We will cover...

• Appendix
• Colon
• Ampulla of Vater
• Anus
• Small intestine
• Esophagus
• Stomach

...in thirty minutes
We will cover...

- Appendix
- Colon
- Ampulla of Vater \(\rightarrow\) **Won-Tak Choi cover**
- Anus **Not much change (N sub)**...in thirty minutes
- Small intestine **Not much change (T1a,N #)**
- Esophagus
- Stomach
AJCC 7th – Appendix chapter

- Goblet cell carcinoid
- Well-differentiated NET
- Adenocarcinoma
- HG NET
AJCC 8th – Appendix chapter

- Goblet cell carcinoid
- Well-differentiated NET
- Adenocarcinoma
- HG NET

+ Low grade appendiceal mucinous neoplasm

Own separate chapter
How I used to understand Appendiceal Mucinous Tumors

“Mucinous cystadenoma”
How I used to understand Appendiceal Mucinous Tumors

“LAMN – low risk”
3% risk of peritoneal recurrence
How I used to understand Appendiceal Mucinous Tumors

“LAMN – high risk” 36% risk of peritoneal recurrence
“By definition, LAMNs are associated with obliteration of the muscularis mucosae”
• Tis (LAMN): “confined by muscularis propria.”
• T1 or T2 not applicable to LAMN

"Acellular mucin or mucinous epithelium that extends into subserosa or serosa should be classified as T3 or T4a respectively.”
AJCC 8th for: Acellular Mucin on Appendix Serosa or Mesoappendix

Tis → T4a

Stage IIB
AJCC 8th

If acellular mucin elsewhere in peritoneum

T4a
M1a
Stage IVa
...and if Cellular Mucin on Appendiceal Serosa?

“LAMN – high risk” 36% risk of peritoneal recurrence
If cellular mucin elsewhere in peritoneum

<table>
<thead>
<tr>
<th>Ext of Dx</th>
<th>Perit mucin</th>
<th>n</th>
<th># f/u</th>
<th>Med f/u</th>
<th>Recurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>RLQ</td>
<td>Acellular</td>
<td>28</td>
<td>12</td>
<td>41 mo</td>
<td>1</td>
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<tr>
<td>Outside RLQ</td>
<td>acellular</td>
<td>4</td>
<td>2</td>
<td>185 mo</td>
<td>0</td>
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<tr>
<td>RLQ</td>
<td>cellular</td>
<td>4</td>
<td>4</td>
<td>85 mo</td>
<td>2</td>
</tr>
<tr>
<td>Outside RLQ</td>
<td>cellular</td>
<td>38</td>
<td>23</td>
<td>51 mo</td>
<td>18</td>
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</table>

T4a
M1b
Stage IVa

<table>
<thead>
<tr>
<th>LAMN</th>
<th>Tis</th>
<th>T4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obliterates MM</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Intact M Propria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acellular mucin on APP Serosa or mesoapp</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cellular mucin on APP Serosa or mesoapp</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>LAMN</td>
<td>Tis</td>
<td>T4a</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>-----</td>
<td>-----</td>
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<tr>
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<td>X</td>
</tr>
<tr>
<td>Cellular mucin on APP Serosa or mesoapp</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Intraperitoneal acellular mucin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal cellular mucin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Until we know better...

- Submit entire appendix
- Report on margin
COLON

- T3 vs T4a
- LN-Size of Cancer
“Penetration of visceral peritoneum”

T4a

Direct Extension
Colon T4a Now Includes

- **Gross** perforation of bowel through tumor
- Invasion of tumor through areas of inflammation to serosa
Colon T4a Now Includes

- **Gross** perforation of bowel through tumor
- Invasion of tumor through areas of inflammation to serosa

![Diagram showing tumor invasion through inflammation]

[Image of histological section showing tumor cells and inflammation]
Colon T4a Now Includes

• Gross perforation of bowel through tumor
• Invasion of tumor through areas of inflammation to serosa

"Tumors with perforation in which the tumor cells are continuous with the serosal surface through inflammation also are considered T4a"
Colon T4a Now Includes

