

Role of Specimen X-ray in Evaluation of Breast Specimens

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Making Cancer History®

Breast Cancer

- Complex and multifaceted disease
- Include great variety of entities
- Show considerable variation
 - Clinical
 - Morphologic
 - Molecular

Features Used to Categorize Breast Ca

- Patient related
 - Age, genetic background
- Tumor related
 - Stage
 - Histologic features
 - ✓ Type, grade, LVI
 - Biomarker expression
 - ✓ ER/PR/Her2/neu

Breast Cancer

- Nottingham Prognostic Index
- St. Gallen Criteria
- NCCN Clinical Practice Guidelines
- Adjuvant Online

Breast Cancer

- Traditional staging and standard histopathological evaluation remain the cornerstone of clinical management
- Not all BCs presenting at the same stage have the same underlying biology

Breast Cancer

- Tumor size
- Lymph node status
- Distant metastasis

Breast Cancer

- Therapy decisions
- Recognizes extremes prognostic spectrum

TNM Staging

PRIMARY TUMOR (T)

- Clinical size
 - clinical examination
 - imaging studies
- Pathologic size
 - measurement of invasive component

TNM Staging

PRIMARY TUMOR (T)

Pathologic size

- Size of the invasive carcinoma before any tissue is removed for special studies
- If multiple core biopsies performed, original tumor site should be reconstructed on the basis of combination of imaging and histologic findings

TNM Staging

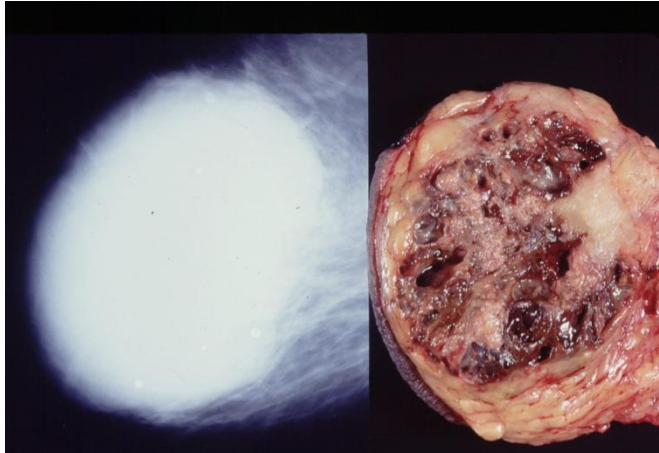
PRIMARY TUMOR (T)

- Tis: In situ ca
- T1: ≤ 2 cm invasive ca
- T2: 2-5 cm invasive ca
- T3: > 5 cm invasive ca
- T4: Skin involvement or inflammatory ca

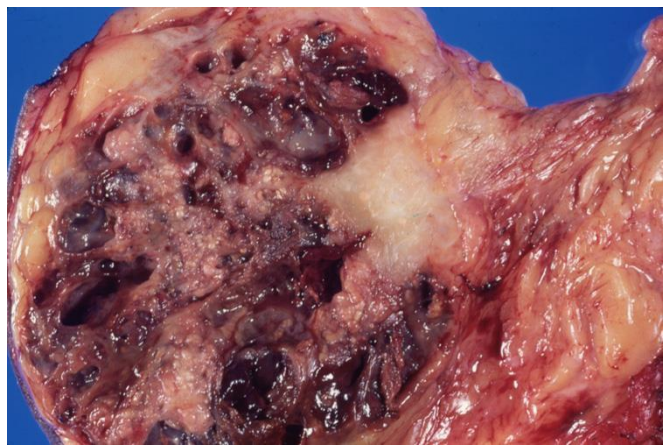
Tumor Size



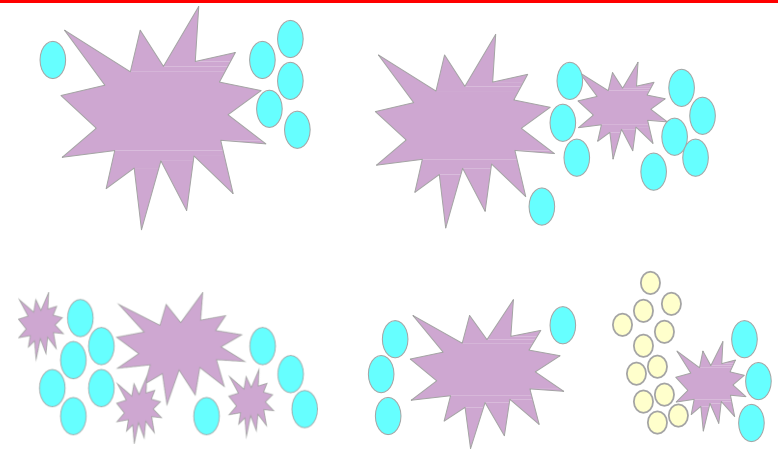
Tumor Size



Tumor Size



Tumor Size



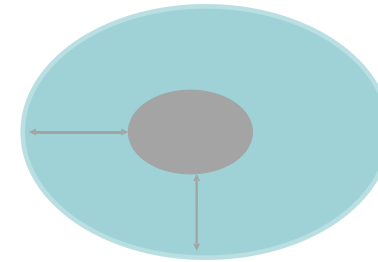
TNM Staging

PRIMARY TUMOR (T)

Multiple Simultaneous Ipsilateral Primary
Carcinomas Microscopically separate foci
of tumor

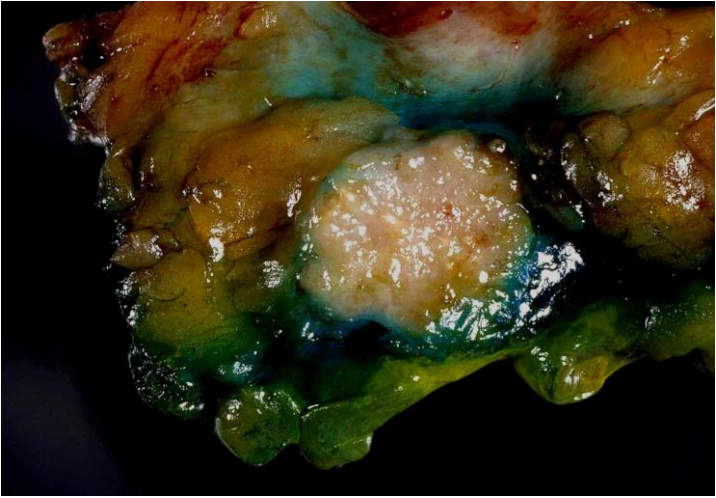
- Largest focus is used for T designation
- Separate T designations are not assigned for smaller tumors

Tumor Size



- Clearly defined mass
- Gross measurement

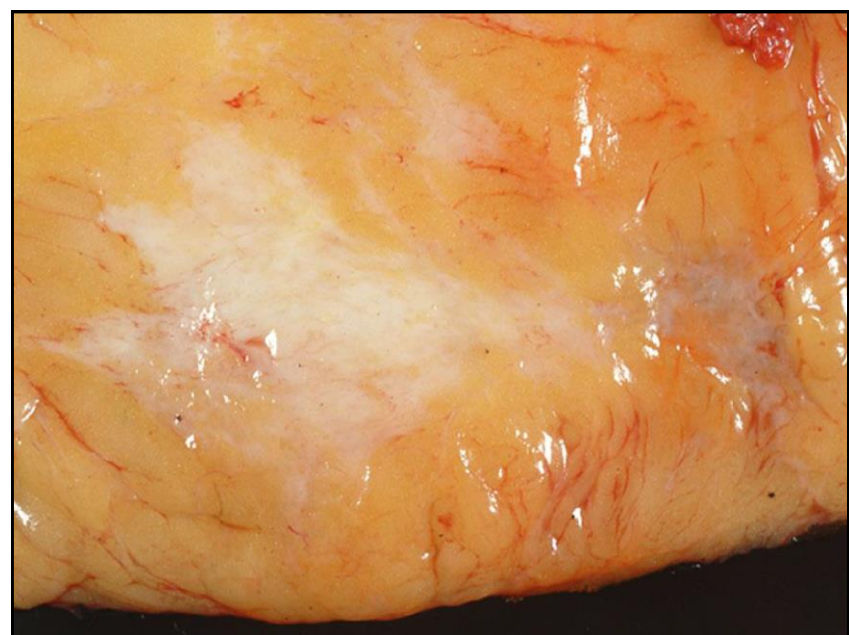
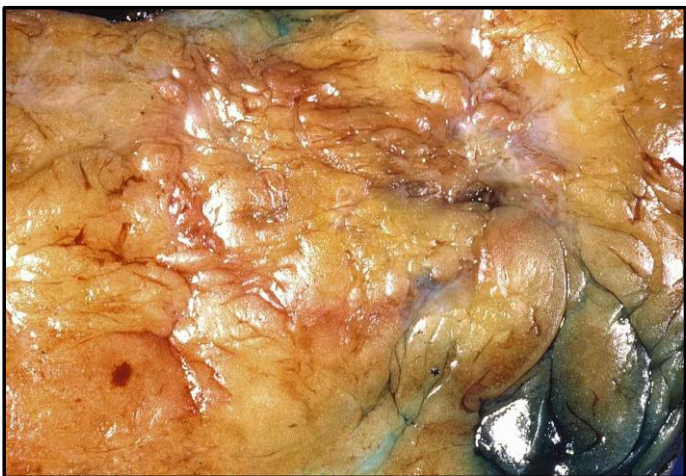
Gross Inspection



