Breast Cytology

- Minimally invasive, accurate and reliable diagnostic method.
- Follow high-risk cancer patients
- Detect early lesions
- To obtain prognostic and predictive information

Breast FNAC
Still used in developed countries?

- One day clinic
- Palpable lesions
- Axillary nodes
- Metastatic sites
ASSESSMENT OF AXILLARY NODES

• US-guided FNAC is indicated in a newly diagnosed breast cancer if axillary nodes appear suspicious or clinical examination is equivocal.

• FNAC can be requested when the node is palpable but thought to be reactive.

• Setting of locally advanced breast cancer when neoadjuvant chemotherapy is planned.

Pre-operative diagnostic procedure

The choice of sampling method in any centre should be determined by:

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

ASSESSMENT OF AXILLARY NODES

• If the result is positive for malignancy, the patient will proceed for full axillary clearance and the SNLB is avoided.

• If the result is negative, the patient will proceed to SNLB as a negative FNAC does not confidently exclude nodal metastasis.

• Failure to visualize all lymph nodes during US, small sized metastasis and preoperative CT are main causes for discrepancy.
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.

Accuracy of FNAC

The accuracy of FNAC depends on three main factors:

- a sample that is adequate and representative of the lesion.
- suitable processing and staining without artifact.
- accurate interpretation of the cytological material with a clear report conveyed to the rest of the clinical team.

Breast FNA

How not to be washed away?

- Doing the technique with quality...
- Coupled with image....
- Solving specific problems...

FNAC

Multistep technique

- Clinical examination
- Image-guided (US)
- Aspiration
- Slide preparation
- Fixation and staining
- Cytological interpretation

TRIPLE ASSESSMENT APPROACH

- Clinical
- Imaging
- Cytology

BBB: 98% benign – follow up
MMM: 1% error – surgery
Other: biopsy

Quality of the smear
Collect sample directly into prefilled Cytolyt® tubes

CYTOLOGICAL CRITERIA OF BENIGN LESIONS

- Cohesive epithelial groups without or with mild nuclear overlapping and presence of myoepithelial cells
- Apocrine cells
- Naked nuclei

CYTOLOGICAL CRITERIA OF MALIGNANCY

- Nuclear pleomorphism
- Dirty background No naked nuclei
- Loss of cohesiveness Isolated cells with cytoplasm

HOW REPORT BREAST FNAC?

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>NHBS (UK) 2001</th>
<th>SNH recommendations (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Unsatisfactory</td>
<td>Unsatisfactory</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>Benign</td>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>Suspicious, probably benign</td>
<td>Atypical/Indeterminate</td>
<td></td>
</tr>
<tr>
<td>C4</td>
<td>Suspicious, probably malignant</td>
<td>Suspicious/probably malignant</td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>Malignant</td>
<td>Malignant</td>
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</table>
Current evidence indicates that the use of non-operative diagnosis substantially reduces the number of unnecessary operations performed both for benign disease and for malignancy, with reduced discomfort and inconvenience to the patient.

What is the role of breast FNAC in benign lesions, malignant lesions and “gray zone” lesions?

Benign Lesions

35-year old female presented with a 25 mm well-defined nodule in the right breast. Mammography and US are compatible with fibroadenoma. There is no family history of breast cancer.

- Well-circumscribed mass (similar to fibroadenoma).
- High cellular smears with irregular groups and single atypical cells. The cells are large, pleomorphic with prominent nucleoli. Background rich in lymphocytes.
- Definitive diagnosis requires the demonstration of well defined borders.
- They are frequently associated with germinal mutation of BRCA-1.

Inflammatory conditions

- A high yield of inflammatory cells and multinucleated giant cells.
- Keratin and squamous metaplastic cells.
- The identification of giant cells with keratin at cytoplasm is an important clue for the diagnosis.
- Reactive epithelial cells.
BENIGN – FAT NECROSIS

- More frequent in women with large breasts.
- In general there is a history of recent severe trauma, surgery or radiotherapy, although that does not exist in some cases.
- There may present as a palpable nodule or just a focal area of pain.

