Update on Colonic Serrated (and Conventional) Adenomatous Polyps

Robert D. Odze, MD, FRCPC
Chief, Division of GI Pathology
Professor of Pathology
Brigham and Women’s Hospital
Harvard Medical School
Boston, MA

Maui, HI 2018

Serrated Pathway of Colon Carcinogenesis

- Silencing of DNA mismatch repair genes by methylation of promoter region of genes
- MSI-High colorectal cancer
- Lack of APC, Kras and p53 mutations
- Serrated morphologic phenotype

Serrated Pathway of Colon Cancer: The Hypothesis

Normal → HP → SSP → MSI-H Invasive CRC

BRAF
CIMP
MSI
Classification of Serrated Colonic Polyps
(WHO 2010 Modified)

1. Non-Dysplastic Serrated Polyps
   - Normal architecture, normal proliferation
     - Microvesicular hyperplastic polyp
     - Goblet cell hyperplastic polyp
     - Mucin-poor hyperplastic polyp
   - Abnormal Architecture, abnormal proliferation
     - Sessile serrated adenoma/polyp

2. Dysplastic Serrated Polyps
   - Sessile serrated polyp with dysplasia
   - Serrated adenoma (traditional)
   - Conventional adenoma with serrated architecture

3. Unclassifiable serrated polyp (either with or without dysplasia)

---

Microvesicular HP

- Sessile
- Microvesicular mucin
- Left>right colon
- Generally<0.5 cm

---

Goblet Cell Rich HP

- Sessile
- Minimal serration
- Elongated crypts
- ↑ goblet cells
Mucin Poor HP

- Sessile
- No mucin
- ↑ serration
- Small cells with ↓ cytoplasm
- Dilated crypts

Hyperplastic Polyps

<table>
<thead>
<tr>
<th>Molecular Features</th>
<th>Microvesicular</th>
<th>Goblet Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Braf</td>
<td>80%</td>
<td>Rare</td>
</tr>
<tr>
<td>Kras</td>
<td>Rare</td>
<td>54%</td>
</tr>
<tr>
<td>CIMP-high</td>
<td>68%</td>
<td>Rare</td>
</tr>
<tr>
<td>P53</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Sessile Serrated Polyp

Synonyms

Sessile serrated Adenoma
Giant (large) hyperplastic polyp
HP with dysmaturation
HP with increased proliferation
HP with altered proliferation
Atypical HP
SSP Clinical Features

- More often located in the right colon
- Sessile, broad
- Usually >0.5 cm
- Up to 9% of all polyps
  - Account for ~1/3 to 1/4 of the serrated polyps

Sessile Serrated Polyp

- Flat, broad, sessile
- Distorted crypts
- Aberrant diff/prolif
- Rt>left colon
- Generally >0.5 cm
- 9% of all colonic polyps
Sessile Serrated Polyp With Dysplasia
Molecular Abnormalities of Colon Polyps and Cancer

<table>
<thead>
<tr>
<th>Polyp/cancer</th>
<th>CIMP high</th>
<th>MLH1 methylation</th>
<th>MSI</th>
<th>Braf</th>
<th>Kras</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Ad</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Cancer CIN</td>
<td>+/-</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Cancer Lynch</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Cancer CIMP-high</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>HP</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SSA/P</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>SSA/P with dys</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>TSA</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>


Molecular Features of Colorectal Hyperplastic Polyps and Sessile Serrated Adenoma/Polyps from Korea