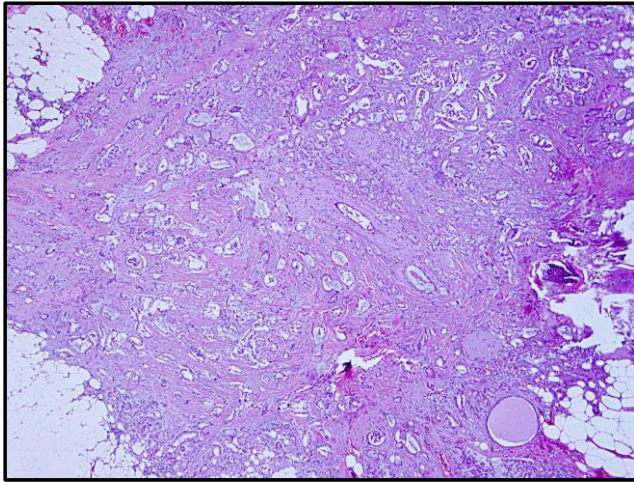
Gross Inspection



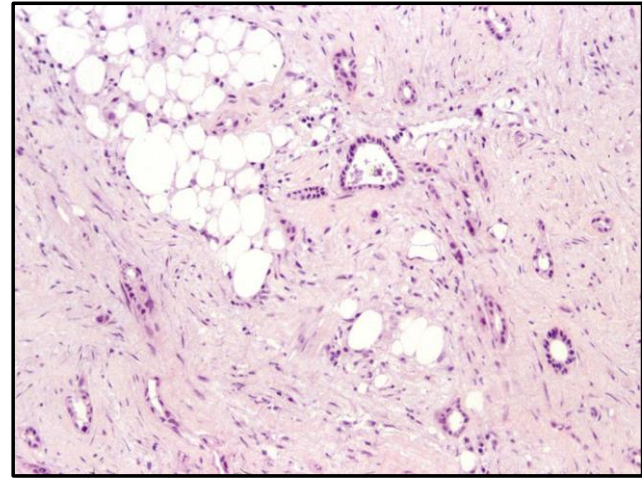
Tumor Size



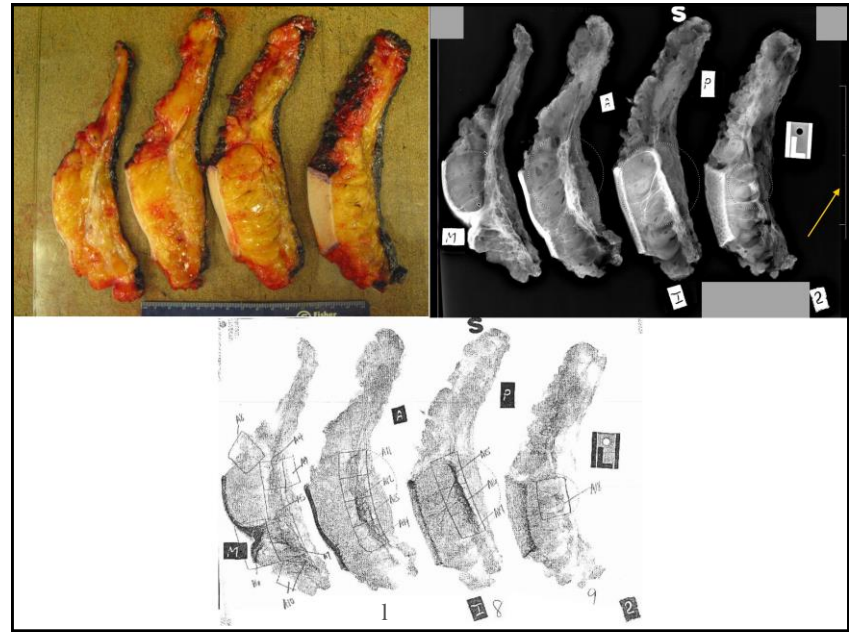
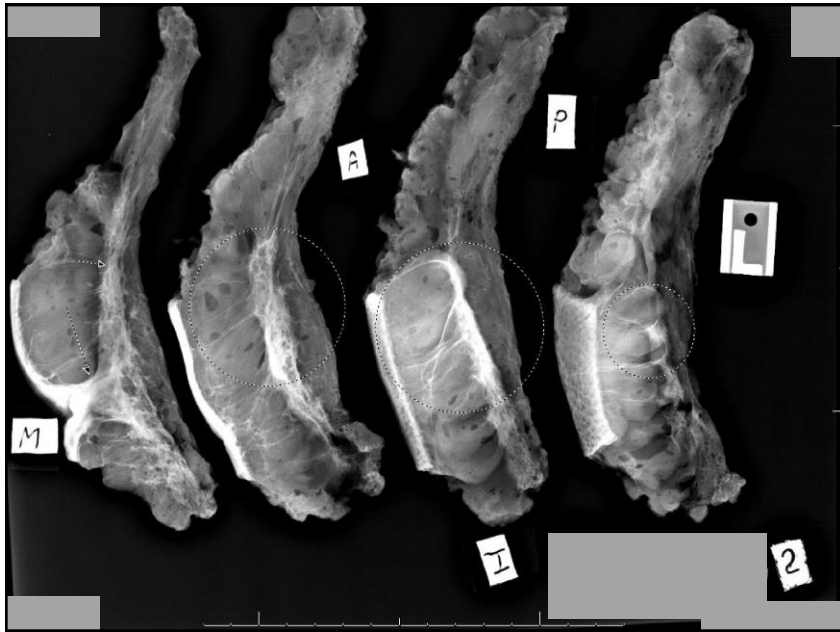
Breast Cancer



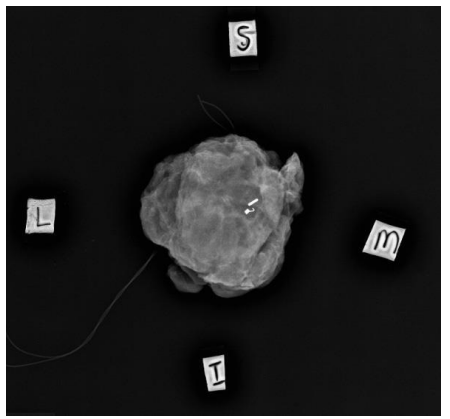
Breast Cancer

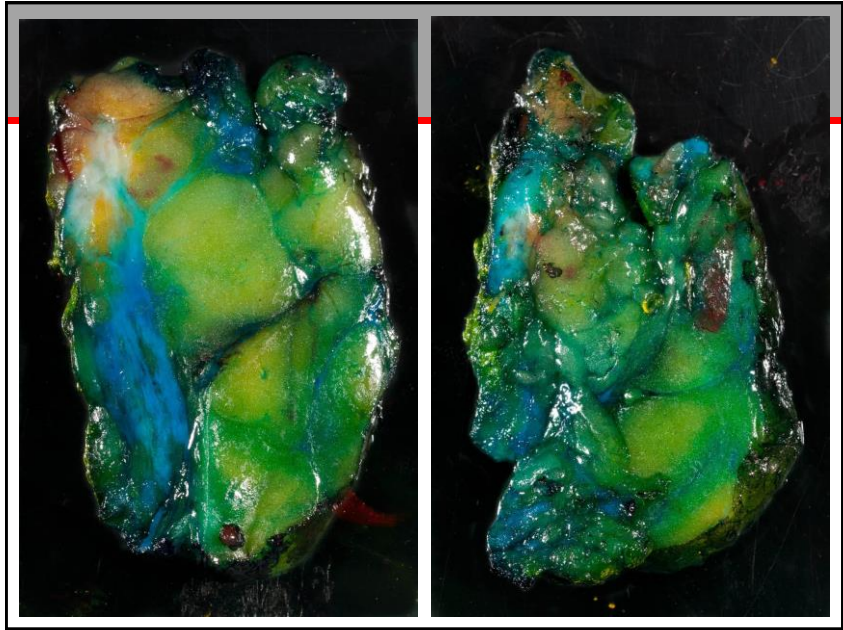
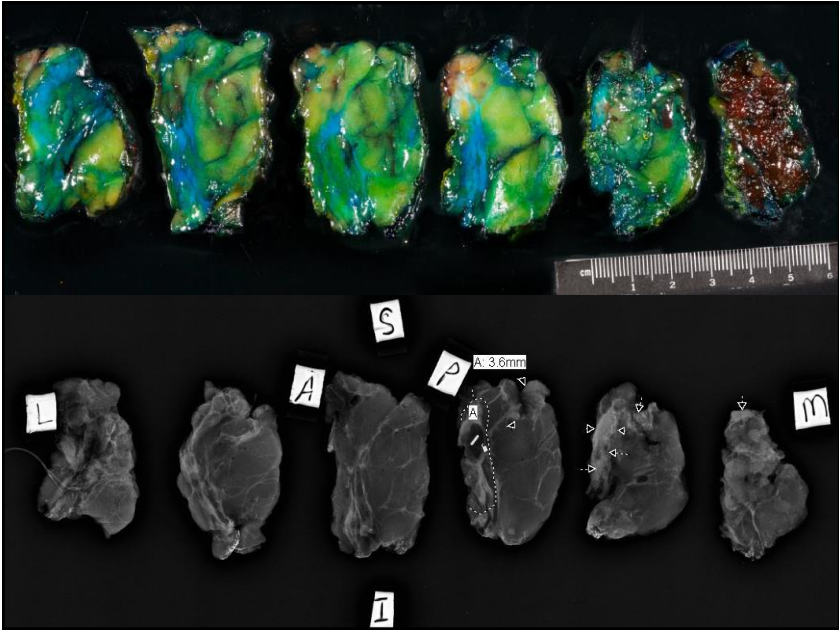


