Controversies on the Management of High Risk Breast Lesions on Core Biopsy: An Update on the Literature

Dianne Georgian-Smith MD
Brigham and Women’s Hospital
Associate Professor of Radiology, Harvard Medical School
Boston, MA

Thomas J Lawton MD
Director, Seattle Breast Pathology Consultants
Seattle, WA
High Risk Lesions: Management

• Objectives:
  – To review literature 2004-2009*:
    • Lobular carcinoma in-situ (LCIS)
    • Atypical lobular hyperplasia (ALH)
    • Solitary benign papilloma
    • Radial scar/complex sclerosing lesion
    • Flat epithelial atypia (FEA)
  – To illustrate management controversies stemming from conflicting data in the literature

*(Radiologic Clinics of NA 2010; Breast Imaging)
Demographics:

- My profession is:
  - A. Radiologist – Board Certified
  - B. Radiologist – Resident in training
  - C. Surgeon
  - D. Pathologist
  - E. Nurse
  - F. Radiology Technologist/ Sonographer
  - G. Other
My current practice location:
Demographics

- 84 chose to participate
- 48% from East Coast region
- 16% from outside US
- Nearly 99% were radiologists
- 98% were board-certified; 2% residents
- 55% have been in practice > 10 years
LCIS- classic

• Case 1A: 54 y/o woman, screening mammogram. Undergoes stereo core bx for cluster of calcifications (See Fig 1A) using 11g vac ast needle, 12 cores; adequate sample of cores.

• Path dx: LCIS only. Calcs present in association with LCIS and in surrounding ducts and lobular units.
Fig 1A

CC magnification
LCIS- classic

• Case 1A: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of LCIS, surgical excision is recommended.
  – C. The case is rad/path discordant because LCIS is incidental without imaging correlate; recommend surgical excision
LCIS-classic results

- 14% rad/path concordant, imaging f/up
- 66% rad/path concordant but due to LCIS recommend surgery
- 20% rad/path discordant because LCIS is incidental without imaging correlate; recommend surgery
ALH

• Case 1B: Same scenario clinically and radiographically.
• Path dx: ALH only. Calcs present in association with ALH and in surrounding ducts and lobular units.
Fig 1B

CC magnification
ALH

• Case 1B: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of ALH, surgical excision is recommended.
  – C. The case is rad/path discordant because ALH is incidental without imaging correlate; recommend surgical excision
ALH results

- 25% rad/path concordant, imaging f/up
- 66% rad/path concordant, but due to presence of ALH surgery is recommended
- 9% rad/path discordant because ALH is incidental without imaging correlate; recommend surgery
LCIS- pleomorphic

• Case 1 C: Same clinical scenario, but the calcifications have this appearance (see Fig 1C).
• Path dx: Pleomorphic LCIS. Calcs present in association with LCIS and in surrounding ducts and lobular units.
Fig 1C: LCIS - pleomorphic
Case 1C: What is your recommendation?

- A. The case is rad/path concordant; imaging f/up
- B. The case is rad/path concordant, but due to presence of LCIS, surgical excision is recommended.
- C. The case is rad/path discordant because LCIS is incidental without imaging correlate; recommend surgical excision
LCIS-pleomorphic results

- 8% rad/path concordant, imaging f/up
- 65% rad/path concordant, but due to LCIS recommend surgery
- 27% rad/path discordant because LCIS is incidental without imaging correlate; recommend surgery
### ALH vs. LCIS vs. pLCIS

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<tr>
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<th>ALH</th>
<th>LCIS</th>
<th>pLCIS</th>
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<tbody>
<tr>
<td>Concordant; imaging follow-up</td>
<td>25%</td>
<td>14%</td>
<td>8%</td>
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<tr>
<td>Concordant; recommend surgery</td>
<td>66%</td>
<td>66%</td>
<td>65%</td>
</tr>
<tr>
<td>Discordant; recommend surgery</td>
<td>9%</td>
<td>20%</td>
<td>27%</td>
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Literature 2004-2009
Lobular Neoplasia Underestimation Rates:

<table>
<thead>
<tr>
<th>Low prevalence (N=4)</th>
<th>High Prevalence (N=9)</th>
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<tbody>
<tr>
<td>• 0% (0/12) [40]</td>
<td>• 4% (1/25) [35] excluding rad-path discordance</td>
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<tr>
<td>• 0% (0/21) [41]</td>
<td>• 14% (3/21) [24]</td>
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<tr>
<td>• 1% (1/87) [37]</td>
<td>• 16% (1/6) [25]</td>
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<tr>
<td>excluding rad-path discordance</td>
<td>• 19% (10/52) [30]</td>
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<tr>
<td>• 2% (2/98) [36]</td>
<td>• 20% (7/35) [26]</td>
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<td></td>
<td>• 23% (38/164) [31]</td>
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<td></td>
<td>• 25% (5/20) [27]</td>
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<td></td>
<td>• 37% (13/35) [28]</td>
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<td>• 50% (9/18) [29]</td>
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Lobular Neoplasia Underestimation Rates:

- High Prevalence
- Low Prevalence
Lobular Neoplasia (LN) Literature

• LN Supporting Surgical Follow-up
    • 14 institutions: 278/ ~ 32,000 cores (0.9%) ALH/ LCIS
      – 59% (164/278) surgical follow-up- surg path reviewed
      – 23% upgrade rate: 25% (17/ 67 LCIS); 22% (21/97 ALH)
  – Issues:
    – Selection for surgery unknown/not uniform across institutions
    – ? f/up for cases that did not go to surgery (41%)
    – Rad/path concordance/discordance variable
      • 15/82 (17%) of concordant cases upgraded
Lobular Neoplasia (LN) Literature

- LN Supporting Imaging Follow-up
    - 333 cores LCIS/ALH; 41% (N=136) surgical follow up
      - ADH + LN = 49 cases
      - LN only = 87 cases
      - Ca in LN: 2% (1/48 ALH); 23% (9/39 LCIS)
        » 6/9 LCIS cases- discordant rad/path; remaining 3 LCIS non-classic/pleomorphic
        » Ca upgrade 1/87 (1%) for LN+ excluding rad/path discordance and non-classic morphology
      - BUT- NO FOLLOW UP ON ~ 60% OF CASES.
Lobular Neoplasia (LN) Pathology Issues

• Variable definitions for distinguishing ALH and LCIS
• Most commonly used definition is vague and subjective
• Inter-observer variability
Lobular Neoplasia: Definitions

- At least 50% of the acinar units in a lobule should be “filled and distended” by lobular neoplastic cells for a diagnosis of LCIS
- Definition of “distended” is at least 8 lobular neoplastic cells spanning any acinar unit
Lobular Neoplasia

- Normal lobule
- ALH
- LCIS
Borderline Epithelial Lesions of the Breast

• Darryl Carter (Yale)
• Robert Fechner (UVA)
• Richard Kempson (Stanford)
• David Page (Vanderbilt)
• Paul Peter Rosen (MSKCC)
# Results for Lobular Neoplasia

<table>
<thead>
<tr>
<th>L1</th>
<th>CIS</th>
<th>AH</th>
<th>AH</th>
<th>AH</th>
<th>H&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>H</td>
<td>AH</td>
<td>AH</td>
<td>H&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
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<td>H</td>
<td>H</td>
<td>AH</td>
<td>H</td>
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<td>AH</td>
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<td>H&lt;sup&gt;b&lt;/sup&gt;</td>
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Benign Papilloma

• Case 2A: 42 y/o woman, nodule retroareolar on screening mammogram; small hypoechoic, circumscribed mass (See Fig 2). US core biopsy- 14 g tru-cut, 5 cores.

