

Male Breast Cancer

Pathogenesis · Morphology · Clinicopathologic correlation

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Learning objectives

Recognize

Relate male ductal anatomy to clinical presentation.

Explain

Assess familial, hormonal and environmental risk factors.

Diagnose

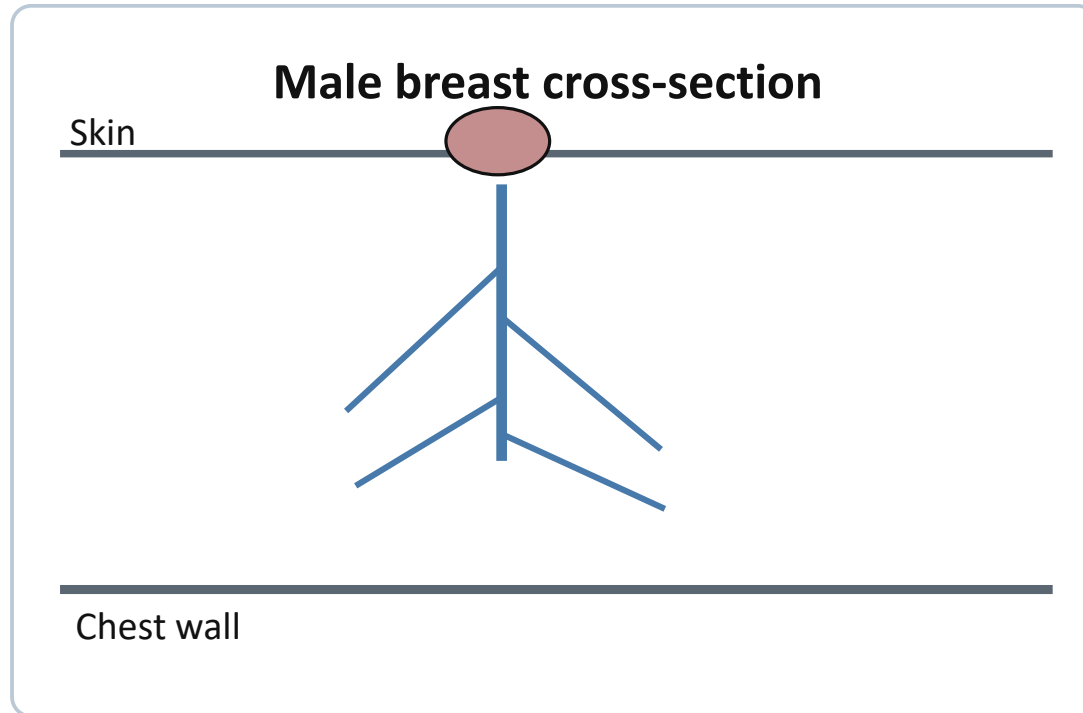
Interpret morphology, grade and ER/PR/HER2 profiles.

Integrate

Explain regional spread, prognosis and treatment logic.

Male breast: The substrate for carcinoma

Schematic



Why location matters

Male breast epithelium is concentrated in relatively large ducts close to the nipple.

Diagnostic implication

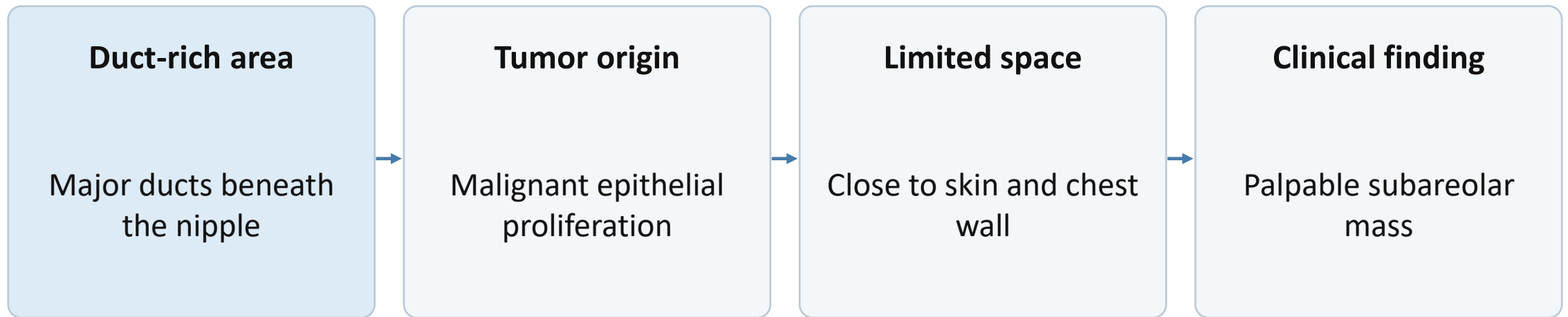
This duct-centered anatomy helps explain the usual subareolar presentation.

Ducts predominate; Lobules are sparse

- The normal breast contains major ducts, branching ducts and terminal lobular units.
- In males, epithelial tissue remains mainly in the large ducts near the nipple.
- Lobules are generally undeveloped in the male breast.
- The anatomic substrate helps explain why duct-type carcinomas dominate.