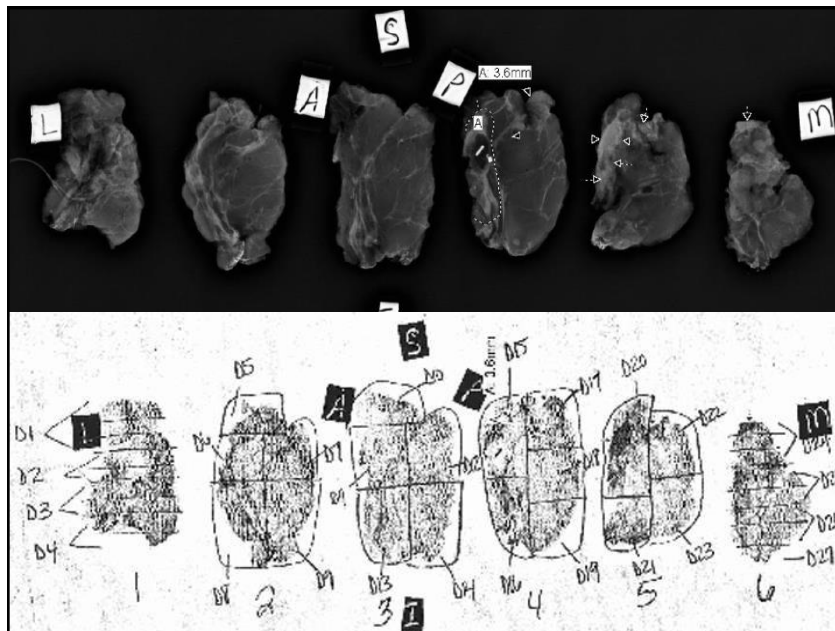




Specimen X-ray







TNM Staging

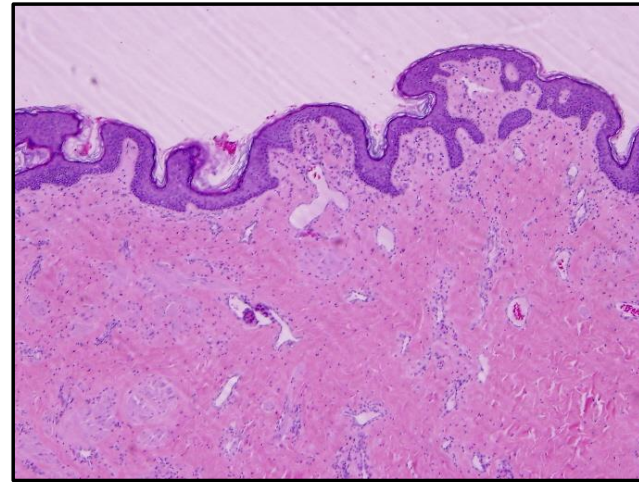
PRIMARY TUMOR (T) Inflammatory Carcinoma

- Clinicopathologic entity
 - diffuse erythema and edema of breast
 - often without an underlying palpable mass
 - imaging studies show skin thickening with or without a mass
 - Biopsy shows tumor emboli in dermal lymphatics

