BREAST CORE-NEEDLE BIOPSY: Potential and limitations

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General-Secretary of the International Academy of Cytology
President of the International Society of Breast Pathology

No financial disclosures
Technique to biopsy a breast mass depends on:

- Whether mass is palpable
- Its location

- Fine needle aspiration
- Core needle biopsy
- Radiology-assisted biopsy
- Stereotactic biopsy
- Ultrasound-guided biopsy
- Wire-localized biopsy
- Excisional biopsy
The choice of sampling method in any center should be determined by:

• the sensitivity and specificity of the technique in the center.

• the diagnostic information required for malignant lesions.

• patient comfort and costs.

• the availability of staff skilled and experienced in using the procedures, particularly FNAC sampling and interpretation.
BREAST FNAC X CNB

• In terms of pathological diagnosis, both methods are accepted to be highly accurate in the assessment of breast lesion.

• CNB is more used in: non-palpable screen-detected calcifications, borderline lesions and when mammography does not show invasion signs.

• Lack of expertise in cytology is one of the most frequent cause of use CNB.
Breast Fine Needle Aspiration Biopsy Cytology
Using the Newly Proposed IAC Yokohama
System for Reporting Breast Cytopathology:
The Experience of a Single Institution

Diana Montezuma¹,³ Daniela Malheiro³,³ Fernando C. Schmitt³,³
¹Portuguese Institute of Oncology, Porto, Portugal; ²Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil; ³Institute of Molecular Pathology and Immunology, University of Porto, Porto, Portugal; ⁴Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal; ⁵Medical Faculty, University of Porto, Porto, Portugal

Table 4. Advantages and disadvantages of breast fine needle aspiration biopsy and core needle biopsy

<table>
<thead>
<tr>
<th>Fine needle aspiration biopsy</th>
<th>Core needle biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy procedure, without anesthesia</td>
<td>Relatively easy procedure, done with local anesthesia</td>
</tr>
<tr>
<td>Hardly any complications</td>
<td>Low rate of complications</td>
</tr>
<tr>
<td>Lower costs, suitable for low-income countries</td>
<td>Higher costs (equipment and histopathology)</td>
</tr>
<tr>
<td>Shorter turnaround time</td>
<td>Longer turnaround time</td>
</tr>
<tr>
<td>Allows rapid on-site evaluation of specimen adequacy</td>
<td>Does not allow on-site evaluation</td>
</tr>
<tr>
<td>Possible therapeutic aspiration of cystic lesions</td>
<td>Therapeutic aspiration is not possible</td>
</tr>
<tr>
<td>Allows evaluation of immunostains</td>
<td>Allows evaluation of immunostains</td>
</tr>
<tr>
<td>Allows HER-2 evaluation (e.g., by FISH)</td>
<td>Allows HER-2 evaluation by FISH or immunostain</td>
</tr>
<tr>
<td>Cannot detect angio or neural invasion</td>
<td>Can detect angio or neural invasion</td>
</tr>
<tr>
<td>Difficulty in some specific diagnoses (papillary lesions, radial scar, fibroadenoma versus benign phyllodes, etc.)</td>
<td>More accurate in the diagnosis of such specific lesions</td>
</tr>
</tbody>
</table>
Breast Fine Needle Aspiration Biopsy Cytology
Using the Newly Proposed IAC Yokohama System for Reporting Breast Cytopathology:
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*Portuguese Institute of Oncology, Porto, Portugal; †Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil; ‡Institute of Molecular Pathology and Immunology, University of Porto, Porto, Portugal; §Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal; ‡Medical Faculty, University of Porto, Porto, Portugal

Table 3. Sensitivity, specificity, PPV, NPV, and accuracy rate of breast cytology

<table>
<thead>
<tr>
<th>Category</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category A</td>
<td>97.56%</td>
<td>100%</td>
<td>100%</td>
<td>98.62%</td>
<td>99.11%</td>
</tr>
<tr>
<td>Category B</td>
<td>97.98%</td>
<td>99.65%</td>
<td>99.49%</td>
<td>98.62%</td>
<td>98.97%</td>
</tr>
<tr>
<td>Category C</td>
<td>98.28%</td>
<td>54.79%</td>
<td>68.21%</td>
<td>98.62%</td>
<td>49.25%</td>
</tr>
</tbody>
</table>