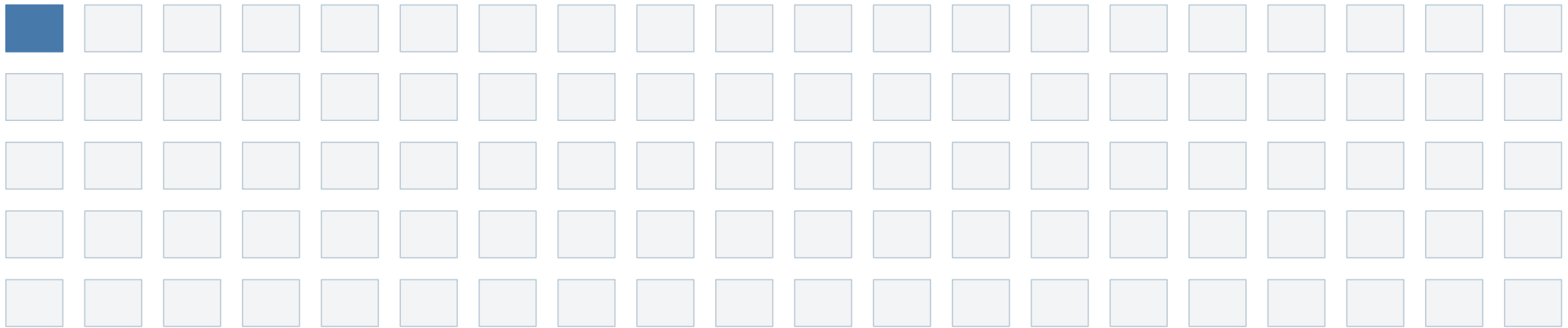
Anatomic explanation of the central mass

Schematic



The site of origin contributes directly to the presenting clinical pattern.

Male breast cancer is uncommon



1 of 100

Male incidence as ~1% of female incidence.

Population lifetime risk remains low

0.13%

Reported lifetime risk in males

Interpretation

Population risk is small; An affected first-degree relative or pathogenic germline variant changes individual risk.

U.S. Burden: Textbook estimate for 2025

2,800

Estimated U.S. New male cases in 2025

510

Estimated U.S. Male breast-cancer
deaths in 2025

A historical estimate quoted by Robbins, not a 2026 surveillance update.

Risk-factor categories

Demographic

Increasing age; Western-country residence

Familial

First-degree affected relative; Inherited predisposition

Hormonal / metabolic

Exogenous estrogen, obesity, infertility

Exposure / history

Radiation, alcohol, prior benign breast disease

Increasing age is an important risk factor

- Older age among the leading epidemiologic associations.
- A new breast mass in an older male should not be assumed benign.
- Age is a risk factor—not a diagnostic criterion.
- Interpret the age effect together with family history and examination.

Family history changes the prior probability

- A first-degree relative with breast cancer is a recognized risk factor.
- Family history should include breast cancer in female and male relatives.
- A pathogenic familial susceptibility variant may be present.
- Absence of a striking family history does not exclude a hereditary cause.

BRCA2 is the major familial susceptibility gene

~6%

Male BRCA2 carriers developing breast cancer (as reported by Robbins)

Important denominator

This is risk among male carriers—not the proportion of male tumors caused by BRCA2.

BRCA2 prevalence varies across cohorts

4%–40%

Reported BRCA2 germline mutation frequency among male breast-cancer cases

Sampling matters

Robbins explicitly attributes this wide range to the population tested.

Other inherited susceptibility genes

BRCA1

Increased risk, lower than with BRCA2

PALB2

Higher-than-baseline susceptibility

PTEN

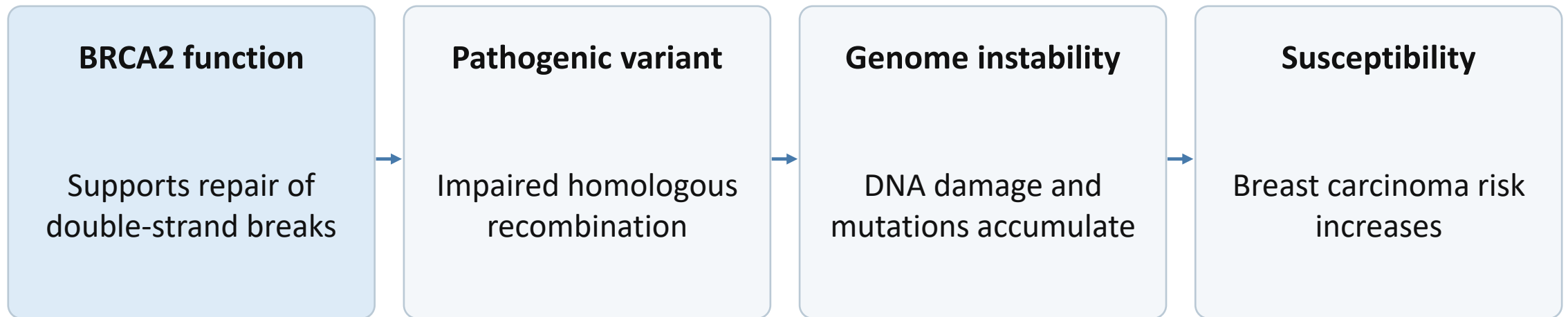
A lower-risk association in the male context

TP53

A lower-risk association in the male context

BRCA2 and homologous recombination repair

Schematic



Mechanistic association; Progression is not deterministic for every carrier.

Keep two BRCA2 denominators separate

- Risk among male BRCA2 carriers: Approximately 6% develop breast cancer.
- Prevalence among affected male cases: 4%–40% depending on cohort.
- These figures answer different epidemiologic questions.
- Neither estimate can be substituted for the other.