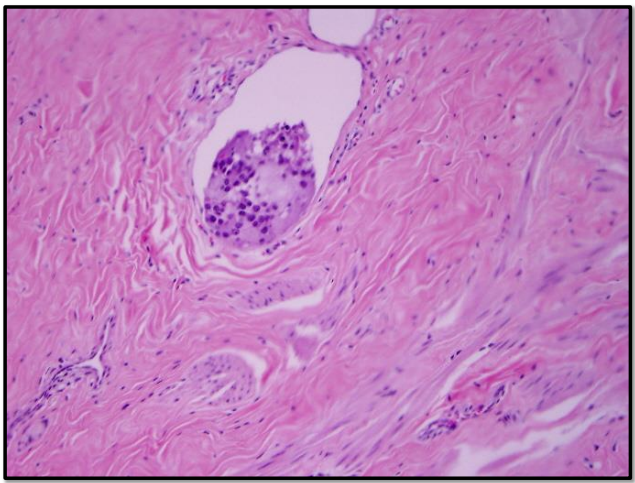
Inflammatory Breast Cancer



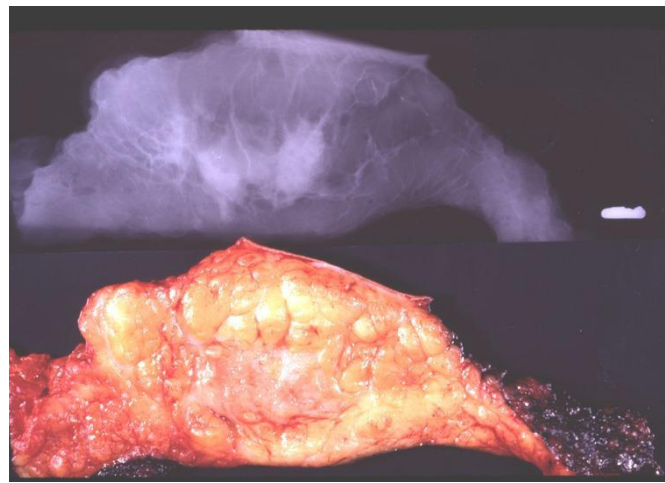
Inflammatory Breast Cancer



Inflammatory Breast Cancer



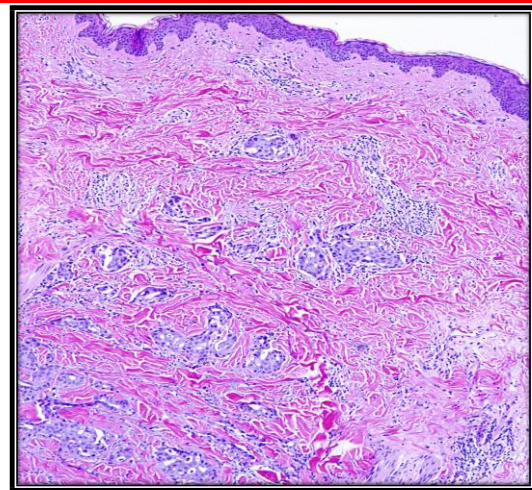
Tumor Size



Tumor Size



Breast Cancer

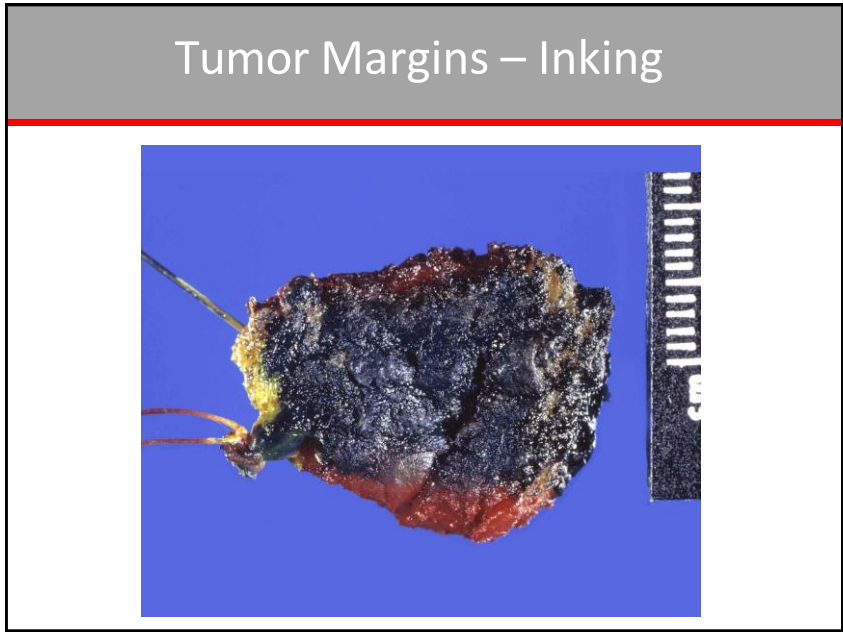


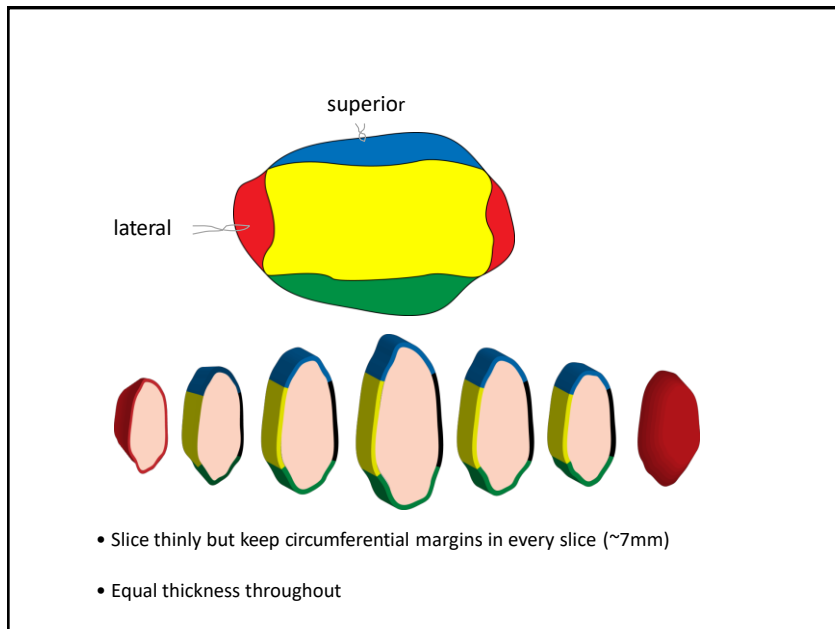
Breast Cancer

- Tumor Stage
- Margin Status

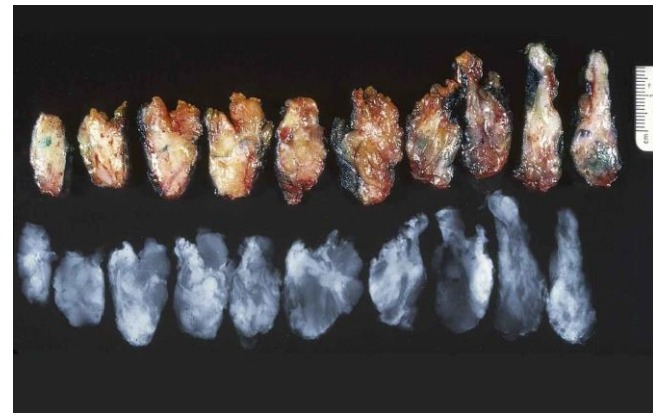
How are Margins Assessed?

- Gross inspection
- Frozen Section
- Touch imprints
- Specimen x-rays

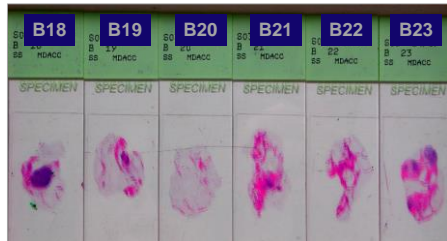
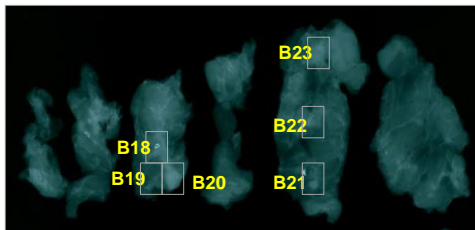




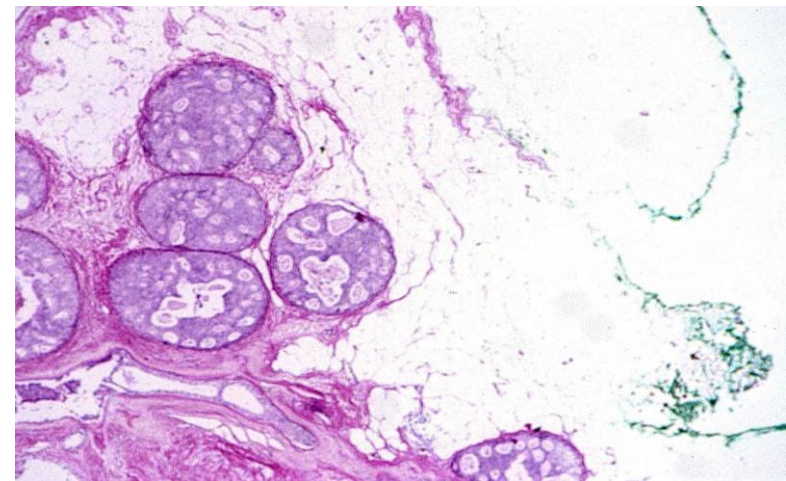
Radiographic Evaluation of Specimen

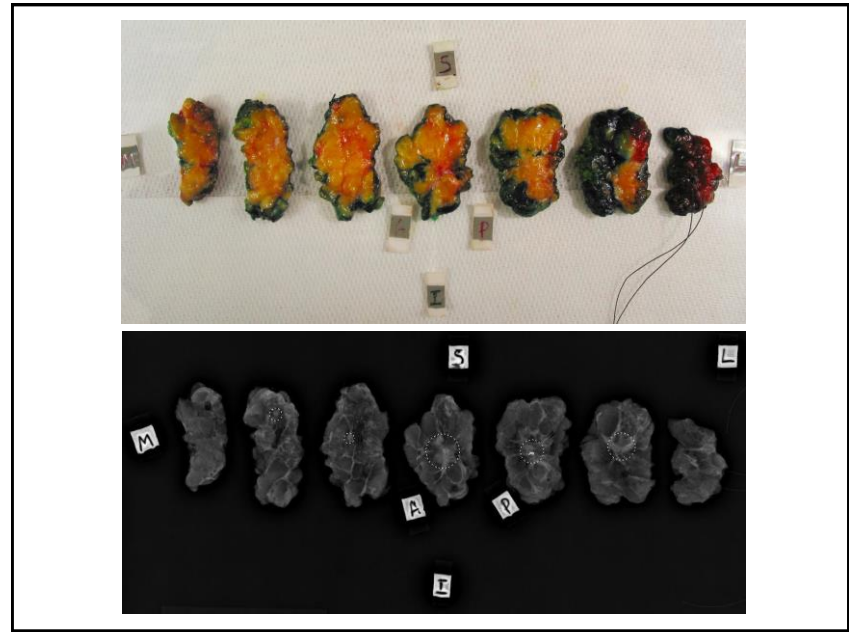
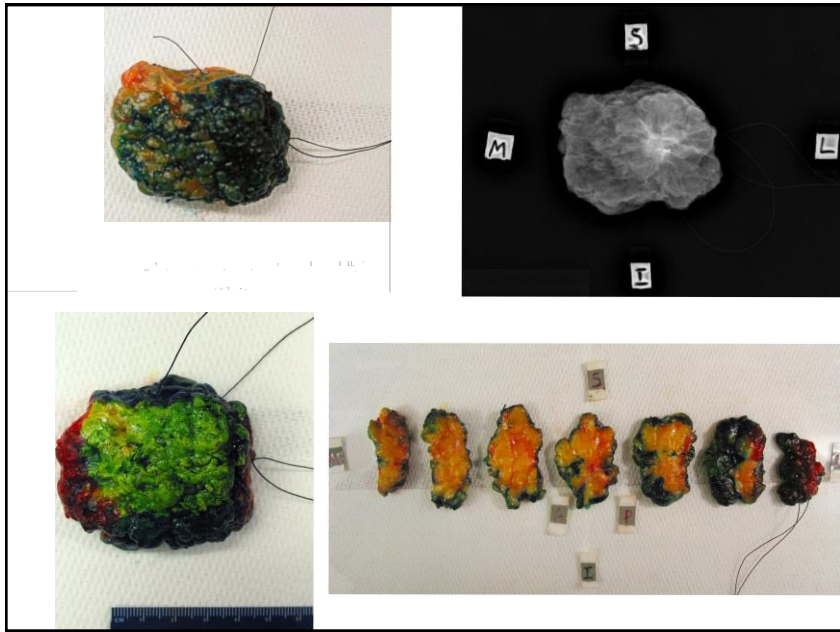


