Il carcinoma del colon retto

Referto anatomo-patologico: quali informazioni deve contenere?

Paola Castelli

IRCCS-Ospedale SC Don Calabria, Negrar di Valpolicella
paola.castelli@sacrocuore.it

Dataset for Pathology Reporting of Colorectal Cancer

Recommendations From the International Collaboration on Cancer Reporting (ICCR)

(Ann Surg 2022; 275:e549–e561)

- Qualità del report istologico
- Gruppo multidisciplinare di esperti internazionali
- 18 elementi «core» (essenziali) e 7 «non-core» (raccomandati)
- Scopo:

  -promuovere dataset condivisi per la patologia CR

  -migliorare la comunicazione tra clinici e patologi

TABLE 1. Core and Non-Core Elements for Reporting

Core Items	Non-Core Items
Neoadjuvant therapy	Clinical information
Operative procedure	Plane of sphincter excision*
Tumor site	Plane of mesocolic excision*
Tumor dimensions (maximum)	Measurement of invasion beyond muscularis propria
Perforation	Tumor budding
Relation of tumor to anterior peritoneal reflection*Plane of mesorectal excision*	Coexistent pathology
Histological tumor type	Ancillary studies
Histological tumor grade	
Extent of invasion	
Lymphatic and venous invasion	
Perineural invasion	
Lymph node status	
Tumor deposits	
Response to neoadjuvant therapy	
Margin status	
Histologically confirmed distant metastases	
Pathological staging	
Ancillary studies	

*These items are only relevant to certain specimen types—see text for details.

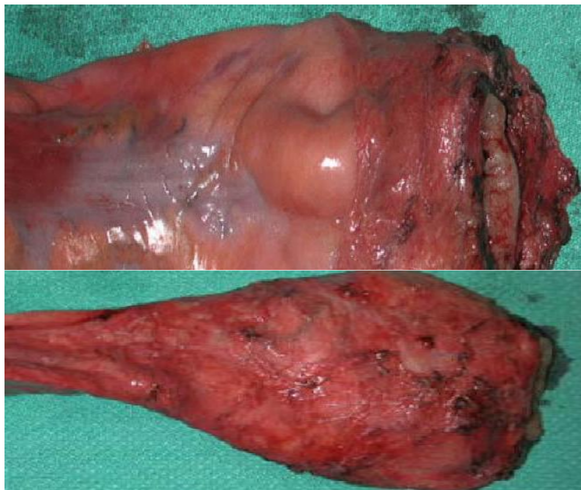
Informazioni cliniche

- Essenziali per il campionamento ottimale del P.O. e per l’interpretazione istologica (forme familiari, IBD…..) ma….
- Non dipendono dal patologo e per questo sono state inserite nella categoria «non-core»
- Due eccezioni:

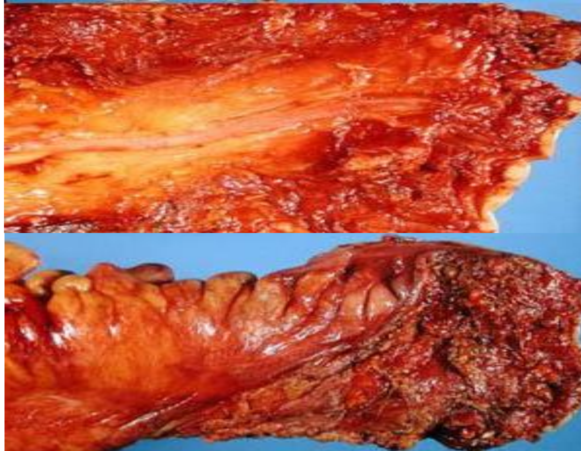
-tipo di intervento chirurgico

-terapia neoadiuvante

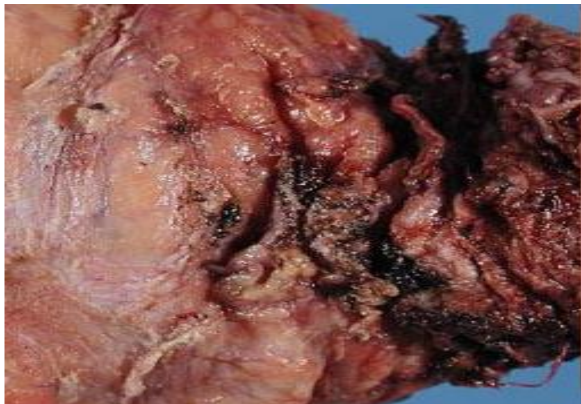
Metodo di Quirke: 3 Gradi



3- Completa
- MR intatto, superficie liscia
- Solo minime irregolarità
- Non difetti più profondi di 5 mm
- Non conizzazione verso il margine distale
- CRM liscio al taglio



2- Quasi completa
- Moderata quantità di MR
- Superficie irregolare, difetti > 5 mm in profondità, che non si estendono alla m. propria (eccetto l'inserzione dell' elevatore dell' ano)
- Moderata "conizzazione"
- Moderate irregolarità del CRM



▪ **1- Incompleta**

Piccola quantità di MR

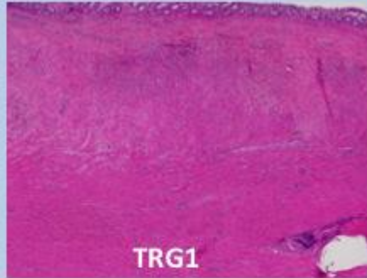
Difetti che si arrivano alla m.propria

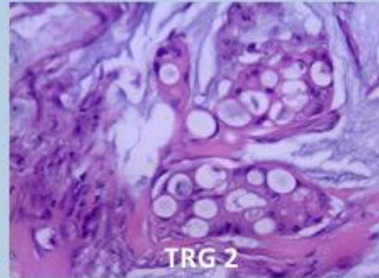
CRM molto irregolare

Particolarita’ nel P.O. del retto

Terapia neoadiuvante: TRG

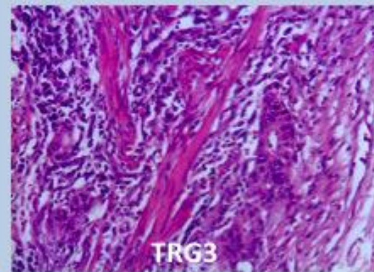
Mandard good responders (TRG1 + TRG2)

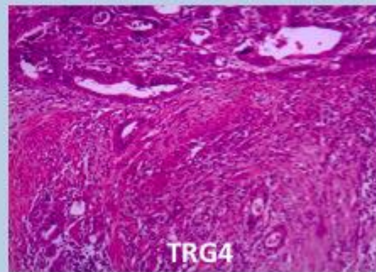


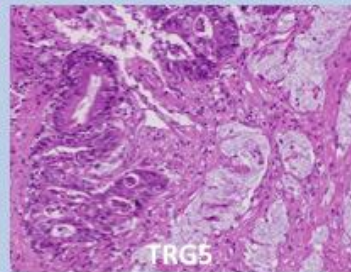


TRG 1	No viable cancer cells, complete response
TRG 2	Single cells or small groups of cancer cells
TRG 3	Residual cancer outgrown by fibrosis
TGR 4	Significant fibrosis outgrown by cancer
TRG 5	No fibrosis with extensive residual cancer

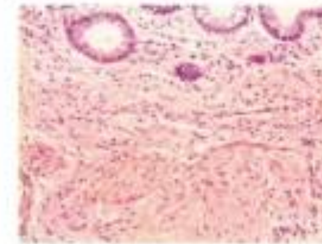
Mandard poor responders (TRG3 +TRG4 + TRG5)

