

Other malignant tumors of the breast

Breast lymphomas · implant-associated ALCL · skin malignancies · secondary tumors

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Learning objectives

- Distinguish primary mammary carcinoma from breast involvement by non-mammary malignancies.
- Recognize the breast lymphoma spectrum, including implant-associated ALCL and Burkitt lymphoma.
- Select morphology-guided immunohistochemistry and integrate clinical history.

Four groups outside conventional breast carcinoma

Hematolymphoid



B-cell and T-cell lymphomas

Implant-associated



ALCL of the peri-implant capsule

Cutaneous



Malignancy arising in breast skin

Metastatic



Extramammary malignancy in breast

The numerical context: Uncommon, not negligible

< 5%

- Together, hematolymphoid tumors, cutaneous malignancies, and extramammary metastases constitute <5% of malignant breast tumors.
- The predominant differential remains a primary mammary carcinoma.
- Small prevalence makes deliberate clinical and histologic recognition important.

The breast contains several diagnostic compartments

Epidermis and dermis



Cutaneous primary malignancy

Parenchyma



Primary carcinoma or lymphoma /
metastasis

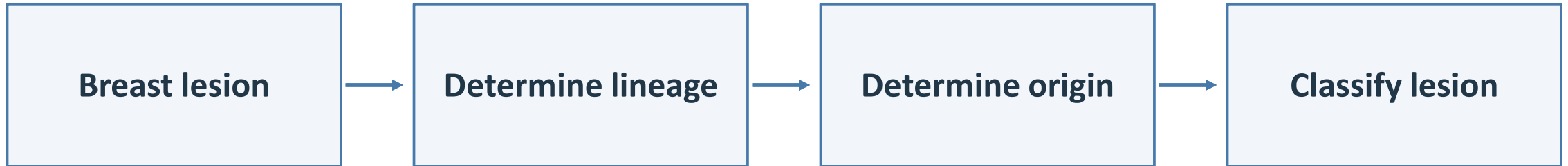
Peri-implant capsule



Implant-associated ALCL

Schematic: Compartments shown separately for site-of-origin reasoning

“Tumor in the breast” does not establish its origin



- Anatomic location is distinct from tissue lineage and site of origin.
- A core biopsy may sample a secondary process rather than a mammary primary.
- Lineage, clinical history, and distribution must be reconciled before final classification.

Three questions at the first sign-out review

1

Is the neoplasm epithelial, lymphoid, melanocytic, or another lineage?

2

Does the patient have systemic disease, an implant, or a prior extramammary malignancy?

3

Is the lesion centered in breast tissue, skin, or the implant capsule?

Red flags on a limited core biopsy

Lymphoid pattern

Discohesive monotonous lymphoid cells rather than cohesive gland-forming epithelium.

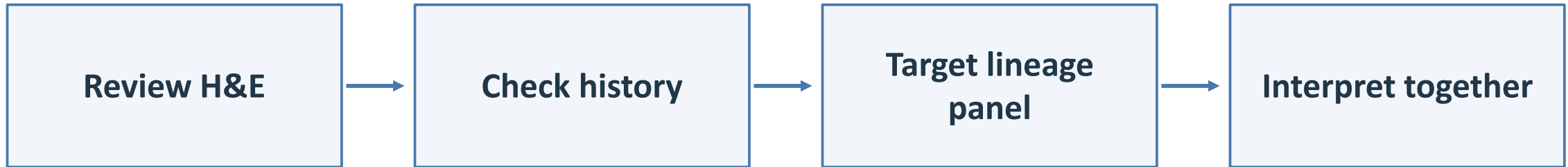
Non-mammary pattern

Unexpected melanocytic or other non-mammary cytomorphology.

Clinical discordance

No demonstrable in situ mammary lesion, especially with a known extramammary cancer.

First-line lineage triage is a differential, not a panel for every case



- Morphology and history determine targeted immunostains.
- Broad epithelial markers help establish epithelial differentiation; CD45 and lineage-specific lymphoid markers assess hematolymphoid disease.
- Melanocytic markers can help when morphology/history raises melanoma.

A negative mammary marker alone is not proof of metastasis

- Mammary carcinomas vary in expression of differentiation markers.
- No single immunostain perfectly identifies primary breast carcinoma.
- Convergent morphology, in situ component, panel results, and clinical history carry more weight.

Breast lymphoma: Primary or secondary involvement

Primary breast lymphoma

Primary breast lymphoma arises/presents predominantly in breast tissue without established disseminated lymphoma.

Secondary breast involvement

Secondary breast lymphoma represents involvement by lymphoma occurring elsewhere.