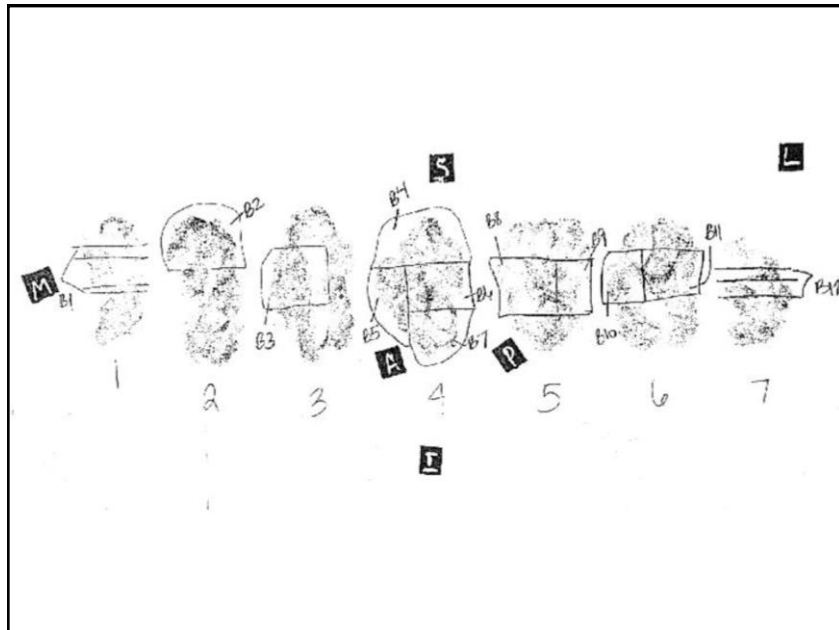
Radiographic Evaluation and Mapping



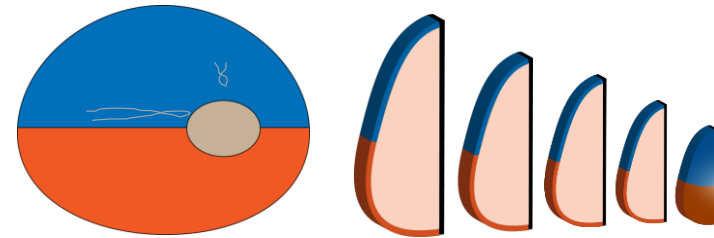
Margin Evaluation



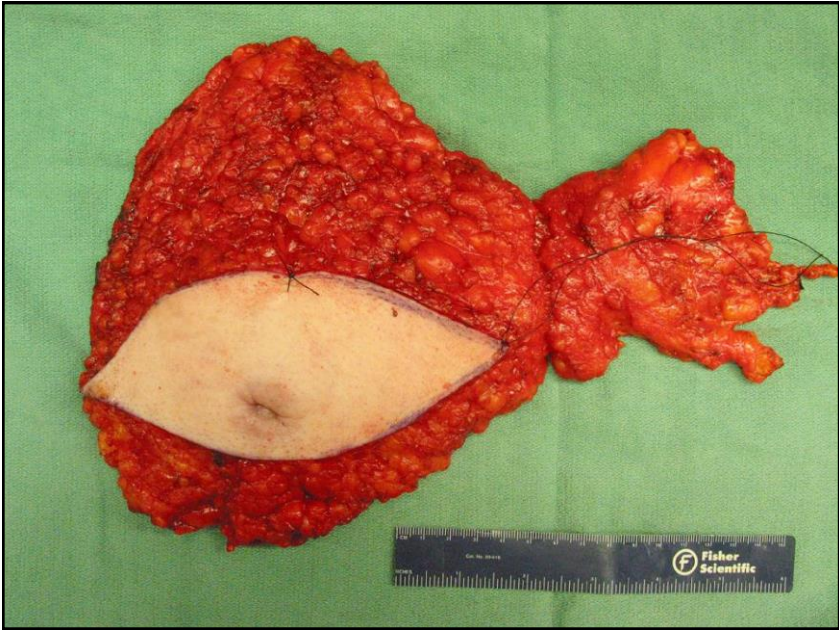


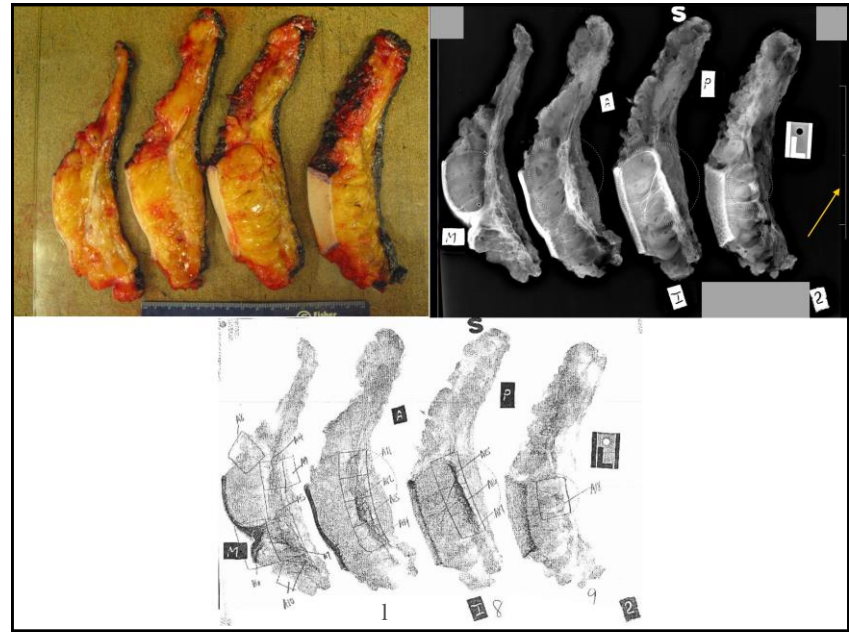


Margin Evaluation



- Slice thinly but keep circumferential margins in every slice (~1.5 cm)
- Equal thickness throughout





Neoadjuvant Chemotherapy

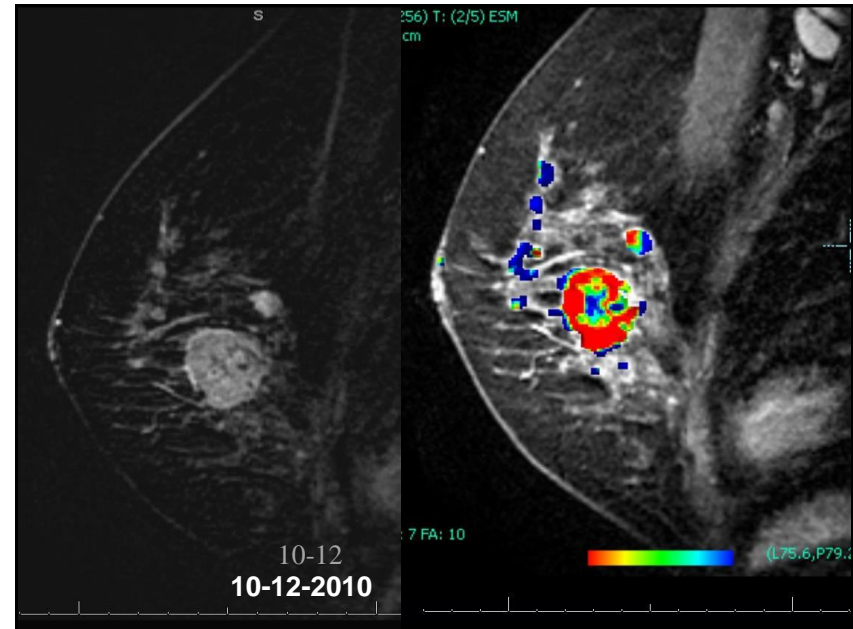
- Standard therapy for locally advanced breast carcinoma
- Increasingly used for early stage operable disease
- A wide range of pathologic changes can occur after neoadjuvant chemotherapy

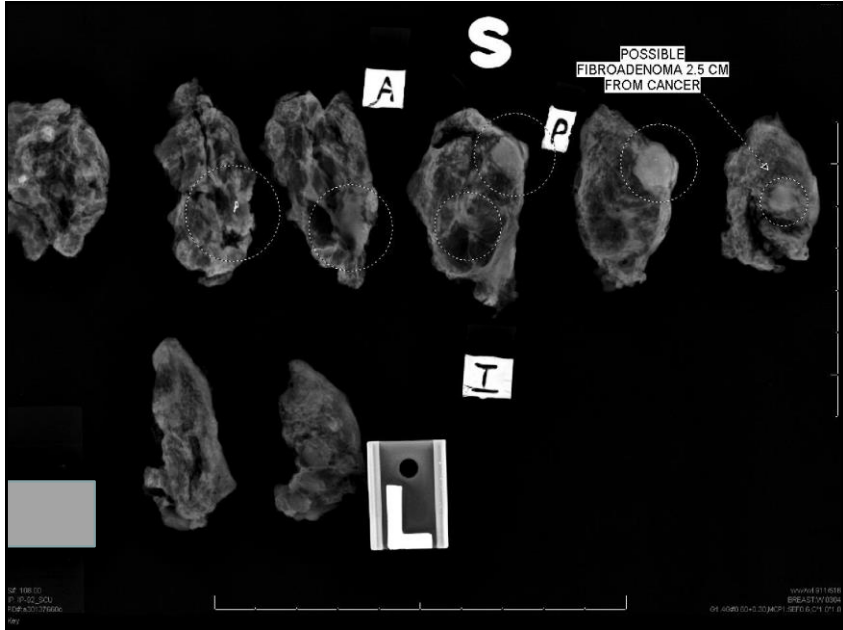
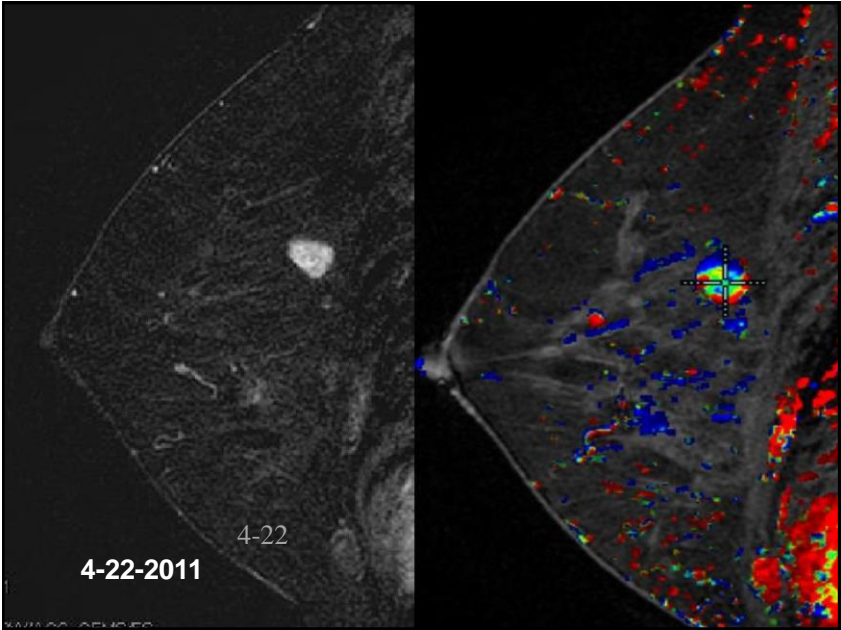
Indications of Neoadjuvant Chemotherapy

