Recurring Problems in the Frozen Section of Adnexal Masses

John Bishop, M.D. & Edwin Alvarez M.D.

UC Davis Pathology and Laboratory Medicine Symposium

24 October, 2014
We have no financial interests to declare.

Objectives:
- Apply sampling and interpretive criteria to reduce frozen section discrepancy rates in ovarian masses.
- Discuss the surgical and clinical consequences of such discrepancies.
Epithelial Ovarian Neoplasms

- **Incidence**
  - Carcinoma 22,000 yearly (2013)
  - Borderline Ovarian Tumor (BOT) 3000/yr

- **Ave age**
  - 53yo carcinoma
  - 44yo BOT

- **BOT**
  - 2/3 serous, 1/3 mucinous

Siegel 2013
Epithelial Ovarian Neoplasms

- Role of surgery
  - Diagnosis
    - No preop diagnosis
  - Cytoreduction
    - To improve survival with adjuvant chemo
  - Staging
    - Fertility preservation
    - Ovarian function
# Ovarian Carcinoma

<table>
<thead>
<tr>
<th>Histology</th>
<th>Mean age diagnosis</th>
<th>Overall %</th>
<th>Stage I-II %</th>
<th>Stage III-IV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous high grade</td>
<td>57</td>
<td>68</td>
<td>17</td>
<td>83</td>
</tr>
<tr>
<td>Clear cell</td>
<td>53</td>
<td>12.2</td>
<td>71-97</td>
<td>2.5-39</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>57</td>
<td>11.3</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Mucinous</td>
<td>52</td>
<td>3.4</td>
<td>97</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Kobel, Behbakht 1998, Hoskins
## EOC - Survival

<table>
<thead>
<tr>
<th>Histology</th>
<th>Early stage</th>
<th>Advanced stage survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous - high grade</td>
<td>57% 10yr</td>
<td>40.8</td>
</tr>
<tr>
<td>Clear cell</td>
<td>87% 10yr</td>
<td>21</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>95% 10yr</td>
<td>50.9</td>
</tr>
<tr>
<td>Mucinous</td>
<td>95% 10yr</td>
<td>14.6</td>
</tr>
</tbody>
</table>

Mackay 2010, Kobel 2010
BOTs

- **Stage**
  - I: 82.3  II: 7.6  III: 10.1
  - Stage II-III: Serous: 24.1%  Mucinous: 3.8%

- **Recurrence**
  - Overall recurrence: 8%, deaths 4.5%
  - MV risk factors for recurrence:
    - Stage: 2.8
    - Fertility preservation: 3.5
    - Incomplete staging: 2.2
    - Tumor residual: 3.4
    - Organ preservation: 2.3
Surgical dilemma in apparent stage I ovarian neoplasm

- Diagnosis may not be clear
- Need to stage
  - 30% upstage
  - avoid unnecessary procedures
- Wish to preserve fertility
- Wish to preserve ovarian function
Case 1

- 63 year old woman presents with an adnexal mass, NOS (duration 35 years??)
- The right tube and ovary weigh 4,850 gm greatest dimension of 26.4 cm
- Characterized as solid-cystic (70% solid)
- (The left ovary was unremarkable)
Gross Cut Surface
Four (4) blocks submitted for frozen section
FS Dx: Mucinous Tumor with Borderline Features
Final Dx: Mucinous Carcinoma, Well Differentiated

- pT1c NX

- Appendectomy: Neuroendocrine Tumor (G1, “carcinoid”)
Context - ‘Benchmark’

- Frozen section – Permanent discrepancy rate between 1.1 and 3.3%
  - Raab, SS; Tworek, JA; Souers, R; Zarbo, RJ. The Value of Monitoring Frozen Section-Permanent Section Correlation Data Over Time. Arch Pathol Lab Med. 2006; 130:337-342
  - White, VA; Trotter, MJ. Intraoperative Consultation/Final Diagnosis Correlation. Arch Pathol Lab Med. 2008; 132:29-36

<table>
<thead>
<tr>
<th>414 Patients</th>
<th>Benign</th>
<th>LMP</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS Sensitivity</td>
<td>97%</td>
<td>62%</td>
<td>88%</td>
</tr>
<tr>
<td>FS Specificity</td>
<td>81%</td>
<td>96%</td>
<td>99%</td>
</tr>
</tbody>
</table>
Most common mistakes

