What Pathology can tell us in the approach of localized colorectal cancer

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Singapore General Hospital
ESMO 2017 Singapore Nov
Do we still need pathologists
Scope

- Pathology reporting
- Gross
- Histopathology
- Molecular / MSI

Stratify patients, Prognostic and Predictive markers
Modified Dukes' staging classification of colorectal cancer.

Staging Classification of Colorectal Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Extent of tumor</th>
<th>A (no deeper than submucosa)</th>
<th>B₁ (not through bowel wall)</th>
<th>B₂ (through bowel wall)</th>
<th>C₁ (not through bowel wall; lymph node metastases)</th>
<th>C₂ (through bowel wall; lymph node metastases)</th>
<th>D (distant metastases)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5-year survival (%)</td>
<td>&gt;90</td>
<td>80–85</td>
<td>70–75</td>
<td>50–65</td>
<td>&gt;90</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

- mucosa
- muscularis mucosa
- submucosa
- muscularis propia
- serosa
- fat
- lymph nodes

liver
lung
bone
skin
Scope

• Pathology reporting
  • Gross
  • Histopathology
  • Molecular / MSI
Pathology reporting

- Pathology report:
- Colon resection;
- Adenocarcinoma.
Reporting data

• specimen type, tumor site, tumor size, macroscopic tumor perforation, histologic type, histologic grade, microscopic tumor extension,
• margins (proximal, distal and radial
• treatment effect (for tumors treated with neoadjuvant therapy),
• lymphovascular invasion,
• perineural invasion,
• tumor deposits (discontinuous extramural extension),
Reporting data

• TNM staging (including the total number of lymph nodes examined and the total number of nodes involved)
• Leading edge of the tumor (infiltrative or expansile),
• presence or absence of tumor budding,
• assessment of histologic features that are suggestive of MSI such as tumor-infiltrating lymphocytes, peritumoral Crohn-like lymphoid response and the percentage of mucinous component.
Scope

- Pathology reporting
- **Gross**
- Histopathology
- Molecular / MSI
Gross
Gross

- Margins
- Vascular margin, serosal
- Tumour description, size depth
- Deepest invasion
- Other mucosal lesions - polyps, diverticular disease
- Lymph nodes (ALL), mesenteric deposits etc
Two methods of dissection and fixation

Longitudinal opening avoiding tumour & leave to fix

Longitudinal opening from either end keeping tumour intact. Leave to fix with wick of paper towel in lumen

Transverse sections through tumour & mesorectum

Depth of tumour closest distance to mesorectal margin

Select representative sections of tumour for processing (e.g. C-G) & include all lymph nodes present (e.g. H).

Lay out serial sections from proximal to distal and photograph

Large tumours may require composite blocks of tumours from mucosa to mesorectal margin.
Gross Orientation

Anterior resection and abdominoperineal (AP) resections

Lateral

Anterior peritoneal reflection

Anterior resection includes sigmoid colon & a segment of mesocolon without anus

Anterior

AP resection includes anus

Sigmoid mesentery

Posterior

Mesorectum
Gross pathology - TME assessment

- Macroscopic Assessment of Mesorectal Excision in Rectal Cancer: A Useful Tool for Improving Quality Control in a Multidisciplinary Team. Eduardo García-Granero
Table 1: Assessment of the quality of mesorectal excision or completeness of resection*.

<table>
<thead>
<tr>
<th></th>
<th>Complete</th>
<th>Nearly complete</th>
<th>Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesorectum</td>
<td>Intact, smooth</td>
<td>Moderate bulk, irregular</td>
<td>Little bulk</td>
</tr>
<tr>
<td>Defects</td>
<td>Not deeper than 5 mm</td>
<td>Unexposed muscularis propria</td>
<td>Exposed muscularis propria</td>
</tr>
<tr>
<td>Coning</td>
<td>No coning</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>CRM</td>
<td>Smooth, regular</td>
<td>Irregular</td>
<td>Irregular</td>
</tr>
</tbody>
</table>

CRM, circumferential resection margin.

