EASY-PEASY!

SIMPLIFYING BREAST CANCER
8th AMERICAN JOINT COMMITTEE ON CANCER (AJCC) STAGING SYSTEM

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DISCLOSURE

THERE IS NO CONFLICT OF INTEREST

TEACHING POINTS

- Describe and illustrate the 8th American Joint Committee on Cancer's (AJCC) staging system for breast cancer.
- Discuss the major changes in the 8th AJCC's staging
- Emphasize radiologist's role in recognizing and reporting breast cancer imaging findings that can change staging and clinical / surgical management.

TABLE OF CONTENTS

CLICK HERE IN ANY SLIDE
TO RETURN TO TABLE OF CONTENTS

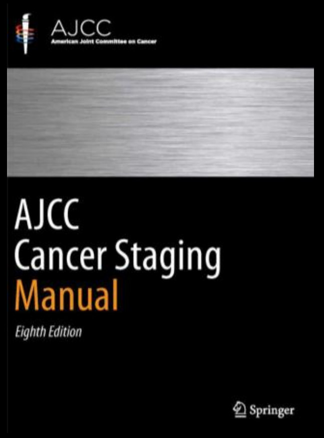
CHOOSE ONE AND CLICK

INTRODUCTION

Which are the goals of a cancer staging?

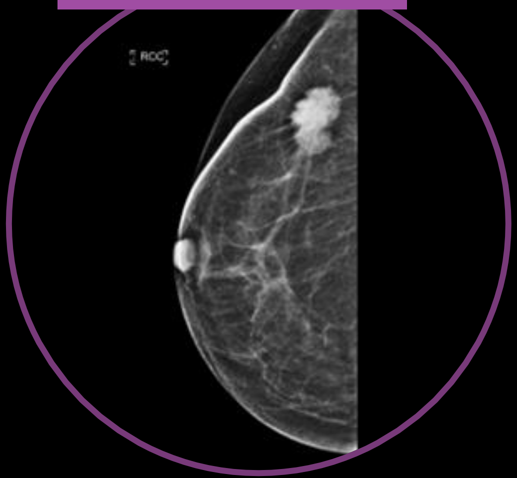
- To determine the extent of disease
- To help implement a treatment plan
- To inform prognosis

The most recent edition of the American Joint Committee on Cancer (AJCC) Staging Manual, the 8th edition, was adopted on January 1st, 2018.

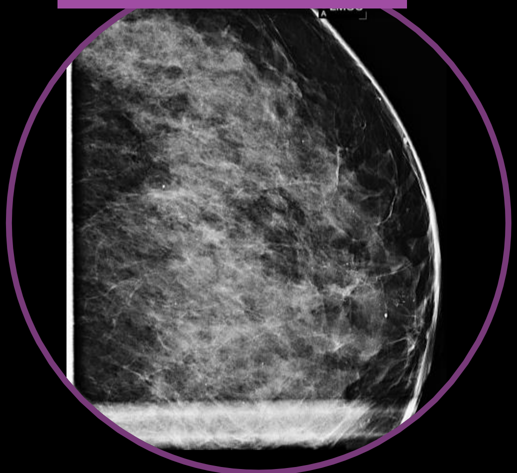


Breast staging system applies to:

Invasive Carcinoma



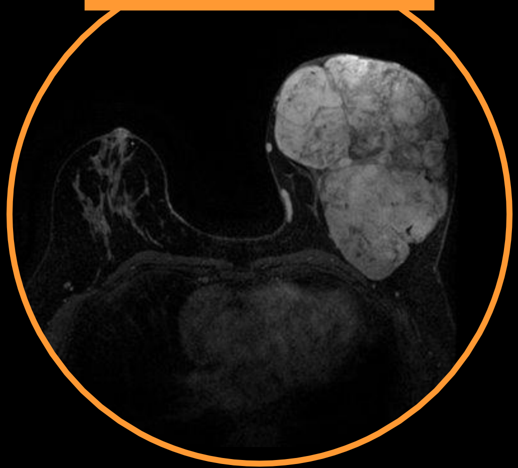
Ductal Carcinoma In Situ



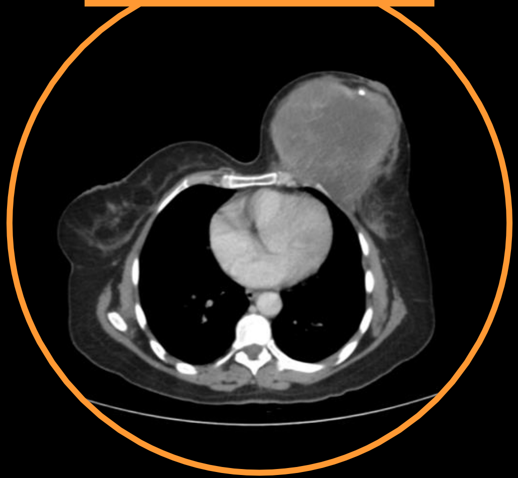
Breast staging system DOES NOT apply to:

Breast Lymphoma

Phyllodes Tumor



Breast Sarcoma



Staging system applied:

Breast lymphoma - hematologic malignancies

Phyllodes tumor and breast sarcoma - soft tissue sarcoma

INTRODUCTION

7th AJCC Edition (2010) → 8th AJCC Edition (2018)

What has changed?

Lobular carcinoma in situ (LCIS) is removed from Tis category (LCIS is treated as a benign entity)

Satellite tumor nodules in skin (T4b) must be separate from primary tumor and macroscopically identified

Adoption of prognostic stage

Response to neoadjuvant chemotherapy is evaluated as complete response, partial response and no response

Two staging system:

Anatomic Stage: based solely on anatomic extent of cancer. Appropriate for regions of world where biomarkers cannot be routinely obtained.

- Size of the primary tumor
- Nodal status
- Distant metastasis

Prognostic Stage

- T, N, M categories
- Tumor grade
- Human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), progesterone receptor (PR) status
- Oncogene expression
- Multigene panels

ANATOMIC STAGING SYSTEM

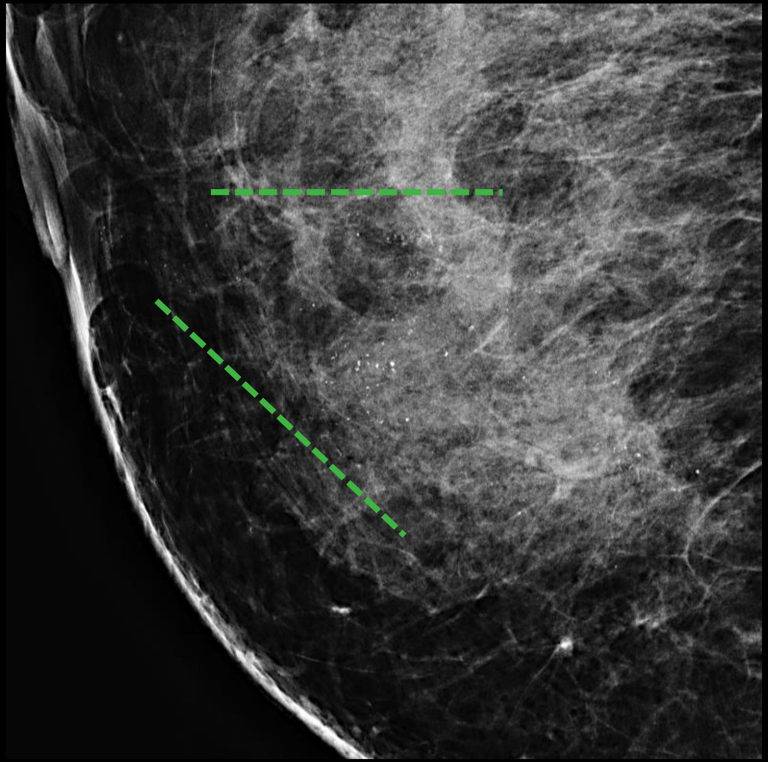
T Category

TX: Primary tumor cannot be assessed

T0: No evidence of primary

Tis: Ductal carcinoma in situ (DCIS) OR Paget disease

(NOT associated to invasive carcinoma)



Mammographic image shows
segmental pleomorphic calcifications

Breast MR image shows abnormal
right nipple enhancement (circle)

Teaching point:
The size of noninvasive carcinomas (Tis)
does not change the T category,
but it may influence therapeutic decisions

Teaching point:
Lobular carcinoma in situ (LCIS) is removed from Tis category. LCIS is treated as a benign entity and is removed from TNM staging.