- **Gross** perforation of bowel through tumor
- Invasion of tumor through areas of inflammation to serosa

- Free tumor cells on serosa with underlying erosion of mesothelium, mesothelial hyperplasia +/- inflammatory reaction
- Perforation in which tumor cells continuous with serosa through inflammation
Does that mean tumor close to surface + serosal reaction?
What T4a is NOT

Per AJCC & CAP: Tumors that are close to serosal surface with serosal reaction = T3

“Multiple level sections and/or additional section of the tumor should be examined in these cases”
"T3" with + Serosal Cytology

19% of T3 tumors had + cyto if:
- CA <1mm from serosa
- fibroinflammatory rxn
- vascular proliferation
- hemorrhage or fibrin deposition
- reactive mesothelial cells

46% of T3 <1 mm had + cyto comparable to 55% of T4

Obviously needed a more representative section put through!
T4a
Direct tumor extension to serosa

T3
Tumors <1 mm from serosa is T3
- AJCC & CAP → additional tissue blocks of tumor & examine multiple level sections to look for serosal involvement
Colon – Lymph Nodes

“Suboptimal node count may lead to further dialogue between surgeon and pathologist to support the opportunity for further evaluation (e.g. fat clearance techniques) of the node bearing specimen to assure that a maximum node assessment is reached.”

Lymph Node Evaluation

- The AJCC and College of American Pathologists recommend examination of a minimum of 12 lymph nodes to accurately stage colon cancers. The literature lacks consensus as to what is the minimal number of lymph nodes to accurately identify stage II cancer. The minimal number of nodes has been reported as >7, >9, >13, >20, and >30. The number of lymph nodes retrieved can vary with age of the patient, gender, tumor grade, and tumor site. For stage II (pN0) colon cancer, if fewer than 12 lymph nodes are initially identified, it is recommended that the pathologist go back to the specimen and resubmit more tissue of potential lymph nodes. If 12 lymph nodes are still not identified, a comment in the report should indicate that an extensive search for lymph nodes was undertaken. The pathologist should attempt to retrieve as many lymph nodes as possible. It has been shown that the number of negative lymph nodes is an independent prognostic factor for patients with stage IIIB and IIIC colon cancer.
Per NCCN

Adverse Prognostic Factors

• <12 LN
• Lymph/vasc invasion
• Poor diff histology (unless its MSI)
• PNI
• Margin status
Positive lymph nodes

**AJCC**

N: tumor in LN $\geq 0.2$ mm
- If $<0.2 = \text{N0i+}$
- ITCs = single tumor cells or small clusters of cells $\leq 0.2$ mm without stromal response

**CAP**

- Single tumor cells or small clusters of cells $\leq 0.2$ mm = \text{N0}
- Either single focus in single node, multiple foci within single or multiple nodes

*Do not match*
Tiny Focus

N0(i+)$\quad$ Stromal rxn
ITCs = Single tumor cells or small clusters of cells ≤0.2 mm without stromal response

N1

N0(i+)
Tumor Deposits

Discrete nodule of cancer in pericolic/perirectal fat or mesentery without identifiable lymph node tissue or vascular structure

- No size rule (AJCC 5th)
- No contour rule (AJCC 6th)

Adverse prognostic factor; adjuvant therapy warranted in cases that are N1c regardless of T (bumps pt to stage III)
AJCC: Specify # of Tumor Deposits

- AJCC: # of tumor deposits should be recorded as 1-4 vs. 5 and up (typo?)
- CAP just says record # of TD

AJCC: Large vessel invasion

- Tumor involving endothelium lined spaces that have elastic lamina +/- smooth muscle layer

- Extramural venous invasion: independent adverse prognostic factor & risk factor for liver mets
  - In UK, venous invasion should be detected in at least 30% of CRC resections
Venous invasion particularly important in stage II CRC: it may prompt oncologists to consider adjuvant chemotherapy.
Tumor Budding?