• Pathology: Intraductal papilloma; no atypical hyperplasia or carcinoma. Surrounding tissue with proliferative fibrocystic changes.
Fig 2: Benign Papilloma
Benign Papilloma

• Case 2A: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of papilloma, surgical excision is recommended.
  – C. The case is rad/path discordant because papilloma is incidental without imaging correlate; recommend surgical excision
Papilloma—14 gauge/5 cores results

- 42% rad/path concordant, imaging f/up
- 58% rad/path concordant, but due to papilloma recommend surgery
Benign Papilloma

- Case 2B: 42 y/o woman, nodule retroareolar on screening mammogram; small hypoechoic, circumscribed mass (See Fig 2). US core biopsy- 11 g vac- ast, 12 cores.
- Pathology: Intraductal papilloma; no atypical hyperplasia or carcinoma. Surrounding tissue with proliferative fibrocystic changes.
Benign Papilloma

• Case 2B: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of papilloma, surgical excision is recommended.
  – C. The case is rad/path discordant because papilloma is incidental without imaging correlate; recommend surgical excision
Papilloma – 11 gauge/12 cores results

- 62.5% rad/path concordant, imaging f/up
- 37.5% rad/path concordant, but due to papilloma recommend surgery
## Papillomas and Sample Size

<table>
<thead>
<tr>
<th>Concordant; imaging f/up</th>
<th>14 gauge 5 cores</th>
<th>11 gauge 12 cores</th>
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<tr>
<td></td>
<td>42%</td>
<td>62.5%</td>
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<tr>
<td>Concordant; recommend surgery</td>
<td>58%</td>
<td>37.5%</td>
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### Literature 2004-2009

#### Benign Papilloma Underestimation Rates:

**Low Prevalence (N=9)**
- 0% (0/25) [50]
- 0% (0/67) [51]
- 0% (0/17) [52]
- 0% (0/63) [53]
- 0% (0/40) [54]
- 0% (0/35) [56]
- exclude symptomatic pts and rad-path discordance
- 0% (0/42) [58] exclude rad-path discordance
- 0% (0/19) [62]
- 2% (1/43) [57]

**High Prevalence (N=7)**
- 7% (4/56) [46]
- 9% (9/104) [61]
- 9% (4/47) [60]
- 10.5% (9/86) [47]
- 17% (20/117) [48]
- 19% (15/80) [59]
- 29% (7/24) [49]
Benign Papilloma Underestimation Rates

- High Prevalence
- Low Prevalence
Benign Papilloma Literature

• Supporting Surgical Follow-up
    • 50/3864 cores-25 surg f/up; 10 cases f/up 2+ yrs (70%)
    • 14% (5/35 Ca -- 4 DCIS; 1 IDC)
  • Review of 5 Malignant Cases:
    – 3 cases - growth or new mass at follow-up
    – 1 case – developed bloody nipple discharge
    – 1 case – self-selected. DCIS 1 cm distal to benign papilloma; hence incidental
• Hence in asymptomatic women with negative mammograms, upgrade rate was 0%
Benign Papilloma Literature

- Supporting Surgical Follow-up
    - Excised *all* benign papillomas, N= 80
      - 15 Ca/ 80 (19%)- BUT “majority of malignant lesions were found immediately adjacent to the papilloma”; more details of discordance not given.
  - Bernik et al. [Bernik SF, Troob S, Ying BL et al. The Am J of Surgery 2009; 197:473 ]
    - 4/47 (9%) Ca in surg excision + additional 13/47 (28%) atypia in “the surrounding tissues” defined as “within 3 cm of the indexed papillary lesion.”
Papilloma: Pathology Issues

- Definition of atypia on core biopsies is subjective
- Criteria used to distinguish ADH from DCIS involving a papilloma are not standardized
Distinguishing ADH from DCIS in Papillomas

- Some authors feel any focus which meets the criteria for non-comedo DCIS within a papilloma should be diagnosed as such
  (Elston CE and Ellis IO. The Breast. Churchill Livingstone, 1998)

- Others suggest that in cases in which a proliferation qualifying as non-comedo DCIS is present in <30% of the lesion, a diagnosis of ADH is suggested
  (Tavassoli FA. Pathology of the Breast, 2nd Ed. Appleton and Lange, 1999)

- Others suggest that the proliferation qualifying as non-comedo DCIS be > 3 mm before a diagnosis of DCIS within a papilloma is made; if less than or equal to 3 mm, a diagnosis of ADH is suggested
Radial Scar

• Case 3A: 45 y/o woman, baseline mammogram. New architectural distortion. (Fig 3); US guided core bx, 14 g tru-cut, 5 cores.