The distinction is clinical as well as histopathologic.

Why “primary” requires staging context

- Breast histology confirms lymphoma lineage; It cannot alone demonstrate that the breast is the primary site.
- Clinical examination, imaging, nodal status, and prior lymphoma history are needed.
- Ipsilateral axillary disease may coexist with primary breast lymphoma in classic clinical definitions.

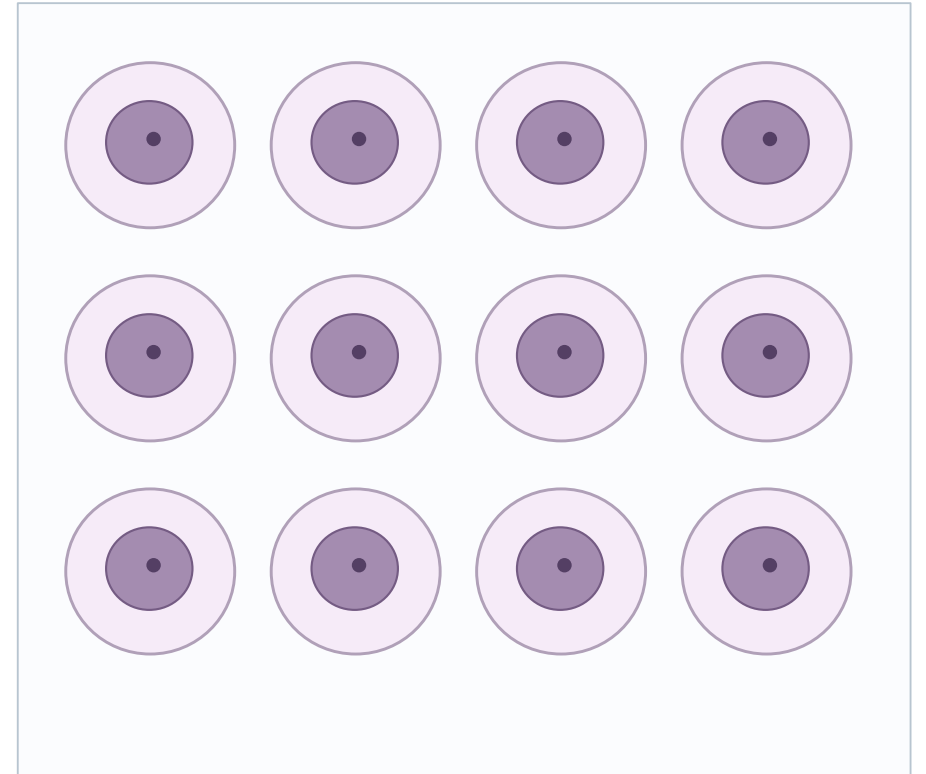
Most primary breast lymphomas are B-cell neoplasms

B-cell

- B-cell tumors as the dominant group among primary breast lymphomas.
- Diffuse large B-cell lymphoma (DLBCL) is the most common subtype.
- The mammary site does not override the lymphoma subtype diagnosis.

DLBCL: The morphologic clue is a destructive large-cell infiltrate

- Typical DLBCL shows sheets of large atypical lymphoid cells.
- Nuclei commonly have open chromatin and conspicuous nucleoli.
- Loss of normal mammary architecture follows diffuse neoplastic infiltration.



Original cellular schematic — not histologic evidence

DLBCL expresses a mature B-cell program

- CD19 and CD20 expression support a mature B-cell lineage.
- CD10 and BCL6 may be expressed; Phenotype varies across cases.
- Histology and immunophenotype must exclude other defined large B-cell entities.

DLBCL is biologically heterogeneous



- BCL6 deregulation can interfere with normal germinal-center differentiation and growth control.
- BCL2 dysregulation supports cell survival in some tumors.
- MYC alteration is not unique to DLBCL and requires context-sensitive classification.

The lymphoma–carcinoma morphological divide

Lymphoma

Lymphoma often consists of discohesive hematolymphoid cells infiltrating native stroma.

Breast carcinoma

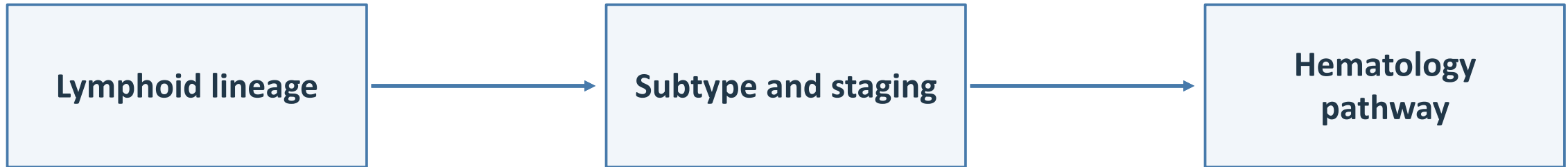
Invasive breast carcinoma typically demonstrates epithelial differentiation, albeit sometimes subtle.

