Breast: Difficulties in Core Biopsies

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No conflicts of interest
Role of Core Needle Biopsy

- To eliminate need for surgical excision of benign lesions
- To definitively diagnose malignancy
- Allow surgical planning and consideration for possible neoadjuvant therapy

Superior to FNA
Advantages

- ↓ no. of surgeries in women with IBC
- Less invasive
- Less expensive
- Less scarring on subsequent imaging
- Confirm multiple foci and determine appropriate surgical procedure

Challenges

- Limited material
- Disruption frequent
- Sampling error
Accuracy

• Excellent agreement with open bx.
• Accuracy, sensitivity, specificity
  – 0.98, 0.88, 0.98 (mostly palpable)
  – 0.98, 0.91, 1.00 (non-palpable)
  – ↑ when ≥ 6 cores
  – ↑ with experienced radiologist

• Original and review pathologist 96% concordance

*Wei et al, Med Onc, 2010
*Fajardo et al, Acad Rad, 2004*
False Negatives

• 1-15% for malignancy
  – Lower with 11G/vacuum

• Causes:
  – Sampling/Suspicious mass – not explained by histologic findings
  – Calcifications – not identified in the core

• Calcs > mass
• DCIS > invasive
Key to success

• Does my diagnosis correlate with the radiologic findings?

• Know the indication for the biopsy !!!!!
Triple Test

Clinical Radiology Pathology

Must correlate!

*Important for pathologist to appreciate imaging categories and pathology correlation*

Multidisciplinary rounds
Specimen x-ray
Role of the Pathologist in the Evaluation of Calcifications
Calcifications

• Specimen radiograph mandatory for any biopsy performed for calcifications
  – *Separate cores with calcs from those without*

• If calcs seen on mammo but none in specimen x-ray:
  – ability to make dx ↓ from 82 to 40%

• Dx more likely in cores bearing calcs on specimen x-ray than those without
  – 84 vs 71%
Specimen radiograph is mandatory for image-guided biopsy for calcifications

U/S-guided needle bx

Must reconcile the findings in specimen radiograph and mammogram with microscopic findings
Calcifications

- Examine ≥ 3 levels
  - intervening unstained levels may be retained for ER/PR vs. other IHC
- If indication = Ca+2, must make every effort to find
- Pattern/distribution
  - Always report if calcs are seen and where
- Number
  - More numerous in radiograph or microscopically?
- Size
  - Is the size of the observed calcs consistent with those targeted? (size threshold of 100µm on imaging)
Audience participation 1

- 58 y.o woman with linear branching calcifications on mammography
- Stereotactic core biopsy
- Calcifications are reported as being present in the specimen x-ray
True or false

Pathology correlates with radiology
Findings are benign
Patient returns to screening programme
False

Calcifications not in keeping with linear branching morphology

Cut deeper levels
No Calcs?

- Polarize - ? calcium oxalate
- X-ray blocks
- Cut deeper levels

• Still none?
  - Lost calcs
    - Loss during processing/sectioning
      - Destruction by fixatives
      - Dislodged by microtome
      - Rupture of cyst during biopsy – fall-out
Microcalcifications: calcium oxalate
Microcalcifications: calcium oxalate
Categories

- Benign
- Malignant
- Uncertain
- Suspicious
Hamartoma

• *Highlights importance of rad-path correlation*

• Circumscribed/encapsulated
  – Ducts, lobules, fibrous tissue, fat (variable)

• Typical mammographic appearance
  – Obviating need for CNB in most
Hamartoma - CNB

- “Benign fibrous and fatty breast tissue”

Was the lesion sampled?

- Are the characteristic imaging features present?