ANATOMIC STAGING SYSTEM

FMUSP InRad HCFMUSP

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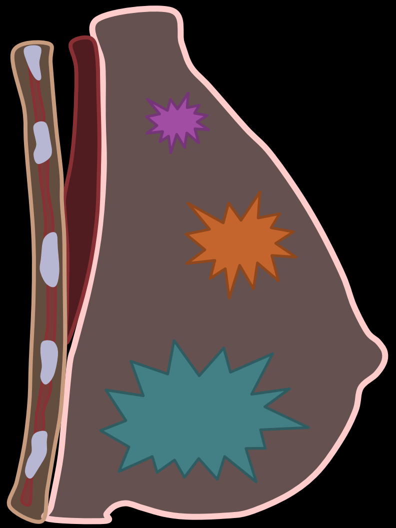
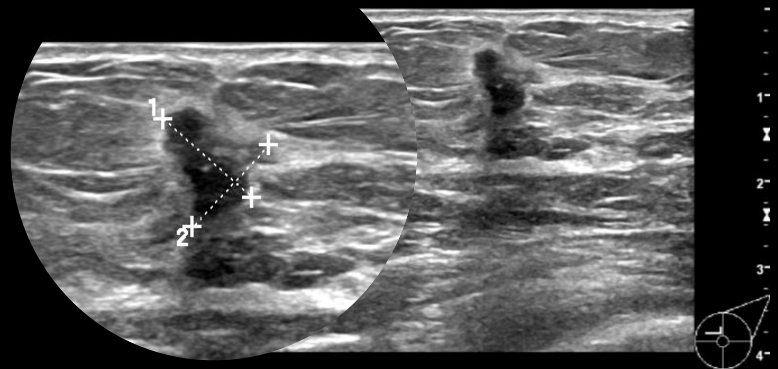
T Category



T1: Tumor size ≤ 2 cm

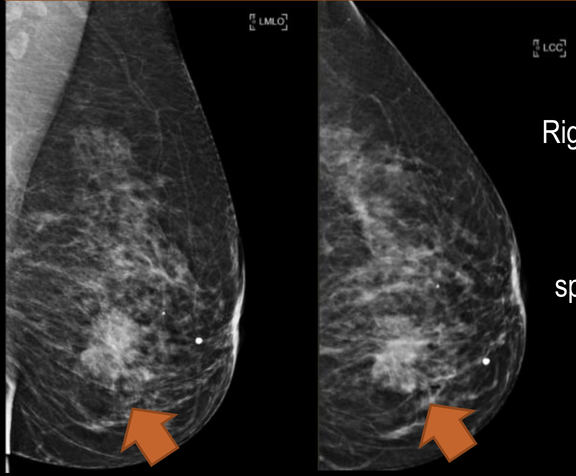


US images show indistinct mass measuring 0.8 x 0.8 x 0.6 cm

Teaching point:
If there is more than one malignant mass in the same breast, the size of the **largest tumor** should be used for staging purposes

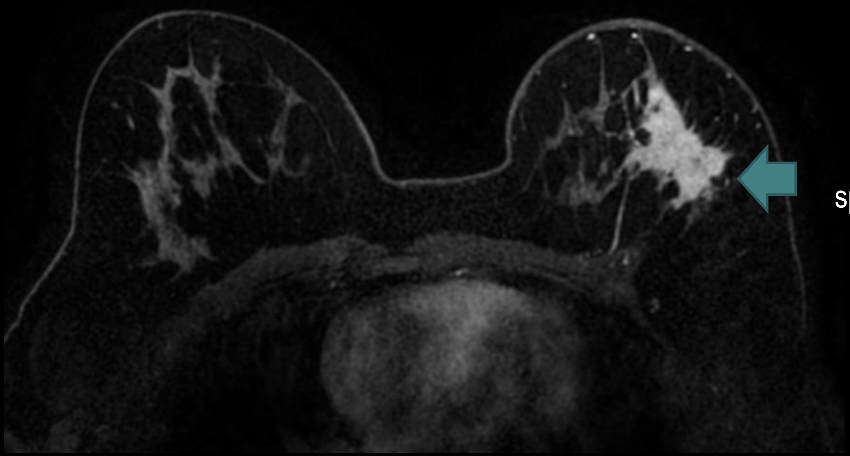
Teaching point:
The same tumor may have different measurements using different modalities (mammography / ultrasound / MR).
MR imaging demonstrates better correlation with tumor size.