Morphology determines whether CD45/B-cell markers or broad cytokeratin assessment is prioritized.

A focused DLBCL work-up has more than one purpose

- Lineage: CD45 with CD20/PAX5 and other appropriate B-cell markers.
- Classification: Selected germinal-center, activation, EBV, and genetic investigations as clinically indicated.
- Exclusions: Other aggressive B-cell lymphoma entities and non-lymphoid mimics.

Primary breast lymphoma is not managed as ordinary carcinoma



- A diagnosis of lymphoma changes systemic staging and the therapeutic pathway.
- Histologic subtype and disease extent determine hematology-directed treatment.
- An incorrect carcinoma label may lead to inappropriate surgical management.

Case: A rapidly growing breast mass

Clinical-pathology problem

- A core biopsy shows diffuse sheets of large atypical cells, no glands, and strong CD20 positivity.
- There is no established prior lymphoma; Staging is not yet complete.
- Question: What can be diagnosed now, and what remains unresolved?

Case resolution: Subtype first; Site designation second

Diagnostic interpretation

- The biopsy supports a large B-cell lymphoma, with DLBCL classification after the appropriate exclusions.
- “Primary breast lymphoma” requires clinical exclusion of a disseminated lymphoma.
- Do not infer primary origin solely from biopsy location.

Implant-associated ALCL is a distinct clinical setting

- Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an uncommon T-cell lymphoma.
- The disorder to breast implants and notes chronic inflammation as a possible contributing mechanism.
- Mechanistic uncertainty should not be translated into a proven single causal pathway.

The relevant compartment is the implant capsule

Implant



Device within capsule

Effusion space



Potential diagnostic cells

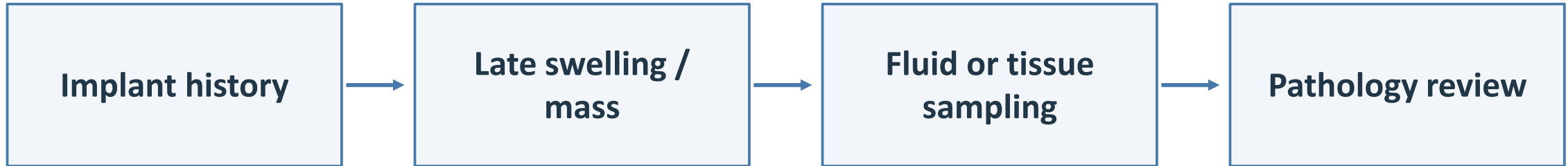
Fibrous capsule



Assess invasion and extent

Schematic: Compartments shown separately for site-of-origin reasoning

Delayed peri-implant change is the clinical trigger

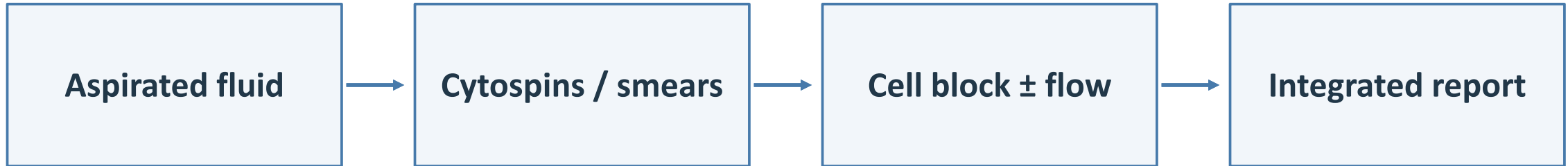


- Late breast swelling, fluid collection, or a new peri-implant mass warrants evaluation.
- An implant-related malignancy must not be presumed from symptoms alone.
- The FDA recommends explicit assessment of BIA-ALCL in symptomatic late peri-implant presentations.

Clinical risk is associated especially with textured devices

- BIA-ALCL is associated particularly with textured-surface implant exposure.
- Implant exposure history should document product type and any preceding implants where possible.
- Risk association does not substitute for cytologic/histologic proof in an individual patient.