• Not required
Perineural

• Should be reported but doesn’t affect stage
Margins: No change

• If ≤1 mm = positive radial margin

<table>
<thead>
<tr>
<th></th>
<th>CA ≤ 1mm from Margin</th>
<th>CA &gt; 1mm from Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Control (no recurrence)</td>
<td>34%</td>
<td>92%</td>
</tr>
</tbody>
</table>

• Positive margin doubles risk of death from disease
• Positive lymph node or intravascular tumor within 1 mm of radial margin

• What do you do?

No Guideline

ESOPHAGUS
(and Stomach Briefly)
LOCATION COUNTS

GE Junction

AJCC 7th – prox 5 cm

AJCC 8th – prox 2 cm

Gastroenterology 1999;117:218-28
AJCC 7th – CA Epicenter w/in prox 5 cm of Stomach, involving GEJ

ESOPHAGUS STAGING
AJCC 8th – CA Epicenter w/in prox 2 cm of Stomach, involving GEJ

\[ = \text{ESOPHAGUS STAGING} \]
AJCC 8th – Epicenter >2 cm distal of GEJ even involving GEJ = STOMACH

ESOPHAGUS
STOMACH
STAGING
AJCC 8th – w/in prox 2 cm of GEJ
NOT involving GEJ = STOMACH

GE Junction UNINVOLVED

ESOPHAGUS
STOMACH
STAGING
Esophagus T category
Not much change

- **T1**
  - **T1a**: invades LP or MM (<2% risk of LN met)
  - **T1b**: invades SM (up to 20% risk of lymph node met)

- **T2**: invades MP

- **T3**: adventia (remember there is no serosa)

- **T4**: (a & b) adjacent structures
Most CA Esophagectomies have been treated

- Assess entire tumor bed for residual cancer
  (Don’t just do one section and report complete response)

- Surgeons may ask you for ~15 LN (NCCN criteria),
  Even post-treatment: # depends on method of surgery

- Treated LN with no cancer
  not considered positive
Most CA Esophagectomies have been treated

Q: Do I have to grade cancers s/p neoadjuvant therapy?

A: AJCC-wise... No
While Eso & Stom Stage groups do include Grade, Separate Stage group for s/p RX does NOT INCLUDE GRADE
Most CA Esophagectomies have been treated

Q: Do I have to grade cancers s/p neoadjuvant therapy?

A: For CAP acc purposes...Yes (no exceptions made post-Rx)
Most CA Esophagectomies have been treated

• TUMOR REGRESSION GRADING
• AJCC mentions Mandard
**AJCC: Mandard system – 5 tier**

**Concordance rate 50.9% (3 pathologists)**

<table>
<thead>
<tr>
<th>TRG1</th>
<th>Complete regression (fibrosis &amp; no detectable CA cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRG2</td>
<td>Fibrosis with scattered CA cells</td>
</tr>
<tr>
<td>TRG3</td>
<td>Fibrosis &amp; CA cells with preponderance of fibrosis</td>
</tr>
<tr>
<td>TRG4</td>
<td>Fibrosis &amp; CA cells with preponderance of CA cells</td>
</tr>
<tr>
<td>TRG5</td>
<td>CA without changes of regression</td>
</tr>
</tbody>
</table>

CAP Tumor Regression Grading

- Optional (besides present/absent)
- Suggests modified Ryan scheme

Modified Ryan Scheme for Tumor Regression Score

<table>
<thead>
<tr>
<th>Description</th>
<th>Tumor Regression Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No viable cancer cells (complete response)</td>
<td>0</td>
</tr>
<tr>
<td>Single cells or rare small groups of cancer cells (near complete response)</td>
<td>1</td>
</tr>
<tr>
<td>Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)</td>
<td>2</td>
</tr>
<tr>
<td>Extensive residual cancer with no evident tumor regression (poor or no response)</td>
<td>3</td>
</tr>
</tbody>
</table>

Sizable pools of acellular mucin may be present after chemoradiation but should not be interpreted as representing residual tumor.

This protocol does not preclude the use of other systems for assessment of tumor response.