*If “yes” → consider hamartoma*
Malignant

DCIS with microinvasion

Invasive carcinoma

Other Malignant

DCIS
Pitfalls

- DCIS with obliterative sclerosis
- Displacement of calcifications
- Displacement of atypical cells
Pitfalls

Beware:

– DCIS with obliterative sclerosis
– Displacement of calcs
– Displacement of atypical cells
Pitfalls

- DCIS with obliterative sclerosis
- Displacement of calcs
- Displacement of atypical cells
DCIS

- 20% upgraded to IBC
- Mass lesions > microcalcs
  - Younger patients
  - Greater extent on mammo
  - High grade
  - Comedo necrosis
- Report: grade, comedonecrosis, calcifications, architecture, microinvasion
- Consider SLN
IBC - What to report?

How much information is required pre-op?

- Neo-adjuvant therapy
  - Full range of prognostic and predictive information

- Proceeding direct to surgery
  - Provision of one set of results only?
    - Avoids misleading/conflicting findings
What to report?

- **Type**
  - May influence pre-op work-up and extent of surgery
    - Good correlation with excision (72-82%)

- **Grade**
  - Can be discordant; still useful
    - Underestimate (less mitoses) (84% for high grade)

- **Size**
  - If entire tumour removed on biopsy
    - Prone to inaccuracies (underestimate in 79%)

- **LVI**
  - Only if unequivocal; beware retraction, 8% sensitivity
Audience Participation 2

65 year old woman, screening detected mass, 1.3 cm
Ultrasound-guided core biopsy
Which action is most appropriate?

A. Observation, lesion is benign
B. Excise, lesion is probably benign
C. Re-biopsy, findings not concordant
D. Wide local excision with sentinel node
E. I’m not sure…..I think I need help
Which action is most appropriate?

A. Observation, lesion is benign
B. Excise, lesion is probably benign
C. Re-biopsy, findings not concordant
D. Wide local excision with sentinel node
E. I’m not sure.....I think I need help
Radial Scar
Invasive Carcinoma

Pitfalls on CNB

– Is it malignant or a benign mimic?
  • e.g. tubular carcinoma vs radial scar
  • Imaging not helpful
Radial Scar

Pitfalls

- Entrapped distorted glands
  → Tubules resembling those of tubular ca.
- Rare absence of MEC IHC staining
- Perineural invasion
- Necrosis present in 10% with UEH

More challenging on CNB
Invasive Carcinoma

Pitfalls on CNB

– Overcalling ILC
– In the setting of a well-circumscribed lesion
  • SA, myoid hamartoma
SA mimicking ILC pattern
Invasive Carcinoma

Pitfalls on CNB
Under calling ILC
- Paucicellular infiltrate
- Chronic inflammation/histiocytes
Stroma appears more cellular than usual
Inflammatory vs. ILC

Pan-CK
Uncertain

Radial Scar

Papillary

CCLs with atypia

Spindle cell lesions

FELCS

ADH

LN
“Uncertain”

- 7.7% of screening biopsies
  - Clinical dilemma
  - Need excision to exclude malignancy

Papillary Lesions

- Heterogeneous
  - Finger-like projections
  - Central FV core
  - Lined by epithelium

- IDP vs. IDP with atypia/DCIS vs. EPC
Benign intraductal papilloma with FEHUT
Intraductal Papilloma

- Sclerosis
  - Obscure papillary nature

- Entrapment
  - Mimics invasion
    - ID MECs
    - Stroma hyalinized
    - Underlying lesion is benign
Benign intraductal papilloma with sclerosis and entrapment
Atypia in Papilloma

- IP with:
  - Low grade cytologic atypia
  - Architectural atypia

- Extent ≤ 3mm
  - If > 3mm → DCIS in IP

- DDx UEH
  - ER
  - CK5

Grin et al. AJSP, 2009 Nov;33(11):1615-23
Atypia within a papilloma
Encapsulated Papillary Carcinoma

- Papillary carcinoma, surrounded by fibrous capsule
- FV cores
  - Single population
- Low to intermediate grade
- MECs lacking from periphery
  - In situ vs invasive?
Fibrovascular Core

No MEC lining FV cores or periphery
Diagnosing Invasive Ca

• Difficult!