T2: Tumor size > 2 cm but ≤ 5 cm



Right mediolateral oblique and craniocaudal mammographic images show spiculated mass (arrow) measuring 3.0 cm

T3: Tumor size > 5 cm



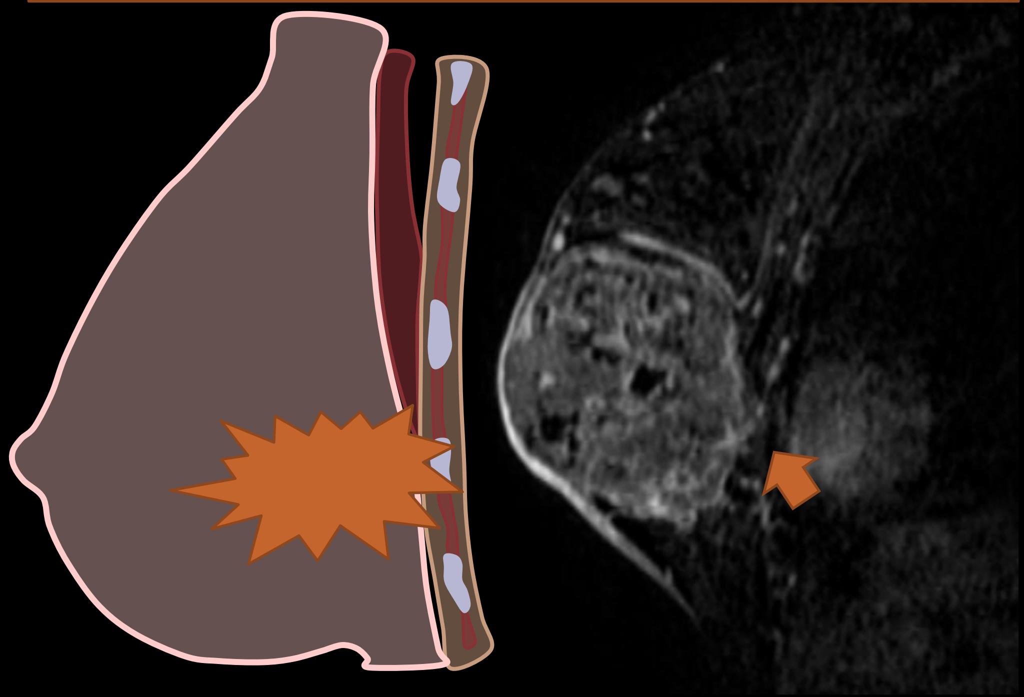
MR image shows an irregular spiculated mass (arrow) with a maximum diameter of 5.8 cm

Teaching point:
Simultaneous bilateral primary carcinomas – each carcinoma is classified and staged as a separate primary carcinoma

ANATOMIC STAGING SYSTEM

T Category

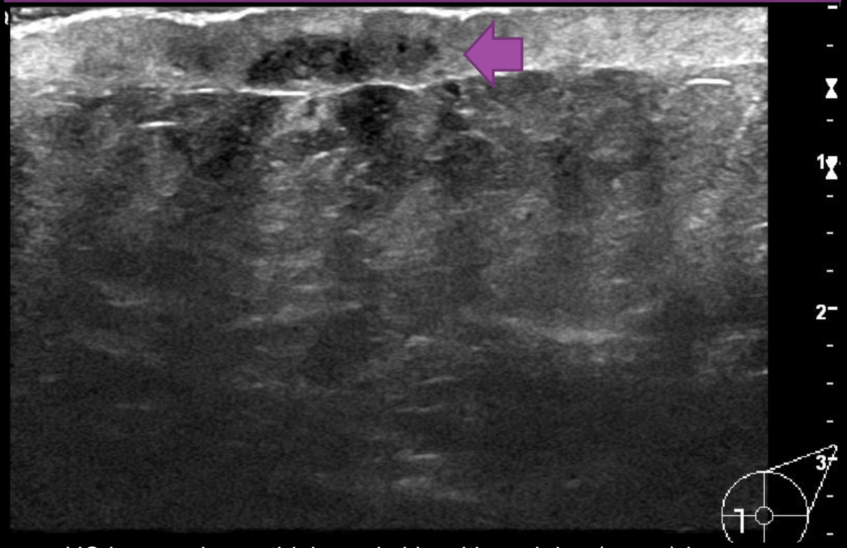
T4a: Tumor with chest wall invasion



Breast MR image shows carcinoma invasion of the chest wall (arrow)