<table>
<thead>
<tr>
<th>Feature</th>
<th>Right (N=21)</th>
<th>Left (N=23)</th>
<th>Right (N=13)</th>
<th>Left (N=7)</th>
<th>Right (N=22)</th>
<th>Left (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KRAS</td>
<td>14.3%</td>
<td>17.4%</td>
<td>28.6%</td>
<td>4.5%</td>
<td>26.7%</td>
<td></td>
</tr>
<tr>
<td>BRAF</td>
<td>76.2%</td>
<td>50.0%</td>
<td>66.2%</td>
<td>93.9%</td>
<td>66.7%</td>
<td></td>
</tr>
<tr>
<td>Methylation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGMT</td>
<td>47.6%</td>
<td>66.7%</td>
<td>17.3%</td>
<td>66.7%</td>
<td>73.3%</td>
<td></td>
</tr>
<tr>
<td>MLH1</td>
<td>95.2%</td>
<td>73.3%</td>
<td>29.3%</td>
<td>73.3%</td>
<td>73.3%</td>
<td></td>
</tr>
<tr>
<td>MSH2</td>
<td>93.3%</td>
<td>100.0%</td>
<td>80.0%</td>
<td>100.0%</td>
<td>80.0%</td>
<td></td>
</tr>
<tr>
<td>APC</td>
<td>28.6%</td>
<td>47.5%</td>
<td>28.6%</td>
<td>100.0%</td>
<td>47.5%</td>
<td></td>
</tr>
<tr>
<td>p16</td>
<td>66.7%</td>
<td>73.3%</td>
<td>30.8%</td>
<td>100.0%</td>
<td>73.3%</td>
<td></td>
</tr>
<tr>
<td>CIMP high</td>
<td>78.6%</td>
<td>69.2%</td>
<td>92.3%</td>
<td>80.0%</td>
<td>92.3%</td>
<td></td>
</tr>
</tbody>
</table>

Kim et al, Am J Pathol 2011;178(9):1278-1300

*p-values by Herman et al
†p-values by Park et al
SSP and Risk of Cancer

- SSP and MSI-H cancers have similar clinical features
  - Right sided, older female patients
- SSP precede MSI-H colorectal cancer
- Associated with hyperplastic polyposis syndrome
  - Heterogenous disorder
  - Familial clustering, underlying hereditary defect unknown
  - Some risk of colon cancer

<table>
<thead>
<tr>
<th>Subjects with High-grade Lesions</th>
<th>N</th>
<th>Subjects with subsequent AP with LGD</th>
<th>All High-grade Lesions</th>
<th>AP with HGD</th>
<th>CRC</th>
<th>Time from Diagnosis of Polyp to Subsequent High-grade Lesions (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSA</td>
<td>40</td>
<td>18</td>
<td>6 (15%)</td>
<td>1</td>
<td>5 (13%)</td>
<td>8.3 (1-15)</td>
</tr>
<tr>
<td>HP</td>
<td>55</td>
<td>7</td>
<td>2 (4%)</td>
<td>1</td>
<td>1 (2%)</td>
<td>2.8 (2-3.6)</td>
</tr>
<tr>
<td>AP</td>
<td>55</td>
<td>26</td>
<td>3 (5%)</td>
<td>2</td>
<td>1 (2%)</td>
<td>3.2 (1.1-5.4)</td>
</tr>
</tbody>
</table>

AP indicates adenomatous polyp; CRC, colorectal carcinoma; HGD, high-grade dysplasia; LGD, low-grade dysplasia; N, number of subjects without prior high-grade lesions; SSA, sessile serrated adenoma; Lu et al, Am J Surg Pathol 2010;34(7):927-934

<table>
<thead>
<tr>
<th>Subjects with High-grade Lesions</th>
<th>N</th>
<th>Subjects with subsequent AP with LGD</th>
<th>All High-grade Lesions</th>
<th>AP with HGD</th>
<th>CRC</th>
<th>Time from Diagnosis of Polyp to Subsequent High-grade Lesions (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSA</td>
<td>40</td>
<td>18</td>
<td>6 (15%)</td>
<td>1</td>
<td>5 (13%)</td>
<td>8.3 (1-15)</td>
</tr>
<tr>
<td>HP</td>
<td>55</td>
<td>7</td>
<td>2 (4%)</td>
<td>1</td>
<td>1 (2%)</td>
<td>2.8 (2-3.6)</td>
</tr>
<tr>
<td>AP</td>
<td>55</td>
<td>26</td>
<td>3 (5%)</td>
<td>2</td>
<td>1 (2%)</td>
<td>3.2 (1.1-5.4)</td>
</tr>
</tbody>
</table>