Exogenous estrogens and hormonal milieu

- Exposure to exogenous estrogens is a textbook-listed risk factor.
- An estrogen– androgen imbalance also contributes to gynecomastia.
- Hormonal effects and malignancy risk are different clinical concepts.
- An enlarged breast is not, by itself, proof of carcinoma.

Obesity and infertility in the risk profile

- Obesity among male breast cancer risk factors.
- Infertility is also included as an epidemiologic association.
- These factors should be documented within a complete risk assessment.
- They are neither necessary nor sufficient for cancer development.

Klinefelter syndrome: Two related findings

Benign breast enlargement

Klinefelter syndrome may be associated with gynecomastia.

Cancer predisposition

Klinefelter syndrome is listed among male breast cancer risk factors.

Radiation and other external exposures

- Prior ionizing-radiation exposure appears' risk-factor list.
- Alcohol consumption is also associated with male breast cancer risk.
- A careful exposure history is relevant to risk characterization.
- An exposure history cannot establish a diagnosis without tissue evaluation.

Additional epidemiologic associations

- Prior benign breast disease is listed as a risk factor by Robbins.
- Western-country residence is another reported association.
- These are group-level associations; They do not define causality for an individual.
- Clinical suspicion still depends on presentation and examination.

Risk assessment: Document the right history

Domain	Specific questions	Clinical relevance
Familial	First-degree affected relative; known BRCA2 variant	Identifies inherited susceptibility
Hormonal	Estrogen exposure; infertility; Klinefelter syndrome	Relevant endocrine background
Exposure	Chest irradiation; alcohol	Potential environmental factors
Metabolic / age	Age; obesity; benign breast history	Modifies risk context

Clinical application: Susceptibility

Teaching vignette — hypothetical

A 63-year-old man with a firm breast lesion reports that his sister was diagnosed with breast cancer and his father carried a pathogenic BRCA2 variant.

Which aspect of his history is most important to integrate with the biopsy findings?

Risk vignette: Interpretation

- A known familial BRCA2 pathogenic variant is a major inherited susceptibility clue.
- First-degree breast-cancer family history independently reinforces concern.
- The lesion still requires standard diagnostic assessment.
- A risk factor informs prior probability; It does not replace pathology.

The dominant cancer is invasive NST

>90%

Invasive carcinoma of no special type

Characteristic phenotype

Typically ER-positive, PR-positive and HER2-negative.

Special histologic types are exceptional

<5%

Special histologic types collectively (Robbins)

Diagnosis

Do not assume that every unusual architecture represents a special histologic type; Classification requires morphology.

Hormone-receptor pattern of the usual tumor

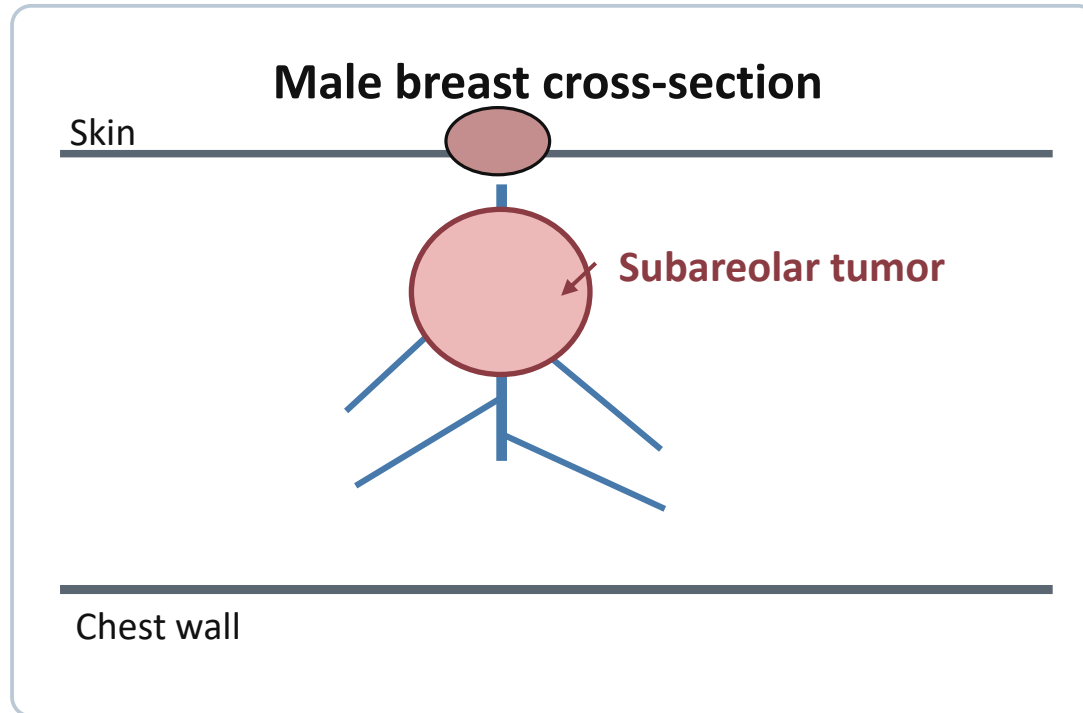
- The dominant male subtype as ER-positive.
- Progesterone receptor is also generally expressed.
- HER2 negativity is characteristic of this dominant category.
- Each tumor requires individual testing; The population pattern is not a substitute.