*Both the whole fresh specimen and formalin-fixed slices are examined to achieve optimal assessment.
Independent predictors of local recurrence were
1) circumferential resection margin (CRM) involvement and
2) noncomplete mesorectum
Gross pathology - Neoadjuvant

Pass scarred area completely
If there is no tumour on microscopy
three levels done
For each block to ensure no microscopic tumour – pathological
Complete response (pCR)
Scope

- Pathology reporting
- Gross
- **Histopathology**
- Molecular / MSI
Histopathology- adenocarcinoma subtypes

○ Carcinomas
  - Adenocarcinoma
    - Cribriform comedo type adenocarcinoma
    - Medullary carcinoma
    - Micropapillary carcinoma
    - Mucinous adenocarcinoma
    - Serrated adenocarcinoma
    - Signet ring cell carcinoma
  - Adenosquamous carcinoma
  - Spindle cell carcinoma
  - Squamous cell carcinoma
  - Undifferentiated carcinoma
Cribriform Comedo

Poor prognosis,
Micropapillary

Poor prognosis
Signet ring

Signet ring poor prognosis.
Features and survival of patients with colorectal mucinous, signet-ring cell or non-mucinous adenocarcinoma: experience at an institution in southern China
Mucinous carcinoma

Associated with MSI-H. Better prognosis if MSI-H
Histopathology – Perineural invasion

Oncology reviews

The role of perineural invasion in predicting survival in patients with primary operable colorectal cancer: A systematic review

H.C. van Wyk, James Going, Paul Horgan, Donald C. McMillan

a Academic Unit of Surgery, College of Medical, Veterinary and Life of Sciences-University of Glasgow, Royal Infirmary, Glasgow UK
b University Department of Pathology, College of Medical, Veterinary and Life of Sciences-University of Glasgow, Queen Elizabeth Hospital, Glasgow UK
Histopathology- Lymphovascular / venous invasion

Intramural and extramural vascular invasion in colorectal cancer

Prognostic significance and quality of pathology reporting

Johannes Betge, Marion J. Pollheimer MD, Richard A. Lindtner MD, Peter Kornprat MD, Andrea Schlemmer, Peter Rehak PhD, Michael Vieth MD, Gerald Hoefler MD, Cord Langner MD
Histopathology – AJCC 8th Ed updates

Outline

• Updates in Colorectal cancer
  Definition of T4a
  Tumor deposits
  Isolated tumor cells
  Tumor budding
**pT3 and pT4**
AJCC 8th edition

<table>
<thead>
<tr>
<th>pT classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT3</td>
<td>Tumor invades through the muscularis propria into pericoloectal tissues</td>
</tr>
<tr>
<td>pT4a</td>
<td>Tumor invades through the visceral peritoneum</td>
</tr>
<tr>
<td>pT4b</td>
<td>Tumor directly invades other organs or structures</td>
</tr>
</tbody>
</table>

**Criteria for serosal involvement**

- Tumor directly extends to involve serosal surface
- Tumor continuous with serosal surface through perforation (inflammatory reaction)

Shepherd, Gastroentrol 1997
Peterson, Gut 2002
Ludeman, Histopathol 2005
Stewart, Histopathol 2006

**Tumor directly extends to serosal surface**

**Colonic adenocarcinoma with perforation**
Not T4a (AJCC 8th)

- Tumor close to serosal surface with serosal reaction
- Deeper levels, additional sections

Tumor ≤1 mm with reaction

<table>
<thead>
<tr>
<th>Study</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panarelli, AJSP 2014</td>
<td>Peritoneal recurrence: 11% in pT3 ≤1 mm</td>
</tr>
<tr>
<td></td>
<td>18% in pT4a</td>
</tr>
<tr>
<td>Shepherd, Gastroenterology 1997</td>
<td>Adverse outcome only with</td>
</tr>
<tr>
<td></td>
<td>Direct invasion of serosal surface</td>
</tr>
<tr>
<td>Lennon, AJCP 2003</td>
<td>Free floating tumor cells</td>
</tr>
<tr>
<td>Douard, AJCP 2004</td>
<td></td>
</tr>
</tbody>
</table>
Histopathology – Tumour deposits

Tumor deposits: AJCC 7th Edition

- Discrete foci of tumor in pericolic fat
- No evidence of residual lymph node tissue