AP indicates adenomatous polyp; CRC, colorectal carcinoma; HGD, high-grade dysplasia; LGD, low-grade dysplasia; N, number of subjects without prior high-grade lesions; SSA, sessile serrated adenoma; Lu et al, Am J Surg Pathol 2010;34(7):927-934
Traditional Serrated Adenoma

- Pedunculated or sessile
- Eosinophilic cytoplasm (↓ mucin)
- Left > right colon
- Any size
TSA
Low-Grade   High-Grade   Adenocarcinoma

TSA with HP/SSP

Traditional Serrated Adenomas
*Molecular Features

<table>
<thead>
<tr>
<th>Gene</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Braf</td>
<td>30-60%</td>
</tr>
<tr>
<td>Kras</td>
<td>10-27%*</td>
</tr>
<tr>
<td>APC</td>
<td>5-28%</td>
</tr>
<tr>
<td>MGMT</td>
<td>17-26%</td>
</tr>
<tr>
<td>P53</td>
<td>10-20%</td>
</tr>
</tbody>
</table>

*Associated with HGD & Carcinoma
Adenoma with Serrated Architecture

Serrated Polyps

Management

<table>
<thead>
<tr>
<th>Hyperplastic Polyp</th>
<th>Biopsy/Polypectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSA/P</td>
<td>-polypectomy (complete)</td>
</tr>
<tr>
<td></td>
<td>-adenoma-like surveillance?</td>
</tr>
<tr>
<td>SSA/P with Dysplasia</td>
<td>-polypectomy (complete)</td>
</tr>
<tr>
<td>Traditional SA</td>
<td>-advanced adenoma surveillance?</td>
</tr>
<tr>
<td></td>
<td>-colectomy for non-complete excisions?</td>
</tr>
</tbody>
</table>

Serrated Polyposis Syndrome*

(formerly Hyperplastic Polyposis)

- ≥5 serrated polyps proximal to sigmoid
  - ≥2 at least 10 mm in size
- ≥1 serrated polyp proximal to sigmoid
  - First degree relative with SPS
- >20 serrated polyps (any size) throughout colon

*No definitive gene mutation identified
Serrated Polyposis Syndrome

**Hallmarks of Genetic Disease**

- Phenotype diversity
- Multiple lesions (HP, SSP, Adenomas)
- Young age of onset
- Strong family history (50% have CRC)
- Restricted ethnicity
- 25-50% synchronous cancer in case series
- 7% risk at 5 years in surveillance
- “Methylator milieu” (Inherited? Acquired?)

Serrated Polyposis Syndrome

**Treatment**

- Screening at ≥40 years or 10 years younger than affected relative, 5 year intervals
- Surgery (extended Rt hemi or subtotal colectomy)
- Annual surveillance residual colon
- Endoscopic management is an option
  - Clear all proximal serrated polyps
  - Clear all >5 mm in size

Colonic Neoplastic Precursor Lesions

1. Benign conventional adenomas
   - Non-advanced (tubular, LGD, <1 cm)
   - Advanced (villous, HGD, >1 cm)
2. Malignant Colon Polyps
**Advanced vs Non-Advanced Adenoma**

- Criteria differ between studies
- No uniform/validated criteria for villi or HGD
- Can endoscopy discriminate 0.9 from 1.1 cm accurately?