CONCLUSIONS

- Appendix
- Colon
- Ampulla of Vater

- Anus
- Small intestine

- Esophagus
- Stomach

Main Changes Here
CONCLUSIONS

• Appendix – LAMN
• Colon
• Ampulla of Vater
• Anus
• Small intestine
• Esophagus
• Stomach
CONCLUSIONS

• Appendix – LAMN
• Colon- T3 vs T4; LN met size
• Ampulla of Vater
• Anus
• Small intestine
• Esophagus
• Stomach
CONCLUSIONS

• Appendix – LAMN
• Colon- T3 vs T4; LN met size
• Ampulla of Vater
• Anus
• Small intestine
• Esophagus
• Stomach
For More GI Cancer Staging this USCAP

• Wendy Frankel: Colon Cancer Grossing  
  • Arthur Purdy Stout Session Sunday AM

• Rupert Langner: Tumor Regression Grading in Esophageal Cancer  
  • GIPS Sunday PM
Special Thanks:

Laura Lamps  Henry Appelman  Karen Choi
AMPULLARY

• Subtyping
• T Category Changes
AJCC vs. CAP
Pancreatobiliary vs. Intestinal Subtypes
Ampullary AdenoCA

AJCC vague about subtyping

CAP has subtypes listed (no longer optional)

• “Controversial,” “not conclusive”
• Prospective randomized study shows no diff in adj Rx effect
  - Large indeterminate group (56%)

JAMA 2012;308 (2):147-156
**CAP**

**No longer Optional to Subtype**

<table>
<thead>
<tr>
<th>Previous</th>
<th>Current</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histologic Type (select all that apply) (Note C)</strong></td>
<td><strong>Histologic Type (Note C)</strong></td>
</tr>
<tr>
<td>___ Adenocarcinoma</td>
<td>___ Adenocarcinoma</td>
</tr>
<tr>
<td>+ ___ Adenocarcinoma, pancreaticobiliary type</td>
<td>+ ___ Adenocarcinoma, pancreaticobiliary type</td>
</tr>
<tr>
<td>+ ___ Adenocarcinoma, invasive intestinal type</td>
<td>+ ___ Adenocarcinoma, invasive intestinal type</td>
</tr>
<tr>
<td>___ Medullary carcinoma</td>
<td>___ Medullary carcinoma</td>
</tr>
<tr>
<td>___ Invasive papillary adenocarcinoma</td>
<td>___ Invasive papillary adenocarcinoma</td>
</tr>
<tr>
<td>___ Mucinous adenocarcinoma</td>
<td>___ Mucinous adenocarcinoma</td>
</tr>
<tr>
<td>___ Clear cell adenocarcinoma</td>
<td>___ Clear cell adenocarcinoma</td>
</tr>
<tr>
<td>___ Signet-ring cell carcinoma</td>
<td>___ Signet-ring cell carcinoma</td>
</tr>
<tr>
<td>___ Adenosquamous carcinoma</td>
<td>___ Adenosquamous carcinoma</td>
</tr>
<tr>
<td>___ Squamous cell carcinoma</td>
<td>___ Squamous cell carcinoma</td>
</tr>
<tr>
<td>___ Hepatoid adenocarcinoma</td>
<td>___ Hepatoid adenocarcinoma</td>
</tr>
<tr>
<td>___ High-grade neuroendocrine carcinoma</td>
<td>___ High-grade neuroendocrine carcinoma</td>
</tr>
<tr>
<td>___ Large cell neuroendocrine carcinoma</td>
<td>___ Large cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td>___ Small cell neuroendocrine carcinoma</td>
<td>___ Small cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td>___ Undifferentiated carcinoma</td>
<td>___ Undifferentiated carcinoma</td>
</tr>
<tr>
<td>___ Undifferentiated carcinoma with osteoclast giant cells</td>
<td>___ Undifferentiated carcinoma with osteoclast giant cells</td>
</tr>
<tr>
<td>___ Mixed adenoneuroendocrine carcinoma</td>
<td>___ Mixed adenoneuroendocrine carcinoma</td>
</tr>
<tr>
<td>___ Other (specify): _________________</td>
<td>___ Other histologic type not listed (specify): _________________</td>
</tr>
<tr>
<td>___ Carcinoma, not otherwise specified</td>
<td>___ Carcinoma, not otherwise specified</td>
</tr>
</tbody>
</table>