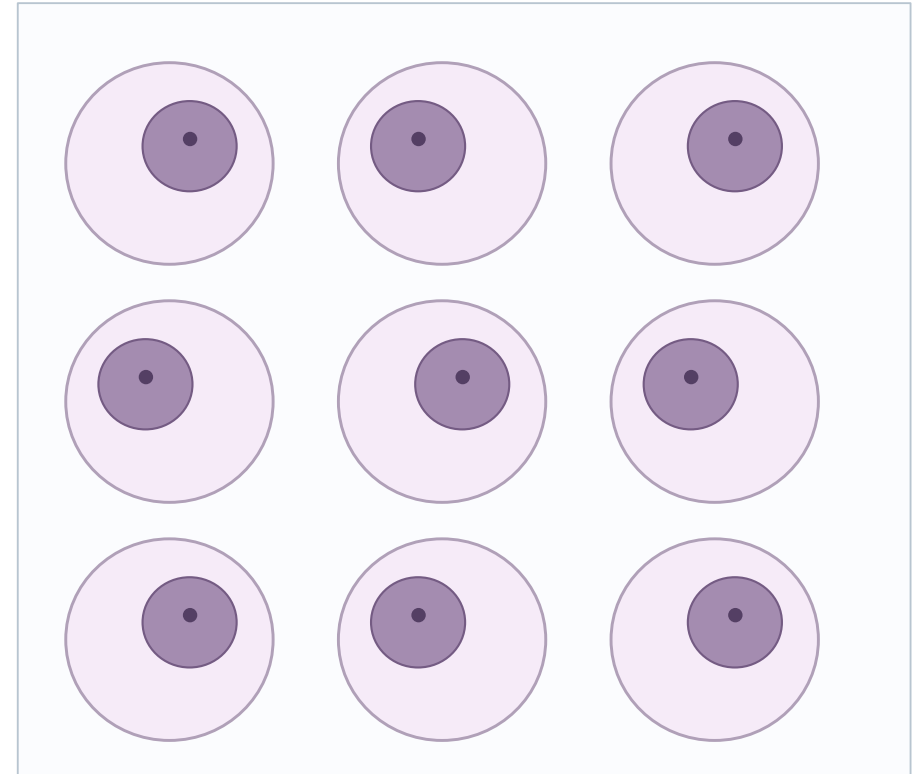
Late peri-implant effusion: Material allocation matters



- Fresh seroma fluid is needed for cytomorphology and creation of a cell block.
- The cell block supports immunohistochemistry; Ancillary flow cytometry may be useful.
- Pathology requisitions should explicitly mention possible implant-associated lymphoma.

BIA-ALCL cytology: Large atypical cells

- Aspirates may contain large pleomorphic cells with prominent nucleoli and irregular nuclei.
- Some cells show kidney- or horseshoe-shaped “hallmark” nuclei.
- The inflammatory background can coexist with malignant cells and should not falsely reassure.



Original cellular schematic — not histologic evidence

The defining immunophenotypic pattern

CD30

Strong CD30 expression in the neoplastic cells is characteristic.

ALK

ALK protein is typically negative in BIA-ALCL.

T-cell markers

T-cell marker expression can be variable or incomplete.

CD30 positivity is necessary context—not sufficient by itself

- Reactive activated lymphocytes may also stain for CD30.
- Diagnosis requires cytologic atypia, lesion context, and an appropriate immunophenotypic profile.
- Isolated CD30-positive cells do not independently establish BIA-ALCL.

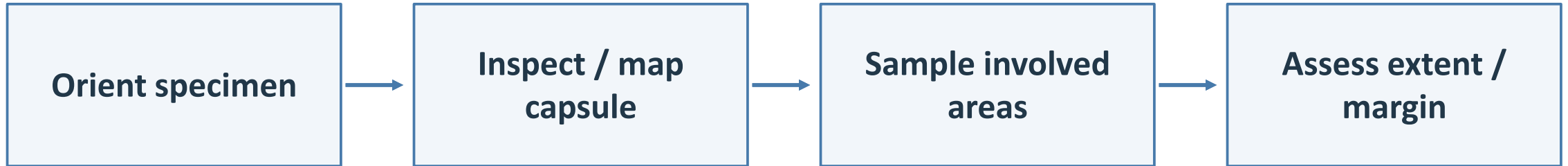
Avoid a false-negative work-up of low-cellularity fluid

- A specimen with few diagnostic cells can be nondiagnostic despite suspicious clinical findings.
- A clear request for cell block and targeted stains improves specimen use.
- Persistent suspicion warrants specialist review and consideration of repeat or additional tissue sampling.