Why invasive lobular carcinoma is unusual

- Lobular carcinoma ordinarily relates to breast lobular differentiation.
- Male breast epithelium is mainly confined to large ducts.
- The very limited lobular apparatus helps explain rarity of lobular carcinoma.
- A genuine special subtype remains possible, but needs morphologic confirmation.

Central location drives the clinical pattern

Schematic



Why location matters

The usual malignant mass arises near large ducts beneath the nipple.

Diagnostic implication

Even a small tumor can abut the skin and chest-wall structures.

Palpable mass: The canonical presentation

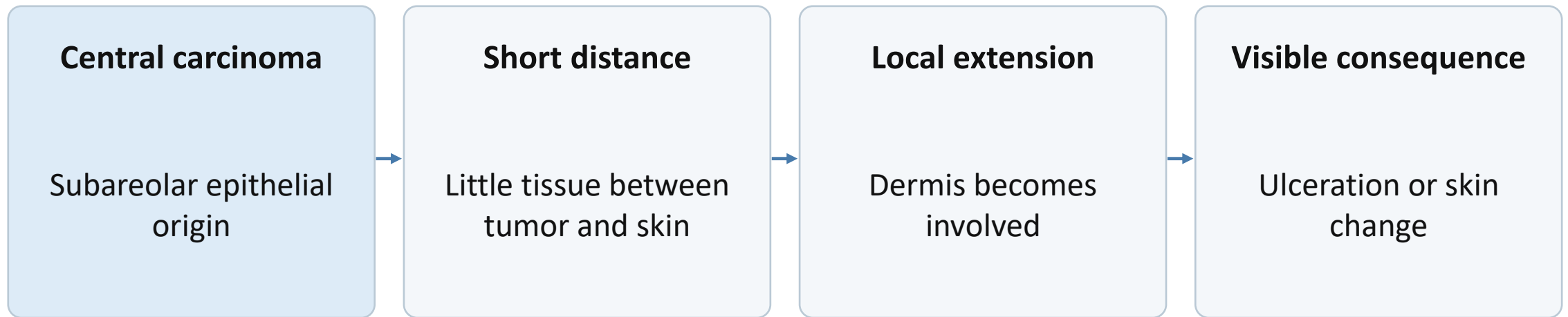
- The primary clinical presentation is a palpable subareolar mass.
- Typical tumor size at presentation as 2–3 cm.
- A new firm unilateral lesion must not be dismissed as physiologic enlargement.
- Local examination includes the nipple, skin and regional nodes.

Nipple discharge is another presenting clue

- Nipple discharge may accompany male breast carcinoma.
- A central ductal lesion can communicate with the nipple apparatus.
- A discharge complaint needs assessment in the context of a mass and examination.
- The symptom alone does not determine histologic type.

Skin invasion can occur in a small tumor

Schematic



The apparent size of a mass need not reflect its potential for local extension.

Close chest-wall relationship matters

- The male breast offers little separation from the underlying thoracic wall.
- Relatively small cancers may reach adjacent deep structures.
- Chest-wall invasion is a staging-relevant feature.
- Local extension should be documented separately from tumor size.

Gross appearance of invasive carcinoma NST

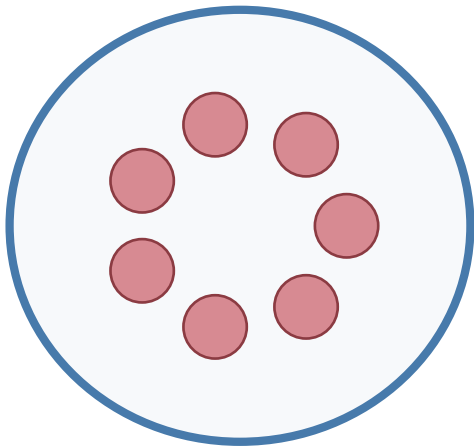
- The parent section describes a hard, irregular mass as a common gross pattern.
- An exuberant desmoplastic response produces dense fibrous stroma.
- Gross boundaries may be less clear than the palpated mass.
- These are general invasive NST features, not a male-specific diagnostic signature.

What histologic invasion means

Schematic

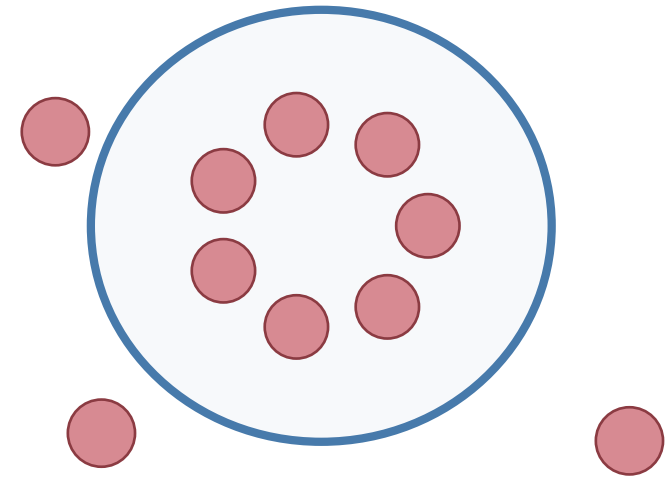
Intact duct

Carcinoma confined within the duct remains bounded by the epithelial–stromal interface.