Inflammatory diseases

Moderate to high cellularity.
- Foam cells (sometimes multinucleated)
- Collapsed fat cells.
- Inflammatory cells.
- Sometimes, presence of worrisome nuclei atypical

Cyto logical interpretation

BENIGN – Cysts

- It is the most common benign tumour of the breast.
- Solitary nodule (most), sometimes multifocal and/or bilateral.
- Usually are non-tender well-circumscribed nodules.
- Biphasic proliferative lesion (epithelial and stromal elements) is similar to the structures of the terminal lobular-ductal unit (TLDU).

Rules to evaluate cysts

- After complete aspiration of the cyst, it is especially important to re-evaluate the area (US) to determine if a residual breast mass is present.
- If a residual mass is found, a second aspiration should be performed.
- Be careful with apocrine changes
CYTOLOGICAL CRITERIA OF FIBROADENOMA

- large branching, monolayer sheets of uniform epithelial cells
- fragments of fibromyxoid stroma
- numerous single, bare bipolar nuclei (myoepithelial cells)

CYTOLOGICAL INTERPRETATION

Fibroadenoma

CYTOLOGICAL INTERPRETATION

Benign epithelial proliferative lesion

<table>
<thead>
<tr>
<th>Predominant pattern</th>
<th>Cystic</th>
<th>Solid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low cellularity of epithelial cells</td>
<td>Moderate to high cellularity</td>
<td></td>
</tr>
<tr>
<td>Foam cells and apocrine metaplasia frequently present</td>
<td>Cohesive epithelial groups without or with mild nuclear overlapping and presence of myoepithelial cells</td>
<td></td>
</tr>
<tr>
<td>Fluid background</td>
<td>Heterogeneous cell population; mild variation in the size and shape of the nuclei (oval, round, or spindle)</td>
<td></td>
</tr>
<tr>
<td>Inflammatory cells can be present</td>
<td>Bipolar naked nuclei in the background</td>
<td></td>
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</tbody>
</table>

BREAST FNAC: solving problems “Gray zone”

- Papillary Lesions
- Epithelial Proliferative Lesions
- Fibro-epithelial Lesions

CYTOLOGICAL INTERPRETATION

Papillary Lesions

- Cellular smears.
- Papillary three-dimensional arrangements.
- Complex folded and branching sheets of epithelial cells.
CYTOLOGICAL INTERPRETATION
Papillary Lesions

- Columnar cells in rows, palisades and single.
- Variable nuclear atypical
- Epithelial cells with cytoplasm vacuoles

Is it possible to distinguish benign and malignant Papillary breast tumours on FNA?

Cytological findings favouring malignant

- Higher cellularity
- Papillary three-dimensional arrangements without a central fibro-vascular core (cell balls)
- Tall columnar cells frequent.
- Isolated cells with cytoplasm.
- Absence of bare nuclei, apocrine metaplasia and rare macrophages.

CYTOLOGICAL INTERPRETATION
Papillary Carcinoma

PAPILLARY LESIONS: CNB helps?
European guidelines on breast cancer screening

CYTOLOGICAL INTERPRETATION

Epithelial proliferative lesions

- Moderate to high cellularity.
- Epithelial cell groups with overlapping and without or w/ few myoepithelial cells.
- Bipolar naked nuclei in the background absent or in few numbers.
- Less cell cohesively in the borders of the cell groups with occasional isolated epithelial cells with preserved cytoplasm.
- 20% are malignant at biopsy.

Fibroepithelial lesions

PHYLLODES TUMOUR

- Biphasic proliferative lesion (epithelial and stromal elements) similar to fibroadenoma but with predominance of the stroma over the epithelium
- Fibromyxoid stromal fragments are larger than those seen in fibroadenomas and are highly cellular with fibroblastic spindle cells.
- The presence of isolated stromal cells with spindle nuclei and abundant pale cytoplasm is suggestive of PT.
Atypia
FIBROADENOMA

BREAST FNAC: solving problems
Malignant Lesions

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

• Imaging typically shows a dense mass with stellate margin, simulating malignancy.
• High cellular yield.
• Cells showing moderate atypia with intact, abundant and granular cytoplasm.

