A Practical Approach to the Evaluation of Fibroepithelial Lesions

Edi Brogi MD PhD
Attending Pathologist
Director of Breast Pathology
Overview

• Fibroadenomas (FAs)
• Phyllodes Tumors (PTs)
  – Morphology and diagnostic criteria
  – Fibroepithelial lesions (FELs) in adolescents
  – Re-excision of positive margins of PT
  – Differential diagnosis of FELs at CBX
Fibroadenoma

• Very common tumor
• Mean age 25-30 years (range 10-90)
• Occurs in women
  • rare in men
    – usually in a background of gynecomastia
  • can occur in ectopic breast tissue (axilla, vulva)
• Predisposing factors
  – No documented genetic alteration, but some families have multiple affected members
  – Cyclosporin A (immunosuppressant) treatment
    • Multiple bilateral FAs, rapid growth; may simulate PT
Fibroadenoma

• Clinical presentation
  – Round-ovoid “rubbery” mass
  – Size usually <3 cm
  – May undergo infarction \(\rightarrow\) +/- pain (nipple bleeding rare)
    • post-trauma (FNA, cbx, other)
    • during pregnancy
    • idiopathic
Expanded intralobular stroma

intracanalicicular

pericanalicicular
Morphologic features

- **Glands:stroma ratio uniform throughout**
- Mitoses rare to absent
- No necrosis
  - Infarction rare
- Multinucleated stromal cells may be present

“Usual” FA
FA and invasive carcinoma

• F/U study of 1835 women with any FA found 2.17 Relative Risk (RR) of subsequent invasive carcinoma

• No increased RR in women with usual FA and no family hx of breast carcinoma

Fibroadenoma Subtypes

- “adult/usual” FA
- myxoid FA
- complex FA
- “juvenile” FA
Myxoid FA

- May be part of Carney’s complex
- Carney’s complex associated with mutations of \textit{PRKAR1A} (regulatory subunit 1A of protein kinase A) gene, located at 17q22-24
- Multiple myxomas
  - atrial myxoma → may cause sudden death
    - unknown how many pts with myxoid FA have Carney’s complex
- No increased risk of carcinoma
Myxoid FA can mimic mucinous carcinoma
Myxoid FA can mimic mucinous carcinoma

- 16/17 cases of myxoid FA with increasing size misdiagnosed as mucinous carcinoma by U/S examination
  Yamaguchi *Hum Pathol* 2011;42:419-423

- misdiagnosis of mucinous carcinoma on review of FNA material

- CBX misdiagnosis
• FA with at least one of the following lesions:
  – sclerosing adenosis
  – apocrine metaplasia
  – usual ductal hyperplasia
  – cysts
  – Often Ca$^{2+}$ in hyperplastic epithelium
Complex FA

- Typically smaller than usual FA
  - Average size of complex FA about half that of usual FA
    1.3±0.57 cm (range 0.5-2.6) vs 2.5±1.44 cm (range 2.1-6.9) (p<0.001)


- Constituted 22.7% of 2458 FAs in the series by Dupont et al.
- 3.1 Relative Risk (RR) of subsequent breast carcinoma
  - vs 2.17 RR for all women with any type of FA
- 3.71 RR in women with complex FA and family hx of breast carcinoma

Complex FA and CBX

• No epithelial atypia at cbx → no excision if concordant rad-path findings

• CBX DDX
  – Adenosis may mask the underlying FA
  – Papilloma
  – invasive carcinoma
Juvenile FA

- “juvenile” is descriptive term
- relatively more common in adolescents and young women, but can occur at any age

### 34 FAs in Adolescent Girls (<18 years old)

<table>
<thead>
<tr>
<th></th>
<th>11 Adult FA</th>
<th>23 Juvenile FA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (% of all FAs)</td>
<td>11 (32%)</td>
<td>23 (68%) (8 variant juvenile FAs)</td>
</tr>
<tr>
<td>Race or ethnicity*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>African American</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mean Age at Menarche (years)**</td>
<td>12 (6 pts)</td>
<td>12 (14 pts)</td>
</tr>
<tr>
<td>Median Time from Menarche to Diagnosis (months)***</td>
<td>72 (6 pts)</td>
<td>36 (14 pts)</td>
</tr>
</tbody>
</table>

*Race/Ethnicity information available for 31 pts
**Information available for 20 patients
***1 pt with Juvenile FA variant 12 mo prior to menarche

Ross D et al. MSKCC study (submitted)
FELs in Adolescents (≤18 years old)
MSK study by Ross et al.