Variability in interpretation

<table>
<thead>
<tr>
<th>Distance from Invasive Front</th>
<th>Study</th>
<th>Size of Tumor Deposit</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 mm</td>
<td>Ueno, Am J Surg 2014</td>
<td>&lt;3 mm</td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td>Nagoyoshi, Dis Colon Rectum 2014</td>
<td>Only if grossly identified</td>
</tr>
<tr>
<td>&gt;10 mm</td>
<td>Gopal, Mod Pathol 2014</td>
<td></td>
</tr>
</tbody>
</table>

AJCC definition

- No minimum distance
- No minimum size

Venous invasion or tumor deposit

<table>
<thead>
<tr>
<th>VI with extravascular spread</th>
<th>VI confined to vessel wall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldstein (2000)</td>
<td>Tumor deposit</td>
</tr>
<tr>
<td>Lin (2015)</td>
<td>Tumor Deposit</td>
</tr>
<tr>
<td>Nagoyoshi (2014)</td>
<td>Vascular invasion</td>
</tr>
<tr>
<td>Ueno (2011)</td>
<td></td>
</tr>
</tbody>
</table>

Tumor deposits: AJCC 8th Edition

- Tumor focus in the pericolic/perirectal fat or in adjacent mesentery within the lymph drainage area of the primary tumor, but without identifiable lymph node or vascular structure
- Vessel wall or its remnant (H&E, elastic, or any other stain): vascular (venous) invasion
- Tumor focus in or around a large nerve: PNI
Histopathology - Isolated tumour cells

<table>
<thead>
<tr>
<th>Size of nodal metastasis</th>
<th>AJCC 7th edition</th>
<th>AJCC 8th edition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2 to 2 mm</td>
<td>Microscopicasis pN1mi</td>
<td>Use pN1 pN1mi not necessary</td>
</tr>
<tr>
<td>Less than 0.2 mm</td>
<td>Isolated tumour cells (ITC)</td>
<td>Less than 0.2 mm Use N0 No definite recommendation for using N0(i+)</td>
</tr>
</tbody>
</table>
**Histopathology - Tumour Budding**

- Def;
  - is defined as a single tumor cell or a cell cluster consisting of four tumor cells or less
  - Assessed on HE
  - in one hotspot (in a field measuring $0.785 \text{ mm}^2$) at the invasive front


**Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016.**

Lugli A\textsuperscript{1}, Kirsch R\textsuperscript{2}, Ajoka Y\textsuperscript{3}, Bosman F\textsuperscript{4}, Cathomas G\textsuperscript{5}, Dawson H\textsuperscript{1}, El Zimaity H\textsuperscript{6}, Fléjou JF\textsuperscript{7}, Hansen TP\textsuperscript{8}, Hartmann A\textsuperscript{9}, Kakar S\textsuperscript{10}, Langner C\textsuperscript{11}, Nagtegaal I\textsuperscript{12}, Puppa G\textsuperscript{13}, Riddell R\textsuperscript{2}, Ristimäki A\textsuperscript{14}, Sheahan K\textsuperscript{15}, Smyrk T\textsuperscript{16}, Sugihara K\textsuperscript{17}, Terris B\textsuperscript{18}, Ueno H\textsuperscript{19}, Vieth M\textsuperscript{20}, Zlobec I\textsuperscript{1}, Quirke P\textsuperscript{21}. 

![SingHealth Logo](SingHealth.png)
Histopathology – Tumour budding

Tumour budding scored as three tier system. Separate from tumor grade
Histopathology - Tumour budding

Consensus statements
Counting tumor buds

- The hot spot method (single field at the invasive front, size 0.785 mm²)
  - Scan the entire invasive front in all tumor sections
  - Choose a "hotspot"
  - Count in 20x field
  - Apply appropriate correction factor based on microscope

