



BREAST CANCER

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Epidemiology:

The most common non-skin malignancy of women

2nd most common cause of cancer deaths in women, following carcinoma of the lung.

the incidence and mortality are improving with the increased screening and decreased use of hormone replacement therapy.

Risk factors:

Age:

- incidence increases rapidly after age 30
- 75% of women with breast cancer are >50 yrs

Gender

- The incidence in men is only 1% of that in women.

Family History of Breast Cancer.

- multiple affected first-degree relatives with early-onset breast cancer.

Risk factors:

Geographic Factors.

- higher in the Americas and Europe than in Asia and Africa
- migrants from low incidence to high-incidence areas tend to acquire the rates of their new home countries due to change in diet, reproductive patterns, breastfeeding practices and adoption of Western habits.

Race/Ethnicity.

- highest rate in women of European descent.
- Hispanic and African American
→ develop cancer at a younger age and develop aggressive tumors.

Risk factors:

Reproductive History.

- Early age of menarche < 12, nulliparity (never pregnant), absence of breastfeeding, and older age at first pregnancy > 35 are all associated with increased risk → due to increased the exposure to estrogenic stimulation.

Ionizing Radiation.

- Chest Radiation

Other Risk Factors.

- Postmenopausal obesity
- postmenopausal hormone replacement
- mammographic density
- alcohol consumption

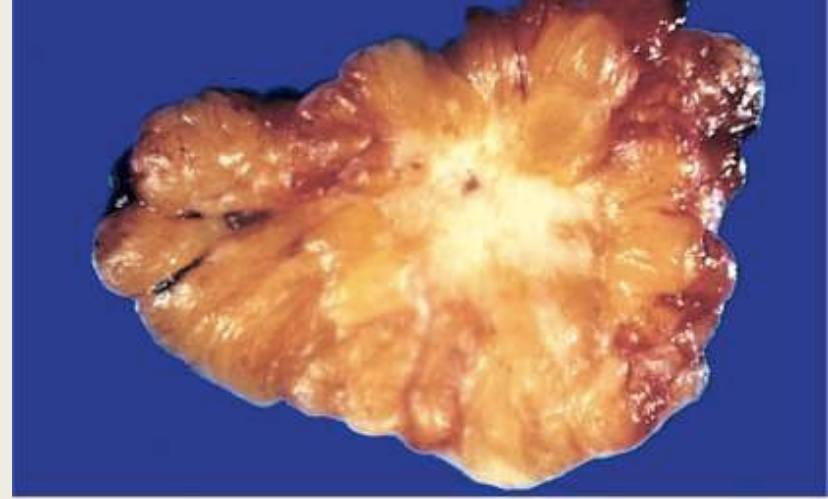
Pathogenesis:

- Factors that contribute directly to the development of breast cancer can be grouped into:
 - *genetic:*
 - *BRCA1 and BRCA2*
 - *HER2 amplification*
 - *TP53; PTEN;*

 - *Hormonal:*
 - Estrogen related

 - *environmental*

Morphology:



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Location:

- *upper outer quadrant (50%)*
- *central portion- subareolar (20%).*
- *Lower outer quadrant 10%*
- *Upper inner quadrant 10%*
- *Lower inner quadrant 10%*

4% have bilateral primary tumors or sequential lesions in the same breast.

Breast carcinoma:

A. Noninvasive: (confined by a basement membrane and do not invade into stroma or lymphovascular channels), include:

1. Ductal carcinoma in situ (DCIS)
2. Lobular carcinoma in situ (LCIS)

B. Invasive (infiltrating):

1. Invasive ductal carcinoma-NOS → 70% to 80%
2. Invasive lobular carcinoma → 10% to 15%
3. Carcinoma with medullary features → 5%
4. Mucinous carcinoma (colloid carcinoma) → 5%
5. Tubular carcinoma → 5%
6. Other types

