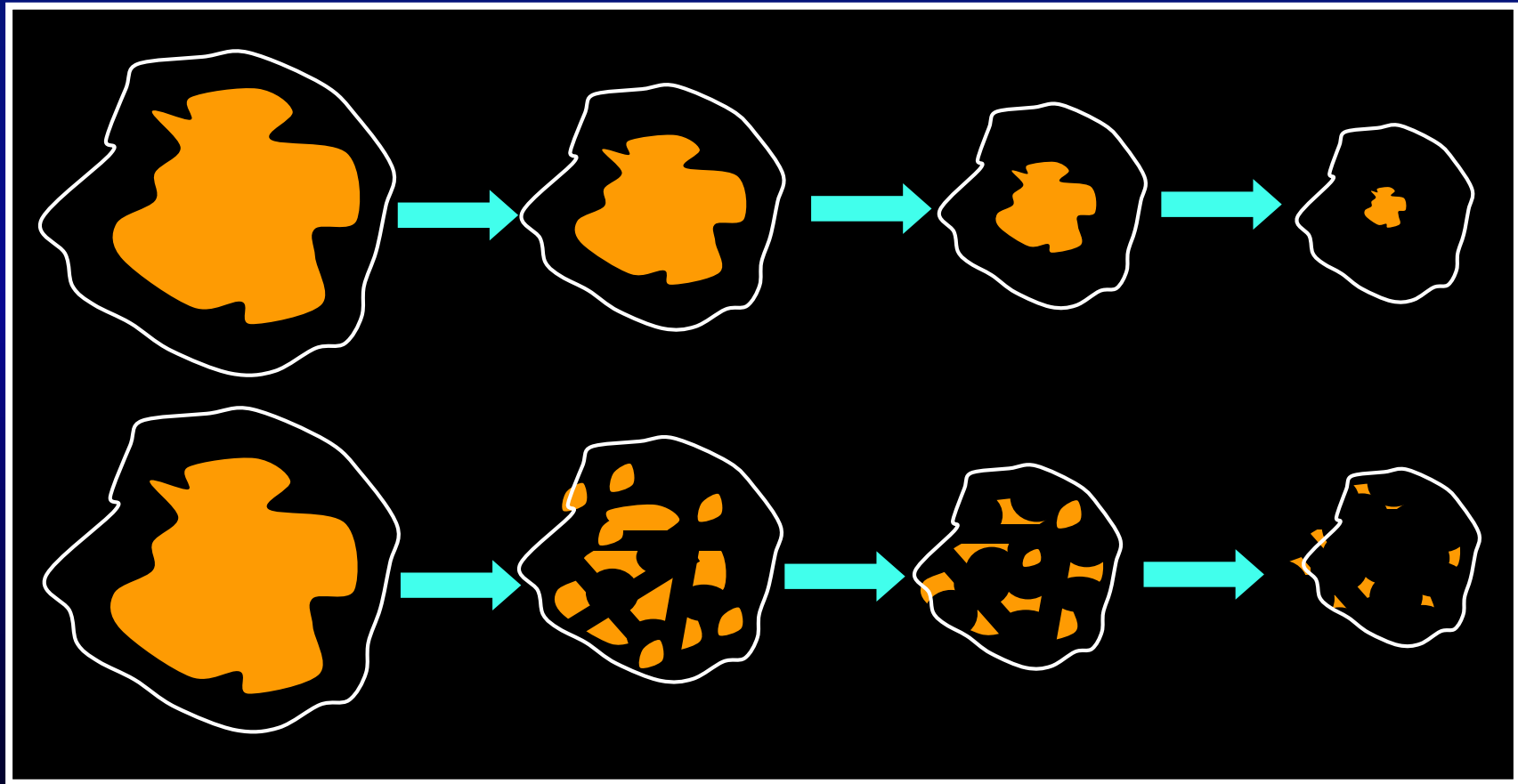


Sentinel Node Biopsy

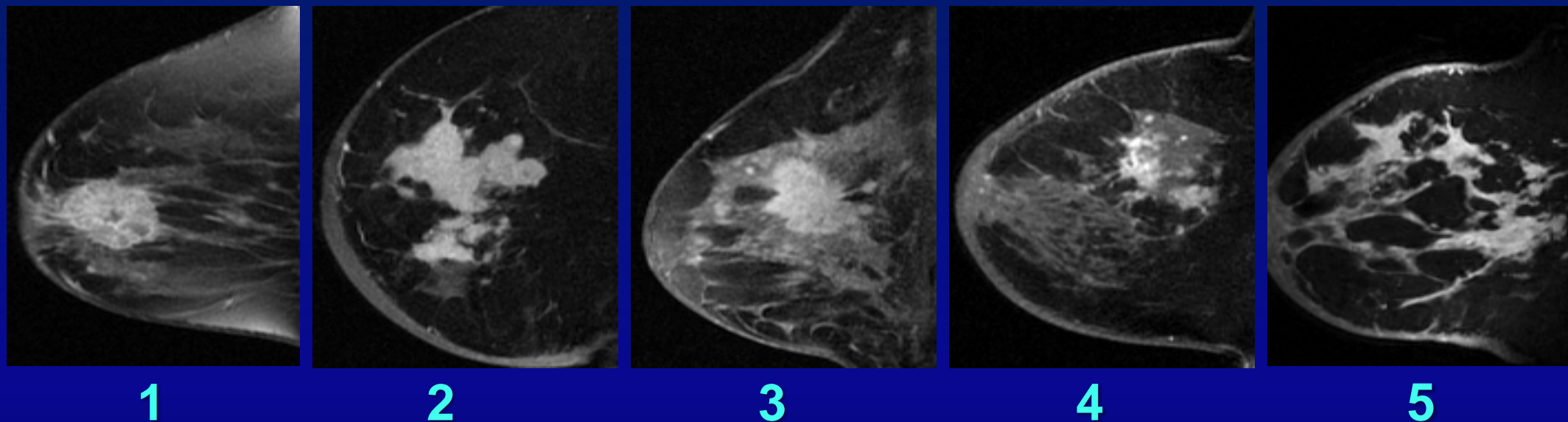
How Do Tumors Shrink in Response to NC?



What is Adequate Surgical Resection after NC?



MRI Phenotypes



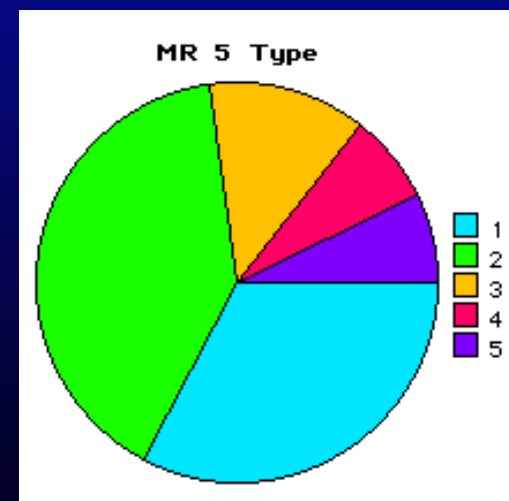
1: Single predominant mass with identifiable rim, displacing