Conversion table

<table>
<thead>
<tr>
<th>Eyepiece FN Diameter (mm)</th>
<th>Eyepiece FN Radius (mm)</th>
<th>Specimen FN radius (mm)</th>
<th>Specimen Area (mm²)</th>
<th>Normalization Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>9.0</td>
<td>0.450</td>
<td>0.636</td>
<td>0.810</td>
</tr>
<tr>
<td>19</td>
<td>9.5</td>
<td>0.475</td>
<td>0.709</td>
<td>0.903</td>
</tr>
<tr>
<td>20</td>
<td>10.0</td>
<td>0.500</td>
<td>0.785</td>
<td>1.000</td>
</tr>
<tr>
<td>21</td>
<td>10.5</td>
<td>0.525</td>
<td>0.866</td>
<td>1.103</td>
</tr>
<tr>
<td>22</td>
<td>11.0</td>
<td>0.550</td>
<td>0.950</td>
<td>1.210</td>
</tr>
<tr>
<td>23</td>
<td>11.5</td>
<td>0.575</td>
<td>1.039</td>
<td>1.323</td>
</tr>
<tr>
<td>24</td>
<td>12.0</td>
<td>0.600</td>
<td>1.131</td>
<td>1.440</td>
</tr>
<tr>
<td>25</td>
<td>12.5</td>
<td>0.625</td>
<td>1.227</td>
<td>1.563</td>
</tr>
<tr>
<td>26</td>
<td>13.0</td>
<td>0.650</td>
<td>1.327</td>
<td>1.690</td>
</tr>
</tbody>
</table>

Consensus statements
Counting tumor buds

Three-tier system for reporting

<table>
<thead>
<tr>
<th>Tumor budding score (0.785 mm²)</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>5-9</td>
<td>≥10</td>
<td></td>
</tr>
</tbody>
</table>
Neoadjuvant

Pass scarred area completely
If there is no tumour on microscopy
three levels done
For each block to ensure no
microscopic tumour – pathological
Complete response (pCR)
Histopathology - Post neoadjuvant therapy resections (rectum)

- Definition of complete pathological response
- Timing of surgery
- Acellular mucin pools do not count as residual disease

References:

Significance of acellular mucin pools in rectal carcinoma after neoadjuvant chemoradiotherapy

Definition of complete response

- (1) absence of any tumor cells in the primary tumor;
- (2) absence of tumor cells in all resected material, including lymph nodes;
- (3) absence of invasive tumor cells in resected material; or even
- (4) near-total absence of invasive tumor in the resected material.

Pathologic Response to Preoperative Therapy: Does It Mean What We Think It Means? *Annals of Surgical Oncology*

John C. Mansour and Roderich E. Schwarz
Factors predicting for complete response

Rectal

Well-differentiated tumor

Noncircumferential tumor

Low pretreatment CEA

Treatment to resection interval

Preoperative radiation
• In summary; (1) Pathologic complete response is likely an important independent predictor of survival for patients with rectal cancer.

• (2) Major histologic regression of hepatic metastases has been associated with improved survival in limited analysis.
• (3) pCR in the primary tumor does not equate to complete eradication of disease.
• (4) The local pathologic effect of chemoradiation may not be fully realized depending on the timing of resection.
## Histopathology – Tumour regression grade

<table>
<thead>
<tr>
<th>Description</th>
<th>Tumor regression grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>No viable cancer cells</td>
<td>0 (complete response)</td>
</tr>
<tr>
<td>Single cells/small groups of cancer cells</td>
<td>1 (moderate response)</td>
</tr>
<tr>
<td>Residual cancer outgrown by fibrosis</td>
<td>2 (minimal response)</td>
</tr>
<tr>
<td>Extensive residual cancer</td>
<td>3 (poor response)</td>
</tr>
</tbody>
</table>
Scope

- Pathology reporting
- Gross
- Histopathology
- Molecular / MSI
Prognostic and predictive markers

• A prognostic biomarker provides information about the patient's overall outcome, regardless of therapy,
Molecular / MSI

• A predictive biomarker gives information about the effect of a particular therapeutic intervention.
MSI

• patients with MSI-H (or dMMR) colon cancers have higher survival rates than those with MSS tumors

• MMR deficiency is an independent prognostic factor for tumor recurrence

MSI

- Stage II disease, 5 FU therapy is not beneficial in dMMR colorectal cancers.