- Juvenile FAs
  - Stroma monotonous (no periglandular condensation)
  - Stromal collagen fibers
  - Fascicular stromal myofibroblasts
  - Slight intratumoral heterogeneity
  - Some cases admixed with adenosis
Juvenile FA

fairly uniform distribution of glands and stroma
Juvenile FA

Stroma also uniform throughout the lesion
Juvenile FA

Minimal difference between intra- and inter-lobular stroma
Juvenile FA

Stroma may be more cellular in some areas
Some epithelial hyperplasia may be present
Juvenile FA

No stromal atypia
# 34 FAs in Adolescent Girls (≤18 years old)

<table>
<thead>
<tr>
<th></th>
<th>11 Adult FAs</th>
<th>23 Juvenile FAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean size (cm) (range)</td>
<td>2.6 (0.7-4.5)</td>
<td>3.1 (0.5-7)</td>
</tr>
<tr>
<td>Growth pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>intracanalicular</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>pericanalicular</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>Epithelial hyperplasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>present in 9/34 (26%) FAs</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Mean mitotic count</td>
<td>1.3 (0-6)</td>
<td>1.8 (0-7*)</td>
</tr>
</tbody>
</table>

*1 pt gave birth 11 months before diagnosis of FA

Ross D et al. MSKCC study (submitted)
FELs in Adolescents ($\leq$18 years old)  
MSK study by Ross et al.

Mitotic activity easily identified in all FELs of adolescent girls (including FAs) → this finding should not be overinterpreted in this age group
Atypia/Carcinoma in FA

• Usually classic LCIS or ALH
• DCIS less common
  – limited to FA vs secondarily involving a FA
• Invasive carcinoma limited to a FA is rare (lobular > ductal)
• FA near invasive carcinoma may delay diagnosis

ALH in myxoid FA
Complex FA with Focal DCIS
Invasive carcinoma near usual FA
Phyllodes Tumor (PT)

• Fully characterized in 1838 by Johannes Muller
• “cystosarcoma phyllodes”
• “leaf-like” architecture
• The term Phyllodes Tumor is currently preferred

Johannes Muller
1801-1858
Phyllodes tumor (PT)

- Rare (<0.5-1% of all breast lesions)
- Women age 40-50 years (range 6-90)
  - Pts with PT about 15-20 years older than pts with FA
  - Under age \leq 25 yo PTs are rare and usually benign
  - Extremely rare before menarche
  - Few reports of rapid growth during pregnancy or lactation
Phyllodes Tumor

• Li-Fraumeni syndrome (germline p53 mutation; autosomal dominant)

• Relatively more common in women of Asian ethnicity
  • In Australian study, Asian women were
    – 31% of all women with PT
    – 67% of all women with recurrent PT
    – Recurrent PT developed in 32% of Asian women vs 7% non-Asian


• Very few reports in men
Phyllodes Tumor

• Usually presents as mass-lesion
• Average size 4-5 cm (range 1-20)
  – 66% of benign PTs measure ≤3 cm
  – 67% of LG or HG malignant PTs >3 cm
• FA and PT are radiologically similar
• Screening mammography ➔ increased detection of small PTs, benign or malignant
Phyllodes Tumor

- Biphasic (epithelial and stromal) tumor
- Proliferation and expansion of the periductal stroma
- Ducts → clefts
- Stromal fronds project into ducts, with “leaf-like” arrangement
- Fronds do not mold to one another or fill the duct space completely
- Stroma is more cellular and mitotically active near ducts
### Classification of PT

takes into account multiple morphologic features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign PT</th>
<th>Borderline PT</th>
<th>Malignant PT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor border</td>
<td>Well-defined</td>
<td>Well-defined, may be focally permeative</td>
<td>Permeative</td>
</tr>
<tr>
<td>Stromal cellularity</td>
<td>Cellular, usually mild, may be non-uniform or diffuse</td>
<td>Cellular, usually moderate, may be non-uniform or diffuse</td>
<td>Cellular, usually marked and diffuse</td>
</tr>
<tr>
<td>Stromal atypia</td>
<td>Mild or none</td>
<td>Mild or moderate</td>
<td>Marked</td>
</tr>
<tr>
<td>Mitotic activity</td>
<td>Usually few (&lt; 5 per 10 HPF)</td>
<td>Usually frequent (5-9 per 10 HPF)</td>
<td>Usually abundant (≥10 per 10 HPF)</td>
</tr>
<tr>
<td>Stromal overgrowth</td>
<td>Absent</td>
<td>Absent, or very focal</td>
<td>Often present</td>
</tr>
<tr>
<td>Malignant heterologous elements</td>
<td>Absent</td>
<td>Absent</td>
<td>May be present</td>
</tr>
<tr>
<td>Relative proportion of all phyllodes tumors</td>
<td>60-75%</td>
<td>15-20%</td>
<td>10-20%</td>
</tr>
</tbody>
</table>

