Breast Imaging for Pathologists
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PATHOLOGY AND RADIOLOGY:
Two complementary breast imaging specialties

- In-vivo
- Non-invasive
- Multiple time points

- Requires biopsy
- Specific diagnosis
- DNA, RNA, and protein analysis
Breast imaging has created challenges for pathologists –

Cancers are smaller and many cannot be seen grossly -

  invasive carcinoma – 15% grossly occult
  DCIS – 80% grossly occult

More cases of carcinoma in situ and atypical hyperplasia – classification can be difficult.

Core needle biopsies only sample a portion of the lesion.

*Pathologists need to use information from imaging to help find and evaluate image detected lesions.*
BREAST PATHOLOGY WITHOUT MAMMOGRAPHIC SCREENING

3.5 cm palpable invasive carcinomas

Majority of patients have multiple nodal metastases

DCIS rare <5%
Invasive cancers ~1 cm

Majority without lymph node metastases

DCIS ~30%

ADH, FEA

“Whatever it is, it’s very, very little.”
Modalities used for Image Guided Core Needle Biopsy

- Mammography ~50% of cases
- Ultrasound ~50% of cases
- MRI ~5% of cases
Mammography – Two types

Standard – two view

MLO (medial lateral oblique): visualizes the upper outer quadrant and axilla.

CC (cranial caudal): visualizes the breast back to the chest wall.

Tomosynthesis (3D mammography)

Additional views are taken at multiple angles and displayed as 1 mm thick high resolution images.

This technique can detect subtle changes in breast texture – often caused by radial sclerosing lesions or diffusely infiltrating cancers.
Mammography - Principles

X-rays penetrate tissues to different degrees:

- Adipose tissue - penetrates well - black
- Fibrous tissue - penetrates less well - white
- Normal breast tissue – mixture of both – mottled gray
- Mass forming lesion – replaces adipose tissue - white
- Calcifications and metal – does not penetrate - white
The fibrous breast stroma of young women is replaced with adipose tissue with age.
Mammographic Lesions

Masses 45%

Architectural distortion or asymmetry 10%

Calcifications 45%
Radiologists describe masses in terms of overall shape and margin.

Margin is an indication of how a lesion interacts with the surrounding breast tissue and is characteristic of specific lesions.

Shape is not very important for differential diagnosis and should not be confused with margin.

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Each type of margin generates a differential diagnosis of the types of lesions with this growth pattern.

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Masses with circumscribed margins are most often benign:

- 65% fibroadenomas
- 20% cysts
- 9% other benign
- 3% DCIS
- 3% invasive carcinoma
Fibroadenoma: mass with circumscribed margins

“Popcorn” calcification
Benign lesions: masses with circumscribed margins

- Hamartoma
- Angiolipoma
- Myofibroblastoma
Ductal Carcinoma in Situ

DCIS is rarely detected as a mass with circumscribed margins.

DCIS involving a fibroadenoma.

DCIS forming a nodular mass.
Invasive Carcinoma: mass with circumscribed margins

- Mucinous carcinoma
- Triple negative carcinoma
- Carcinoma with medullary features
Masses with microlobulated/spiculated/angular margins are most often malignant:

97% invasive carcinoma
2% surgical or trauma related scars
<1% radial sclerosing lesions (radial scars) or other rare lesions (fibromatosis, granular cell tumor)
Invasive Carcinoma: mass with irregular margins
Radial sclerosing lesion: mass with irregular margins

The spicules are longer relative to the size of the lesion as compared to invasive carcinomas.

The center may be lucent.
Benign lesions: masses with irregular margins

Granular cell tumor
(can also look circumscribed)

Fibromatosis
(desmoid fibromatosis)
Masses with indistinct or obscured margins are of two types:

Some of these lesions do not have defined margins (e.g. pseudoangiomatous stromal hyperplasia (PASH) or diffusely infiltrative cancers).

Some of these lesions have defined margins but the margins are not well seen due to the surrounding breast tissue.
Masses with obscured or ill-defined margins:

~30% normal breast
~30% benign lesions
~30% invasive carcinoma or DCIS
Mammographic Lesions

- Masses 45%
- Architectural distortion or asymmetry 10%
- Calcifications 45%
Architectural Distortion and Asymmetry

Definitions:

**Architectural distortion:** A localized alteration in the normal breast texture consisting of lines radiating from a point. A central mass is not seen.

