Breast Core Biopsy
Outline of Presentation

- Clinical request form and X-ray should be received
- Fixation – how long?
- Processing - rapid processing?
- Levels – how many as routine?
- Pitfalls – microcalcifications & tubular carcinoma Vs sclerosing lesions

Needle Core Biopsy
Principles

- All biopsies for Ca²⁺ should have immediate specimen X-ray
- Representative nature of the calcification should be confirmed by a radiologist
- Specimen should be sent, with completed clinical request form, in fixative to laboratory
- X-ray should be sent with request form – the distribution and amount on X-ray can be helpful histopathologically

Fixation – how long?
ER & Formalin Fixation of Cores

- 24 ER⁺ carcinomas fixed for 3, 6, 8 & 12 hrs & 1, 2 & 7 days & Q score (0-7) performed
- Mean Q score / block = 2.46 for blocks fixed for 3 hrs, 5.75 after 6 hrs & 6.70 for blocks fixed for 8 hrs
- Difference between max & mean nearly 0 at 6-8 hrs fixation
- For core biopsies, means for ER-disparate & ER-similar results at 1.2 and 6.3 hours, respectively
- Minimum fixation time for reliable IHC ER results 6 to 8 hours regardless of type or size of specimen
Microwave Fixation
- Not new
- "Histological fixation by microwave heating"

How many levels?
3. After processing, hematoxylin and eosin stained sections from one level are usually sufficient for core biopsies from most lesions, but core biopsies taken for the investigation of microcalcification should have a minimum of three levels examined. In practice, most laboratories choose to examine all core biopsies from screen-detected lesions on at least three levels initially. In problematic cases, further levels and immunohistochemical studies may be helpful.

UK NHSBSP Non-operative Guidelines

Needle Core Biopsy Handling
Calcification in core biopsy
- Targeted specimen examination
- Cell safe capsules, or similar, may be useful
- 3 levels - e.g. 1, 5 & 10 as routine

If not present – what are the options?
- More levels (through) block
- Check with radiologist regarding the presence of calcification!

Sources of “missing” microcalcification
Calcium Oxalate
- Calcium oxalate in 23% of diagnostic biopsies excised for mammographic microcalcifications
  Radi. Arch Pathol Lab Med.1989;113; 1367-9
- Polarized light microscopy
- Silver nitrate / rubeanic acid with 5% acetic acid pre-treatment
  Tornos. Am J Surg Pathol. 1990; 14;961-8

Core Biopsy - Microcalcifications
If calcification seen in specimen X-ray:
- histologically in 78%
- diagnosis in 81%

If no calcifications on specimen X-ray:
- histologically in 13% &
- diagnosis in 38%

Liberman. Radiology. 1994;190;223-5

- Multidisciplinary discussion re representative nature of the calcification essential

Sources of “missing” microcalcification
Disappearance in formaldehyde?
- 150 cores from 2 specimens in ethanol
- 41 radiographically proved microcalcifications into 4 different solutions:- 10% formaldehyde, 0.9% sodium chloride, electrolyte solution & 74.1% ethanol with 10% 2-propanol
- Specimens radiographed again after 1 & 3 days
- Within 3 days, total radiographic disappearance of microcalcifications in all cores in solutions with high water content
- Those in ethanol, microcalcifications - no change
- A non-aqueous fixative (e.g. ethanol) better preservative of microcalcifications in breast cores than various aqueous solutions, possibly because calcium compounds are water-soluble
Tubular Carcinoma Vs Radial Scar

- May be clinically, radiologically and macroscopically indistinguishable – stellate lesions
- Pale fibrous areas with spiculate appearance and ill-defined radiation of fibrous bands into surrounding fat
- Microscopically both may have central fibrous/fibro-elastotic area with central entrapped tubular structures
- Associated epithelial hyperplasia/atypia/DCIS

Tubular Carcinoma Histology

- ‘Pure’ type has stellate configuration with central fibrosis and elastosis; “sclerosing” type characterised by a diffuse & haphazard infiltration of tubules into adjacent connective & adipose tissue
- Tubules are small, angulated, oval or rounded, lined by a single layer of epithelium
- Tumour cells are small & uniform with mild to moderate nuclear atypia – if score 3, then NOT tubular carcinoma
- Cytoplasmic apical snouts may be present
- Connective tissue stroma is usually desmoplastic
- 90% of tumour area must show these features (>50% if other element is cribriform)

Tubular Carcinoma Clinical Features

- 0.8-2.3% of invasive breast carcinomas
- Higher proportion in screen-detected series
- By definition, are grade 1 lesions (usually TPM = 121)
- 5-year & 10 year overall survival rates approx 94% & 88% respectively; death is more likely to be from unrelated causes