WHO 2012
### Classification of PT

**takes into account multiple morphologic features**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign PT</th>
<th>Low Grade Malignant PT</th>
<th>High Grade Malignant PT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor border</strong></td>
<td>Well-defined</td>
<td>Well-defined, may be focally permeative</td>
<td>Permeative</td>
</tr>
<tr>
<td><strong>Stromal cellularity</strong></td>
<td>Cellular, usually mild, may be non-uniform or diffuse</td>
<td>Cellular, usually moderate, may be non-uniform or diffuse</td>
<td>Cellular, usually marked and diffuse</td>
</tr>
<tr>
<td><strong>Stromal atypia</strong></td>
<td>Mild or none</td>
<td>Mild or moderate</td>
<td>Marked</td>
</tr>
<tr>
<td><strong>Mitotic activity @MSKCC</strong></td>
<td>&lt;2 per 10 HPF</td>
<td>3-5 per 10 HPF</td>
<td>&gt;5 per 10 HPF</td>
</tr>
<tr>
<td><strong>Stromal overgrowth</strong></td>
<td>Absent</td>
<td>Absent, or very focal</td>
<td>Often present</td>
</tr>
<tr>
<td><strong>Malignant heterologous elements</strong></td>
<td>Absent</td>
<td>Absent</td>
<td>May be present</td>
</tr>
</tbody>
</table>

*Use of lower cutoff of mitotic activity in Benign PT → recurrence less likely*

Diagnosis is based on constellation of findings

@MSKCC
Benign PT

- Circumscribed or very focally infiltrative
- Stromal heterogeneity (areas of different cellularity)
**Benign PT**

- Overall low cellularity
- Mild stromal atypia
- Few mitoses
  - <2 mitoses/10 HPF @MSK
  - <5 mitoses/10 HPF WHO 2012
- Epithelial hyperplasia in 74% cases
Low grade malignant (borderline) PT

- Peripheral infiltration
- Stromal heterogeneity
- +/- necrosis
Low grade malignant (borderline) PT

- Moderate cellularity
- Moderate stromal atypia
- Moderate mitoses
  - 3-5 mitoses/10 HPF @MSK
  - 5-9 mitoses/10 HPF  WHO 2012
- Rare heterologous elements
- Epithelial hyperplasia in 83% cases
High grade malignant PT

- Infiltrative margins and satellite nodules
- Stromal heterogeneity
- High cellularity
- Increased vascularity
- Necrosis
High grade malignant PT

• Marked nuclear atypia
• Frequent mitoses
  >5 mitoses/10 HPF @MSKCC
  >10 mitoses/10 HPF  WHO 2012
• Epithelial hyperplasia in 51% cases
High-Grade Malignant PT
Intratumoral heterogeneity
stromal overgrowth

no epithelial component at final 40X magnification

(=10X ocular piece and 4X objective)

Frequent finding in primary PTs that develop distant mets
Heterologous elements

- Can occur in High-Grade PT
  - Less common in Low Grade PT

- **Liposarcoma**
- **Rhabdomyosarcoma**
- **Angiosarcoma**
- **Chondrosarcoma**
Liposarcomatous component does not seem to confer worse prognosis
Prognosis of PT

• Local recurrence

• Distant metastases
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,1 Aye Aye Thike,1 Wai Jin Tan,1 Minn Minn Myint Thu,1 Inny Busmanis,1 HuiHua Li,2 Wen Yee Chay,3 Min-Han Tan,4 The Phyllodes Tumour Network Singapore*