Peri-implant mass: Sample the solid component

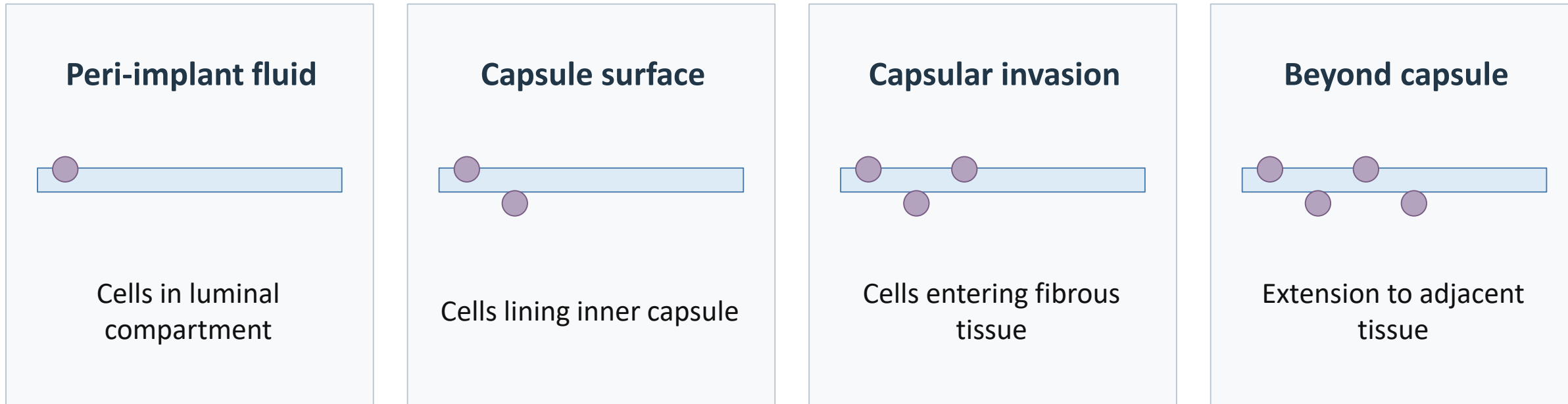
- A discrete mass requires tissue sampling to define infiltrative disease.
- The morphology and immunophenotype still need to establish lymphoma, not carcinoma or another mass lesion.
- Capsule involvement must be evaluated separately from luminal effusion cytology.

Capsulectomy examination is an anatomic assessment



- Document the implant–capsule relationship and any focal thickening or mass.
- Sample the capsule sufficiently to detect luminal, intracapsular, and extracapsular lymphoma.
- Margins and extent are meaningful only when the specimen and orientation are adequate.

Progression can extend from lumen to surrounding tissue



Schematic: Progression in relation to fibrous capsule; Not a histologic image

Reactive peri-implant inflammation is a key mimic

Reactive response

Inflammation, foreign-body reaction, and some reactive cells can coexist in a capsule.

BIA-ALCL

Search for an atypical cohesive or dispersed population of large cells with concordant immunophenotype.

CD30 staining must be interpreted with cell identity and architectural distribution.

A negative ALK result is supportive, not a stand-alone diagnosis

- ALK negativity helps distinguish BIA-ALCL from ALK-positive systemic ALCL.
- ALK-negative T-cell lymphomas and other lesions remain in the broader differential.
- The peri-implant clinical and anatomic presentation is critical.

Prognostic evaluation depends on disease extent

- Disease confined to fluid/capsule differs clinically from a mass with infiltration outside the capsule.
- Pathology should report detectable extension and margin status when assessable.
- Multidisciplinary management uses extent, not CD30 staining intensity, to guide decisions.

Case: Delayed swelling around an implant

Clinical-pathology problem

- Several years after placement, a patient develops recurrent unilateral swelling and a peri-implant effusion.
- Fluid cytology shows large pleomorphic cells; Cell block is strongly CD30 positive and ALK negative.
- Question: What additional context and specimen evaluation are necessary?

Case resolution: Confirm lineage and map the lesion

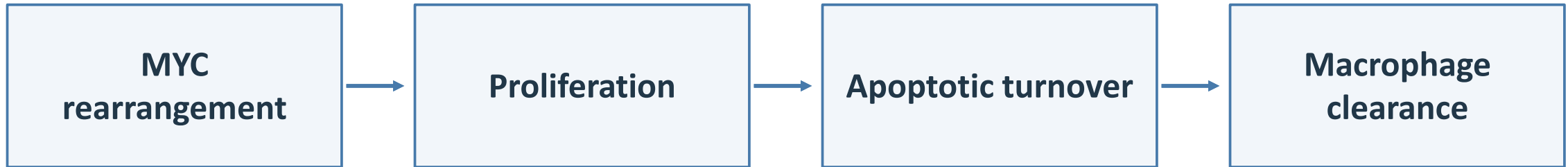
Diagnostic interpretation

- Interpret morphology and full panel to establish BIA-ALCL rather than relying on CD30 alone.
- Assess imaging for a mass; Examine excised capsule for infiltration and extent when available.
- Communicate the diagnosis for coordinated specialist management.