Invasive cancer

Malignant epithelial cells extend beyond the ductal boundary into surrounding tissue.



Conceptual diagram, not a histologic specimen

Microscopic morphology of invasive NST

- Invasive malignant epithelial glands, nests or sheets infiltrate stroma.
- A desmoplastic reaction may dominate the surrounding tissue.
- Architecture varies with tumor differentiation.
- Morphology establishes subtype; ER/PR/HER2 describe treatment-relevant biology.

Grade: Tubule formation

- Well-differentiated tumors retain substantial glandular differentiation.
- Poorly differentiated tumors form fewer recognizable tubules.
- The degree of tubule formation contributes to Nottingham grade.
- Tumor type and grade are related but separate observations.

Grade: Nuclear pleomorphism

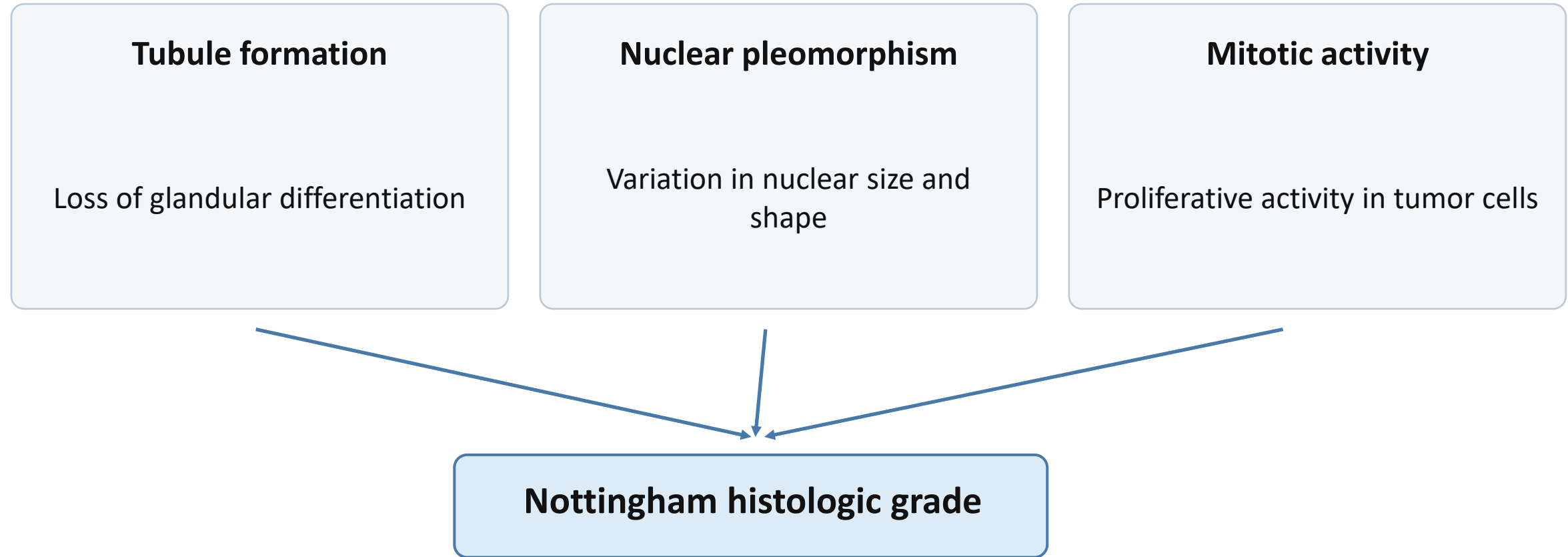
- Lower-grade tumors have more uniform nuclear morphology.
- Higher-grade tumors show larger, irregular and more variable nuclei.
- Nuclear appearance is scored separately from glandular formation.
- This is a microscopy-based assessment, not a biomarker assay.

Grade: Mitotic activity

- Mitotic activity reflects cellular proliferation in tumor tissue.
- Grade 3 carcinomas characteristically show more mitotic figures.
- Necrosis may accompany highly proliferative, poorly differentiated cancers.
- A high mitotic rate is not interchangeable with HER2 positivity.

Nottingham grading combines three features

Schematic



Three core predictive biomarkers

Schematic

ER

Nuclear receptor

Endocrine therapy

PR

Nuclear receptor

Hormone-signaling context

HER2

Cell-surface receptor

HER2-directed therapy

Tumor biology guides treatment selection; Phenotype must be measured, not inferred.

ER assessment: A nuclear IHC biomarker

- ER immunohistochemistry detects nuclear receptor expression.
- The parent section defines ER positivity as at least 1% of tumor nuclei staining.
- ER predicts likelihood of benefit from endocrine therapy.
- The dominant male subtype is ER-positive, but results must be reported per tumor.

PR expression supplies additional context

- PR expression is usually assessed by nuclear immunohistochemistry.
- ER-positive carcinomas frequently coexpress PR.
- Low PR expression can be associated with less favorable outcomes in ER-positive disease.
- Receptor results should be interpreted as a panel, not as isolated labels.

HER2 testing: Protein and amplification

- HER2 is assessed using membrane immunohistochemistry.
- In situ hybridization can evaluate HER2 gene amplification.
- HER2 positivity has important predictive implications for targeted agents.
- Most male cancers are HER2-negative.