+ = optional
**CAP**

“This panel able to classify 92% of cases”

<table>
<thead>
<tr>
<th>Ampullary CA Subtype</th>
<th>CK20</th>
<th>CDX2</th>
<th>MUC2</th>
<th>MUC1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pancreato-biliary</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
</tbody>
</table>

### Ampullary CA Subtype

<table>
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<tr>
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<tr>
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<td>+</td>
<td>+</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Pancreato-biliary</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
</tr>
</tbody>
</table>

CAP

“This panel able to classify 92% of cases”

## CAP

“This panel able to classify 92% of cases”

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<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Pancreato-biliary</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

### No prognostic significance (overall survival)

### Large ambiguous category (40%)

<table>
<thead>
<tr>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Pancreato-biliary</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

CAP: Two-Tier Approach

1
PB Histology + MUC1 + CDX2 − = Pancreatobiliary type

2
Everything else = Intestinal type
# Ampullary T category Subdivided

<table>
<thead>
<tr>
<th>T1</th>
<th>Limited to Ampulla of Vater or Sphincter of Oddi</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>Invades Duodenal wall</td>
</tr>
<tr>
<td>T3</td>
<td>Invades Pancreas</td>
</tr>
<tr>
<td>T4</td>
<td>Invades peripancreatic tissue or adj organs/structures</td>
</tr>
</tbody>
</table>

**T1a – Limited to AmpVater or Sph Oddi**

**T1b – Invades beyond AmpVater or Sph Oddi +/- Duod Submucosa**
## Ampullary T category Subdivided

<table>
<thead>
<tr>
<th></th>
<th>PREVIOUS</th>
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</thead>
<tbody>
<tr>
<td><strong>T1</strong></td>
<td>Limited to Ampulla of Vater or Sphincter of Oddi</td>
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**T1a** – Limited to AmpVater or Sph Oddi

**T1b** – Invades beyond AmpVater or Sph Oddi +/- Duod Submucosa
## Ampullary T category Subdivided

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</tr>
<tr>
<td>T4</td>
<td>Invades peripancreatic tissue or adj organs/structures</td>
</tr>
</tbody>
</table>

T3a – Invades Pancreas up to 0.5 cm

T3b – Invades >0.5 cm into pancreas or peripancreatic soft tissue or duod serosa or periduodenal tissue
# Ampullary T category Subdivided

<table>
<thead>
<tr>
<th>T1</th>
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</thead>
<tbody>
<tr>
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<td>Invades Pancreas</td>
</tr>
<tr>
<td>T4</td>
<td>Invades peripancreatic tissue or adj organs/structures</td>
</tr>
<tr>
<td>T4</td>
<td>Involves celiac axis, SMA, +/- common hepatic artery irresp of size</td>
</tr>
</tbody>
</table>

- **T3a** – Invades Pancreas up to 0.5 cm
- **T3b** – Invades >0.5 cm into pancreas or peripancreatic soft tissue or duod serosa or periduodenal tissue
Grading: Back to Well, Mod, Poor

- **AJCC 7th:**
  - Low (well, moderate)
  - High (poorly diff, undiff)

- **AJCC 8th: back to:**
  - G1 – well
  - G2 – moderate
  - G3 – poor
  - G4 - undifferentiated

Not part of Staging (as it is in Appendix)
Perineural

- Should be reported but doesn’t affect stage
AJCC: Large vessel invasion

- Tumor involving endothelium lined spaces that have elastic lamina +/- smooth muscle layer

- Extramural venous invasion: independent adverse prognostic factor & risk factor for liver mets
  - In UK, venous invasion should be detected in at least 30% of CRC resections
Venous invasion particularly important in stage II CRC: it may prompt oncologists to consider adjuvant chemotherapy.
Tumor Budding?