Teaching point:
Involvement of the pectoral muscles *alone* (without involvement of the ribs, intercostal muscles or serratus anterior muscles) **are not** considered T4a

T4b: Tumor with macroscopic skin changes



US image shows thickened skin with nodules (arrow) in a patient with ipsilateral breast mass **in another quadrant**

Male patient with carcinoma breast invasion of the skin characterized by ulcerated lesion

T4c = T4a + T4b

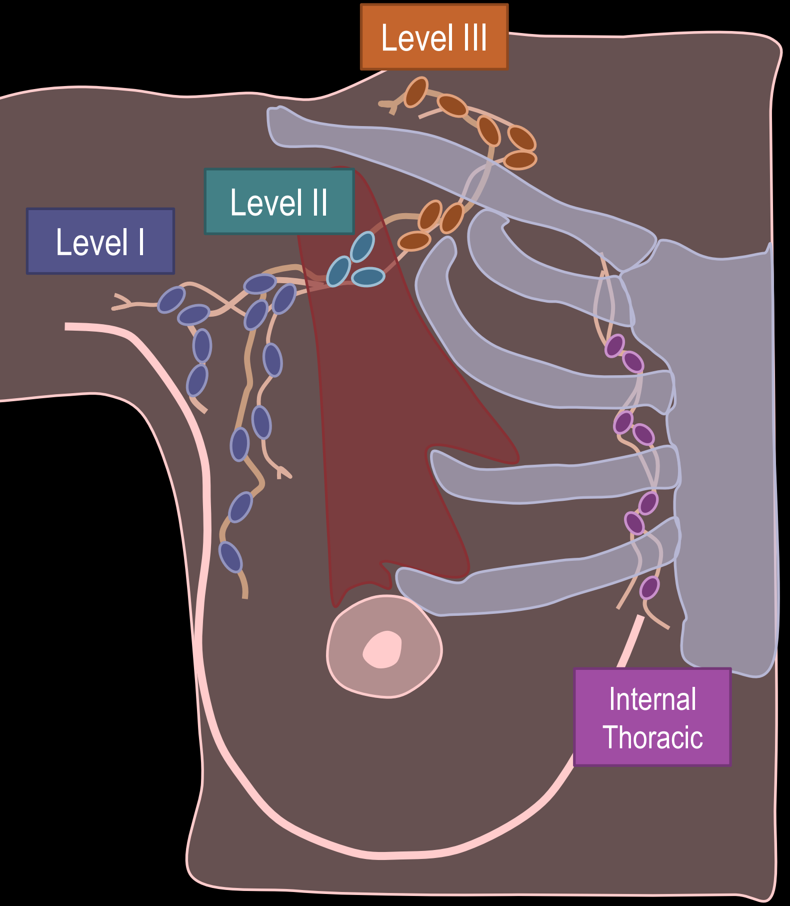
T4d: Inflammatory carcinoma

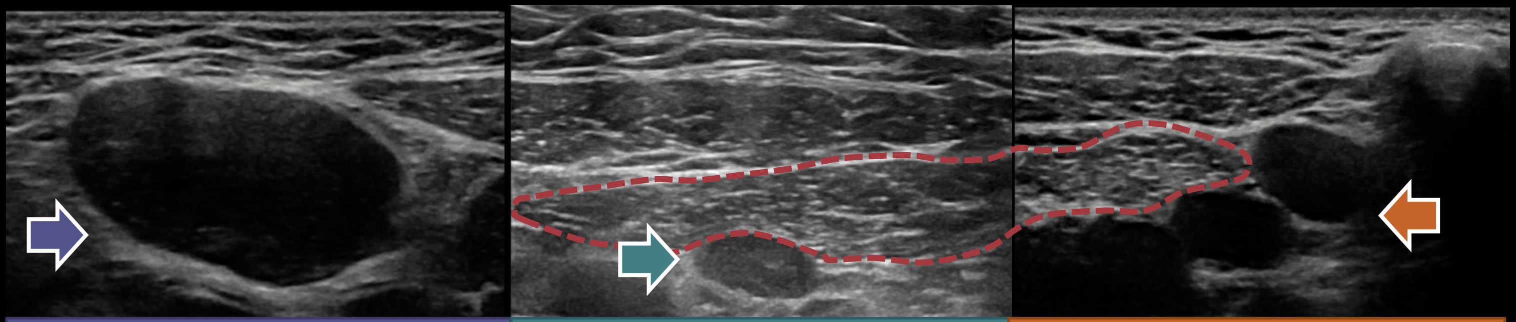
Mammographic image shows skin thickening and diffuse increased density