• Pathology: Radial scar. See comment.
  • A smooth muscle myosin heavy chain immunostain was performed to confirm that the irregular glands in this lesion are “entrapped” benign glands and not invasive (tubular) carcinoma.
Fig 3: Radial Scar
Radial Scar

• Case 3A: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of radial scar, surgical excision is recommended.
  – C. The case is rad/path discordant because radial scar is incidental without imaging correlate; recommend surgical excision
Radial scar—14 gauge/5 cores results

- 10% rad/path concordant, imaging f/up
- 89% rad/path concordant, but due to radial scar surgery is recommended
- 1% rad/path discordant because radial scar is incidental with imaging correlate
Radial Scar

• Case 3B: 45 y/o woman, baseline mammogram. New architectural distortion. (Fig 3); US guided core bx, 11 g tru-cut, 12 cores.

• Pathology: Radial scar. See comment.
  • A smooth muscle myosin heavy chain immunostain was performed to confirm that the irregular glands in this lesion are “entrapped” benign glands and not invasive (tubular) carcinoma.
Radial Scar

• Case 3B: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of radial scar, surgical excision is recommended.
  – C. The case is rad/path discordant because radial scar is incidental without imaging correlate; recommend surgical excision
Radial scar—11 gauge/12 cores results

- 23% rad/path concordant, imaging f/up
- 77% rad/path concordant, but due to radial scar surgery recommended
# Radial Scar and Sample Size

<table>
<thead>
<tr>
<th></th>
<th>14 gauge 5 cores</th>
<th>11 gauge 12 cores</th>
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<tbody>
<tr>
<td>Concordant; imaging f/up</td>
<td>10%</td>
<td>23%</td>
</tr>
<tr>
<td>Concordant; recommend surgery</td>
<td>89%</td>
<td>77%</td>
</tr>
<tr>
<td>Discordant; recommend surgery</td>
<td>1%</td>
<td>0%</td>
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</table>
Literature 2004-2009
Radial Scar Underestimation Rates:

<table>
<thead>
<tr>
<th>Low Prevalence (N = 3)</th>
<th>High Prevalence (N = 4)</th>
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<tbody>
<tr>
<td>0% (0/80) [72]</td>
<td>4% (5/125) [70]</td>
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<tr>
<td>0% (0/27) [73]</td>
<td>8% (5/62) [74]</td>
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<tr>
<td>0.7% (2/281) [76]</td>
<td>9% (1/11) [75]</td>
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<tr>
<td>excluding 9 cases that missed primary lesions</td>
<td>22% (6/27) [69]</td>
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</table>
Radial Scar Underestimation Rates

- High Prevalence
- Low Prevalence
Radial Scar (RS) Literature

• Supporting surgical follow-up:
    • 227/ ~15,000 cores (1.4%) – “included a RS at path”
    • 184/ 227 (81%) surgery or 24+ month f/up
  • Two Core Groups per Needle type and gauge:
    – 14 g Tru-cut (ave # of cores 6); 100 benign RS at core
    – 11 g Vac-Ast (ave # of cores 32); 25 benign RS at core
Radial Scar (RS) Literature

• Supporting surgical follow-up:
  – Becker et al.
    • 14g Tru-cut: N= 100
      – 50 surg f/up; 4/50 (8%) Ca
      – 50 imag f/up; 1/50 (2%) Ca
    • 11 g Vac-ast: N= 25
      – 9 surg f/up; 0% Ca
      – 16 imag f/up; 0% Ca

• Overall: 5 Ca/125 (4%)
Radial Scar (RS) Literature

• Supporting surgical follow-up:
    • 11 Ca at surg path/ 281 (4%) RS cores reviewed
      – Core tracks identified
      – Only 6/11 had RS on core biopsy; 2 of which had ADH
      – 9/11 cores missed lesion by average ~ 5 mm (1-20 mm)
      – Needle gauge and type not specified.
      – Imaging directed- not specified
Radial Scar: Pathology Issues

• Pathologists CAN distinguish tubular carcinoma from radial scar on core biopsy
• Immunohistochemistry can aid in that distinction but often on H/E alone the diagnosis can be made
Radial Scar
Flat Epithelial Atypia (FEA)