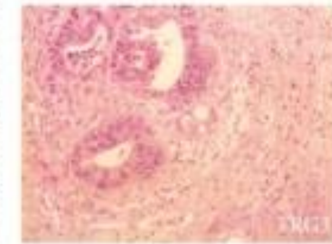




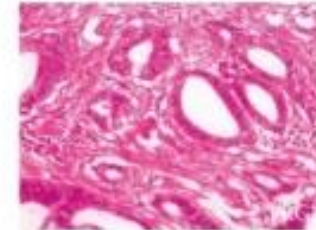


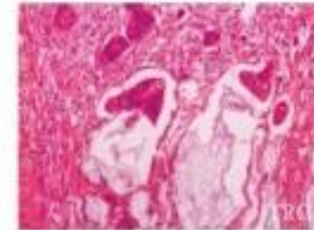
Dworak good responders (TRG3 + TRG4)

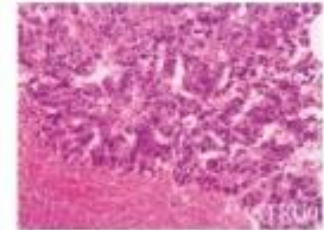




Dworak bad responders (TRG0 + TRG1 + TRG2)







Dworak TRG system	
TRG0	No regression
TRG1	Dominant tumor mass with obvious fibrosis and/or vasculopathy
TRG2	Dominant fibrotic changes with few tumor cells or groups (easy to find)
TRG3	Very few (difficult to find microscopically) tumor cells in fibrotic tissue with or without mucus substance
TRG4	No tumor cells, only fibrotic mass (total regression)

Quando l’istologia fa la differenza

- PT1: chirurgia vs «watch and wait»
- STADIO II: fattori di rischio per la chemioterapia adiuvante
- STADIO III (LN+): chemioterapia
- MMR-deficient: immunoterapia negli stadi IV, non beneficio per la terapia adiuvante con 5-FU negli stadi II

PT1: fattori di rischio

<table>
<tr><td>Sessile ‘low risk’ pT1 CRC</td><td>Low-grade (G1-2)
Infiltration depth <1000 µm
No vessel invasion (L0, V0)
Tumor budding BD1</td></tr>
<tr><td>Pedunculated ‘low risk’ pT1 CRC</td><td>Low-grade (G1-2)
Haggitt Level 1-2
No vessel invasion (L0, V0)
Tumor budding BD1</td></tr>
<tr><td>Sessile/pedunculated ‘high risk’ pT1 CRC</td><td>Not all low-risk factors present</td></tr>
<tr><td colspan="2">Clinical consequence: All high-risk tumors must be discussed at interdisciplinary tumor rounds</td></tr>
</table>

Truninger et al, Swiss Medical Forum 2022

PT1: fattori di rischio

Endoscopically resected pT1 CRC (‘malignant polyp’)

Clinical question – could lymph nodes be positive?

<1% 35%

Watch and wait Hemicolectomy

STADIO II

Recommendation 1.3. ACT should be offered to patients with stage IIB and stage IIC colon cancer (ie, T4, lesions either penetrating visceral peritoneum or invasive of surrounding organ, respectively), with a discussion of the potential benefits and risks of harm associated with ACT (Type: Evidence-based; benefits may outweigh harms; Evidence quality: moderate; Strength of recommendation: weak).

Recommendation 1.4. ACT may be offered to patients with stage IIA (ie, T3) colon cancer with high-risk features, including sampling of fewer than 12 lymph nodes in the surgical specimen, perineural or lymphovascular invasion, poorly or undifferentiated tumor grade, intestinal obstruction, tumor perforation, and/or grade BD3 tumor budding (≥ 10 buds) (Type: Evidence-based; benefits may outweigh harms; Evidence quality: low; Strength of recommendation: weak).