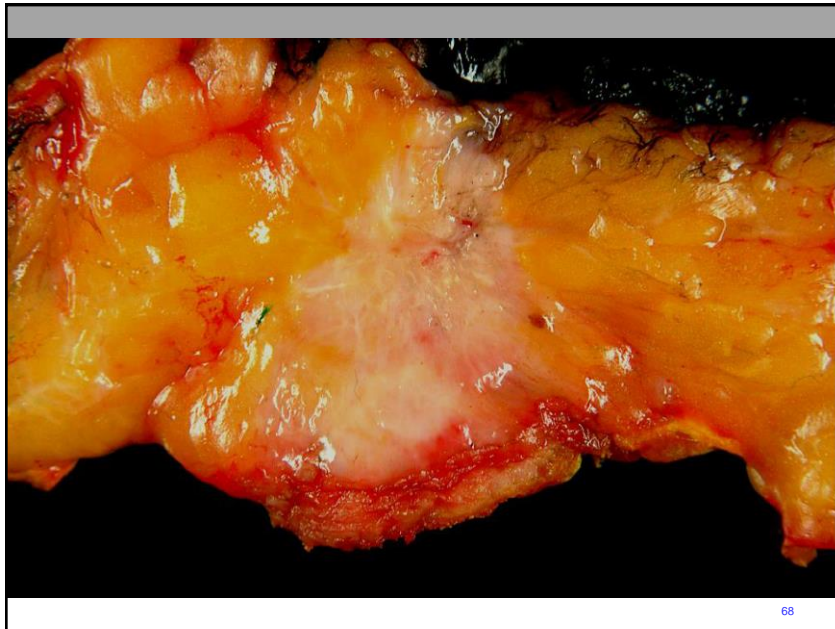
- Management of locally advanced invasive breast ca including inflammatory breast ca
- 'Down-staging' of large inoperable cancers to permit surgical resection
- Routine management of women with high risk disease who would require adjuvant chemotherapy based on biological tumour characteristics and clinical-radiological findings

Specimen Handling

- One of the most critical steps in accurately evaluate response to NAC is the macroscopic (gross) assessment of the specimen
- A multidisciplinary approach with close clinical/ radiological correlation to map the precise location of the tumor bed is preferable to exhaustive blind sampling

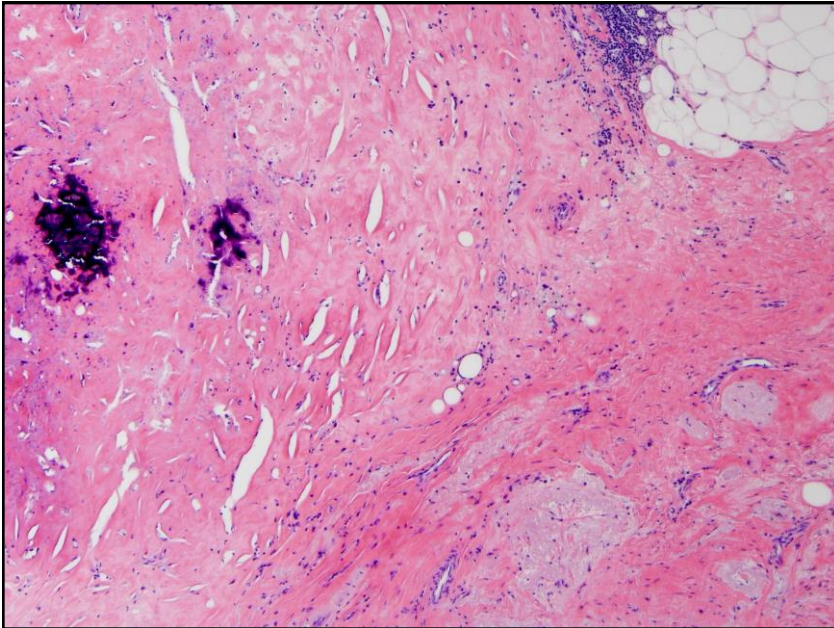




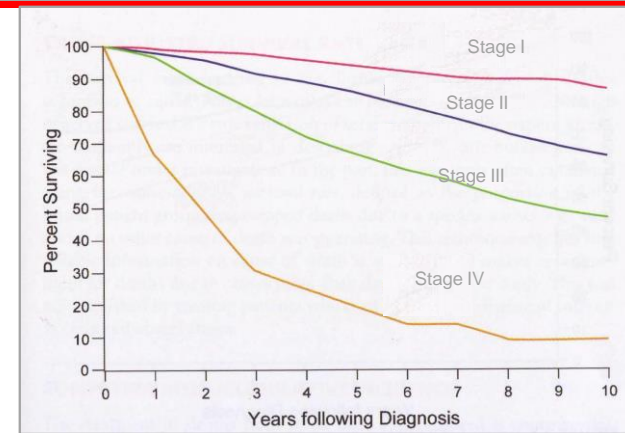


Neoadjuvant Chemotherapy

- The tumor bed consisted of an area of histiocytes and lymphocytes. No residual carcinoma was identified
- Sixteen lymph nodes were excised
- All were negative for metastatic carcinoma



Neoadjuvant Chemotherapy



Her expected survival is over 90%

Methods to Determine Response to NAC

- Clinical/imaging methods
 - False negative 40-60%
 - False positive 20-30%

Histopathologic evaluation is gold standard

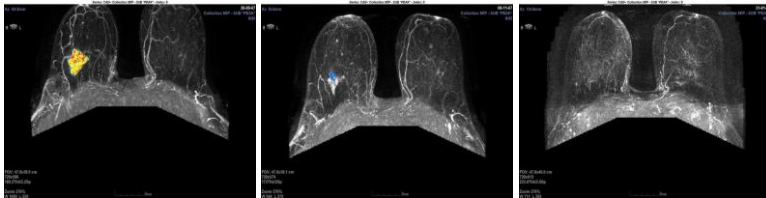
Neoadjuvant Chemotherapy

Pathological Response

- PCR is defined as complete absence of invasive carcinoma in the breast and no residual metastatic ca in lymph nodes
- PCR occurs 5-30% of patients with locally advanced breast carcinoma after NAC

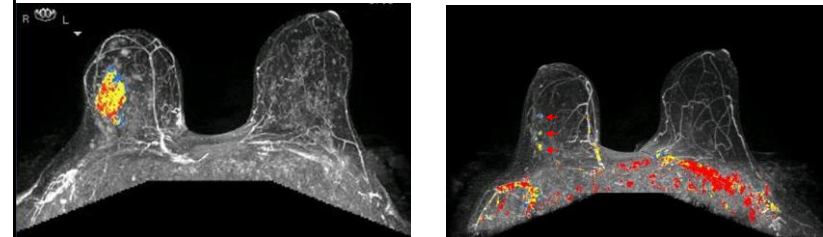
Patterns of Tumor Response

Concentric shrinking



Patterns of Tumor Response

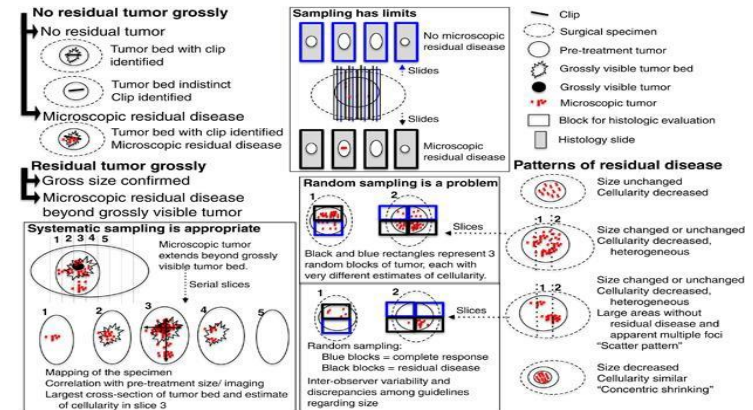
Scatter pattern



Measuring Tumor Size post NAC

- Tumor size more difficult to assess after NAC
- If there is a single lesion present on pre-treatment imaging, then treat residual disease as a single tumor, especially if tumor cells are present within a reactive stromal background consistent with a solitary tumor bed

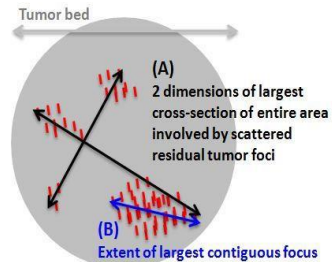
Standardization of pathologic evaluation and reporting of postneoadjuvant specimens in clinical trials of breast cancer: recommendations from an international working group



Provenzano E et al. Mod Pathol 2015;1185-201

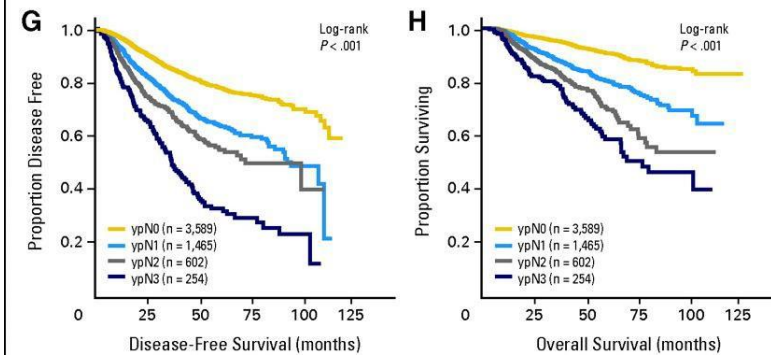
Measuring Tumor Size post NAC

- 7th edition AJCC – largest contiguous area of tumour cells (B)
- The combination of size and residual tumor cellularity is the best indicator of response