Biomarker roles are not interchangeable

Measure	What it contributes	Why it matters
ER	Tumor endocrine phenotype	Predicts endocrine treatment sensitivity
PR	Additional hormone receptor information	Refines interpretation of ER-positive cancers
HER2	Growth-receptor status	Predicts HER2-targeted therapy benefit
Grade	Tumor differentiation and proliferation	Prognostic tumor biology information

Gynecomastia: A common benign mimic

- Gynecomastia is the most frequent benign lesion in the male breast.
- It typically presents as button-like subareolar enlargement.
- The enlargement may be unilateral or bilateral.
- It reflects relative estrogenic effects rather than malignant epithelial invasion.

Gynecomastia: Ductal hyperplasia and fibrosis

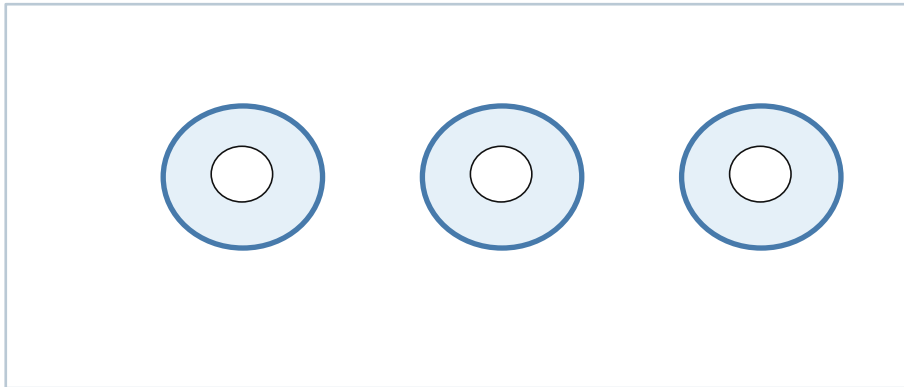
- Histology shows increased duct lining epithelial cells.
- Dense collagenous connective tissue accompanies the epithelial proliferation.
- Lobules are almost never formed.
- These features differ fundamentally from infiltrating malignant glands.

Benign proliferation versus stromal invasion

Schematic

Benign enlargement

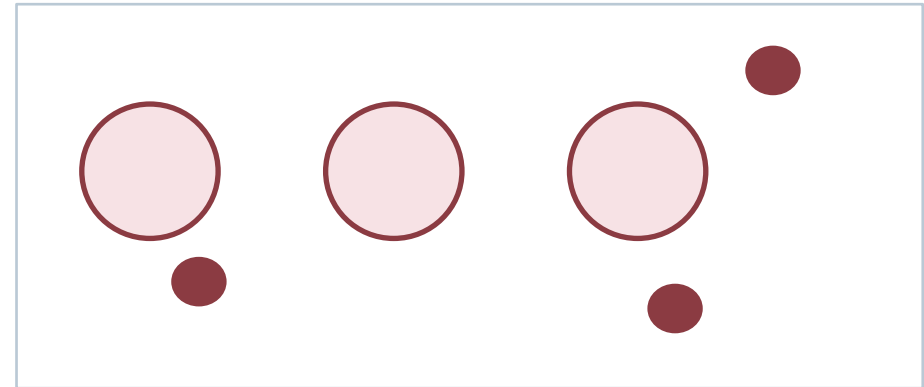
Increased ductal epithelium and connective tissue; Almost no lobule formation.



Gynecomastia: Schematic

Invasive malignancy

Atypical cells infiltrate tissue outside normal duct boundaries.



Carcinoma: Schematic

Male subareolar lesion: Clinical distinction

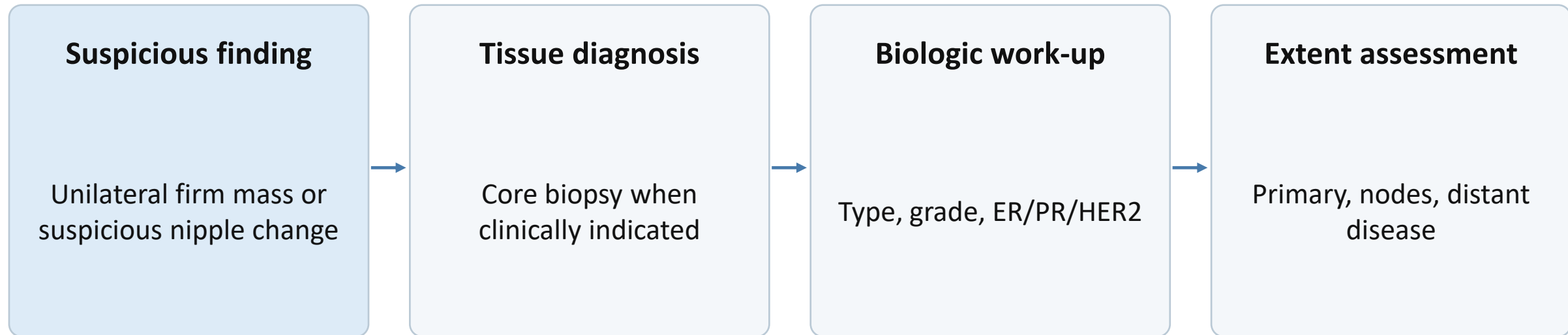
Feature	Gynecomastia	Invasive carcinoma
Typical pattern	Button-like subareolar enlargement	Palpable discrete subareolar mass
Tissue process	Benign ductal and stromal proliferation	Infiltrative epithelial malignancy
Nipple / skin	Not defining in source	Discharge and possible ulceration
Regional spread	Not expected for benign process	Axillary nodes may be involved

Microscopic distinction: The decisive boundary

Histologic parameter	Gynecomastia	Invasive carcinoma NST
Ductal epithelium	Hyperplastic, within ducts	Malignant cells breach normal compartments
Surrounding stroma	Increased collagen	May show desmoplasia with infiltrating tumor
Tumor differentiation	No malignant carcinoma grading	Nottingham grade is applicable
Clinical interpretation	Benign lesion	Requires stage and receptor evaluation

From suspicious mass to pathologic diagnosis

Schematic



Exact investigation sequence depends on clinical findings and institutional pathways.