NONINVASIVE (IN SITU) CARCINOMA

- **include:**

1. Ductal carcinoma in situ, DCIS

2. Lobular carcinoma in situ, LCIS

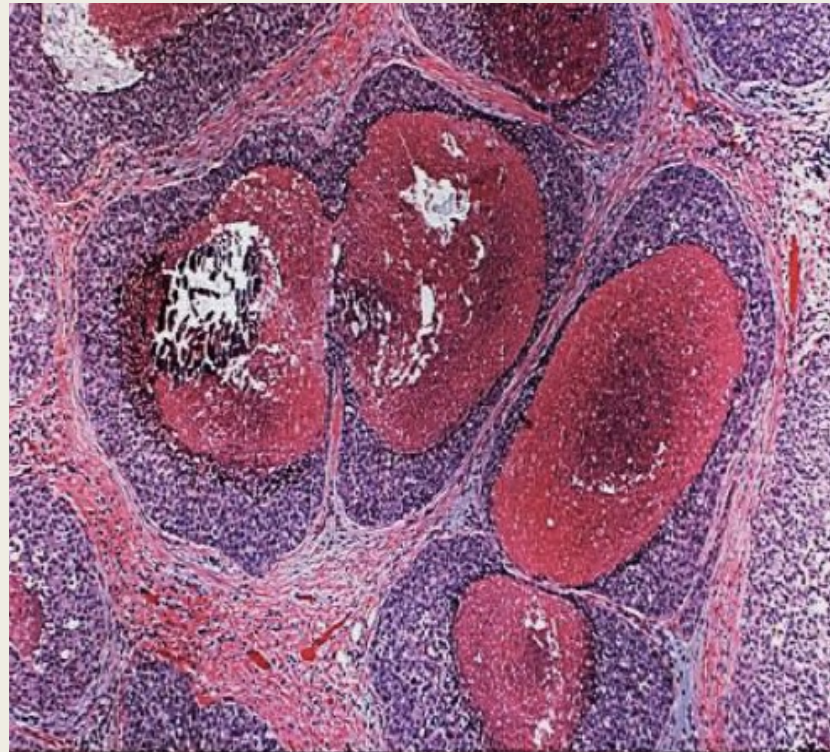
- **By definition both confined by a basement membrane and do not invade into stroma or lymphovascular channels**

LOBULAR carcinoma in-situ (LCIS)

- Malignant clonal proliferation of cells within lobules and ducts
- Cells grow in a discohesive fashion → an acquired loss of the tumor suppressive adhesion protein E-cadherin.
- The term “lobular” was used to describe this lesion because the proliferation takes **an appearance resembling lobules**

Ductal carcinoma in-situ (DCIS)

- malignant clonal proliferation of epithelial cells within ducts and lobules.
- DCIS has a wide variety of histologic appearances including:
 - *solid, comedo, cribriform, papillary, and micropapillary*



The background of the slide is a grayscale micrograph of breast tissue. It shows several lobules, which are clusters of cells. One prominent lobule in the center-right is significantly enlarged and distorted, with cells that are more densely packed and irregular in shape compared to the surrounding normal lobules, illustrating the concept of an infiltrating mass. The overall image is framed by a thick black L-shaped border on the left and bottom sides.