• EPC lack MEC around periphery
  – IHC not useful

• Pseudoinvasion

• True invasion
  – Recognisable pattern of invasive carcinoma
  – Beyond capsule, into fat/normal breast

  ↓

*May not be included in biopsy*
Management

- Atypia in IP → excise
- EPC → excise
- Benign IP → ?
  - Risk of upgrade to malignancy (0-36%)
  - Sampling or difficult dx.
  - ? Preventive
  - ? Excise all vs. prolonged follow-up vs. VACB

- Consider:
  - Small, no atypia, generously sampled by VACB, no residual lesion post-core imaging

Beware epithelial displacement
### Benign papillomas on CNB – Upgrade Rate

<table>
<thead>
<tr>
<th>Study</th>
<th>Benign Excised</th>
<th>Benign on Excision</th>
<th>Atypical on excision</th>
<th>Malignant on excision</th>
<th>Total Upgrade N(%)</th>
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</thead>
<tbody>
<tr>
<td>Jakate et al, 2012</td>
<td>90</td>
<td>74</td>
<td>12</td>
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<td>16 (17.8%)</td>
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<td>Kim et al, 2011</td>
<td>136</td>
<td>120</td>
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<td>16 (12%)</td>
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<td>Bennett et al. 2010</td>
<td>45</td>
<td>45</td>
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<tr>
<td>Jung et al. 2010</td>
<td>154</td>
<td>144</td>
<td>0</td>
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<td>10 (6%)</td>
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<td>Chang et al. 2010</td>
<td>100</td>
<td>83</td>
<td>13</td>
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<td>Ahmadiyeh et al. 2009</td>
<td>29</td>
<td>28</td>
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<td>1 (3%)</td>
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<td>Jaffer et al. 2009</td>
<td>104</td>
<td>87</td>
<td>8</td>
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<td>17 (16%)</td>
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<td>Bernik et al. 2009</td>
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<tr>
<td>Shandarajah et al. 2008</td>
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<td>Sakr et al. 2008</td>
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<td>75</td>
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<tr>
<td>Rizzo et al. 2008</td>
<td>86</td>
<td>65</td>
<td>12</td>
<td>9</td>
<td>21 (24%)</td>
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<tr>
<td>Kil et al. 2008</td>
<td>76</td>
<td>70</td>
<td>0</td>
<td>6</td>
<td>6 (8%)</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>1029</strong></td>
<td><strong>886 (86%)</strong></td>
<td><strong>62 (6%)</strong></td>
<td><strong>81 (8%)</strong></td>
<td><strong>143 (14%)</strong></td>
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</tbody>
</table>
Audience Participation 3

47 year old woman, fine pleomorphic calcifications
Stereotactic core biopsy performed
Very little tissue obtained, mostly fat, with focal epithelial element....multiple additional levels cut
Most appropriate action

A. Benign, continue routine screening
B. Re-biopsy patient
C. Excise, it’s at least atypical
D. Excise, it’s malignant
E. I’m not sure.....help needed!!
Most appropriate action

A. Benign, continue routine screening
B. Re-biopsy patient
C. Excise, it’s at least atypical
D. Excise, it’s malignant
E. I’m not sure…..help needed!!
FEHUT  ADH
Core Biopsy Diagnosis

Atypical Ductal Hyperplasia
ADH

Dx. depends on quantitative features
=> can’t be diagnosed reliably on core biopsy

“Atypical intraductal epithelial proliferation”
or
“...at least amounting to ADH...”

Be conservative in borderline cases
Should pass “bilateral mastectomy test”
Management - ADH

- Excise mammographic abnormality
- Not infrequently part of larger DCIS
  
  *Nature of biopsy => quantitative criteria not met*

- Underestimation of malignancy
  - Rates of upgrade to DCIS or invasive cancer (18-87% using 14G)
  - Vacuum-assisted methods 11G
    - Lower underestimation rate (10-39%)
    - Removal of entire lesion
  - DCIS>>IBC (25%)
53 year old woman
Mammo: asymmetric density
U/S: mass with microlobulation of margins

U/S-guided core biopsy
What next?