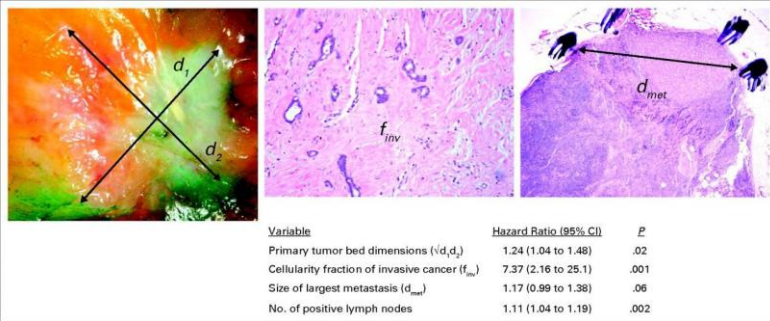
Significance of nodal response

Nodal status post NAC a strong predictor of outcome



von Minckwitz G et al. JCO 2012;30:1796-1804

Residual Cancer Burden System MDACC



- Cellularity of residual carcinoma over the tumor bed
- Presence of lymph node metastasis
- Size of the largest lymph node metastasis

Residual Cancer Burden

The screenshot shows the MD Anderson Cancer Center website with the Residual Cancer Burden Calculator tool. The calculator interface includes the following fields:

- (1) Primary Tumor Bed:**
 - Primary Tumor Bed Area: (mm) X (mm)
 - Overall Cancer Cellularity (as percentage of area): (%)
 - Percentage of Cancer That is in situ Disease: (%)
- (2) Lymph Nodes:**
 - Number of Positive Lymph Nodes:
 - Diameter of Largest Metastasis: (mm)

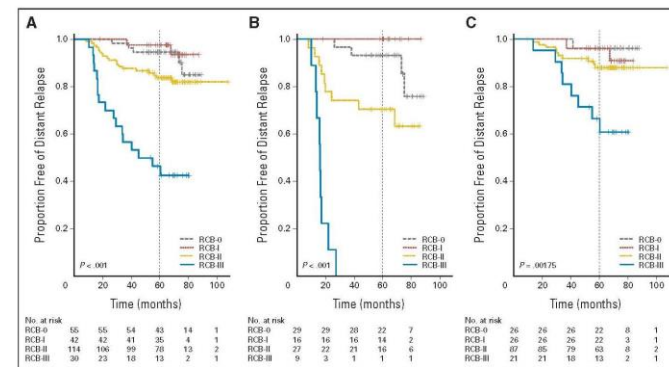
Buttons for "Reset" and "Calculate" are present. Below the calculator, it states: "The following parameters are required from pathologic examination in order to calculate Residual Cancer Burden (RCB) after".

Systems of Categorizing Response To Neoadjuvant Treatment

Residual Cancer Burden System (MDACC)

- RCB-0 No carcinoma in breast or lymph nodes (pCR)
- RCB-1 Minimal residual disease (marked response)
- RCB-2 Moderate response
- RCB-3 Minimal or no response (chemoresistant)

Residual Cancer Burden



- Likelihood of distant relapse in patients with residual cancer burden
- A: entire paclitaxel plus fluorouracil, doxorubicin, and cyclophosphamide cohort
 - B: subset without adjuvant hormone treatment
 - C: subset who received adjuvant hormone treatment

J Clin Oncol. 25(28):4414-22, 2007

What do we look at in the pathologic examination after NAC?

All prognostic factors important before treatment are also important after treatment

- Residual Tumor pattern
- Tumor size
- LVI
- Lymph node status
- Histologic type and grade
- Tumor biomarkers

Neoadjuvant Chemotherapy

- Identification of “Tumor Bed” essential
- Can be very difficult if there is a marked clinical/imaging response
- Requires thorough evaluation

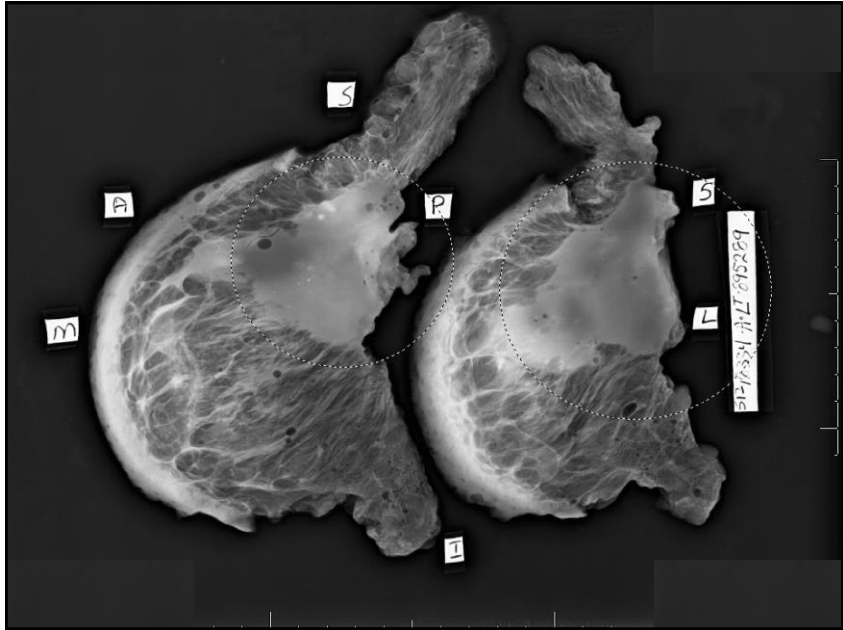
Tumor Bed

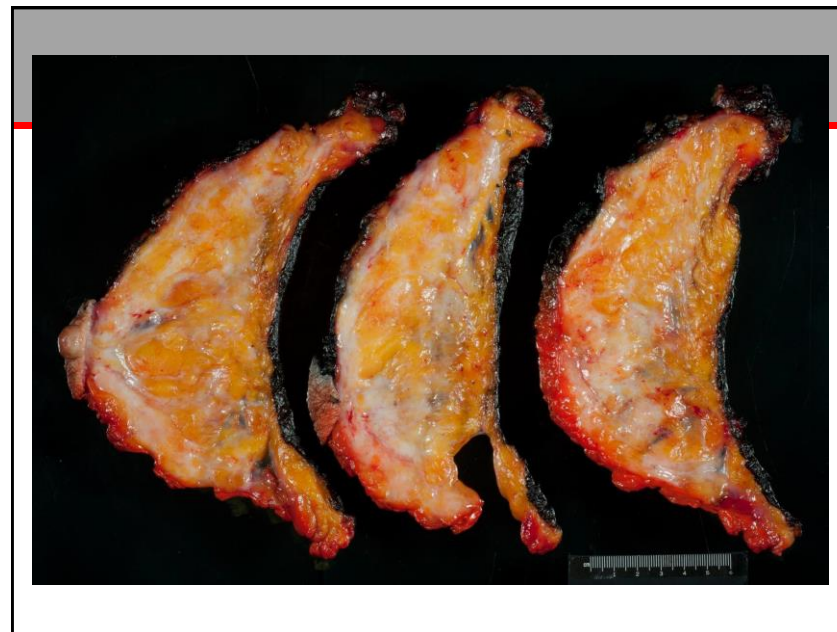
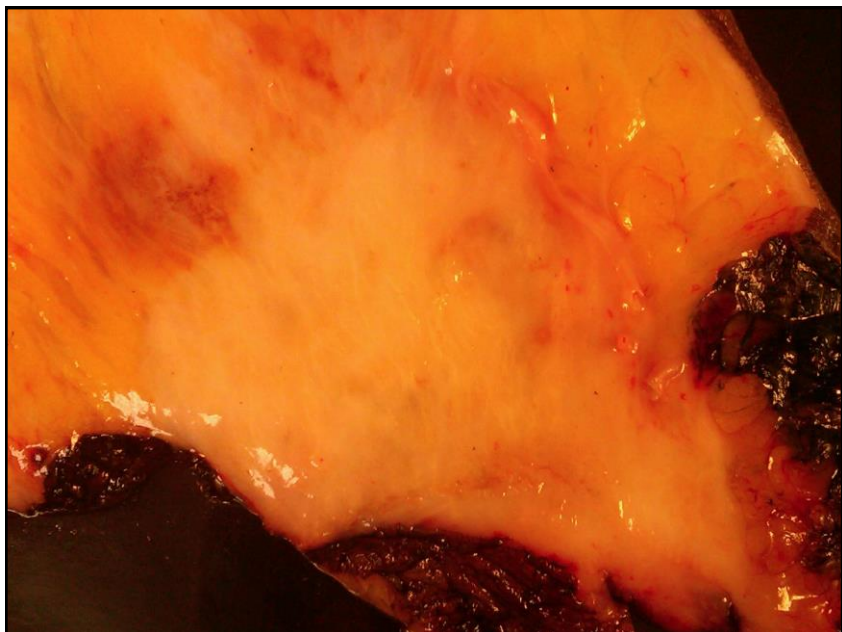
How extensively these specimens need to be sampled?