Benign Granular Cell Tumour

BREAST FNAC: solving problems
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.

CYTOLOGICAL CRITERIA OF INVASIVE DUCTAL CARCINOMA

Cellular smear, w/variable cell pattern, sometimes plasmacytoid appearance

Nuclear pleomorphism

Loss of cohesion
**CYTOLOGICAL INTERPRETATION**

**Invasive lobular carcinoma**

- Variable cellularity. In some cases very poor cell yield.
- Cells single and in small clusters, short single files common.
- Epithelial cells have small dark nuclei with scanty cytoplasm. The lack of pleomorphism can be cause of a false-negative diagnosis.
- Intracytoplasmic lumina/vacuoles.

**Mucinous carcinoma**

- Well defined and circumscribed tumour (similar to fibroadenoma).
- Abundant background mucinous, atypical cells in small solid aggregates, single files or isolated. The mucin stains violet to blue with MGG or pink on HE staining.

**Metaplastic carcinoma**

- Is an invasive ductal carcinoma with metaplastic changes: squamous cells, spindle cells, osteoid or chondroid.
- Smears can show different cell types: ductal, spindle or squamous.
- Sometimes we can observe multinucleated giant cells and myxoid material.
- Can be cystic at aspiration and with necrotic material.

**Tubular carcinoma**

- Variable cellularity (moderate to intense). At low magnification a pattern somewhat similar to fibroadenoma.
- Cells arranged mostly in tubular structures with comma-like pattern.
- Epithelial cells are uniform and bland. The lack of pleomorphism can be cause of a false-negative.
- Bare nuclei are present in rare cases.

**Invasive micropapillary carcinoma**

- Highly cellular smears composed by angulated small groups of cohesive cells with papillary configurations without fibro vascular cores.
- Cells showing nuclear atypical, irregular nuclear contours and prominent nucleoli.
- Cytoplasm vacuoles are rarely seen.
- Background is clean with rare isolated neoplastic cells.
**CYTOLOGICAL INTERPRETATION**

**Apocrine carcinoma**
- Malignant cells have a large dense eosinophilic granular cytoplasm with large nuclei with prominent nucleoli.
- Neoplastic cells are isolated, sometimes without cytoplasm and in small aggregates.
- Necrosis is frequent.

**Breast carcinoma with osteoclast-like giant cells**
- Cellular smears composed by cohesive groups of epithelial cells, with low grade of atypia.
- Groups of plump spindle cells as well as isolated atypical epithelial cells.
- Presence of osteoclast-like multinucleated cells at periphery of the epithelial cells or in the background of the smears.

**Adenoid cystic carcinoma**
- Highly cellular
- Pattern of large tissue fragments, consisting of cells with poorly defined cytoplasm, minimal cytological atypia and myoepithelial cells.
- Background may have dispersed bare nuclei and/or dispersed intact atypical cells.
- Hyaline spherules, varying from mucinous to collagenous

**Metastatic malignancy**
- **METASTATIC MELANOMA**
- **METASTATIC OVARIAN CARCINOMA**

**Other malignancy**
- **NON-HODGKIN LYMPHOMA**

**Inflammatory diseases**
- **BENIGN – INTRAMAMMARY LYMPH NODE**
Breast FNAC

How not to be washed away?

QUALITY

QUALITY

QUALITY

Technical factors

False-positives
- Bad quality of smears
- Fixation artefacts

False-negatives
- Operator dependent
- Characteristics of the lesion:
  - Size of the lesion
  - Size of the breast
  - Location
  - Histological type

Breast FNAC

How not to be washed away?

- Aspiration should be direct to a define target.
- FNAC is a multi-step procedure and to obtain a good material is essential for the diagnosis.
- The cytological diagnosis should be done only with the knowledge of the clinical context and preferential in a multidisciplinary environment.
- Negative results can not solve the patient problem.