• Not required

My cheatsheet:
• Scan for hot spot
• Count tumor buds (cluster of cells 4 or less) at 20x
• If your eyepiece says 22, divide # of tumor buds by 1.21

Report # of buds and what it is by consensus 3 tiered system

Low: 0-4
Interm: 5-9
High: ≥10

Tell clinician:
• Cancer in polyps:
  -low is ok,
  -interm/high predicts LN mets
• Stage 2 colon CA (invades past MP): it is adverse prognosticator (survival); may be important in chemo decisions
  - Low/ interm ok,
  - high = bad prog

Mod Pathol. 2017 Sep;30(9):1299-1311.
1. Define the field (specimen) area for the 20x objective lens of your microscope based on the eyepiece field number (FN) diameter.

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Specimen Area (mm²)</th>
<th>Normalization Factor</th>
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<tbody>
<tr>
<td>19</td>
<td>0.416</td>
<td>0.816</td>
</tr>
<tr>
<td>19</td>
<td>0.708</td>
<td>1.000</td>
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<tr>
<td>20</td>
<td>0.600</td>
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<tr>
<td>26</td>
<td>1.327</td>
<td>1.690</td>
</tr>
</tbody>
</table>

2. Select the H&E slide with greatest degree of budding at the invasive front.

3. Scan 10 individual fields at medium power (10x objective) to identify the “hotspot” at the invasive front. For surgical resection specimens, scan 10 fields.

4. Count tumor buds in the selected “hotspot” (20x objective). Selected hotspot indicated in red.

5. Divide the bud count by the normalization factor (figure 2) to determine the tumor bud count per 0.785 mm². Select the budding (Bd) category based on bud count and indicate the absolute count per 0.785 mm² (see reporting example).

- Reporting example: Tumor budding: Bd3 (high), count 14 (per 0.785 mm²).

*Mod Pathol*. 2017 Sep;30(9):1299-1311.
Pathologic Eval: Impact on Overall Survival

• Both post-therapy pathologic stage & extent of residual CA → independent predictors of overall survival (p = 0.02; p=0.04)

<table>
<thead>
<tr>
<th></th>
<th>Overall Survival rate p = 0.003</th>
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<tbody>
<tr>
<td></td>
<td>2 years</td>
</tr>
<tr>
<td>No residual carcinoma on pathology exam (30%)</td>
<td>78%</td>
</tr>
<tr>
<td>Residual carcinoma</td>
<td>55%</td>
</tr>
</tbody>
</table>
Stage 4A

- Any t with any N and M1a: intraperitoneal acellular mucin without identifiable tumor cells
  - This has very low rate of recurrence, prolonged time even >10 years, may not need HIPEC
- Any T with any N, M1b, G1 (intraperitoneal met only including peritoneal mucinous deposits containing tumor cells
- AJCC considers “serosal involvement of the appendix by acellular mucin may demonstrate excellent outcome with only localized surgical resection.” but lumps acellular and cellular together as T4a
8th vs 7th

- 4 pages on prognostic factors
- D
- CEA
- Tumor regression score
- CRM
- LVI
- PNI
- MSI
- KRAS, NRAS
- BRAF

- Prognostic Factors (site specific factors) recommended for collection: a list
- CEA
- TD
- CRM
- PN
- MSI
- Tumor regression grade
- KRAS
High levels of MSI (MSI-H) occur in ~15% colorectal carcinomas, associated with right sided colon cancers with good prog

Hallmark of Lynch

Sporadic usually but may occur in pts with germline DNA MMR gene mutation (Lynch)

MSI H good prognostic factor and also predicts poor response to 5-FU chemo

However, oxaliplatin addition in FOLFOX regimens negates adverse effects of MSI-H

BRAF mutation + MSI-H (there is an association) have significantly worse prognosis in Stage III and IV colon cancers (node mets or dist mets resp)
• MSI-H good
• MSI-H + BRAF not as good
• Still better than MSS without BRAF
• Which is better than MSS with BRAF

• Use FDA approved assay or standard genotyping/next-gen sequencing for BRAF
• Not IHC for BRAF
CAP

• Used to have a “features suggestive of Microscatellite instability” section (tumo infiltrating lymphocytes, Crohn like lymphocytic reaction, mucinous/signet ring, medullary)

• But now there is universal MSI testing recommended for <70 years