Table 7 Grade of original and initial local recurrences of PT

<table>
<thead>
<tr>
<th>Original tumour grade</th>
<th>Recurrent tumour grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>= Benign</td>
<td>27</td>
</tr>
<tr>
<td>Benign</td>
<td>↑ Borderline</td>
<td>17</td>
</tr>
<tr>
<td>Benign</td>
<td>↑ Malignant</td>
<td>4</td>
</tr>
<tr>
<td>Borderline</td>
<td>= Borderline</td>
<td>10</td>
</tr>
<tr>
<td>Borderline</td>
<td>↑ Malignant</td>
<td>2</td>
</tr>
<tr>
<td>Borderline</td>
<td>↓ Benign</td>
<td>4</td>
</tr>
<tr>
<td>Malignant</td>
<td>= Malignant</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>73</td>
</tr>
</tbody>
</table>

Recurrent PT grade
- same as index PT in 46/73 (63%)
- higher than index PT in 23/73 (31.5%)
- Lower than index PT in 4/73 (5.5%)

Benign PT <5 mitoses/10 HPFs; Borderline 5-10 mitoses/10HPF; Malignant >10 mitoses/10 HPF
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,¹ Aye Aye Thike,¹ Wai Jin Tan,¹ Minn Minn Myint Thu,¹ Inny Busmanis,¹ HuiHua Li,² Wen Yee Chay,³ Min-Han Tan,⁴ The Phyllodes Tumour Network Singapore*

Table 2  Relationship of grade of phyllodes tumour with recurrence (p<0.001)

<table>
<thead>
<tr>
<th>Grade of phyllodes tumour</th>
<th>WITHOUT RECURRENCE</th>
<th>WITH RECURRENCE</th>
<th>TOTAL CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>392 (89.1%)</td>
<td>48 (10.9%)</td>
<td>440 (100%)</td>
</tr>
<tr>
<td>Borderline</td>
<td>95 (85.6%)</td>
<td>16 (14.4%)</td>
<td>111 (100%)</td>
</tr>
<tr>
<td>Malignant</td>
<td>38 (70.4%)</td>
<td>16 (29.6%)</td>
<td>54 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>525 (86.8%)</td>
<td>80 (13.2%)</td>
<td>605 (100%)</td>
</tr>
</tbody>
</table>

Benign PT <5 mitoses/10 HPFs
Borderline 5-10 mitoses/10HPF
Malignant >10 mitoses/10 HPF
Prognosis of PT

• **Local recurrence**
  – Recurrent PT: usually same or higher grade
  – Local recurrence more common for LG or HG PTs

• **Distant metastases**
  – Rare; only <1% PTs develop distant mets
  – more common in HG-PT with stromal overgrowth, necrosis, >5 cm size


  – Benign PTs → LG or HG recurrence before mets
Local recurrence >> distant mets; most series combine the two for analysis
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,¹ Aye Aye Thike,¹ Wai Jin Tan,¹ Minn Minn Myint Thu,¹
Inny Busmanis,¹ HuiHua Li,² Wen Yee Chay,³ Min-Han Tan,⁴ The Phyllodes Tumour
Network Singapore*

Table 5: Recurrent pattern stratified according to the grade of PT

<table>
<thead>
<tr>
<th>Grade</th>
<th>Local recurrence</th>
<th>Metastases</th>
<th>Local recurrence and metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>48</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Borderline</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Malignant</td>
<td>4</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

Benign PT <5 mitoses/10 HPFs
Borderline 5-10 mitoses/10HPF
Malignant >10 mitoses/10 HPF
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,¹ Aye Aye Thike,¹ Wai Jin Tan,¹ Minn Minn Myint Thu,¹ Inny Busmanis,¹ HuiHua Li,² Wen Yee Chay,³ Min-Han Tan,⁴ The Phyllodes Tumour Network Singapore*

Table 6  Sites of metastases of PT

<table>
<thead>
<tr>
<th>Site</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung and pleura</td>
<td>9 (75.1%)</td>
</tr>
<tr>
<td>Lung and Liver</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Vertebra</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Soft tissue (infraclavicular tumour)</td>
<td>1 (8.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>12 (100%)</td>
</tr>
</tbody>
</table>

Histologically confirmed cases include three metastases to the lung and one metastasis to the left infraclavicular region. Remaining cases were radiologically detected. PT, phyllodes tumours.