Teaching point:
Inflammatory carcinoma is primarily a clinical diagnosis (diffuse erythema and edema involving at least a third of the breast skin)

ANATOMIC STAGING SYSTEM

N Category





Level I: below the lower edge of the pectoralis minor muscle	Level II: underneath the pectoralis minor muscle	Level III: medial the pectoralis minor muscle

Targeted US images show right axillary lymph nodes (arrows) with atypical characteristics. Pectoralis minor muscle (brown dashed lines).

N0: No regional nodal metastases

N1: Metastases to movable ipsilateral level I and/or level II axillary nodes

N2: Metastases to fixed or matted
ipsilateral level I and / or level II axillary nodes
OR
ipsilateral internal mammary nodes without axillary involvement

N3: Metastases to ipsilateral level III axillary nodes
OR
ipsilateral internal mammary nodes
OR
ipsilateral supraclavicular nodes

Teaching point:
axillary lymph nodes
are described according to their position relative to the pectoralis minor muscle

Teaching point:
contralateral
axillary lymph nodes
are considered
distant metastasis

ANATOMIC STAGING SYSTEM

M Category

M0: No evidence of distant metastases
M1: Distant metastases

Abdomen CT shows multiple liver metastases (arrows) in a patient with breast carcinoma

Teaching point:
In patients with T1 or T2 N0 or N1 cancer, routine use of imaging to detect occult distant metastasis is **discouraged**, based on its low yield and because of the risk of false-negative

Teaching point:
For patients with clinical stage IIIA and higher locoregional disease, the diagnostic tests can be considered in the absence of clinical signs and symptoms of distant metastasis

Post Neoadjuvant Therapy Staging

- Assigned after neoadjuvant therapy
- Clinical posttreatment T category (ypT) is determined by the largest single focus of residual tumor by examination or imaging
- Clinical pretreatment and posttreatment node status (ycN) is defined by clinical and imaging findings with or without FNA or biopsy. If definitive resection of the nodes is performed, the pathologic information for this category is ypN
- The M category for patients treated with neoadjuvant therapy is the category assigned for pretreatment clinical stage prior to initiation of the treatment

Teaching point:
If a cancer was classified as inflammatory (T4d) before neoadjuvant chemotherapy, the cancer is classified inflammatory cancer after therapy, **even if complete resolution of the inflammatory findings** is observed during treatment

ANATOMIC STAGING SYSTEM

Anatomic Stage	T	N	M
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T0	N1mi	M0
	T1	N1mi	M0
Stage IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Early cancer

Locally advanced

Simplifying….

<table>
<tr><th colspan="6">M0</th></tr>
<tr><td></td><td>N0</td><td>N1mi</td><td>N1</td><td>N2</td><td>N3</td></tr>
<tr><td>Tis</td><td>Stage 0</td><td></td><td></td><td></td><td></td></tr>
<tr><td>T0</td><td rowspan="2">Stage IA</td><td rowspan="2">Stage IB</td><td rowspan="2">Stage IIA</td><td rowspan="4">Stage IIIA</td><td rowspan="5">Stage IIIC</td></tr>
<tr><td>T1</td></tr>
<tr><td>T2</td><td>Stage IIA</td><td></td><td>Stage IIB</td></tr>
<tr><td>T3</td><td>Stage IIB</td><td></td><td></td></tr>
<tr><td>T4</td><td>Stage IIIB</td><td></td><td colspan="2">Stage IIIB</td></tr>
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<table>
<tr><th colspan="2">M1</th></tr>
<tr><td></td><td>Any N</td></tr>
<tr><td>Any T</td><td>Stage IV</td></tr>
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** N1mi refers to nodal micrometastasis (<0.2 cm)