Radial Scar/Complex Sclerosing Lesion Histology

- Central fibro-elastotic scarring with entrapped tubules/glands
- These have a double layer of epithelium & myoepithelium
- Tubules may have flattened appearance, although may appear angulated due to surrounding fibrosis
- Stroma not desmoplastic, although previous FNA or core biopsy may obscure this
- Tubular structures do not extend to periphery but radiating, peripheral fibrocystic changes
- Associated hyperplasia frequent
- Double-layer can be confirmed by IHC for myoepithelial cells

Smooth Muscle Actin

- Smooth muscle actin is still probably the most commonly used myoepithelial cell marker
- Specific and sensitive
- But, stains stromal myofibroblasts & vascular smooth muscle cells

S100 & Cytokeratins

- S100 protein & specific cytokeratins (5, 7, 14 and 17) stain myoepithelial cells
- Staining not specific & not optimally sensitive
**Smooth Muscle Myosin Heavy Chain**
- Myoepithelium in normal breast, DCIS & sclerosing lesions
- Some myofibroblasts (about 8%)

**Calponin**
- Myoepithelial cells, similar to myosin
- Also subset of myofibroblasts

**Heavy caldesmon**
- Only fraction of myoepithelial cells

*Wang NP et al. Applied Immunohistochemistry 1997; 5; 141 - 151*

**CD10 (common acute lymphoblastic leukemia antigen/CALLA)**
- Myoepithelial cells of normal breast & benign lesions
- Negative in vessels
- Less background staining than SMA
- Moritani S et al. Mod Pathol. 2002;15:397-405

- Strong circumferential staining in 18% ducts bearing DCIS vs 48% with SMMHC
- Myoepithelial cells NOT detected in 32% ducts with CD10 vs 13% with SMMHC
- CD10 shows non-specific staining of epithelial cells

**P63**
- Nuclear staining
- Myoepithelial cells
- Negative in vessels & stromal myofibroblasts
- 11% of tumors at least focal p63 expression
- Valuable in metaplastic carcinomas

*Noel JC et al. Ann Pathol. 2004;24:319-23*

**Which Myoepithelial Stain?**
- Dependent on personal and laboratory preference
- On a particular histological problem to solve
- Combination of SMMHC & p63?

**Needle Core Biopsy Reporting Categories**
- B1 Normal tissue
- B2 Benign lesion
- B3 Of uncertain malignant potential
- B4 Suspicious
- B5 Malignant

*UK NHSBSP Non-operative Guidelines*

**Radial Scar in Core Biopsy**
**B3 Category Because.........**
- May show intra-lesional heterogeneity
- Associated with atypia/DCIS & low grade invasive cancer
- Co-existing malignancy may be focal and not present in cores
Outcome of B3 Diagnoses
Nottingham Data

<table>
<thead>
<tr>
<th>Reason for B3 diagnosis</th>
<th>Excision biopsy</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Epithelial atypia (+/- other lesion, RS, papillary lesion etc)</td>
<td>24/9 (61%)</td>
<td>25/7</td>
</tr>
<tr>
<td>Radial scar or papillary lesion without atypia</td>
<td>2/2 (8%)</td>
<td>29/2</td>
</tr>
<tr>
<td>Overall (not all shown)</td>
<td>29 (31%)</td>
<td>65</td>
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</tbody>
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Outcome of Radial Scars

- 198 impalpable radial scars - 157 lesions surgical excision (n = 102) Vs mammo surveillance
- Carcinoma in excision in 26% with atypical hyperplasia in core Vs 4% of lesions without atypia
- Malignancy missed in 9% biopsied with a spring-loaded device & in 0% biopsied with a directional vacuum-assisted device
- Missed in 8% with <12 specimens/lesion Vs 0% with 12 or more cores
- Lesion type, size, type of imaging guidance (stereotactic or US) not significant in determining presence of malignancy

Brenner RJ. AJR Am J Roentgenol. 2002;179:1179-84

Summary
Core biopsy handling & avoiding pitfalls

- Core biopsies should be received with full clinical information (and X-ray)
- Cores with microcalcification can helpfully be separately identified
- Fixed, ideally, for 6 hours (or microwave)
- Routine processing & embedding
- 3 levels for cores with microcalcification initially, although may need more on occasions
- Polarised light
- Low threshold for requesting immunohistochemistry
- Some lesions cannot be unequivocally diagnosed (B3 - uncertain malignant potential or B4 - suspicious) on core biopsy
- Multidisciplinary discussion