Category A: only malignant cases considered positive; category B: suspicious and malignant cases considered positive; category C: atypical, suspicious, and malignant cases considered positive. NPV, negative predictive value; PPV, positive predictive value.
A sensitivity and specificity comparison of fine needle aspiration cytology and core needle biopsy in evaluation of suspicious breast lesions: A systematic review and meta-analysis

Mei Wang a, Xiaoning He b, Yaping Chang a, Guangwen Sun c, Lehana Thabane a, d, e, f, g, h, *

*The Breast 31 (2017) 157–166*

Table 5
Subgroup analysis based on publication year for accuracy of FNAC and CNB.

<table>
<thead>
<tr>
<th>Category (prevalence)</th>
<th># of studies (# of participants)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FNAC % (95% CI) (P value), (I²)</td>
<td>CNB % (95% CI) (P value), (I²)</td>
</tr>
<tr>
<td>Year of publication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007 or later (69%)</td>
<td>7 (682)</td>
<td>81 (77–84)</td>
<td>88 (85–91)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(&lt;0.001), (84.4)</td>
<td>(0.079), (47)</td>
</tr>
<tr>
<td>Before 2007 (60%)</td>
<td>5 (1112)</td>
<td>70 (66–73)</td>
<td>86 (83–88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(&lt;0.001), (89.6)</td>
<td>(&lt;0.001), (95.1)</td>
</tr>
<tr>
<td>Pooled estimate</td>
<td>12 (1802)</td>
<td>74 (72–77)</td>
<td>87 (84–88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(&lt;0.001), (88.5)</td>
<td>(&lt;0.001), (88.3)</td>
</tr>
</tbody>
</table>

**Conclusion:** Our study suggests that both of FNAC and CNB have good clinical performance. In similar circumstances, the sensitivity of CNB is better than that of FNAC, while their specificities are similar. FNAC could be still considered the first choice to evaluate suspicious nonpalpable breast lesions.
Core-Needle Biopsy of Breast Cancer Is Associated With a Higher Rate of Distant Metastases 5 to 15 Years After Diagnosis Than FNA Biopsy

Roland B. Sennerstam, MD, PhD; Bo S. H. Franzén, PhD; Hans O. T. Wiksell, PhD; and Gert U. Auer, MD, PhD

Cancer Cytopathology October 2017
CORE NEEDLE BIOPSY

• Standard of care for the initial assessment of non-palpable breast lesions

• Methods
  – Stereotactic mammography
  – Ultrasound
  – Magnetic resonance imaging (MRI)
DEVICES OF CNB

- **Spring-loaded** and discharge a cutting needle into the breast tissue
- Multiple needle insertions needed
- Used to sample mass lesions

- **Vacuum Assistance** following needle insertion to draw tissue into the cutting chamber and to facilitate sample collection
- Larger specimens
- Permits the collection of numerous, contiguous samples with a single needle insertion
- Used to sample microcalcifications

Core needle biopsy

Position | Vacuum | Cut | Remove
CORE NEEDLE BIOPSY

Samples
CORE NEEDLE BIOPSY

• Knowing clinical history and imaging findings, including radiological differential diagnosis is essential.

• The pathological diagnosis on core biopsy must be concordant with the imaging studies.

• Discordant diagnoses must be reconciled; may require repeat biopsies or surgical excision.
### Core Needle Biopsy

**Some nightmares...**

<table>
<thead>
<tr>
<th>IMAGING</th>
<th>PATHOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spiculated Mass</strong></td>
<td>Any benign diagnosis (except radial scar)</td>
</tr>
<tr>
<td><strong>Circumscribed Mass</strong></td>
<td>Benign, non-specific diagnosis</td>
</tr>
<tr>
<td><strong>“Malignant” Calcifications</strong></td>
<td>Any benign diagnosis, even if calcifications are present</td>
</tr>
</tbody>
</table>
PATHOLOGY REQUISITION on CNB