**Conventional Adenomas**

- Villous
- Tubular

**Tubular or Villous?**
### “Advanced” Adenomas: Pathologists Don’t Agree

| 19 GI Pathologists \(^1\) | 21 Adenomas | \(|2 - 100\%|\) |
|--------------------------|-------------|-------------|
| 90\% agreement           | 48\%        | 62\%        |
| 80\% agreement           | 67\%        | 71\%        |
| Kappa                    | 0.49        | 0.43        |

\(^1\)GI pathologists agreed less than general pathologists
\(^2\)Ranged of percent villosity; 2-100%
Conventional Adenomas

Reporting Issues

• Status of margins
• Size
• Dysplasia (if <1 cm)

Malignant Colorectal Polyp

Pathology

1. Definition/Terminology
2. Tissue Handling: Endoscopy/Pathology
3. Pathology Assessment
   - Prognostication
   - Reporting
4. Summary

Malignant Colorectal Polyp

Definition

Adenoma with submucosal invasive adenocarcinoma

≠ High grade dysplasia
≠ Intramucosal adenocarcinoma
Adenomas Terminology

WHO

Dysplasia/Intraepithelial neoplasia
- No BM invasion

Intramucosal adenocarcinoma
- LP or MM invasion

Submucosal adenocarcinoma
- Invasion beyond MM

pTis

pTis

pT1

"HGD"

"Invasive Adenoca"

Malignant Colon Polyp

Invasive Adenocarcinoma

Information Pathologists Need to Know

- Shape of Polyp (pedunculated, sessile)?
- Excised in total vs. piecemeal?
- Deepest (stalk) tissue margin

Do not pin, cut, or ink anything
Place in formalin ASAP!
Polypectomy vs. Colectomy

Factors

1. Patient factors
   - Age, co-morbidities, resectability, genetics (lynch), cancer phobia

1. Pathologic factors
   - Gross (sessile vs. pedunculated)
   - Microscopic

Unfavorable (High Risk) Features*

Summary

- Poor differentiation (high grade)
- LVI
- Positive margin (or <1 or 2 mm²)
- Tumor budding/ dedifferentiation
- Mucinous, cribriform morphology
- Sessile morphology (SM>1 cm)
  (Tumor depth and width)

* Indications for colectomy due to risk of LNM, recurrence, metastasis and mortality
Frequency of Carcinoma at colectomy or Followup Post Polypectomy for MCP

<table>
<thead>
<tr>
<th>Studies</th>
<th># Polyps</th>
<th>Unfavorable Outcome (Total)</th>
<th>Unfavorable Outcome (Low Risk* Polyps)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21</td>
<td>1227</td>
<td>135 (11%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Low Risk: Margin>2 mm, low grade Tumor, no LVI

Seitz et al Dis Colon Rectum 2004;47: 1789-1797

Poor differentiation

- 6-9% malignant polyps (should be <20%)
- Poor differentiation in any part of tumour but particularly at invasive edge (some studies required 50% of polyp)
- Patterns:
  - <50% gland lumina
  - mucinous
  - signet ring
  - tumour 'buds' with >5 cells
  - Gleeson pattern 4 like cribriform arrangements
  - Undifferentiated carcinoma
  - NOT true tumour budding (<5 cells)
## Tumor Differentiation

- **Risk:**
  
<table>
<thead>
<tr>
<th>Residual disease</th>
<th>Metastasis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (average)</td>
<td>18%</td>
<td>23%</td>
</tr>
<tr>
<td>Odds ratio - Hassan</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>% Odds ratio - Ueno</td>
<td>20%</td>
<td>29% (multivariate)</td>
</tr>
</tbody>
</table>

- **Problem** = Interobserver agreement is not good
  - Kappa = 64-70%
  - 0.14: Terris et al Mod Path 2012;20(2)1052A

---

## LVI

- Usually associated with another adverse prognostic factor
- Vascular invasion does not add to risk when other adverse factors are already present
- Interobserver agreement is poor/moderate – 37-77%