Breast Burkitt lymphoma: An uncommon but distinctive presentation

- Massive bilateral breast involvement in young patients, sometimes during pregnancy or lactation.
- This pattern should prompt consideration of a high-grade lymphoma alongside epithelial and inflammatory causes.
- The clinical setting is a clue, not a criterion sufficient for diagnosis.

Burkitt lymphoma is a rapidly proliferating mature B-cell neoplasm



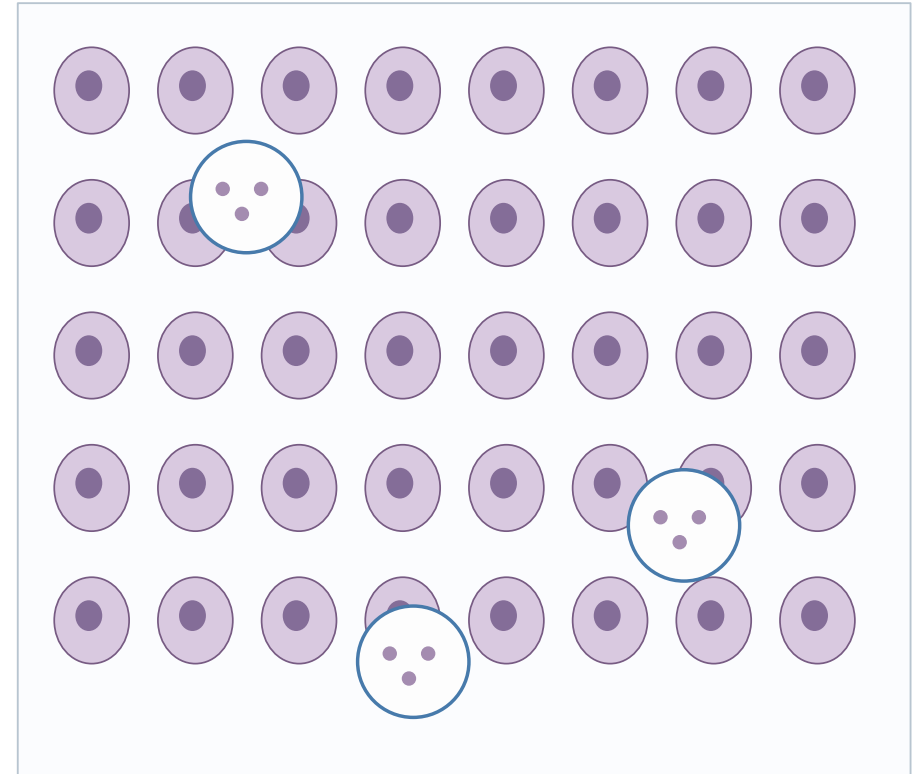
- MYC deregulation drives a marked increase in cellular growth and metabolic activity.
- Very high proliferation and apoptosis can occur together.
- High cellular turnover helps explain the frequent conspicuous “starry-sky” pattern.

MYC rearrangement: Essential molecular context

- Burkitt lymphoma is associated with MYC rearrangement, usually involving an immunoglobulin locus.
- The classic translocation is IGH::MYC, t(8;14).
- MYC alteration alone is not synonymous with Burkitt lymphoma; Morphology and phenotype remain necessary.

“Starry sky” is a morphologic pattern, not a diagnosis

- Interspersed macrophages ingest apoptotic fragments among dense tumor cells.
- Their relatively pale cytoplasm produces the lighter “stars.”
- The pattern is compatible with Burkitt but can occur in other rapidly proliferating disorders.



Original cellular schematic — not histologic evidence

Burkitt lymphoma immunophenotype

- The cells express mature B-cell markers including CD19 and CD20.
- CD10 and BCL6 support germinal-center differentiation.
- BCL2 is typically absent; Ki-67 activity is characteristically very high.

Distinguish Burkitt from other high-grade B-cell lymphomas

Burkitt lymphoma

Morphology, broad phenotype, and MYC partner alterations must be integrated.

DLBCL / other HGBCL

DLBCL can also proliferate rapidly and can show MYC-related changes.

Current WHO-HAEM5 classification requires attention to other genetically defined high-grade B-cell entities.