Mandatory items

- Identification of the patient
- Laterality and location of the targeted lesion
- Indication for the biopsy: mass, arquitectural distortion, non-mass enhancement on MRI, etc...
- Radiologist differential diagnosis
- Level of radiologic suspicion: usually provided by BIRADS category
- Image-guidance method
- Size of needle used
- Number of obtained cores
RADIOLOGY-PATHOLOGY CORRELATION
Possible solution: PASH involving two or more adjacent lobules ("diffuse") is significantly more often associated with a mass lesion than focal PASH.
Discordance with imaging

- 33-year old female presented with a 15 mm ill-defined nodule in the right breast. Mammography and US are compatible with carcinoma.
Benign Granular Cell Tumour
CNB

Histological Processing

• If the indication for CNB is mammographic microcalcifications, a specimen radiograph should be obtained by the radiologist, and the samples with the calcifications submitted separately.

• CNB specimens should be submitted in their entirely for microscopic evaluation.

• No universal agreement about the number of levels that should be cut from blocks of CNB specimens: in general three levels from each block for initial evaluation and additional levels are cut as necessary.
CNB for microcalcifications
CNB and microcalcifications
Differences between Pathology and Radiology

• Histology can see more microcalcifications.

• Digital technology beats analog mammograms for calcification.

• Some calcifications can wash out of a specimen

- Can especially be a problem on stereotactic core biopsy when the calcifications have been removed on the post biopsy film, but no calcium seen in the specimen x-rays.
HOW REPORT BREAST CNB?

**B1. Normal tissue:** normal breast or other normal tissue including adipose tissue, may include microcalcification associated with atrophic TDLUs.

**B2. Benign lesion:** FA, fat necrosis, duct ectasia...

**B3. Lesion of uncertain malignant potential:** includes ADH, LN, fibroepithelial lesions with cellular stroma, papillary lesions, FEA, radial scar.

**B4. Suspicious:** a definitive malignant diagnosis (DCIS or invasive carcinoma) is not possible because of crush artefact, poor fixation or a small questionable focus of non-diagnostic cells.

**B5. Malignant:** an unequivocal malignant diagnosis (includes DCIS and invasive carcinoma).
• Histopathological diagnosis:
  - Benign lesions
  - Atypical ductal lesions:
    • atypical columnar cell lesion (FEA)
    • atypical ductal hyperplasia
  - Atypical lobular lesions: lobular neoplasia
  - Ductal carcinoma in situ (DCIS)
  - Invasive carcinoma

• Ductal carcinoma in situ (DCIS):
  - Nuclear grade: low, intermediate, high
  - Presence or not of microinvasion

• Invasive carcinomas:
  - Histological type: ductal/NST, lobular, special subtypes
  - Histoprognostic grade (modified SBR grade: I, II, III)

• Prognostic and predictive factors
  - Hormonal receptors (ER, PR):
    • % of positive cells; nuclear intensity (low, moderate, strong)
    • ASCO/CAP: + if > 1% staining, irrespectively of the intensity
  - HER2 status:
    • negative: score 0 or score 1+
    • positive: score 3+
    • equivocal: score 2+ → retest with ISH (SISH or FISH)
CORE NEEDLE BIOPSY
Diagnostic problems

- ADH vs low grade DCIS
- Identify invasion in DCIS
- DCIS vs LCIS
- Histological typing
- Papillary lesions
- Spindle cell lesions
- Columnar cell lesions
- Mucocoele-like lesion vs. mucinous carcinoma
- Fibroepithelial lesions
- Vascular lesions

SIMILAR TO THOSE ENCOUNTERED IN EXCISIONAL BIOPSIES
BREAST FNAC: solving problems
“Gray zone”

✓ Fibro-epithelial Lesions
✓ Papillary Lesions
✓ Spindle cell lesions
✓ Epithelial Proliferative Lesions

SIMILAR TO THOSE ENCOUNTERED IN CNB
Fibroepithelial lesion on CNB

- Diagnosis of fibroadenoma on CNB is usually straightforward.
- If it looks like a fibroadenoma, call it a fibroadenoma.
- Excision not required.
CYTOLOGICAL CRITERIA OF FIBROADENOMA

- Large branching, monolayer sheets of uniform epithelial cells
- Fragments of fibromyxoid stroma
- Numerous single, bare bipolar nuclei (myoepithelial cells)
Fibroepithelial lesion on CNB with increased stromal cellularity

- How cellular is too cellular?