---

## Vascular invasion

<table>
<thead>
<tr>
<th>Residual disease</th>
<th>Metastasis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (average)</td>
<td>18%</td>
<td>35% (LN)/5% (H)</td>
</tr>
<tr>
<td>Odds ratio - Hassan</td>
<td>1</td>
<td>2**</td>
</tr>
<tr>
<td>% Odds ratio - Ueno</td>
<td>31% (multivariate)</td>
<td></td>
</tr>
</tbody>
</table>

---

Hassan et al Dis Colon Rectum 2005;48:1586-96
Ueno et al Gastroenterology 2004;127:105-94
## Tumor Margin

![Tumor Margin Image]

> 2mm - clear

\[\Rightarrow \text{POSITIVE} \]

## Margin of resection

- positive variously defined
  - In diathermy artefact
  - 1 HP field
  - <1mm
  - <2mm
- Ueno et al. Gastroenterology 2004;127:385-94  \(\Rightarrow\) only diathermy artefact involvement significant
- \(\geq 1\) mm clearance
- general agreement that \(\geq 2\)mm is definitely clear
- positive margin -33% (using all definitions)

## Unfavorable Histology/ Outcome

<table>
<thead>
<tr>
<th>Author</th>
<th>Cases</th>
<th>Margin</th>
<th>&quot;Unfavorable&quot; Histology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper</td>
<td>140</td>
<td>&lt;1 mm</td>
<td>71 (50%)</td>
<td>20%</td>
</tr>
<tr>
<td>Volk</td>
<td>47</td>
<td>&lt;2 mm</td>
<td>30 (66%)</td>
<td>33%</td>
</tr>
<tr>
<td>Seitz</td>
<td>114</td>
<td>Clear</td>
<td>60 (52%)</td>
<td>27%</td>
</tr>
</tbody>
</table>

Poor diff, LVI, Margin <1 mm or <2 mm or clear
**Tumor Budding**

- Identified as a significant prognostic factor in several papers:
  - Ueno et al. Gastroenterology 2004;127:883-44
  - Tateishi et al. Mod Pathol 2010;1:1-5
- Uniform definition lacking – range from any budding to strict definition:
  - Ueno paper = >5 buds (of <5 cells) in any one 20X field (FD = 0.785mm²);
  - Sohn paper = >10 buds
- Reproducibility?

**Tumour budding**

- Identified as a significant prognostic factor in several papers
- Uniform definition lacking – range from any budding to strict definition
  - Ueno paper = >5 buds (of <5 cells) in any one 20X field (FD = 0.785mm²);
  - Sohn paper = >10 buds
- Reproducibility?

**Polyp morphology**

- Pedunculated vs sessile
- Sessile - overall mortality 8x pedunculated polyps
- By definition all sessile polyps are Haggitt level IV (but this over estimates risk based on Haggitt data)
- Reason sessile is worse = increased adverse factors are usually present:
  - poor differentiation
  - vascular invasion
  - positive resection margin**
### Polyp morphology

- Risk for sessile polyp Vs pedunculated polyp – pooled analysis*

<table>
<thead>
<tr>
<th>Residual/recurrent disease</th>
<th>Metastasis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (average) - S</td>
<td>11%/8%</td>
<td>10%/LN/4% (H)</td>
</tr>
<tr>
<td>% (average) - P</td>
<td>3%/0.5%</td>
<td>10%/LN/3% (H)</td>
</tr>
</tbody>
</table>

Odds ratio - Hassan

<table>
<thead>
<tr>
<th></th>
<th>Hassan et al Dis Colon Rectum 2005;48:1588-96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds</td>
<td>4</td>
</tr>
<tr>
<td>ratio</td>
<td>1/4</td>
</tr>
<tr>
<td>-</td>
<td>10</td>
</tr>
</tbody>
</table>

*approximation (multivariate)