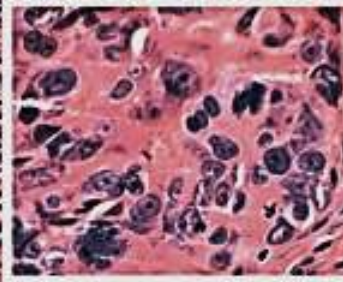
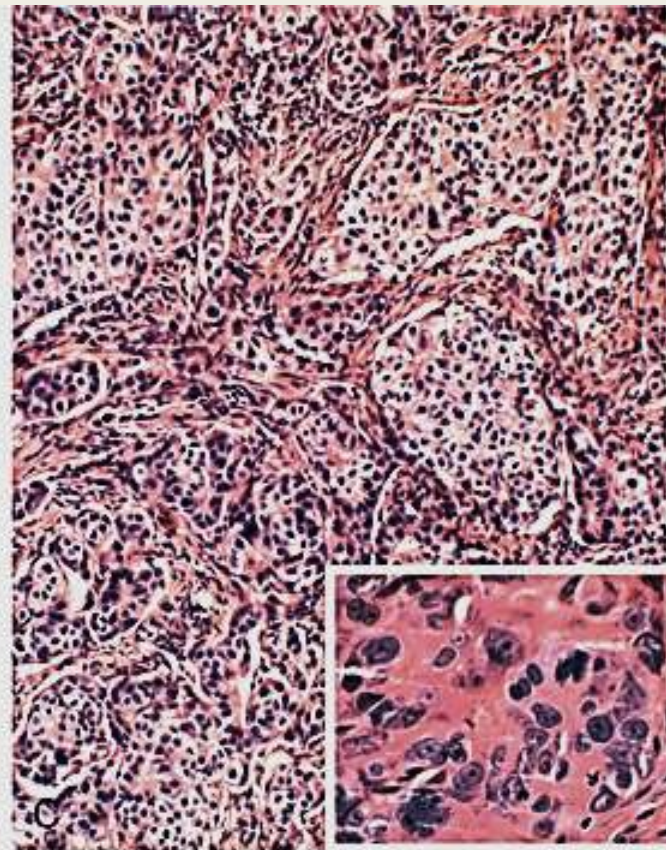
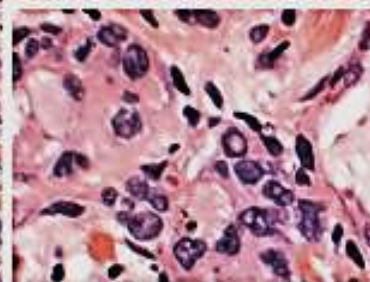
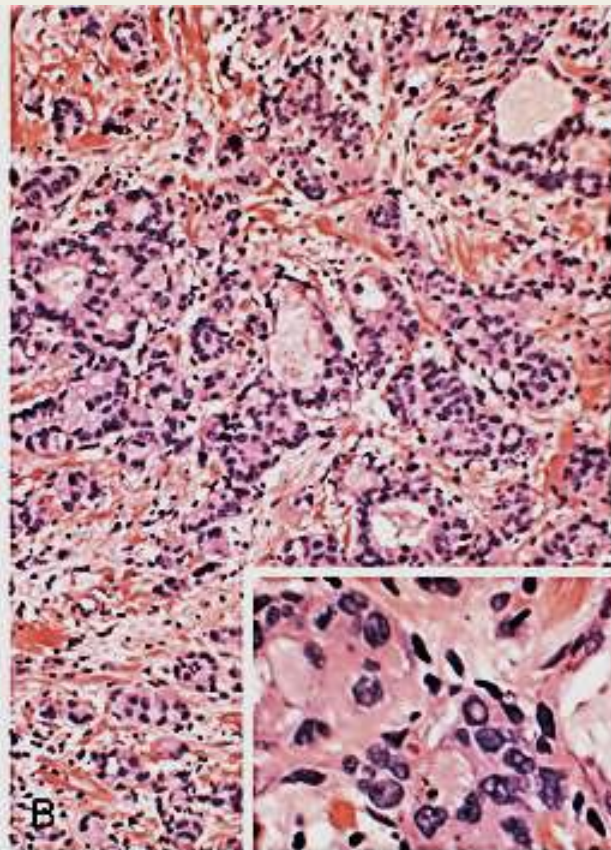
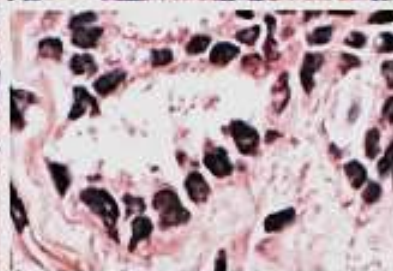
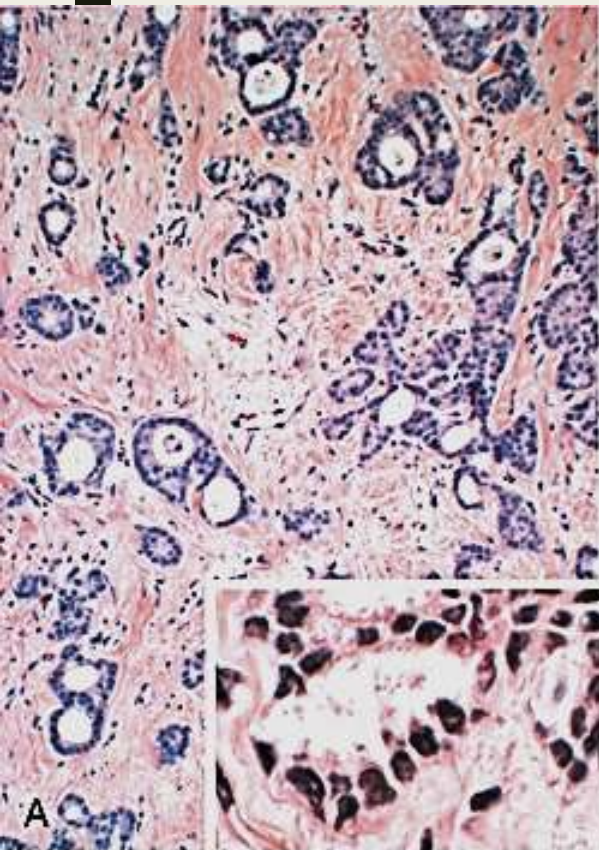
**INVASIVE (INFILTRATING)
BREAST CARCINOMA**