Morphology of MSI-H

- HNPCC, Mucinous, crohns like infiltrate
- Medullary, poorly differentiated grade
- Sporadic
- Sessile serrated pathway
Microsatellite instability

- Immunohistochemistry MMR IHC
- MSI PCR, Bethesda Panel
- Highly concordant (~ 90-96%)
• concurrent use of MSI testing, MMR protein IHC, and BRAF c.1799T>A (V600E) mutation analysis would detect almost all dMMR CRCs, would classify 94% of all new CRCs into these MMR subgroups
MSI PCR

- PCR Bethesda panel- tumour and normal tissue
- (5 loci, mono and dinucleotide repeats)

![Graph comparing normal and tumor tissue](image)
MSI PCR

Panel 1:
Normal rect tissue

Panel 1:
Tumorous rectal tissue
MSI*

Panel 2:
Normal rect tissue

Panel 2:
Tumorous rectal tissue
MSS*
Role of immunohistochemistry

- MMR IHC
- MLH1
- PMS2
- MSH2
- MSH 6

(Other Antibodies PMS1, MSH3, MLH3, EPCAM etc)
MMR IHC

MLH1/PMS2, MSH2/MSH6
MMR IHC

- Criteria repeat
- Internal controls
- (Lymphocytes,
- Normal colonic crypts
- Not staining

- Tumour shows very weak or very focal staining- best repeat.
IHC MMR proteins

- Interpretation:
  - Positive - > 10 % strong to moderate staining of nucleus
  - Negative - complete loss of staining in all tumour cells
  - Equivocal - < cannot be assessed – repeat stain can be ordered- MSI PCR
IHC for MMR proteins

- Results:
- All 4 positive
- Normal - Positive expression of DNA mismatch repair proteins in adenocarcinoma.
MMR IHC

• Any one negative
• Abnormal - Negative expression of DNA mismatch repair proteins in adenocarcinoma
MMR IHC

• Any one equivocal

• Equivocal - Possible loss of staining, further MSI PCR or repeat IHC.
Stage II Colon Cancer
MSI Status is Prognostic

A. No Adjuvant Chemotherapy

Overall Survival (%)

Years after Randomization

No. at Risk
- Microsatellite stability or low-frequency microsatellite instability
  - 245 238 220 200 176 137 105 82 53
- High-frequency microsatellite instability
  - 42 42 39 38 35 29 23 22 14

P = 0.004
Revised MSI (Microsatellite instability) immunohistochemistry and molecular workflow for colorectal cancer (*resection only*)

1. **Colorectal Adenocarcinoma**
   - Others
     - Pathologist to request for **MSI PCR**
       - Inconclusive
         - Reflex MSI IHC
           - MLH 1 Loss
             - Reflex BRAF V600E mutation analysis
       - MSI S
     - MSI H
   - ≥ N1 or M1
     - Pathologist to request for **MSI PCR** and **KRAS mutational analysis**
       - Inconclusive
         - MSI S
           - Reflex MSI IHC
       - MSI H
Colorectal

- MSI PCR
  - MSS → No further testing
  - MMR IHC
    - Loss of MSH2,6 or PMS2 → Genetic clinic
    - MLH1 loss
      - BRAF V600E present
        - Sporadic
Distribution of mutations in mCRC

KRAS mt (non exon 2 KRAS mt) & NRAS mt ~10%

KRAS mt (exon 2) ~40%

RAS wt ~50%

Rare KRAS Mutations NRAS Mutations

Molecular profiles

- KRAS + PIK3CA mutation: 8%
- BRAF mutation: 3%
- NRAS mutation: 2%
- BRAF + PIK3CA mutation: 5%
- PIK3CA mutation/PTEN loss: 12%

Responsive:
- 15% KRAS, BRAF, NRAS, PIK3CA wild type, no PTEN loss
- 32% KRAS mutation

Non-responsive:
- Molecular aberration to be identified: 23%
The prognostic significance of *KRAS* and *BRAF* mutation status in Korean colorectal cancer patients

Daeyoun David Won, Jae Im Lee, In Kyu Lee, Seong-Taek Oh, Eun Sun Jung and Sung Hak Lee

*BMC Cancer* 2017 17:403

[https://doi.org/10.1186/s12885-017-3381-7](https://doi.org/10.1186/s12885-017-3381-7)  © The Author(s). 2017