- Case 4: 48 y/o woman presents with new cluster of punctate calcifications. Undergoes stereo core bx, 11g vac-ast, 12 cores, adequate sample of calcifications.
- Pathology: Proliferative changes including columnar cell change with focal nuclear atypia (FEA); no carcinoma. Calcifications within FEA and surrounding ducts and lobules.
Fig 4: FEA
FEA

• Case 4: What is your recommendation?
  – A. The case is rad/path concordant; imaging f/up
  – B. The case is rad/path concordant, but due to presence of FEA, surgical excision is recommended.
  – C. The case is rad/path discordant because FEA is incidental without imaging correlate; recommend surgical excision
FEA results

- 27% rad/path concordant, imaging f/up
- 73% rad/path concordant, but due to FEA surgery is recommended
Literature 2004-2009
FEA Underestimation Rates:

<table>
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<tr>
<th>Low Prevalence (N = 3)</th>
<th>High Prevalence (N = 5)</th>
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</thead>
<tbody>
<tr>
<td>0% (0/41) [99]</td>
<td>14% (9/63) [95]</td>
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<tr>
<td>0% (0/20) [100]</td>
<td>17% (2/12) [96]</td>
</tr>
<tr>
<td>0% (0/20) [101]</td>
<td>17.5% (7/40) [94]</td>
</tr>
<tr>
<td>20% (3/15) [97]</td>
<td>21% (3/14) [98]</td>
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FEA Underestimation Rates

High Prevalence
Low Prevalence
FEA Literature

• Supporting surgical excision
  • 40 patients with FEA (25 CCHA/15 CCA)
  • 7 carcinomas (17.5 %) on open biopsy
  • All cancers were in the CCHA group and in lesions 10 mm or greater or those not completely excised
FEA Literature

• Supporting imaging follow-up
    • 63 cases followed for avg. 6.2 years (1-11 years)
    • 9 Ca/ 63 (14%)
      » 7 ipsilateral (mean 3.7 yrs); 2 contralateral (mean 7 yrs)
      » 2/7 ipsilateral- had undergone interval core bx after FEA, before Ca showing ADH
      » 5 patients underwent ipsilateral surgical biopsy within 3 months and no cancers were identified
  
• “Based on our findings, we consider flat DIN1 a marker of slightly increased risk for subsequent development of invasive breast carcinoma“
Case 5: Flat Epithelial Atypia (FEA)
FEA Pathology Issues

• Numerous terms to describe FEA (CAPSS with atypia, columnar cell change/hyperplasia with atypia, clinging carcinoma)
• Criteria to distinguish atypia in columnar cell lesions is somewhat vague
• Inter-observer variability in diagnosing atypia in columnar cell lesions
FEA: Inter-observer variability

• 8 pathologists
• Tutorial given by lead pathologist on CCLs
• 39 images of CCC, CCC with hyperplasia/ atypia, and DCIS sent out
• Diagnoses collected, then same set sent out one week later for repeat review
FEA: Inter-observer variability

- CCC
  -- complete agreement in 9.1%; same in second round
- CCH
  -- complete agreement in 20%; second round up to 60%
- CCC with cytologic atypia (FEA)
  -- complete agreement in 14.3%; second round down to 7.1%
FEA Intra-observer variability

Kappa values ranged from 0.271- 0.832
High Risk Lesions: Summary

Current rates of underestimation of malignancy are inaccurate since most are derived from retrospective studies with the following limitations:

• The incidence of high risk lesions is low
  Number of patients is small in most studies
  Most have no statistical significance

• Data is mainly selected from review of prior surgical pathology files.
  Selection of which patients undergo surgery is unknown
  Follow-up of patients not excised is often poor

• Most studies lack radiology-pathology concordance:
  ? radiographic finding and how suspicious
  ? Clinical presentation, age of patient
  ? proximity of subsequent cancer to the high risk lesion
Wrap-up Question

Now that you have been updated in the literature, your management of High Risk Lesions on core biopsy will:

– A. Not change
– B. Definitely change
– C. Will consider changing
– D. I am now completely confused.
Wrap-up Answers

• 42% won’t change
• 5% definitely change
• 19% will consider changing
• 34% completely confused