Classification Systems

- In all cases of breast cancer, we examine the following Receptors:
 - Estrogen receptor (**ER**);
 - progesterone receptor (**PR**);
 - human epidermal growth factor receptor 2 (**HER2/neu**)
- Cancer can be classified according to expression of hormone receptors into three major groups:
 - ER positive (HER2 negative; $\approx 60\%$)
 - HER2 positive (ER positive or negative; 20%)
 - Triple negative (ER, PR, and HER2 negative; 10%)

Invasive ductal carcinoma

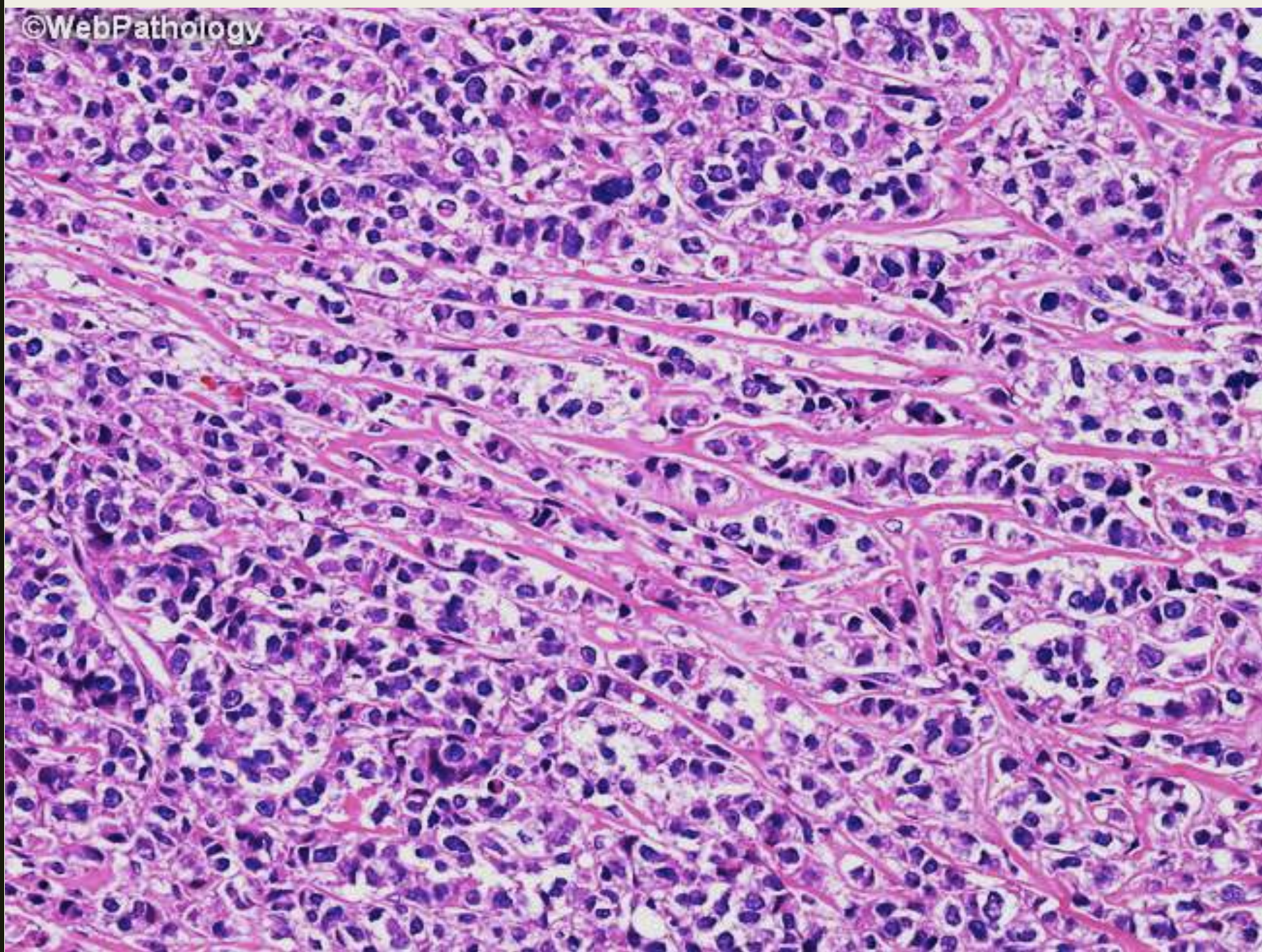
- 70% to 80%
- Also called Carcinomas "not otherwise specified"
- **Precancerous lesion:** usually DCIS
- **Clinical presentation:** mammographic density or hard, palpable irregular mass.
- Receptor profile:
Usually: ER, PR (+), HER2 (-)