LUNG most common site of metastases
Other sites: brain, heart, skin, tongue, etc

Benign PT <5 mitoses/10 HPFs
Borderline 5-10 mitoses/10HPF
Malignant >10 mitoses/10 HPF
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan, Aye Aye Thike, Wai Jin Tan, Minn Minn Myint Thu, Inny Busmanis, HuiHua Li, Wen Yee Chay, Min-Han Tan, The Phyllodes Tumour Network Singapore*

**AMOS**

- **ATYPIA**
- **MITOSES** in 10 HPFs
- **STROMAL OVERGROWTH**
- **SURGICAL MARGIN**

**Points**
- 0 to 40

**Total points**
- 0 to 100
Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,1 Aye Aye Thike,1 Wai Jin Tan,1 Minn Minn Myint Thu,1 Inny Busmanis,1 HuiHua Li,2 Wen Yee Chay,3 Min-Han Tan,4 The Phyllodes Tumour Network Singapore*

This nomogram has not been validated in other populations
PT and margin status

• 1 cm wide margin generally recommended
  – no study has proven need for 1 cm wide margin
• Locally recurrent PTs have higher grade in about 1/3 cases → best to avoid local recurrence
• Re-excision of (+)margins for low grade/borderline and high grade malignant PT always needed

• ?Re-excision of positive margins for Benign PT?
  – YES, IN GENERAL, however...
Few series report “low” recurrence for (small) benign PTs with positive/close margins

• 11/140 (7.9%) recurrences in women with benign PT
  – Surgery: 5 enucleation, 5 lumpectomy with tissue rim, 1 wide excision
• Recurrent PT grade: 7 benign, 3 borderline, 1 malignant
• 9/11 (81%) benign PTs with recurrence had initial size >2.5 cm
• 42 Asian women with benign PT treated by enucleation alone
  – 15/42 (36%) had (+)margins
• No recurrences at 43 months median F/U
  Teo et al. ANZ J Surg. 2012;82(5):325-8
• 31 women with benign PTs excised by percutaneous US-guided vacuum-assisted BX and mean F/U of 75.9 months
• One recurrence (3.3%) at 11 months: 1.3 cm index benign PT → 1.5 cm recurrent benign PT
• Note: percutaneous excision of benign PT is NOT an acceptable practice
DDX of spindle cell lesions at CBX

- Fibroepithelial lesions
  - FA vs PT
  - PASH vs PT

- Non-fibroepithelial lesions
  - Fibromatosis
  - Metaplastic spindle cell carcinoma
  - Sarcoma
CBX: cellular fibroepithelial lesion
DDX of Cellular FEL at CBX

- Cellular Fibroadenoma
- Benign Phyllodes Tumor
- Low Grade (Borderline) Phyllodes Tumor
WHAT IS A CELLULAR FIBROADENOMA?

- FEL with focal or diffuse increased stromal cellularity and no cytologic atypia
- No criteria for defining “hypercellularity”
- Interobserver variation in dx of mild cytologic atypia
  → DDx cellular FA vs benign PT very difficult, even when the entire tumor is examined
- WHO 2012 recommends conservative approach
  – (dx FEL even when entire specimen is examined)
CBX features that correlate with PT diagnosis at surgical excision

- Patient age older than 50 years
- >2 stromal mitoses per 10 HPF
- Increased stromal cellularity
- No epithelial elements in at least one final 100X magnification field
- Infiltrative margins
- Fragmented tissue cores
- Adipose tissue admixed with stroma

Jacobs T. Am J Clin Pathol, 2005
Jara-Lazaro AR, Histopathology 2010
Lee AH Histopathology 2007
Tsang AK Histopathology 2011

- Ki67 index 1.6 (range 0.4-4) in FA vs 6 (range 0-18) in PT
  Jacobs T. Am J Clin Pathol, 2005
- Ki67 index >5% and reduced CD34 staining → favor PT
  Jara-Lazaro AR, Histopathology 2010
CBX  DX: FEL with increased stromal cellularity
Recommend excision
WARNING
epithelial hyperplasia in FEL CBX ➔ do not overcall

ADH
IHC for CKs in 109 PTs
70 benign, 30 borderline, 9 HG

<table>
<thead>
<tr>
<th>KERATIN</th>
<th>% of PTs with CK staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK7</td>
<td>28.4</td>
</tr>
<tr>
<td>34BE12</td>
<td>22</td>
</tr>
<tr>
<td>MNF116</td>
<td>11.9</td>
</tr>
<tr>
<td>AE1:3</td>
<td>8.3</td>
</tr>
<tr>
<td>CAM5.2</td>
<td>1.8</td>
</tr>
<tr>
<td>CK14</td>
<td>1.8</td>
</tr>
<tr>
<td>p63</td>
<td>0</td>
</tr>
</tbody>
</table>