Parametro piu’ forte per un beneficio alla terapia: pT4

Fattori addizionali: L1; V1; alto grado; budding (BD3); PNI, <12 LN

Budding

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

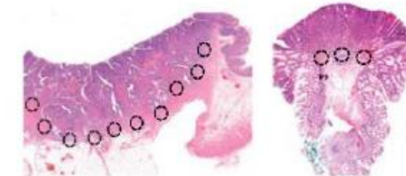
Alessandro Lugli[1,22], Richard Kirsch[2,22], Yoichi Ajioka[3], Fred Bosman[4], Gieri Cathomas[5], Heather Dawson[1], Hala El Zimaity[6], Jean-François Fléjou[7], Tine Plato Hansen[8], Arndt Hartmann[9], Sanjay Kakar[10], Cord Langner[11], Iris Nagtegaal[12], Giacomo Puppa[13], Robert Riddell[2], Ari Ristimäki[14], Kieran Sheahan[15], Thomas Smyrk[16], Kenichi Sugihara[17], Benoît Terris[18], Hideki Ueno[19], Michael Vieth[20], Inti Zlobec[1] and Phil Quirke[21]

1 Define the field (specimen) area for the 20x objective lens of your microscope based on the eyepiece field number (FN) diameter

Eyepiece FN Diameter (mm)	Specimen Area (mm2)	Normalization Factor
18	0.636	0.810
19	0.709	0.903
20	0.785	1.000
21	0.866	1.103
22	0.950	1.210
23	1.039	1.323
24	1.131	1.440
25	1.227	1.563
26	1.327	1.690

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

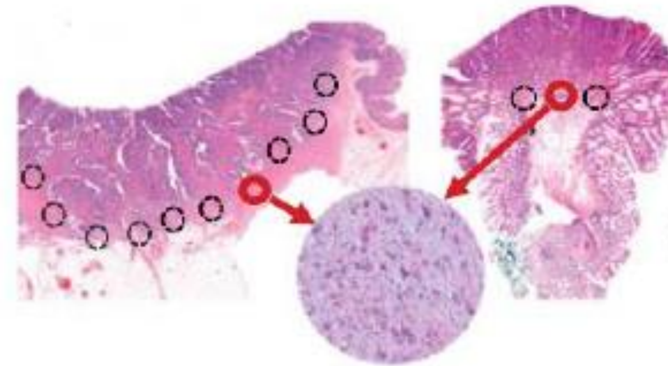


For surgical resection specimens, scan 10 fields

For pT1 endoscopic resections (usually <10 fields available), scan all

Budding

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 0.785mm²**

Select the budding [Bd] category based on bud count and indicate the absolute count per 0.785mm² (see reporting example)

$$\text{Tumor bud count per } 0.785\ \text{mm}^2 = \frac{\text{Bud count (20x objective)}}{\text{Normalization factor}^*}$$

Category	Buds	
Bd1 (low):	0-4 buds	per 0.785 mm²
Bd2 (intermediate):	5-9 buds	per 0.785 mm²
Bd3 (high):	≥10 buds	per 0.785 mm²

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

Lugli et al, Mod Pathol 2017

Budding

pT1 CRC
Tumor budding as a predictor of lymph node metastases
OR 6.44 (95% CI 5.26-7.87; $p<0.0001$)