Kumar et al: Robbins Basic Pathology, 9e.
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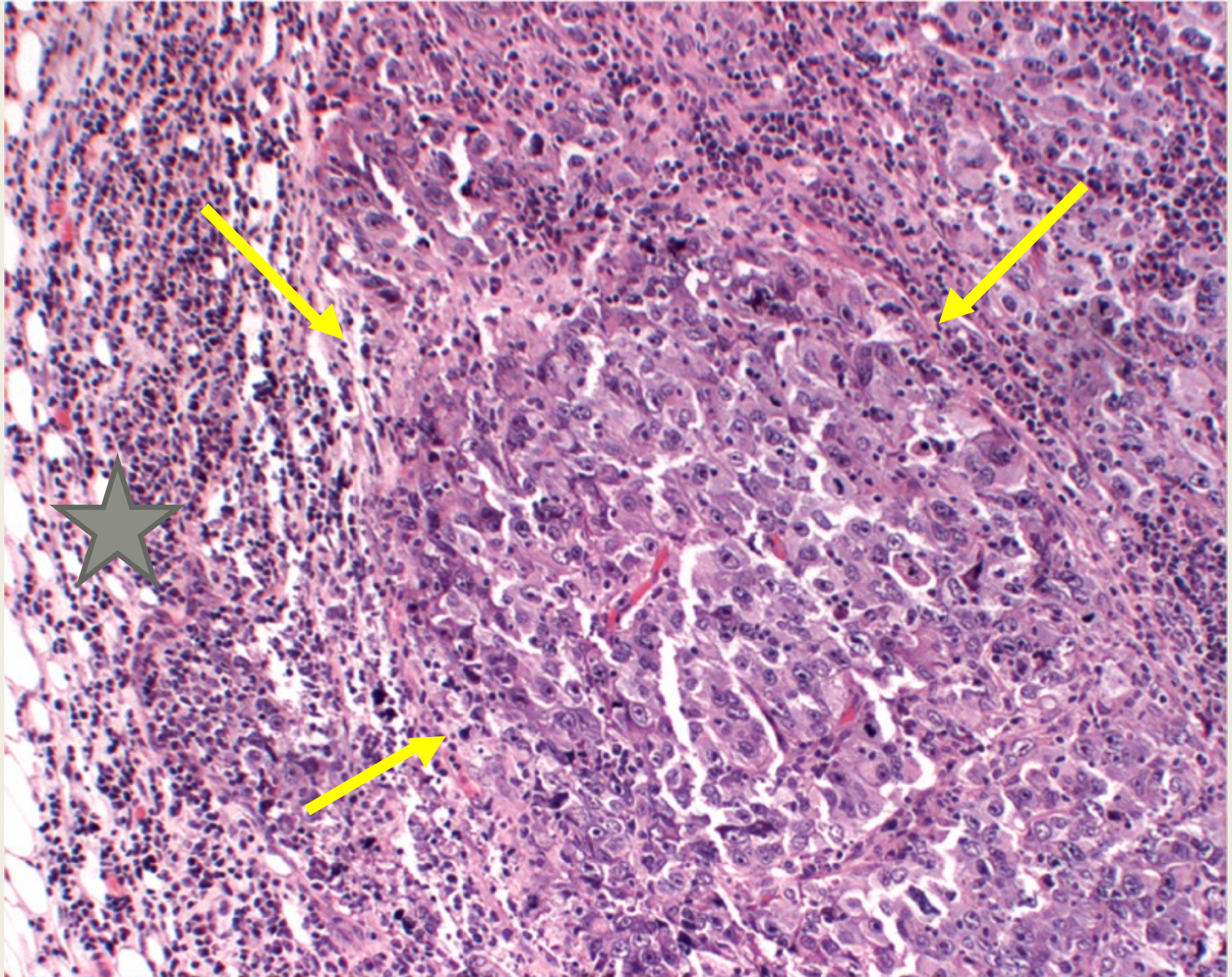
Invasive lobular carcinoma