**Focal asymmetry:** An area of tissue that is denser compared to the same site in the contralateral breast. The area does not have definable margins.
The corresponding lesions can be subtle and may be easily missed unless the pathologist is looking for a diffusely infiltrative process.
Architectural Distortion and Asymmetry

Most common benign diagnoses:

- Radial sclerosing lesions
- Sclerosing adenosis
- Many are non-specific (e.g. uneven involutional changes)

Most common malignant diagnoses:

- Diffusely infiltrative carcinoma with little or no desmoplastic response (often lobular in type)
- DCIS
Mammographic Lesions

Masses 45%

Architectural distortion or asymmetry 10%

Calcifications 45%
Calcifications

Calcium and phosphate are present in extracellular fluid.

Crystallization occurs on a regular repeating matrix.

<table>
<thead>
<tr>
<th>Cell membranes</th>
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<tbody>
<tr>
<td></td>
<td>Secretions: benign or malignant</td>
</tr>
<tr>
<td></td>
<td>Necrosis: benign (fat necrosis) or malignant (epithelial)</td>
</tr>
</tbody>
</table>

| Hyalinized stroma | benign (fibroadenoma, fibrovascular cores of papillomas) |
It is very important to ensure that all the tissue and all the calcifications removed are recovered for pathologic evaluation.

It is helpful for the radiologist to wrap cores in paper and place them into a cassette. The cassette is then placed into a container of formalin.

This ensures that all biopsied tissue is retrieved from the formalin.

If cores are placed directly in a large volume of formalin, it is possible tissue fragments will be missed because they are small or in unusual locations (e.g. stuck to the lid) or that calcifications will be lost.
The appearance of calcifications on the slide may not correspond in size or number to the calcifications on the specimen radiograph:

Specimen radiographs show a 3 dimensional object - slides are essentially 2 dimensional.

Radiologic “calcifications” are often many superimposed small calcifications.

Calcifications may chip out of sections, wash out of sections (e.g. if in cysts), or dissolve if there has been prolonged fixation.

Some “calcifications” may be metallic debris from surgery or trauma.
What radiologists see: Calcifications that are more likely associated with cancer are clustered, irregular, increasing over time, and/or linear and branching.
What pathologists see: There are many additional smaller calcifications in benign tissue that are not correlated with cancer. It is important to be sure the tissue with the radiologically suspicious calcifications are examined.
The radiologist needs to document that the targeted calcifications were sampled by radiographing the cores.

If the targeted calcifications are not present, there is no value in doing additional levels to look for calcifications.

Any calcifications found are not the ones in the area with findings suspicious for carcinoma.
Calcifications

75% benign

25% malignant

75% DCIS

25% invasive
Apocrine cysts

Clustered, rounded calcifications

Blue dome cyst

Clustered, rounded calcifications
The calcifications in apocrine cysts can be calcium oxalate. The clear crystals are easily seen under polarized light.
"Milk of calcium" is a term that refers to calcifications that change position relative to each other when comparing the MLO and CC views.
These calcifications change position with respect to each other in the different mammographic views (ML, MLO, and CC).

In contrast, other types of calcifications are fixed in tissue and do not change position.
Fibroadenomas can present as clusters of calcifications.

The large “popcorn” calcifications are easy to identify.

Smaller calcifications can look like small blue bubbles and are easily missed.
Large psammoma body calcifications can be seen in areas of secretory/lactational change. There is no specific clinical correlation.
Hyalinized ducts can calcify in a linear pattern. This causes concern for DCIS.
Fat necrosis is a common lesion that frequently calcifies.

Because the calcifications are often in fat, they may chip out of the tissue and be very difficult to detect.
Flat Epithelial Atypia and Atypical Ductal Hyperplasia

FEA and ADH are commonly associated with columnar cell change and numerous calcifications.
Calcified blood vessels are usually easily identified on mammography. These calcifications will not be intentionally biopsied but may be present as an incidental finding.

If these are the only calcifications present, other calcifications should be sought.
Some “calcifications” are not calcifications.

Metal fragments from prior surgical excisions can resemble calcifications.

To the radiologist, they appear denser than true calcifications.

Dense hemosiderin can also resemble calcifications.
DCIS – comedo necrosis associated with calcifications

A pattern of branching calcifications is strongly associated with high grade DCIS.

Necrotic debris in the ducts calcifies.
High grade DCIS can be almost completely necrotic.

If ducts are filled with calcifications without evident lining cells, request additional levels to look for tumor cells. They may be quite scarce.