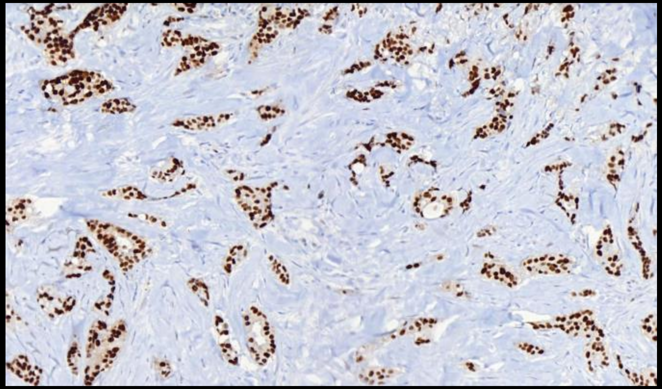
PROGNOSTIC STAGING SYSTEM

Prognostic Markers

Teaching Point:
Besides TNM cancer staging, tumor biology is important in prognosis and treatment response

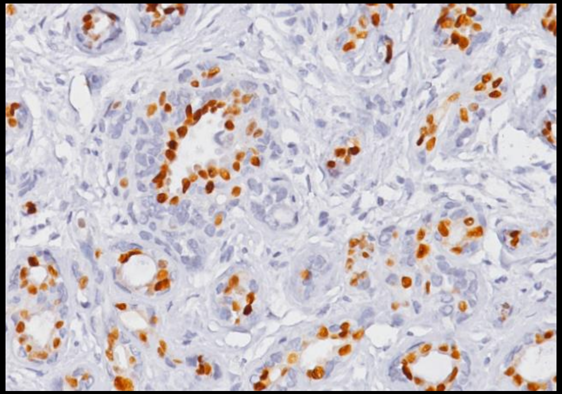
Estrogen Receptor (ER) expression

Positive immunohistochemical staining for ER



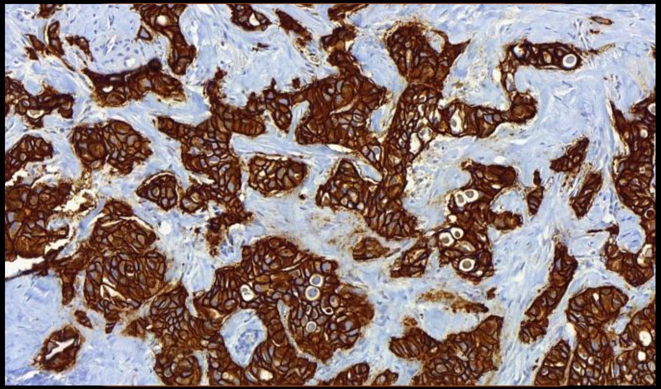
Progesterone Receptor (PR) expression

Positive immunohistochemical staining for PR



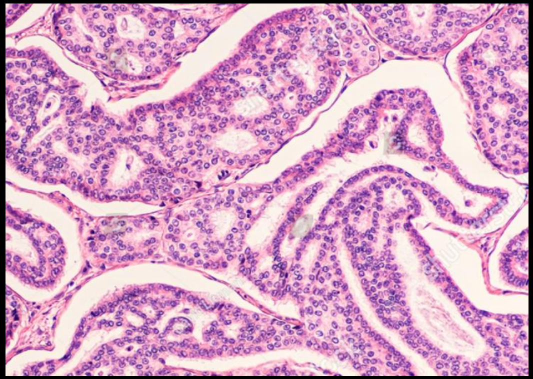
Human Epidermal Growth Factor Receptor-2 (HER-2)

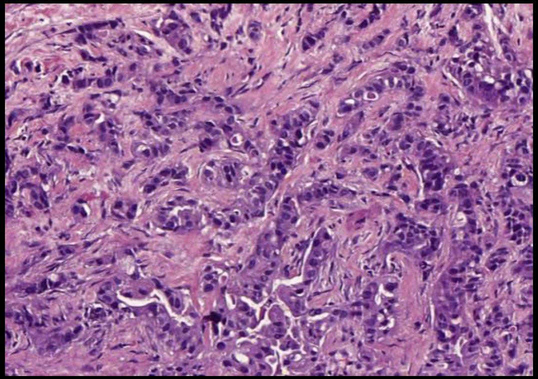
Positive immunohistochemical staining for HER-2



Tumor grade (assessed by Nottingham Grading System)

Low-grade tumors (better prognosis)
Well-differentiated (grade I) → High-grade tumors (worse prognosis)
Poorly-differentiated (grade III)