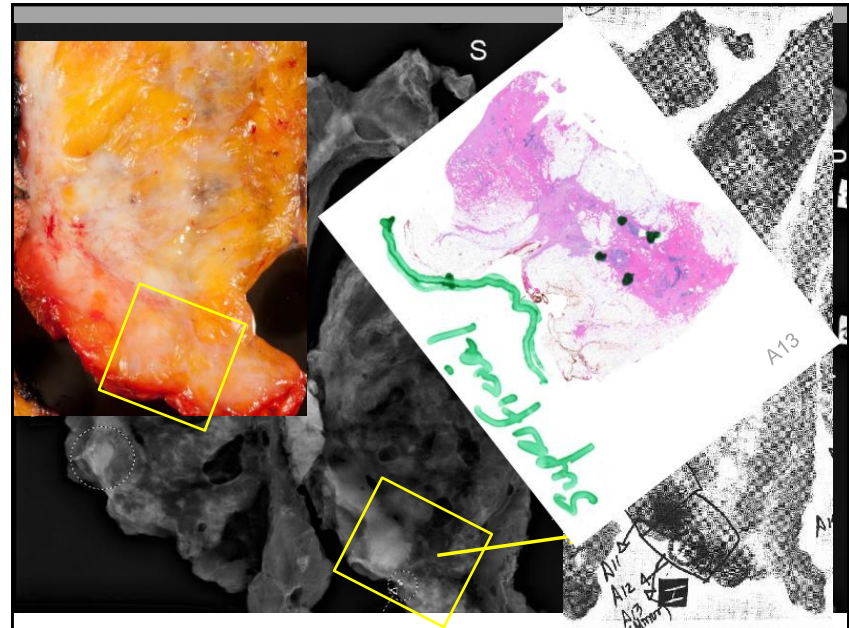
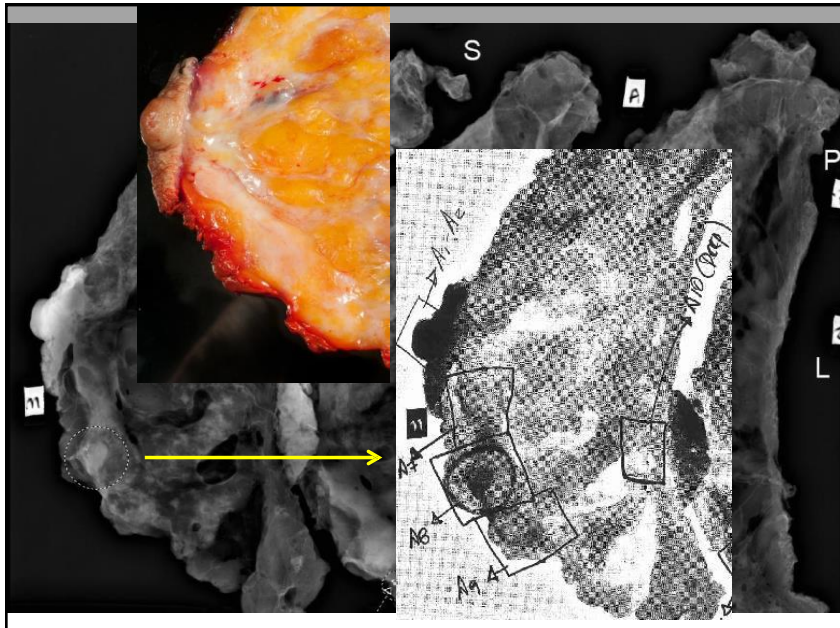
- If gross tumor is present limited sampling is adequate to establish the presence, size and cellularity of residual tumor. 1-2 sections/cm of tumor is reasonable
- If tumor bed is ill defined more extensive sampling is necessary

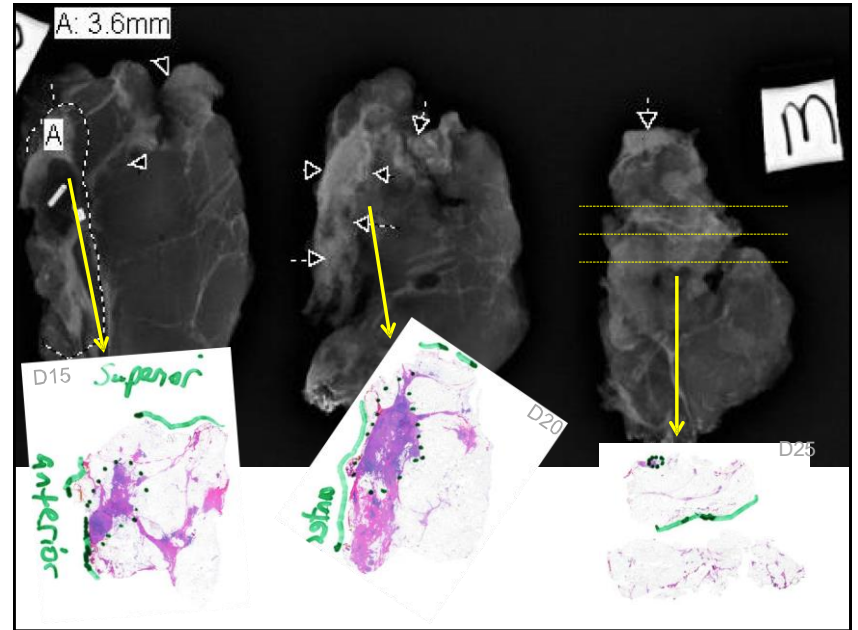
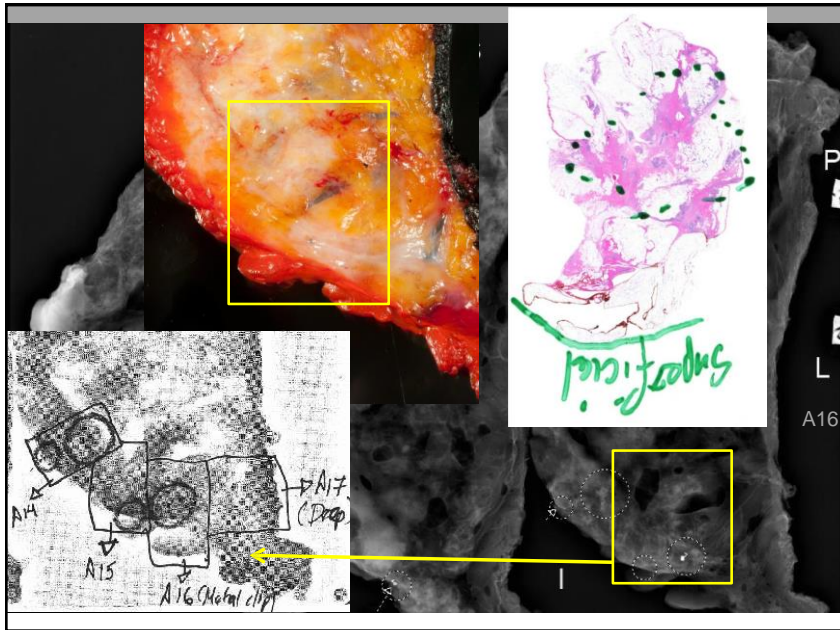
Placement of clip prior to treatment is very helpful

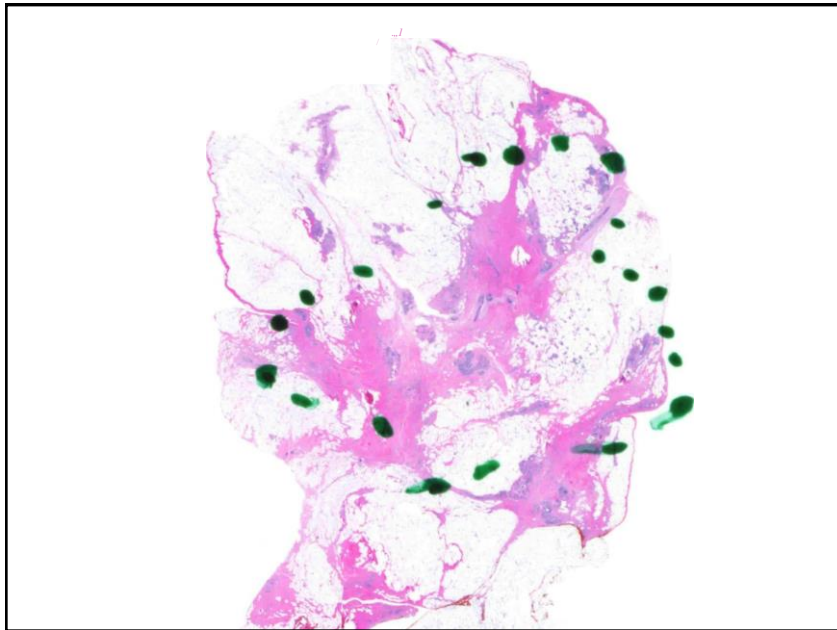












Neoadjuvant Chemotherapy

Take Home Messages

- NAC is being used more frequently
- Pathologic response is an important predictor of survival
- pCR provides the best prognosis
- Multidisciplinary specimen handling is essential for evaluation

Breast Cancer

Take Home Messages

- Appropriate specimen evaluation requires multidisciplinary approach
 - Tumor stage determined by tumor size and lymph node status
 - Margin status
- Specimen X-ray is an essential tool