In this case a large calcification has chipped out of the tissue during sectioning.
Clusters of calcifications can be associated with lower grade DCIS.
Modalities used for Image Guided Core Needle Biopsy

Mammography  ~50% of cases

Ultrasound  ~50% of cases

MRI  ~5% of cases
ULTRASOUND - Principles

Sound waves rebound (echo) from different tissues in distinctive patterns:

- **Adipose tissue:** hyperechoic – white
- **Fibrous tissue:** hypoechoic – gray
- **Fluids:** anechoic with posterior enhancement – black
- **Masses:** hypoechoic with acoustic shadowing - gray with black

Ultrasound is the best modality for distinguishing cysts from solid masses.
ULTRASOUND

US plays an important role to further characterize masses detected by palpation, mammography, or MRI -

- Border (smooth vs irregular)
- Size
- Solid vs. cystic

Core needle biopsies are performed more easily under ultrasound guidance. This is the preferred modality and is used when possible.

The differential diagnosis for masses with circumscribed or spiculated margins is the same as for masses detected by mammography.
<table>
<thead>
<tr>
<th>A. Cystic Circumscribed Anechoic Mass</th>
<th>B. Solid and Cystic Circumscribed Mass</th>
<th>C. Solid Circumscribed Hypoechoic Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
<tr>
<td>D. Solid Circumscribed Hyperechoic Mass</td>
<td>E. Lymph Node</td>
<td>F. Solid Hypoechoic Mass with Spiculated Margins</td>
</tr>
<tr>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
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Almost all benign (e.g. angiolipoma)  

Invasive carcinoma – irregular borders, hypoechoic
Hyperechoic Lesions

Almost all (>95%) of purely hyperechoic lesions are benign.

However, lesions with mixed patterns (hyperechoic and hypoechoic) can be malignant.

Hyperechoic Lesions

Fat necrosis: Adipose tissue adjacent to fibrous tissue.

Angiolipoma: Adipose tissue adjacent to blood vessels.

A hyperechoic pattern occurs when tissues of different echogenicity are adjacent to each other.
Hyperechoic Malignancies

Very rare malignancies have a predominant hyperechoic pattern.

These cancers infiltrate in adipose tissue with little or no desmoplastic response.

These can be subtle malignancies to see on core needle biopsy.

Ductal carcinoma

Lobular carcinoma
Modalities used for Image Guided Core Needle Biopsy

- Mammography ~50% of cases
- Ultrasound ~50% of cases
- MRI ~5% of cases
Magnetic Resonance Imaging - Principles

MRI detects patterns of vascularity as the contrast agent is taken up more rapidly in vascular lesions than in benign lesions or normal breast tissue.

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Enhancement Pattern</th>
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<tbody>
<tr>
<td>Normal breast</td>
<td>non-enhancing or diffusely enhancing during menstrual cycle</td>
</tr>
<tr>
<td>Benign lesions (e.g. fibroadenoma)</td>
<td>slowly enhancing</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td>~ 100% rapidly enhancing</td>
</tr>
<tr>
<td>DCIS</td>
<td>~ 75% are rapidly enhancing</td>
</tr>
</tbody>
</table>
Types of MRI Lesions for Pathology Correlation

Mass forming (margins are defined by blood flow rather than actual shape)

   Irregular mass

   Circumscribed/oval/lobulated/nodular mass

Non-mass forming

   Linear/clumped

   Other (diffuse/stippled/patchy/focal)

However, correlation is more difficult than for other modalities because patterns of blood flow are not seen in tissue sections.
The most common lesions are:

- ~10-15% invasive cancer (typically low grade)
- ~10-15% DCIS (typically high grade)
- ~70-80% benign findings
Fibroadenoma – circumscribed, slow enhancement

DCIS – linear clumped

Site of excision for prior carcinoma

Invasive carcinoma – irregular, rapidly enhancing

Paget disease – skin enhancement

New carcinoma
Pre-treatment MRI can be a helpful modality to evaluate carcinomas after neoadjuvant chemotherapy.

Post-treatment
Masses larger than ~0.5 cm can generally be identified by mammography or US and undergo biopsy using these other modalities.

MRI does not detect calcifications.

Therefore, the majority of lesions undergoing MRI guided biopsy are small masses or non-specific areas of enhancement.

Unless invasive cancer, DCIS, or a definite mass-forming lesion (e.g. fibroadenoma) is identified on the core biopsy, whether or not the biopsy is concordant is the responsibility of the radiologist.
Breast imaging and pathology are complementary techniques to observe breast lesions.

It is very helpful to use both the radiologic appearance and the microscopic appearance to fully evaluate breast lesions – especially on core needle biopsies.

As imaging modalities evolve, it will be important for pathologists to keep up with new technology.

Hopefully, within our lifetimes . . .
Patho-radiology of the Future?

Thank you for your attention!