2: Nodular pattern, irregular borders

3: Diffuse infiltrative pattern

4: Patchy enhancement

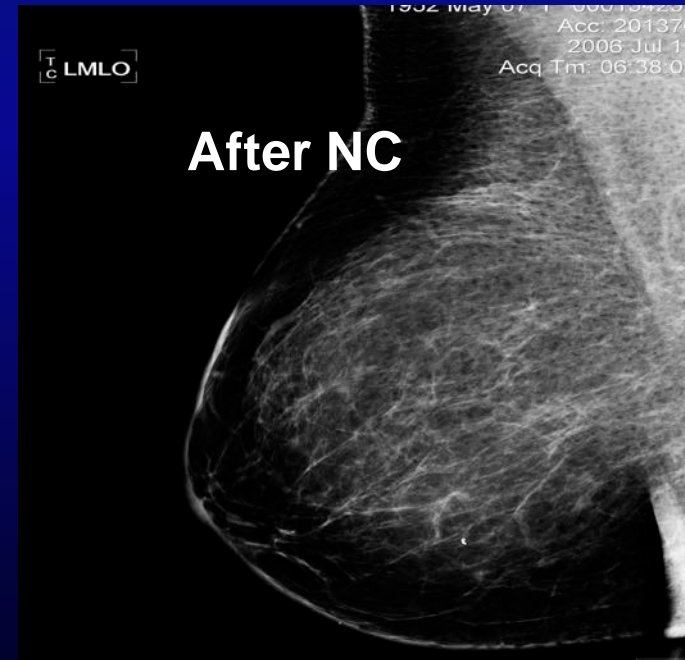
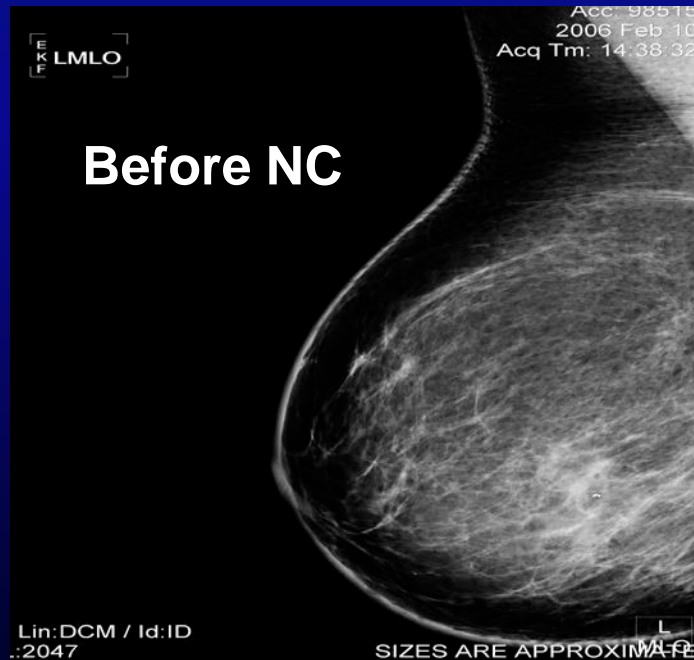
5: Septal spread



Neoadjuvant Chemotherapy

Surgical Planning

- Identification of the exact tumor location in cases of cCR
 - Preoperative titanium clip placement



Management of the Clinically Negative Axilla in Patients Treated with NC

- **SLNB after NC** has become the **arguable standard** for patients with **operable BC**
- Capitalizes on the **down staging effect of NC** in sub-clinically involved axillary nodes
- **Feasibility** and **accuracy of SLNB after NC** has been demonstrated in **multiple studies** and **meta-analyses**
- Although **SLN identification rate is lower** than with upfront SLNB, there is **no difference in FNR** between the two approaches

Optimizing SLNB Performance After NC in Pts with Documented (+) Axillary Nodes Before NC

- **Appropriate candidate selection for SLNB (T_{1-3}, N_1)**
- **Dual agent lymphatic mapping (isotope plus blue dye)**
- **Identification and removal of >2 SNs**
- **Clip placement in the positive node with radiologic clip localization and retrieval**
- **Consideration of performing IHC staining in the SN and consider completion ALND even with N0i+ disease**

Summary

- **Core needle biopsy is the standard diagnostic procedure for primary BC**
- **MRI is not indicated for all pts who undergo BCS but is helpful in the surgical plan in selected cases**
- **Lumpectomy + breast XRT is the preferred surgical option in the absence of absolute contraindications. No “ink on tumor” appears adequate margin for invasive tumors and 2 mm margin is optimal for DCIS**

Summary

- **There has been a recent increase in use of CPM**
- **Nipple-sparing mastectomy requires careful consideration and patient selection**
- **In patients undergoing neoadjuvant chemotherapy, unique primary surgical issues relate to the assessment of the extent of residual disease and the exact location of residual tumor (or tumor bed) in patients with complete clinical and/or radiologic response**

Summary

- **Use of SLNB alone is the standard of care for axillary management when SLN(s) are negative**
- **SLNB alone is increasingly being used in selected patients with positive SLN(s) and following neoadjuvant chemotherapy for appropriately selected candidates**