Core biopsy and pathologic work-up

- A suspicious male breast lesion requires tissue confirmation.
- Core biopsy permits classification of invasive versus noninvasive disease.
- Histologic type and grade are evaluated on tumor tissue.
- ER, PR and HER2 should be assessed for invasive carcinoma.

Regional spread: The axilla is critical

- The male cancer dissemination pattern parallels that of female breast cancer.
- Axillary lymph nodes are a major regional site of spread.
- Regional nodal status is important for staging and prognosis.
- Lymph-node involvement does not itself mean distant metastasis.

About half have axillary nodal involvement

~50%

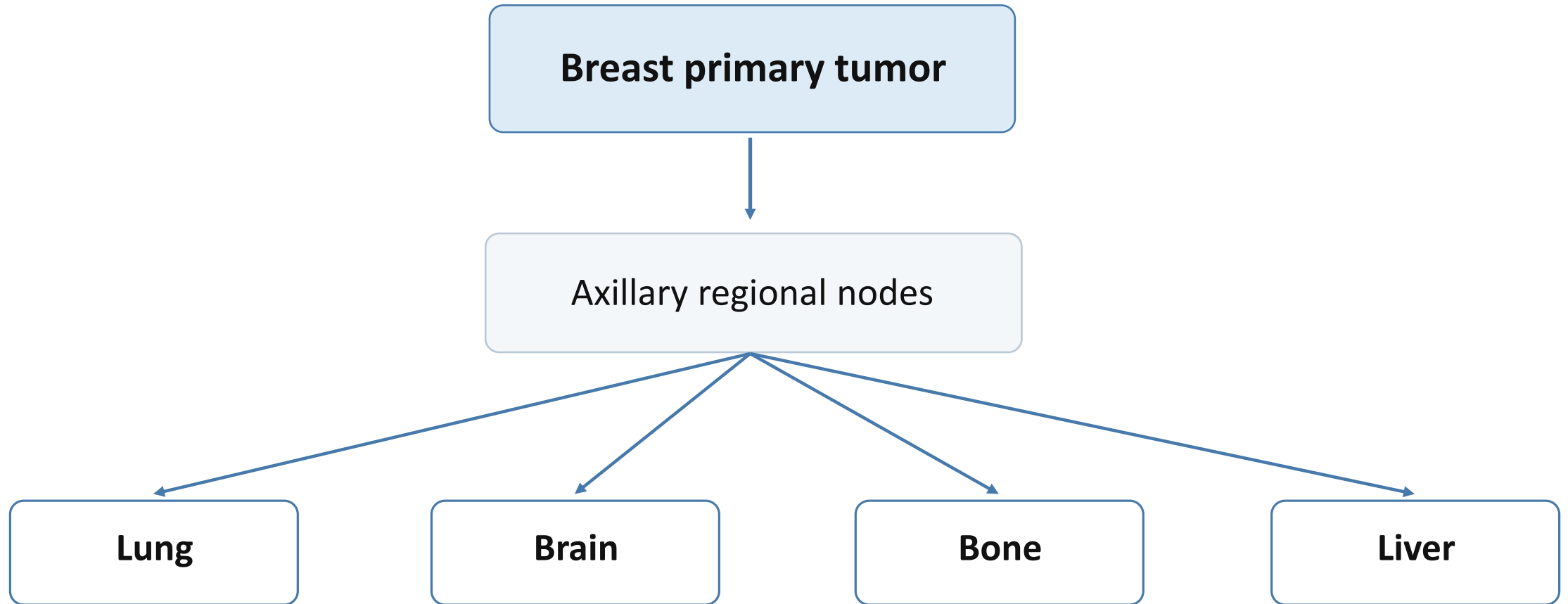
Axillary lymph-node involvement at presentation

Stage is central

Regional nodal involvement affects stage and prognosis; It is not proof of distant metastasis.

Distant metastatic distribution

Schematic



Staging separates tumor, nodes and metastasis

Schematic

T — Primary tumor

Size / local tissue invasion

N — Regional nodes

Axillary and regional spread

M — Distant metastasis

Beyond regional nodal basin

TNM anatomic staging is combined with grade and receptor biology in prognostic staging.

Small size does not eliminate local risk

- A small subareolar carcinoma may contact overlying skin early.
- Skin ulceration or chest-wall invasion reflects local extent.
- Tumor dimension and adjacent-structure invasion must both be assessed.
- Nodal and distant disease are recorded as separate staging components.

Males often present at a higher stage

- Males tend to have more advanced stage at presentation.
- The central location and proximity to adjacent tissues can complicate local extent.
- Nodal involvement is frequent at initial diagnosis.
- Comparing outcomes requires stage adjustment.