Received: 21 January 2017  |  Accepted: 22 May 2017  |  Published: 5 June 2017
Fig. 3
Kaplan-Meier curves for DFS and OS according to KRAS mutation status in combination with BRAF. a DFS according to KRAS mutation status in combination with BRAF and b OS according to KRAS mutation status in combination with BRAF.
Fig. 2
Kaplan-Meier curves for disease-free survival and overall survival according to KRAS or BRAF mutation status. a Disease-free survival (DFS) according to KRAS status, b DFS according to BRAF status, c Overall survival (OS) according to KRAS status and d OS according to BRAF status.
Molecular/ MSI status

Disease-Specific Survival

<table>
<thead>
<tr>
<th>Type</th>
<th>MSI status</th>
<th>BRAF mutation</th>
<th>KRAS mutation</th>
<th>CIMP status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>Stable/Low</td>
<td>Yes</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>Stable/Low</td>
<td>No</td>
<td>Yes</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Stable/Low</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
<tr>
<td>5</td>
<td>High</td>
<td>No</td>
<td>No</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Molecular testing Ras/Raf

- Predictive of response to anti EGFR agents
- Wild type KRAS/NRAS responsive
- Ras mutants – no or poor response to mono or combination TKI therapy
- Braf mutations also show poorer prognosis (V600E)- poor response to TKI monotherapy
Colorectal CA (N2 or M1)

*KRAS + BRAF

- KRAS wild type
  - BRAF wild type
  - NRAS
- KRAS wild type
  - BRAF mutant
- KRAS mutant
  - BRAF wildtype/mutant

T4
Somatic Solid Tumour Panel

<table>
<thead>
<tr>
<th>Somatic Solid Tumour Panel (SSTP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targets</td>
</tr>
<tr>
<td>Hotspots and targeted regions in 133 exons of 29 genes implicated in colon and lung cancer.</td>
</tr>
<tr>
<td>Genes</td>
</tr>
<tr>
<td>KRAS, NRAS, BRAF, EGFR, TP53, PDGFRA, KIT, PIK3CA, FGFR1, FGFR2, FGFR3, ZNRF3, RNF43, APC, PIK3R1, NF1, AKT1, ERBB2, PTEN, STK11, DDR2, CTNNB1, MET, SMAD4, FBX7, NOTCH1, ERBB4, ALK and MAP2K1.</td>
</tr>
<tr>
<td>Amplicon Length</td>
</tr>
<tr>
<td>260 amplicons with an average length of 162bp</td>
</tr>
<tr>
<td>Primer Pool</td>
</tr>
<tr>
<td>260 pairs of primers in 5 pools</td>
</tr>
</tbody>
</table>

Validated for FFPE specimens
Input of 30 ng of DNA
Limit of detection 1-5 %
Somatic Solid Tumour Panel

KRAS, NRAS, BRAF, PIK3CA, PTEN

TP53, APC etc
Summary

- Pathologists are still important
- Pathological examination- Gross pathology, Histopathology, Neoadjuvant
- MSI testing (IHC MMR, MSI PCR)
- Molecular testing Ras/Raf – prognostic and predictive value
- Reflex colorectal workflows
Summary

• Close collaboration between Surgeons, Oncologists and Pathologists is very important

• Further areas, Her2 IHC, MSI –H immunotherapy
Do we still need pathologists
AJCC Vision

...and Where It Fits in the 8th Edition:

Cancer Stage → Comprehensive Cancer Profile

8th Edition Chapter Headings

Definitions of TNM

Prognostic Factors

Clinical Trial Stratification

Prognostic and Risk Assessment Models

Population → Personalized
Acknowledgements

- NCC-DMO
- Su Pin
- Iain
- Matthew
- Simon
- GI team
- NCC-DSO
- Melissa
- Histopathology IHC
- Wing fatt
- Maryam
- Syed
- Xin xiu
- Molecular MSI PCR
- Lynette Oon

- Colorectal Surgeons
- Choon leong
- Min hoe
- Wah siew
- SGH Pathology
- Wei keat
- Rafay
- Wei qiang
- Tracy
- Thane
- TPC- SSTP
- Tan Gek San
- Shi hui
- Tan Hui ying
- Nguyen Ha linh
• Thank you