Why bilateral involvement changes the clinical question

- Two rapidly growing masses in a pregnant/lactating patient raise concern for a systemic hematolymphoid process.
- Bilateral distribution is suggestive but not specific.
- Comprehensive staging and prompt hematology involvement are needed once lymphoma is confirmed.

Case: Bilateral enlargement during lactation

Clinical-pathology problem

- A young lactating patient has rapidly progressive bilateral breast masses.
- Biopsy shows a monomorphic, highly proliferative B-cell infiltrate with abundant apoptotic debris.
- Question: What diagnosis and confirmatory investigations belong at the top of the differential?

Case resolution: Consider Burkitt and confirm the classification

Diagnostic interpretation

- Evaluate CD20, germinal-center phenotype, BCL2, Ki-67, and MYC status in the morphologic context.
- Differentiate Burkitt lymphoma from DLBCL and genetically defined high-grade B-cell lymphoma.
- Do not label the presentation “mastitis” solely because the patient is lactating.

Breast skin is a separate primary cancer compartment

Surface lesion



Epidermal origin

Dermal nodule



Dermal / metastatic differential

Deep mass



Breast parenchymal origin

Schematic: Compartments shown separately for site-of-origin reasoning

Cutaneous squamous malignancy requires an epidermal correlation

- A malignant squamous tumor centered in breast skin should be evaluated as a skin-based lesion.
- Keratinization and intercellular bridges support squamous differentiation when present.
- Determine whether the tumor connects to epidermis and whether another site could be primary.

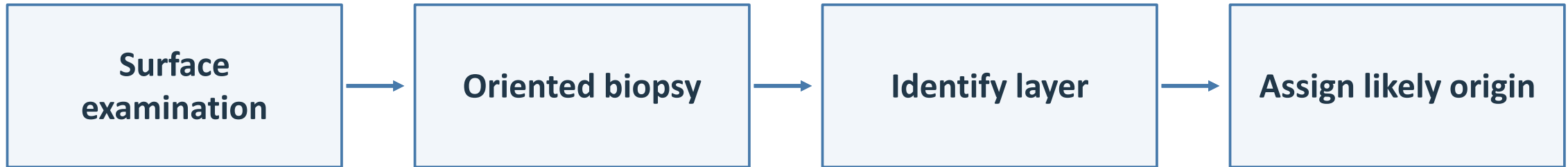
Melanocytic malignancy in breast skin vs breast tissue

- A melanoma centered in the overlying skin differs from melanoma metastatic into breast parenchyma.
- Epidermal junctional/in situ involvement supports a cutaneous primary when documented.
- Clinical skin examination and tissue orientation are important for site assignment.

A dermal tumor can be primary cutaneous or secondary

- A nodule in the dermis is not automatically a primary skin malignancy.
- A metastasis from another primary cancer can involve dermis or subjacent breast tissue.
- Interpret the biopsy with anatomic depth and systemic cancer history.

Skin lesion sampling must preserve anatomic relationships



- Superficial fragments may not show the full epidermis–dermis–breast interface.
- Histologic connection to epidermis is informative when a primary epidermal tumor is suspected.
- Describe where the malignant population is actually located; Avoid guessing origin from a small fragment.

Metastatic disease to breast parenchyma is rare

- Robbins specifically lists melanoma and ovarian carcinoma among common sources of breast metastases.
- A breast lesion may be secondary to an established or previously unsuspected extramammary tumor.
- The major practical issue is differentiation from primary mammary carcinoma.

Clinical history has high diagnostic value

- Review known malignancies, original pathology reports, interval, and treatment history.
- A new breast lesion can still be metastatic even when imaging resembles a localized primary tumor.
- Comparison with prior tumor slides, when available, can be decisive.

Morphology can suggest metastasis before immunostaining

- Features unusual for primary mammary carcinoma should prompt a search for another origin.
- Absence of carcinoma in situ may support—but never prove—a metastatic explanation.
- Certain cell types, pigment, or specialized growth patterns suggest specific extra-mammary primaries.

A breast metastasis usually lacks a mammary in situ precursor

Supports mammary primary

DCIS/LCIS may establish a link to a breast primary in the correct setting.

Raises metastatic differential

Finding no in situ component is not diagnostic of metastasis because many core biopsies omit it.

Use negative evidence cautiously and avoid overconfident interpretation.

Melanoma metastasis can mimic poorly differentiated carcinoma

- Epithelioid melanoma may resemble a high-grade epithelial lesion.
- Pigment may be absent; Cytology alone does not resolve lineage in every case.
- Melanocytic markers need interpretation alongside cytokeratins and clinical history.