Stage-matched prognosis: Important nuance

- Outcomes similar to females after matching for stage.
- A higher stage distribution at diagnosis is not identical to intrinsically worse biology.
- Prognosis depends on stage and tumor biology.
- Avoid comparing unadjusted groups as if their stage distributions were equal.

Separate prognostic from predictive variables

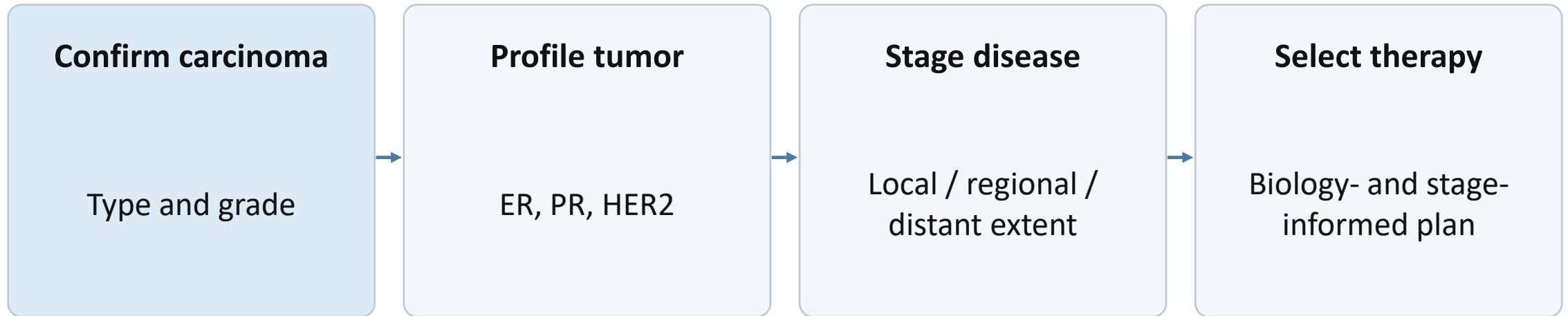
Variable	Chief role	Interpretation
Distant metastasis	Prognostic	Strong determinant of outcome
Axillary nodal status	Prognostic	Regional disease burden
Grade	Prognostic	Differentiation and proliferative behavior
ER / HER2	Predictive and prognostic	Guides endocrine / targeted therapy

Local treatment description

- Mastectomy as the usual local surgical approach.
- Its text also mentions axillary node dissection in male cases.
- Management must address tumor extent and regional nodal disease.
- This textbook statement should not be interpreted as a universal 2026 axillary surgical mandate.

Systemic treatment follows tumor biology

Schematic



Broadly comparable systemic treatment principles in males and females.

Why endocrine treatment is relevant

- The dominant male phenotype expresses ER and PR.
- Endocrine treatments interfere with estrogen receptor signaling.
- Endocrine therapy as central for luminal breast carcinomas.
- Treatment choice depends on clinical setting and patient-level evaluation.

BRCA-associated cancers: Therapeutic context

Schematic



The parent treatment table links germline BRCA1/2 alterations to PARP inhibitor response.

Therapeutic target and diagnostic assay

Target / pathway	Laboratory test	General treatment concept
ER	Nuclear ER IHC	Endocrine blockade or deprivation
HER2	HER2 IHC; ISH amplification	HER2-directed therapy when positive
BRCA1 / BRCA2 HRR	Germline mutation testing	DNA-repair-directed strategies in eligible patients

Case application: Subareolar mass

Teaching vignette — hypothetical

A 70-year-old man presents with a unilateral firm subareolar 2.5-cm mass, intermittent nipple discharge and ipsilateral palpable axillary nodes.

What three disease dimensions should pathology and staging establish?

Case discussion: Histology, phenotype, extent

- Histology: Establish whether an invasive carcinoma of NST or another lesion is present.
- Phenotype: Determine ER, PR and HER2 status; Assign grade when indicated.
- Extent: Evaluate primary tumor, regional nodes and distant spread.
- Clinical suspicion and nodal examination cannot replace histopathologic diagnosis.

Case application: Stage and outcome

Teaching vignette — hypothetical

Two men have ER-positive/HER2-negative invasive NST. One has a localized lesion; The other has axillary nodal involvement and skin ulceration.

Why is receptor concordance insufficient to predict equivalent prognosis?

Case discussion: Biology is not stage

- Shared ER/HER2 phenotype does not equal shared anatomic extent.
- Regional nodes and skin involvement modify stage and prognosis.
- Histologic grade may further distinguish tumor behavior.
- Interpret comparisons after considering disease stage—not sex alone.

Core clinicopathologic conclusions

Rare but consequential

Male risk is low, but new suspicious lesions need evaluation.

Genetic signal

BRCA2 is the leading familial predisposition highlighted by Robbins.

Anatomic pattern

Large central ducts explain the dominant subareolar presentation.

Tumor phenotype

Invasive NST with ER/PR positivity and HER2 negativity predominates.

Extent determines much

Axillary nodes and local invasion are common at presentation.

Stage is essential

Stage-matched male and female outcomes are reported as similar.

Selected sources

Primary textbook

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026). Chapter 23: The Breast; pp. 944–967. Main male breast cancer section: p. 966.

Supplemental clinical guidance

National Cancer Institute. Male Breast Cancer Treatment (PDQ®), Health Professional Version. Used for general diagnostic-workup context; Robbins remains the primary content source.