- Patient follow-up, no surgery necessary
- Complete excision
- Complete excision with sentinel node
- Additional work-up of case
- None of the above
What next?

- Patient follow-up, no surgery necessary
- Complete excision
- Complete excision with sentinel node
- Additional work-up of case
- None of the above
LCIS within sclerosing adenosis

E-cadherin
LCIS vs DCIS - An Important Distinction?

- Yes
  - Clinical significance and management considerations

- LN – indicator of increased risk (traditional)
  - 4-5x - ALH
  - 8-10x – LCIS
  - Bilateral

  *Page et al, Human Pathology 1991; 22;1232-1239*

- LG DCIS – risk is ipsilateral → direct precursor

  *Data shows that LN can act as a non-obligate precursor of IBC*
  *Risk of ipsilateral ↑ x 3*
  *ILC overrepresented*
  *LCIS and ILC – shared genetic alterations*
Should LN be Excised?

- Co-existent high risk lesion e.g. ADH
- Rad-path discordance
- Indeterminate features
- Variant LCIS

*Liberman et al, AM J Roentgenol 1999;173:291-299*
Should LN be Excised?
Classic LN only

- Upgrade 17-36%
  - Studies retrospective, selection bias
  - Small numbers

- Larger studies, rad-path correlation
  - 1-3.4%

Murray et al, Cancer, 2013, 1073-9
Chaudhary et al, Mod Path, 2013, 762-71
Hwang et al. Mod Pathol 2008;21:1208-16
Columnar cell change

Columnar cell hyperplasia

atypia

atypia

Flat Epithelial Atypia
CCL - Management

- Non-atypical
  - Excision not required
    *If calcs are accounted for*

- Atypical lesions
  - Very low risk of progression
  - *Red flag*
  - Excise
## CNB and Excision

<table>
<thead>
<tr>
<th>Study</th>
<th>FEA N</th>
<th>Upgrade N(%)</th>
<th>Invasive N(%)</th>
<th>DCIS N(%)</th>
<th>LN N(%)</th>
<th>ADH N(%)</th>
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<td>Bonnett et al. 2003</td>
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<td>Noel et al. 2009</td>
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<td>Senetta et al. 2009</td>
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<td>Peres et al, 2012</td>
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<td>Biggar et al, 2012</td>
<td>51</td>
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<td>Khoumais, 2013</td>
<td>94</td>
<td>38</td>
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<td><strong>Total</strong></td>
<td>571</td>
<td><strong>174 (30%)</strong></td>
<td><strong>24 (4.2%)</strong></td>
<td><strong>37 (6%)</strong></td>
<td><strong>45 (8%)</strong></td>
<td><strong>68 (12%)</strong></td>
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</table>
Radial Scar/CSL

Ducts radiating from central sclerotic core

Fibrotic/elastotic centre

FEHUT

SA

Papillary change

DCIS

ADH

LN

IMC

Usually associated BPD; 10% AH/CIS, 1-5% IMC
Radial Scar
Results of Outcome Studies Following CNB

- Majority of Studies recommend all RS be excised based on associated atypia in 10-15% of cases
- Carefully performed studies suggests:
  - Rates of missed carcinomas (benign on CNB) 0-5%
  - Majority of “upgrades” had at least AH on Bx
  - Virtually no upgrades if:
    - RS < 1.0 cm, esp if ≤ 6-7 mm
    - Sampled by 11 gauge needle or larger
    - ≥ 12 cores taken

References:
- Brenner 2002
- Sohn 2010
- Cawson 2003
- Rajan 2011
RS Treatment Approach

Incidental Finding

No Further Treatment

Mammo Lesion of Interest

No Atypia
Mammo < 6-7 mm
Well sampled
11 or 8 gauge needle

No Atypia
Limited Sample

Atypia
Malignancy
Mammo discordant

Excision
Take Home Messages

• Radiologic correlation pivotal
  – Does the pathology explain the imaging?
  – If not → reconcile
  – Still discordant? Re-biopsy

• Uncertain category
  – ? Appropriate mgt.

• CNB has limits
  – Be conservative