Chia Y, J Clin Pathol 2012;65:339-347

WARNING
Some PT may show focal CK stain
Management of FEL at CBX

• Any FEL with increased stromal cellularity
  → recommend excision
  – CBX dx of FA does not completely rule out PT

• Consider all features of the lesion and include DDX
DDX of spindle cell lesions at CBX

• Fibroepithelial lesions
  – FA vs PT
  – PASH vs PT

• Non-fibroepithelial lesions
  – Fibromatosis
  – Metaplastic spindle cell carcinoma
  – Sarcoma
Primary Mammary Fibromatosis

• Deep (desmoid-type) fibromatosis
• Women, age 20-50 years
• Trauma, prior surgery, implants
• Palpable mass or incidental finding on imaging
• Recurs locally, no metastases
broad sweeping fascicles
tends to be sharply demarcated from adjacent tissue
prominent vascularity
vessels have dark nuclei and perivascular lymphocytes
inflammation usually confined to tumor periphery
bland cytology
open chromatin, inconspicuous nucleoli
β-catenin staining is not useful in the DDX of mammary spindle cell lesions

- Primary Mammary Fibromatosis is a clonal myofibroblastic proliferation
  - 45% cases activating mutation of β-catenin gene
  - 33% cases Adenomatous Polyposis Coli gene mutation
    - Gardner’s syndrome

→ nuclear staining for β-catenin in 82% cases

β-catenin nuclear staining also in:
- 23% metaplastic carcinomas
- 94% benign phyllodes tumors
- 57% malignant phyllodes tumors

Lacroix-Triki M, Mod Pathol, 2010
<table>
<thead>
<tr>
<th>Feature</th>
<th>FEL</th>
<th>Spindle Cell Carcinoma</th>
<th>Fibromatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fronds</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Elongated ducts/clefts lined by epithelium</td>
<td>Present</td>
<td>Absent</td>
<td>absent</td>
</tr>
<tr>
<td>DCIS and/or Invasive ductal NOS</td>
<td>Not present</td>
<td>May be present</td>
<td>Not present</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>May be focally positive (?)</td>
<td>Focally positive, (usually more than in PT)</td>
<td>Negative</td>
</tr>
<tr>
<td>P63</td>
<td>Negative</td>
<td>Often positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Nuclear β-catenin</td>
<td>May be positive</td>
<td>May be positive</td>
<td>Usually positive (not always)</td>
</tr>
<tr>
<td>Feature</td>
<td>FEL</td>
<td>Spindle Cell Carcinoma</td>
<td>Fibromatosis</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-------</td>
<td>------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Fronds</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Elongated ducts/ clefts lined by epithelium</td>
<td>Present</td>
<td>Absent</td>
<td>absent</td>
</tr>
<tr>
<td>DCIS and/or Invasive ductal NOS</td>
<td>Not present</td>
<td>May be present</td>
<td>Not present</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>May be focally positive (?)</td>
<td>Focally positive, (usually more than in PT)</td>
<td>Negative</td>
</tr>
<tr>
<td>P63</td>
<td>Negative</td>
<td>Often positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Nuclear β-catenin</td>
<td>May be positive</td>
<td>May be positive</td>
<td>Usually positive (not always)</td>
</tr>
<tr>
<td>Feature</td>
<td>FEL</td>
<td>Spindle Cell Carcinoma</td>
<td>Fibromatosis</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-----</td>
<td>------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Fronds</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Elongated ducts/clefts lined by epithelium</td>
<td>Present</td>
<td>Absent</td>
<td>absent</td>
</tr>
<tr>
<td>DCIS and/or Invasive ductal NOS</td>
<td>Not present</td>
<td>May be present</td>
<td>Not present</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>May be focally positive (?)</td>
<td>Focally positive, (usually more than in PT)</td>
<td>Negative</td>
</tr>
<tr>
<td>P63</td>
<td>Negative</td>
<td>Often positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Nuclear β-catenin</td>
<td>May be positive</td>
<td>May be positive</td>
<td>Usually positive (not always)</td>
</tr>
</tbody>
</table>
• Different subtypes of FAs → no substantial clinical impact
• Different types of PT → clinical impact
• Excision of PT with clear margins is recommended
  – judicious approach for Benign PT
• FEL with uncertain features at CBX → excision
  – Rarely FELs may show focal CK positivity
  – β-catenin staining noncontributory in DDX of breast spindle cell lesions