Multigene Panels

Test for the levels of expression of multiple genes in the breast tissue cancer

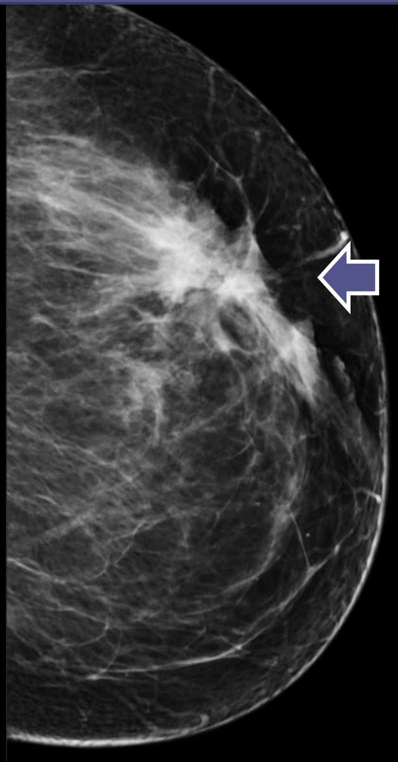
- Oncotype DX Breast Recurrence Score (AJCC Level I of Evidence) = is a genomic test based on assessment of 21 genes; the result is a mathematical formula of the weight expression of each gene combined into a single score

Teaching Point:
The incorporation of prognostic markers into the staging system results in stage migration (downstage or upstage) for some patients

PROGNOSTIC STAGING SYSTEM

Stage Migration

ER + / PR +



Espiculated mass

75% of invasive breast carcinoma are hormone receptor positive

In Luminal type cancer the prognostic stage is **often lower** than the anatomical stage

For example:

Hormone positive T1 N1 M0

Anatomic stage: IIA

Prognostic stage: IB

Down stage

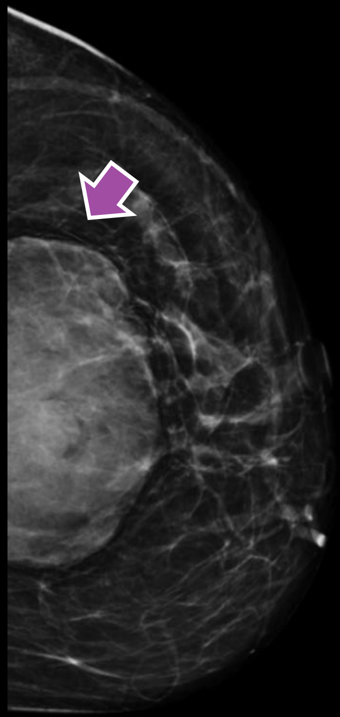
HER 2 positive

Mass with pleomorfic calcifications

Breast cancers that overexpress HER2 are generally associated to high rates of metastasis

In HER2-positive cancer, the anatomical stage and prognostic stage are **often similar**

Triple negative



Rounded well-defined mass

Triple negative corresponds to 15-20% of the breast carcinomas. They have the worst prognosis.

In Triple Negative cancer the prognostic stage is **often higher** than the anatomical stage.

For example:

Triple negative T1 N0 M0

Anatomic stage: IA

Prognostic stage: IB

Upstage

PROGNOSTIC STAGING SYSTEM

New Prognostic Biomarker: Oncotype Dx

- It's a genomic test based on assessment of 21 genes
- Predicts average 10-year distance recurrence risk in patients undergoing endocrine therapy alone
- Low, intermediate or high risk of recurrence (score 0-100)

For example:
For patients with a low-risk recurrence score, the model predicts no additional benefit of chemotherapy

- The 8th edition of the AJCC manual now incorporates Oncotype Dx recurrence scores **to potentially downstage tumors**
- Oncotype Dx applicable only for assigning prognostic stage groups to patients with:
  - T1-2 N0 M0
  - ER positive
  - HER2 negative

T1 N0 M0
or
T2 N0 M0

Any tumor grade
ER positive
HER2 negative
Any PR

Oncotype Dx < 11

Prognostic Stage IA

CONCLUSION

- The 8th edition of the AJCC Cancer Staging Manual combines prognostic biomarkers with the anatomic staging system

- The radiologist’s role in recognizing and reporting breast cancer imaging findings can change staging and clinical / surgical management

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