- 10-15% of all breast carcinomas.
- **Precancerous lesion.** 2/3 associated with LCIS.
- multicentric and bilateral (10% to 20%).
- **Clinical presentation.** Most present as palpable masses or mammographic densities
- Histologically, cells invade stroma **individually** and often are aligned in “**single-file**”
- receptor profile: Usually express ER & PR while HER2 overexpression is rare or absent.



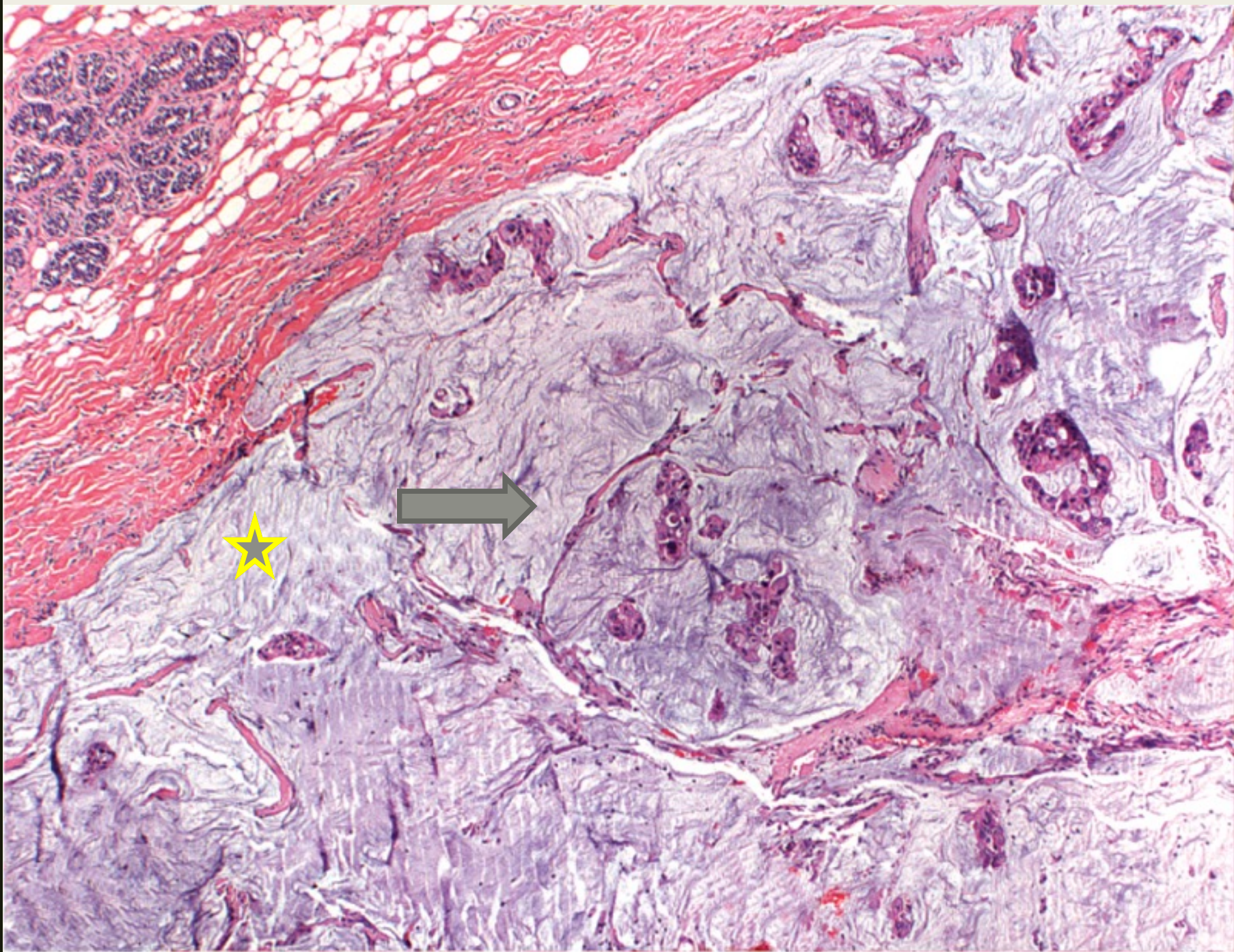
carcinoma with Medullary features:

- 5%
- **Microscopically:** large anaplastic cells with pushing, well-circumscribed borders. With a pronounced lymphocytic infiltrate.
- **Precancerous lesions.** usually absent
- increased frequency in women with ***BRCA1* mutations.**
- receptor profile: Triple negative (ER, PR, and HER2 all negative).



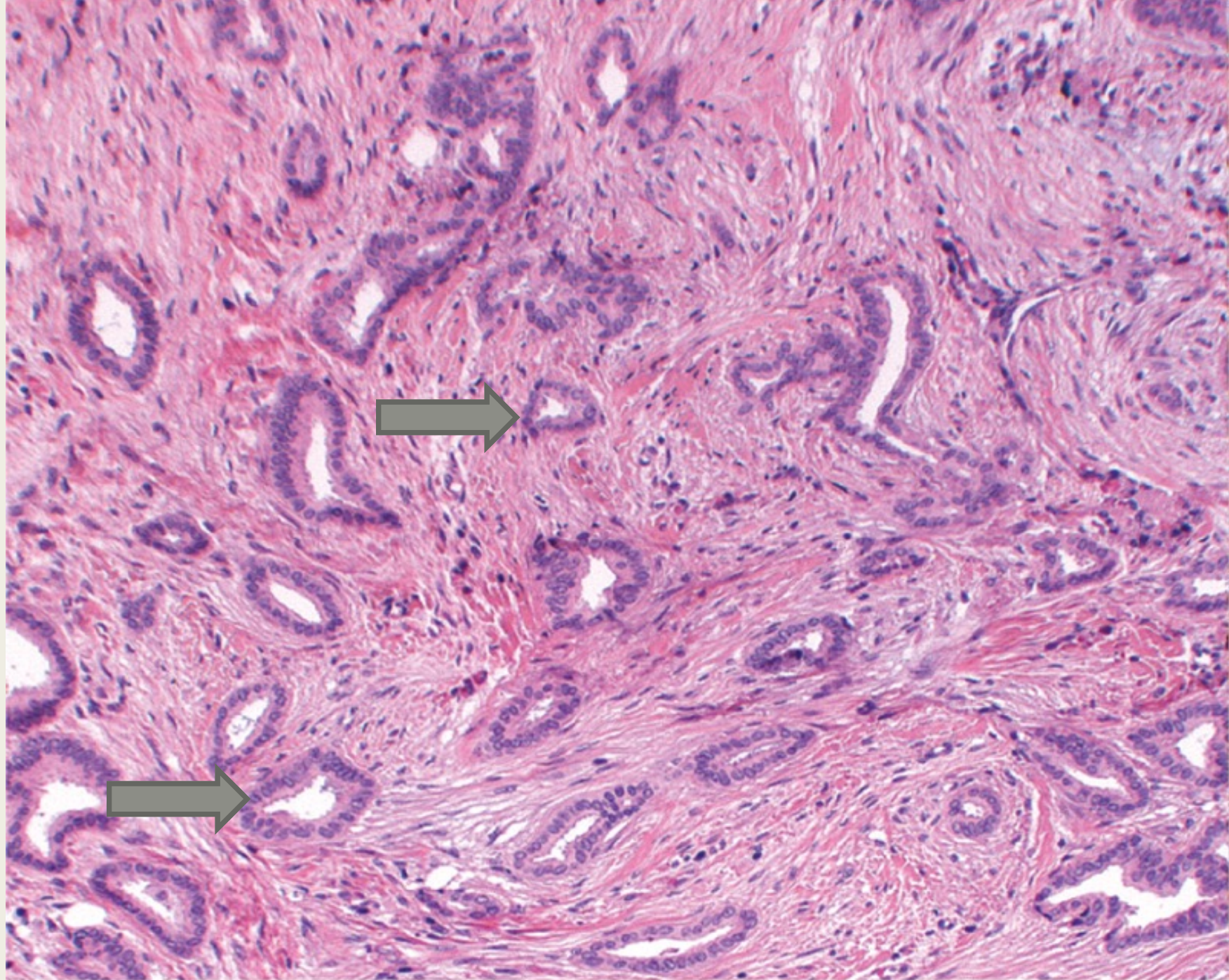
Colloid (mucinous) carcinoma

- a rare subtype.
- **Grossly** the tumors are usually soft and gelatinous.
- **Microscopic picture.** The tumor cells produce abundant quantities of extracellular **mucin** that dissects into the surrounding stroma.
- **receptor profile:** ER-positive, HER2- negative



Tubular carcinomas

- **<5%**
- **Clinical presentation.** Almost always detected as irregular mammographic densities.
- **Microscopically**, well-formed tubules with low-grade nuclei.
- **Lymph node metastases: rare**
- **Prognosis: excellent.**
- **Receptor profile:** ER-positive, HER2- negative



Features Common to All Invasive Cancers

- **Fixation:** adherent to the pectoral muscles or deep fascia of the chest wall
- **retraction or dimpling** of the skin or nipple: adherence to the overlying skin
- **peau d'orange** (orange peel): Involvement of the lymphatic pathways cause localized lymphedema, the skin becomes thickened and exaggerated around hair follicles

Spread of Breast Cancer

- through **lymphatic** and **hematogenous** channels.
- Favored mets are the **bone, lungs, skeleton, liver,** and **adrenals** and (less commonly) the brain, spleen, and pituitary.