SOX10 is an important diagnostic pitfall

SOX10-positive melanoma

SOX10 can be expressed by melanoma and by some triple-negative mammary carcinomas.

SOX10-positive breast carcinoma

SOX10 positivity alone does not distinguish these two processes.

A pan-cytokeratin and a broader melanocytic panel help resolve the differential.

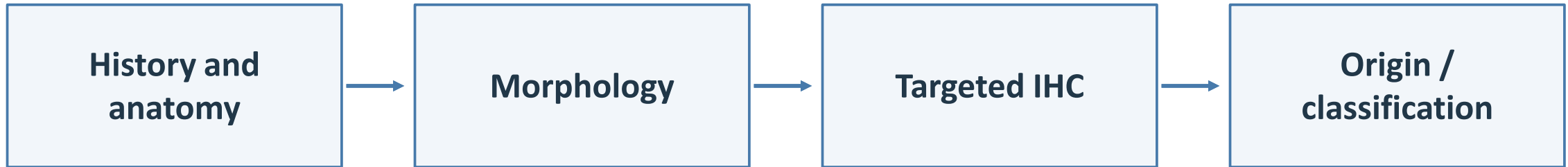
Ovarian carcinoma can metastasize to the breast

- High-grade serous carcinoma from the tubo-ovarian tract may involve breast tissue.
- WT1 and PAX8 can support Müllerian origin in the appropriate morphological context.
- No single marker replaces comparison with the documented ovarian primary.

Lineage panels are hypothesis-driven

Suspected origin	Directed positive lineage evidence	Essential competing differential
Lymphoma	CD45; B/T-cell markers	Poorly differentiated carcinoma
Melanoma	Melan-A, S100, HMB45	SOX10-positive carcinoma
Ovarian serous carcinoma	PAX8, WT1	Primary mammary carcinoma

A practical algorithm for the unfamiliar breast malignancy



- Confirm anatomic compartment and review clinical cancer/implant history.
- Use morphology to classify epithelial, lymphoid, melanocytic, or uncertain lineage.
- Select focused IHC; Compare with prior tissue; Reconcile findings before issuing the final diagnosis.

Case: A pigmented or amelanotic tumor in breast tissue

Clinical-pathology problem

- A patient with previous cutaneous melanoma presents with a new breast nodule.
- Biopsy is an atypical epithelioid proliferation without an identifiable in situ ductal component.
- Question: Which differential and stain interpretation problems matter?

Case resolution: Melanoma versus mammary carcinoma

Diagnostic interpretation

- Compare biopsy with the prior melanoma and assess appropriate melanocytic markers.
- Include epithelial markers because SOX10 can label some breast carcinomas.
- Classify as metastatic melanoma only when the combined evidence supports that origin.

Case: Breast mass in a patient with ovarian carcinoma

Clinical-pathology problem

- An ovarian carcinoma survivor develops a new breast nodule.
- Histology suggests high-grade carcinoma but no mammary in situ lesion is sampled.
- Question: How should a proposed ovarian metastasis be established?

Case resolution: Use a comparative origin panel

Diagnostic interpretation

- Compare tumor morphology with the known tubo-ovarian primary.
- Use PAX8/WT1 and mammary markers as a panel, interpreted in context.
- Do not classify from absent DCIS or one positive marker alone.

The most consequential diagnostic errors are classification errors

1

Calling lymphoma a carcinoma misdirects staging and treatment.

2

Calling metastatic melanoma a mammary primary misstates the site and disease burden.

3

Calling a late peri-implant seroma “benign inflammation” without appropriate evaluation can miss BIA-ALCL.

Integrated pathology report: What must be made explicit

- Tumor lineage, specific subtype, and what evidence supports it.
- Anatomic compartment and the limits of site-of-origin attribution on the submitted specimen.
- Relevant differential, ancillary results, and any need for clinical staging or comparative pathology.

Synthesis: Use origin, lineage and clinical setting

Lymphoid mass



DLBCL, other primary or secondary lymphoma

Late implant effusion



Exclude BIA-ALCL

Skin-based lesion



Classify by cutaneous lineage

**Unexpected
carcinoma**



Consider extramammary metastasis

Five defensible take-home decisions

- Rare breast malignancies need deliberate lineage triage, not blanket stain panels.
- DLBCL dominates primary breast B-cell lymphoma; Primary versus secondary remains a clinical distinction.
- BIA-ALCL requires peri-implant context, cytomorphology, CD30/ALK work-up, and extent assessment.
- Burkitt can affect both breasts in pregnancy/lactation and demands molecularly informed classification.
- Metastatic melanoma or ovarian carcinoma must be distinguished from a mammary primary.

References and evidence boundaries

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