* not an independent risk factor for LN metastasis

However, most (85%) of sessile polyps had surgery

### Pathologic Factors

**Tumor size/depth of invasion**  
(Haggitt, Kichuki/Kudo)

### Haggitt levels

Depth of invasion

Haggitt et al Gastroenterology 1985;89:326-36
Haggitt levels

- Haggitt paper Gastroenterology 1985;89:328-34
  - 8/64 (12.5%) submucosal invasive carcinoma had an adverse outcome (LN mets/tumour related death). These were:
    - Levels 0-2 = 0 cases (0%)
    - Level 3 = 1 case (12.5%)
    - Level 4 = 7 cases (87.5%)**
  - Level 4 is the significant factor
  - 7/28 polyps were level 4 = PPV for adverse behaviour = 25%

Haggitt Levels

Limitations

1. Not clear # level 4 were pedunculated
2. 59 sessile polyps, by def’n level 4
3. Difficult to apply in practice
   - Poor orientation
   - Piecemeal specimens
   - Pedunculated vs sessile
   - Hard to distinguish levels

Kikuchi/Kudo levels

<table>
<thead>
<tr>
<th>Sessile polyps</th>
<th>LN metastasis risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>sm1: slight submucosal invasion from the muscularis mucosae.</td>
<td>3%</td>
</tr>
<tr>
<td>sm2: Intermediate between sm1 and sm3.</td>
<td>8%</td>
</tr>
<tr>
<td>sm3: carcinoma invasion near the inner surface of the muscularis propria.</td>
<td>23%</td>
</tr>
</tbody>
</table>

Overall pT1 = 6-12%
Rectal location

- Rectal location, in particular, the distal 1/3 of rectum is an adverse factor for:
  1. LN metastases (up to 1/3)
  2. Recurrent/Residual disease (5-28%)

Haggitt et al. Gastroenterology. 1985;89:328-36

- Reason is not clear from the literature
- Surgical resection favoured for rectal site

Pathology Reporting

<table>
<thead>
<tr>
<th>Mandatory</th>
<th>Highly recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasion vs. No invasion</td>
<td>Leading Edge characteristics</td>
</tr>
<tr>
<td>Type of Cancer</td>
<td>Tumor budding</td>
</tr>
<tr>
<td>Tumor Differentiation</td>
<td>Dedifferentiation</td>
</tr>
<tr>
<td>LVI</td>
<td>Desmoplasia</td>
</tr>
<tr>
<td>Distance to deep margin (mm)</td>
<td>Mucinous or cribriform</td>
</tr>
<tr>
<td>Status of mucosal margins</td>
<td>Haggitt level (pedunculated)</td>
</tr>
<tr>
<td>Status of cauterized tissue edges</td>
<td>Kikuchi level (sessile)</td>
</tr>
</tbody>
</table>

Piecemeal Polypectomy

*Words of Caution*

- Invasion vs no invasion difficult to evaluate
  - MM breach ➔ Presume invasion
  - LVI

- Cannot assess: Deep margin (unless excised separately) mucosal margins, leading edge, Haggitt or Kikuchi level

- Can assess: Type of tumor, differentiation, and status of cauterized tissue edges

Review with Pathologist at microscope!
### Surgical Resection Recommendations

<table>
<thead>
<tr>
<th>Site</th>
<th>Pedunculated</th>
<th>Sessile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td></td>
<td>Unfavorable features</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Haggitt 4</td>
</tr>
<tr>
<td>Rectum (Upper 2/3)</td>
<td>Same</td>
<td>Same</td>
</tr>
<tr>
<td>Rectum (Lower 1/3)</td>
<td>Same</td>
<td>All</td>
</tr>
</tbody>
</table>

Unfavorable features:
- SM2, 3 (or >1 mm)
- Piecemeal Excision

*N=70 cases

### Summary

1. Direct communication between endoscopist and pathologist is vital
2. Understand the terminology, staging and meaning of unfavorable features
3. Make sure polyps are evaluated in total (Don’t leave cancer in the tissue block!)
4. Don’t ever make false assumptions! Assume the worse