- Mucinous tumors – undercall
- Met vs primary
Predictive Factors in Misdiagnosis of LMP tumors

- Histologic type (mucinous)
- Tumor size (less than 10 cm)
- The borderline component (less than 10%)
- Pathologist’s experience
- Tendency to undercall borderlines
Possible primaries for met mucinous tumors:

- Appendix
- Colon
- Pancreas
- Gall Bladder
- Uterine Cervix
- Small Bowel
- Stomach
- Lung
For a population of cases, Primaries are:

- Unilateral
- Cystic or glandular-papillary-cystic
- Whereas mets are
- Bilateral
- Solid or multinodular solid
- Show surface involvement
For the individual case

- this does not hold well enough because:
  - Many mets are unilateral
  - Most solid tumors are in fact primary
  - Many mets are cystic
Keys to intraoperative exam

- Gross exam including careful inspection of the surface
- Clean cystic lesions well looking for nodules, papillary areas, hemorrhagic areas
- Select samples
- Freeze multiple samples on any complex mucoid lesion
- See or ask: “what does the other ovary look like?”
Malignant mucinous tumors can exhibit loss of most of their mucin

When mucinous tumors are bilateral, that favors metastasis

When a unilateral tumor is <13 cm, that favors metastasis (about 87% of the time)
  - BUT Mets from colon and appy can be quite large

Other signs of mucinous mets incl involvement of surface or of hilum; infiltrative growth, either with nodular or desmoplastic pattern; lots of signet rings
- Mucinous LMP are bilateral 40% of the time;
- may show seromucinous mixture;
- may be associated with endometriosis.
Case 2

- A 60 year old woman presents with a pelvic mass.
- The right adnexa consist of a 180 gm mass 16 cm in greatest dimension.
- Grossly characterized as a soft tan lobulated tumor with some cystic change and hemorrhage.
- (The left ovary was unremarkable)
FS Dx: Malignant ovarian neoplasm, favor stromal tumor
Two (2) blocks were submitted for frozen section
FS Dx: Malignant ovarian neoplasm, favor stromal tumor
Final Dx: Clear Cell Carcinoma

- Overall accuracy 95.7%
- Clear cell carcinoma may be a particularly difficult problem on FS.

<table>
<thead>
<tr>
<th>282 Patients</th>
<th>Benign</th>
<th>LMP</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS Sensitivity</td>
<td>99%</td>
<td>60%</td>
<td>92%</td>
</tr>
</tbody>
</table>
Ovarian Clear Cell Carcinoma

- Tubulocystic
- Papillary
- Solid
- Adenofibromatous
- Cystic pattern with flat lining
Recall that many of features by which we name the tumor ‘clear cell’ are formalin induced/ enhanced, including papillary pattern and clear cytoplasm.

FS may subdue these features.
When in doubt on an ovarian frozen:

- Re-check the gross
- Take more samples
- Check for history in EMR
- Ask about the other ovary and the abdomen generally
Surgeon’s conclusions

- **CONSENT**
  - Learn your patient’s priorities
  - Discuss and document plan for benign, borderline and carcinoma

- OK to return to OR if final path changes
  - Minimally invasive can be easier for patient
  - Discuss before first surgery
  - Educate about limitations of frozen section
Early Stage Mucinous Neoplasm

- Lymph node dissection
  - Omit in apparent stage 1 BOT or mCA

- Appendectomy
  - Omit if normal appearing

- Ovarian wedge resection
  - Consider: 2.5% occult positive

- Restaging – not necessary

- Fertility preservation
  - HR for recurrence 4.2 with Grade 3, stage 1

References: EA

References: EA


Raab, SS; Tworek, JIA; Souers, R; Zarbo, RJ. The Value of Monitoring Frozen Section-Permanent Section Correlation Data Over Time. Arch Pathol Lab Med. 2006; 130:337-342

Tornos, C, Intraoperative Diagnosis of Ovarian Lesions, USCAP short course, March 2011.

White, VA; Trotter, MJ. Intraoperative Consultation/Final Diagnosis Correlation. Arch Pathol Lab Med. 2008; 132:29-36