- Features favoring phyllodes tumor:
  - Fragmentation
  - Epithelium along edges of fragments
  - Imbalance between glands and stroma
  - Mitoses
  - Adipose tissue within the stroma of the lesion

- Excision required.

- Not essential make decision on CNB.
Fibroepithelial Lesions With Cellular Stroma on Breast Core Needle Biopsy

Are There Predictors of Outcome on Surgical Excision?

Timothy W. Jacobs, MD,¹ Yunn-Yi Chen, MD, PhD,² Donald G. Guinee, Jr, MD,¹ Joseph A. Holden, MD,³ Imok Cha, MD,² Donald E. Bauermeister, MD,¹ Beverly Hashimoto, MD,⁴ Dulce Wolverton,⁵ and Grady Hartzog, MD⁴

Histologic Features of Fibroepithelial Lesions With Cellular Stroma in Breast CNB Specimens in Relation to Diagnosis at Surgical Excision*

<table>
<thead>
<tr>
<th>Histologic Feature</th>
<th>Fibroadenoma at Excision (n = 16)</th>
<th>Phyllodes Tumor at Excision (n = 12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stromal cellularity</td>
<td></td>
<td></td>
<td>.017</td>
</tr>
<tr>
<td>Mildly increased</td>
<td>4 (25)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Moderately increased</td>
<td>12 (75)</td>
<td>8 (67)†</td>
<td></td>
</tr>
<tr>
<td>Markedly increased</td>
<td>0 (0)</td>
<td>4 (33)‡</td>
<td></td>
</tr>
<tr>
<td>Stromal cell atypia (grade)</td>
<td></td>
<td></td>
<td>.016</td>
</tr>
<tr>
<td>1</td>
<td>14 (88)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (13)</td>
<td>7 (58)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0 (0)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Stromal cell mitoses</td>
<td></td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Cases with mitoses</td>
<td>2 (13)</td>
<td>9 (75)</td>
<td></td>
</tr>
<tr>
<td>Range (mitoses per 10 high-power fields)</td>
<td>1-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range) relative proportion of stroma to epithelium (%)</td>
<td>55 (50-90)</td>
<td>70 (50-90)</td>
<td>.018</td>
</tr>
<tr>
<td>Stromal overgrowth</td>
<td>0 (0)</td>
<td>1 (8)</td>
<td>.429</td>
</tr>
<tr>
<td>Infiltrative edge§</td>
<td>5/14 (36)</td>
<td>5/8 (63)</td>
<td>.378</td>
</tr>
<tr>
<td>Epithelial hyperplasia</td>
<td>9 (56)</td>
<td>3 (25)</td>
<td>.136</td>
</tr>
<tr>
<td>Stromal cellularity enhanced at epithelium</td>
<td>5 (31)</td>
<td>6 (50)</td>
<td>.441</td>
</tr>
<tr>
<td>Growth pattern:</td>
<td></td>
<td></td>
<td>.445</td>
</tr>
<tr>
<td>Pericanalicular</td>
<td>3 (19)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>Intracanalicular</td>
<td>3 (19)</td>
<td>6 (50)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>10 (63)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>Leaf-like pattern</td>
<td>5 (31)</td>
<td>7 (58)</td>
<td>.250</td>
</tr>
<tr>
<td>Multinucleated stromal giant cells</td>
<td>0</td>
<td>2 (17)</td>
<td>.175</td>
</tr>
</tbody>
</table>
Fibroepithelial lesion on CNB

- An apparently pure spindle cell lesion on CNB may still be a phyllodes tumor.

- Do not exclude the possibility of phyllodes tumor even if no epithelial component is seen.
Papillary lesions on CNB

- Distinction among benign, atypical and malignant papillary lesions is difficult, especially with limited material.

- Sampling issues: otherwise benign papillomas may harbor foci of ADH or DCIS.