- Metastases may appear many years after therapeutic control of the primary lesion
- SCREENING :
 - *mammographic screening*
 - *Magnetic resonance imaging MRI*

PROGNOSIS

1. Tumor stage:

1. *Invasive carcinoma versus carcinoma in situ*
2. *tumor size.*
3. *Lymph node involvement and the number of lymph nodes involved by metastases.*
4. *Distant metastases.*

2. Histologic grade

3. histologic type of carcinoma

4. Lymphovascular invasion

5. estrogen or progesterone receptors expression

6. Overexpression of HER2

- the importance of evaluating HER2 s to predict response to a monoclonal antibody ("Herceptin") against the gene product.

References:

- Diagnostic pathology book, normal histology, 2nd edition, LINDBERG LAMPS
- ❖ Robbins basic pathology, 10th edition
- ❖ Robbins and Cortan Atlas of Pathology, 3rd edition
- ❖ <https://www.webpathology.com>

The image features a central white rectangular area with a black border. Inside this area, the word "QUESTIONS!" is written in a large, bold, black, sans-serif font. The background of the entire image is a collage of various question marks in different colors (blue, yellow, red, green, pink) and patterns (solid, striped, dotted). Below the white area, several hands of different skin tones are raised, suggesting a Q&A session or a public forum.

QUESTIONS!

An aerial photograph of a multi-lane highway with several cars driving on it. The image is framed by a large, thick black L-shaped graphic that forms a partial border around the central text. The background is a light teal color with a subtle, wavy texture.

THANK YOU