- Management controversial: always excision or no excision for incidental papillomas.
PAPILLARY LESIONS: CNB helps?
Reporting needle core biopsies of breast carcinomas

Papillary lesions cannot always be categorized as benign or malignant on needle core biopsy. In this setting the diagnosis of ‘papillary neoplasm’ should suffice. All papillary tumours identified on needle core biopsy should be fully excised, regardless of the presence or degree of architectural and cytological atypia. This rather sweeping recommendation is based on the observation that papillomas may harbour focal papillary carcinoma or be adjacent to carcinoma that was not sampled in the needle core biopsy.¹⁰

European guidelines on breast cancer screening
Papillary lesion on CNB

• The excision of all papillary lesions (PL) is being challenged. The option of prolonged follow-up with imaging has been suggested as an alternative approach, but all palpable or symptomatic PL or any PL with atypia must be excised.

• However, after the diagnosis of intraduct papilloma at CNB, 14% of incidence of carcinoma and 17% of high-risk lesions had been reported in the excision.

• There appears to be insufficient evidence to support a general change to the current protocol of excision of intraduct papilloma with exception of small papillomas with no atypia generously sampled by VACB and with no residual lesion in post-core imaging.
Risk of malignancy in papillary neoplasms of the breast

Claire Liu¹ · Ravi Sidhu¹ · Avi Ostry² · Rebecca Warburton¹ · Jin-Si Pao³ · Carol Dingee¹ · Urve Kuusk¹ · Elaine McKevedt¹

Table 2  Clinical data and association with upstage to malignancy

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Benign (N = 234)</th>
<th>Malignant (N = 83)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>54.8</td>
<td>60.7</td>
<td>0.0005</td>
</tr>
<tr>
<td><strong>Palpability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40 (17.7%)</td>
<td>25 (33.8%)</td>
<td>0.004</td>
</tr>
<tr>
<td>No</td>
<td>186 (82.3%)</td>
<td>49 (66.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Discharge</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>43 (19.4%)</td>
<td>15 (19.7%)</td>
<td>0.944</td>
</tr>
<tr>
<td>No</td>
<td>179 (80.6%)</td>
<td>61 (80.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Family history of breast cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>43 (24.2%)</td>
<td>7 (14.6%)</td>
<td>0.156</td>
</tr>
<tr>
<td>No</td>
<td>135 (75.8%)</td>
<td>41 (85.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical exam size (mm)²</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>15.0 (n = 31)</td>
<td>21.5 (n = 24)</td>
<td>0.037</td>
</tr>
<tr>
<td><strong>Imaging size (mm)²</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.3 (n = 224)</td>
<td>15.3 (n = 83)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td><strong>Biopsy type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U/S guided CNB</td>
<td>197</td>
<td>66</td>
<td>0.140</td>
</tr>
<tr>
<td>No</td>
<td>199</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td><strong>Atypia on CNB (excluding ADH, ALH, FEA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>21</td>
<td>71</td>
<td>&lt;0.000001</td>
</tr>
<tr>
<td>No</td>
<td>213</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

*a of palpable lesions

*b largest image size of MMO, U/S, or MRI

Conclusion  We recommend excision of PN with atypia, concurrent cancerous lesion, or radiologic–pathologic non-concordance, and serial imaging follow up may be considered for image detected PN, less than 1 cm, with no atypia.
SPINDLE CELL LESIONS
Practical approach

- Spindle Cell Lesions
  - Monophasic
  - Biphasic
     - Cytokeratins: CK903, CK5/6, CK14, MNF116, CAM5.2, AE1/3
     - MEC Markers: p63, SMMHC, calponin
       (Evaluate reactivity in stromal spindle cells)

- Myofibroblastoma Fibromatoses
  - β-Catenin
    - +
    - -

- Metaplastic Carcinoma
  - CD34 Bcl2
    - +
    - -

- Phyllodes Tumor
  - Refer to the text for the grading of phyllodes tumor

- Fibromatosis
- Myofibroblastoma
Accuracy and clinical implications of pre-operative breast core needle biopsy diagnoses of fibroepithelial neoplasms and sarcomatoid carcinomas

Alisha D. Ware¹ · Pedram Argani² · Ashley Cimino-Mathews²

Table 1 Pre-operative core needle biopsy diagnoses compared to the excision diagnoses in patients with breast fibroepithelial neoplasms and sarcomatoid (metaplastic) carcinoma

<table>
<thead>
<tr>
<th>Resection diagnosis</th>
<th>n²</th>
<th>Pre-operative core needle biopsy diagnosis, n (%)</th>
<th>Malignant or atypical spindle cell lesion</th>
<th>Phyllodes Tumor</th>
<th>Fibroepithelial lesion</th>
<th>FA</th>
<th>Benign breast tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>MP</td>
<td>6</td>
<td>0</td>
<td>6 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>BLP</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>4 (44%)</td>
<td>4 (44%)</td>
<td>0</td>
<td>1 (12%)</td>
</tr>
<tr>
<td>BP</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>1 (11%)</td>
<td>6 (67%)</td>
<td>2</td>
<td>(22%)</td>
</tr>
<tr>
<td>FA</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>2 (29%)</td>
<td>5 (57%)</td>
<td>0</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>SC</td>
<td>13</td>
<td>10 (77%)</td>
<td>3 (23%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

BLP borderline phyllodes tumor, BP benign phyllodes tumor, FA fibroadenoma, MP malignant phyllodes tumor, n number, SC sarcomatoid (metaplastic) carcinoma
In summary, accurate identification and classification of breast PT on core needle biopsy can be challenging. MP and SC have overlapping features on biopsy, but are more easily differentiated from BP, BLP, and FA. The distinction between MP and SC is vital and will guide treatment management. The distinction between BP and FA in difficult cases may not be as vital, and a core biopsy diagnosis of “fibroepithelial lesion” may be sufficient in such cases, with a note suggesting complete surgical excision. Our findings suggest differing biopsy and patient characteristics in PTs that can guide treatment planning.
Clinical Information

72-year old female with a mass of 5.0 cm in the transition of upper quadrants of the right breast.

CNB was performed.
P63 is consistently expressed in sarcomatoid/metaplastic carcinomas of the breast

Reis Filho JS & Schmitt FC. Histopathology 42: 92-99, 2003
Clinical Information

41-year old female with an ulcerated tumour in the right breast, measuring 25.0 cm.

CNB was performed.
T (17;22)
DERMATOFIBROSARCOMA PROTUBERANS

• DFSP is a rare, locally aggressive cutaneous tumor, characterized by its slow, infiltrative growth and marked tendency to local recurrence.

• The most common location is trunk, with 25% affecting the chest and shoulder areas.

• At least 40 case reports of DFSP in the breast have been reported.

• DFSP is associated with a rearrangement (translocation) between chromosomes 17 and 22. This translocation, t(17;22), fuses part of the COL1A1 gene with part of the PDGFB gene.
Upgrade to Worse Lesion

- Some diagnoses on CNB may be upgraded to a worse diagnosis at excision
  - DCIS
  - ADH
  - Lobular neoplasia
  - Papilloma
  - Radial scar
  - FEA
  - Fibroepithelial lesions
Upgrade to Worse Lesion

- Upgrade to a worse diagnosis at excision is related to:
  
  ✓ Technical factors: gauge of needle, lesion targeted, completeness of removal.
  
  ✓ Pathologic factors: extend of ADH on core, histologic features of ADH
The upgrade rate to carcinoma may be lower than initially reported in studies that lacked radiologic-pathologic correlation.
Lobular neoplasia on CNB

- 48 year-old
- Nodular lesion of 0.8 cm, BIRADS 3
HLA/ CLIS on CNB

Lobular Carcinoma In Situ Diagnosed By Core Needle Biopsy: When Should It Be Excised?
Lavinia P. Middleton, M.D., Shakeitha Grant, Tanya Stephens, M.D., Carol B. Stelling, M.D., Nour Sneige, M.D., Aysegul A. Sahin, M.D.

- 35 cases of lobular neoplasia
  - Classic LCIS (14) lobular neoplasia (4) and ALH (17)
- 17 excised
  - 6 associated with invasive carcinoma; all associated a mass lesion
- 18 cases follow-up twice per year
  - No evidence of progression (6 to 39 months)

Based on these findings, we recommend excisional biopsy of lobular carcinoma in situ, atypical lobular hyperplasia or lobular neoplasia only when it is associated with a synchronous mass lesion.

Middleton et al. Mod Pathol 2003
# Current recommendations for management of high-risk lesion on breast CNB

<table>
<thead>
<tr>
<th>High-risk lesion</th>
<th>Management recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical ductal hyperplasia</td>
<td>Surgical excision</td>
<td>Small volume ADH completely excised by CNB may be observed based on risk assessment and multidisciplinary input</td>
</tr>
<tr>
<td>Atypical lobular hyperplasia and LCIS</td>
<td>Observation with clinical or imaging follow-up or surgical excision</td>
<td>Excision necessary if there is a radiologic-pathological discordance or other high risk lesion present</td>
</tr>
<tr>
<td>Pleomorphic LCIS</td>
<td>Surgical excision</td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>Surgical excision</td>
<td>Active surveillance trials are currently evaluating follow-up after CNB for low-risk DCIS</td>
</tr>
</tbody>
</table>

[Modern Pathology](https://doi.org/10.1038/s41379-018-0137-0)
Features of DCIS associated with microinvasion

- High grade/comedo histology
- Extent (size, number of involved ducts)
- Periductal lymphoid infiltrates.
Malignant Lesions

• Definitive surgery for carcinoma can be planned preoperatively using the triple approach or radiological imaging, clinical examination and FNAC (or CNB). This permits treatment for many malignant lesions in a one-stage operation.
CONTENTS OF THE CNB REPORT

• The diagnosis (correct if possible!)

• Biopsies for calcification
  ✓ Location of calcifications
  ✓ Correlation with image

• Biopsies with invasive cancer
  ✓ Histologic type, grade, maximum size, ER, PR, HER2

• Biopsies with DCIS
  ✓ Nuclear grade, architectural pattern, location, calcification, ER.
How to avoid nightmares on CNB

• It looks like an epithelial malignancy but is it really a carcinoma?

• Is it really a primary breast carcinoma?
  ✓ Histology unusual
  ✓ Absence of in situ component
  ✓ Extensive LVI
  ✓ Triple negative

• Is this even a breast lesion?
How to avoid nightmares on FNA/CNB

• Be aware of the imaging findings and the radiologist’s differential diagnosis – triple diagnosis

• Liberal use of levels and judicious use of immunostains.

• Be conservative; avoid overdiagnosis when findings are equivocal.
Handout online:

Special thanks: Dr Catarina Callé
MSKCC
Backup Slides
Mucinous lesion on CNB

- It is reasonable to view mucocoele-like lesions as part of a spectrum from benign through to mucinous carcinoma with a significant risk of underdiagnosis in CNB. Excision of these lesions is always recommended.
Table III. Diagnostic statistics of the patients’ oestrogen receptor (ER) status according to time of data collection.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 286)</th>
<th>Group 2 (n = 264)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER-positive</td>
<td>75.9</td>
<td>74.6</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>99.5</td>
<td>99.0</td>
</tr>
<tr>
<td>Specificity</td>
<td>79.7</td>
<td>92.5</td>
</tr>
<tr>
<td>PPV</td>
<td>93.9</td>
<td>97.5</td>
</tr>
<tr>
<td>NPV</td>
<td>98.2</td>
<td>96.9</td>
</tr>
<tr>
<td>Concordant pairs</td>
<td>94.8</td>
<td>97.4</td>
</tr>
<tr>
<td>AUROC curve*</td>
<td>0.961</td>
<td>0.972</td>
</tr>
</tbody>
</table>

ER/PR in CNB

Table IV. Diagnostic statistics of the patients’ progesterone receptor (PgR) status according to time of data collection.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 286)</th>
<th>Group 2 (n = 262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PgR-positive</td>
<td>60.1</td>
<td>60.7</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>91.3</td>
<td>89.9</td>
</tr>
<tr>
<td>Specificity</td>
<td>84.2</td>
<td>89.3</td>
</tr>
<tr>
<td>PPV</td>
<td>89.7</td>
<td>92.9</td>
</tr>
<tr>
<td>NPV</td>
<td>86.5</td>
<td>85.2</td>
</tr>
<tr>
<td>Concordant pairs</td>
<td>88.5</td>
<td>89.7</td>
</tr>
<tr>
<td>AUROC curve*</td>
<td>0.881</td>
<td>0.890</td>
</tr>
</tbody>
</table>
# HER testing in CNB

## Table II: Concordance between Her2 status of core-needle biopsy (CNB) and corresponding surgical (Ex) samples in recent studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Arnedos et al., 2009&lt;sup&gt;26&lt;/sup&gt;</th>
<th>Tamaki et al., 2010&lt;sup&gt;28&lt;/sup&gt;</th>
<th>D’Alfonso et al., 2010&lt;sup&gt;29&lt;/sup&gt;</th>
<th>Apple et al., 2009&lt;sup&gt;30&lt;/sup&gt;</th>
<th>Apple et al., 2009&lt;sup&gt;30&lt;/sup&gt;</th>
<th>Park et al., 2009&lt;sup&gt;31&lt;/sup&gt;</th>
<th>Lebeau et al., 2010&lt;sup&gt;32&lt;/sup&gt;</th>
<th>Lee et al., 2012&lt;sup&gt;33&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples tested (n)</td>
<td>327</td>
<td>353</td>
<td>100 (patients)</td>
<td>260</td>
<td>260</td>
<td>104 (patients)</td>
<td>500</td>
<td>300</td>
</tr>
<tr>
<td>Testing method</td>
<td>HIC</td>
<td>HIC</td>
<td>FISH</td>
<td>FISH</td>
<td>HIC</td>
<td>HIC</td>
<td>HIC/FISH</td>
<td></td>
</tr>
<tr>
<td>Overall concordance (%)</td>
<td>98.8</td>
<td>89.3</td>
<td>87</td>
<td>92</td>
<td>98</td>
<td>86.5</td>
<td>90.4</td>
<td>98</td>
</tr>
<tr>
<td>Concordant Her2− [n (%)]</td>
<td>283 (86.5)</td>
<td>182 (96.8)</td>
<td>12 (85.7)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>102 (82)</td>
<td>83 (66)</td>
<td>—</td>
<td>411 (97.4)</td>
<td>261 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>58 (90.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant Her2+ [n (%)]</td>
<td>40 (12.2)</td>
<td>12 (75.0)</td>
<td>100</td>
<td>13 (10)</td>
<td>6 (5)</td>
<td>—</td>
<td>27 (81.8)</td>
<td>33 (97.0)</td>
</tr>
<tr>
<td>Overall discordance (%)</td>
<td>—</td>
<td>10.66</td>
<td>13</td>
<td>8</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Discordant (CNB+/Ex−) [n (%)]</td>
<td>1</td>
<td>0</td>
<td>2 (2)</td>
<td>6 (5)</td>
<td>0 (0)</td>
<td>2</td>
<td>5 (15.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Discordant (CNB−/Ex+) [n (%)]</td>
<td>3</td>
<td>0</td>
<td>2 (2)</td>
<td>4 (3)</td>
<td>3 (2)</td>
<td>1</td>
<td>0 (0)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Indeterminate [n (%)]</td>
<td>4 (1.2)</td>
<td>—</td>
<td>—</td>
<td>0 (0)</td>
<td>33 (26)</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Scored as HIC 0.<br>
<sup>b</sup> Scored as HIC 1+.<br>

HIC = immunohistochemistry; FISH = fluorescence in situ hybridization.

## Rate

<table>
<thead>
<tr>
<th>Rate</th>
<th>HER2 (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>93 (80.94–98.5)</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.6 (98.05–100)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>99 (96.97–99.8)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>97.6 (87.14–99.9)</td>
</tr>
</tbody>
</table>
HER testing in CNB

Evaluation of HER2 in breast cancer: reality and expectations

Fernanda Milanezi†, Dina Leitão, Sara Ricardo, Isabel Augusto & Fernando Schmitt

†Institute of Molecular Pathology and Immunology of Porto University, Rua Roberto Frias, s/n, 4200-465, Porto, Portugal

- Cases with fixation less than 6 hours and crush artifacts.
- CNB with few tumour cells.
- High grade tumour negative on CNB (?).
- Low amplified/borderline cases on CNB.