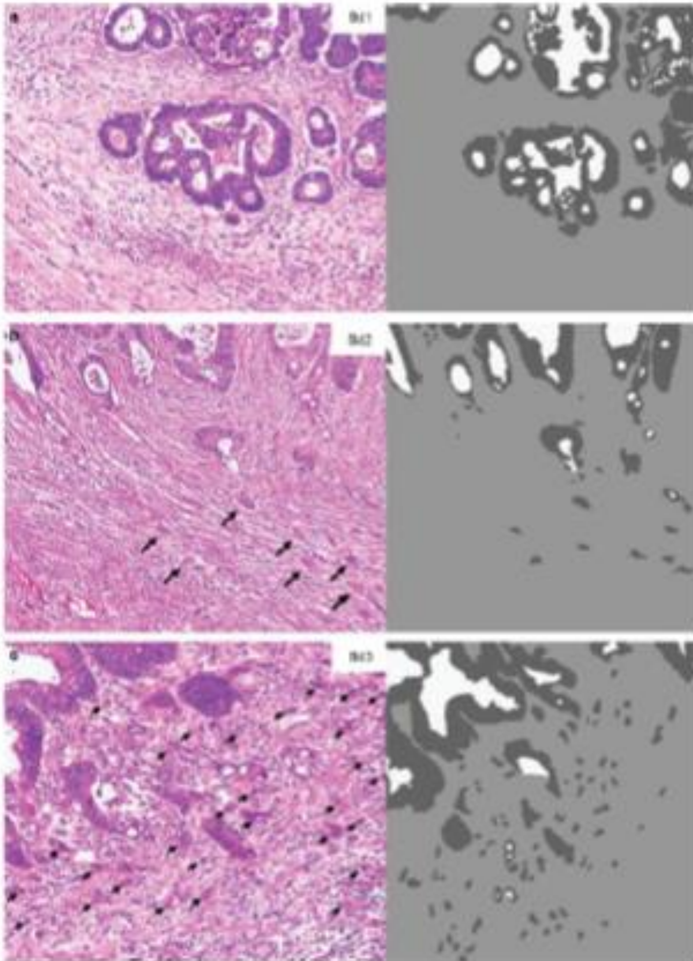
Clinical implication: resection

Stage II CRC
Tumor budding as a factor of tumor progression and survival
OR for 5-year OS 6.25 (95% CI 4.04-9.67; $p<0.0001$)

Clinical implication: adjuvant therapy

Cappellesso et al, Hum Pathol 2017; Petrelli et al, J Gastrointest Cancer 2015

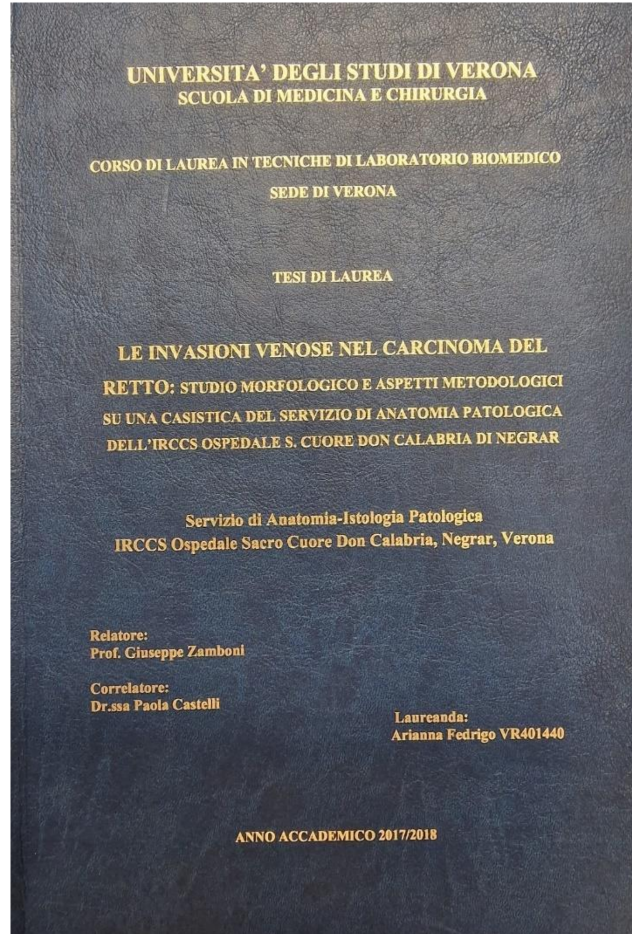
Budding



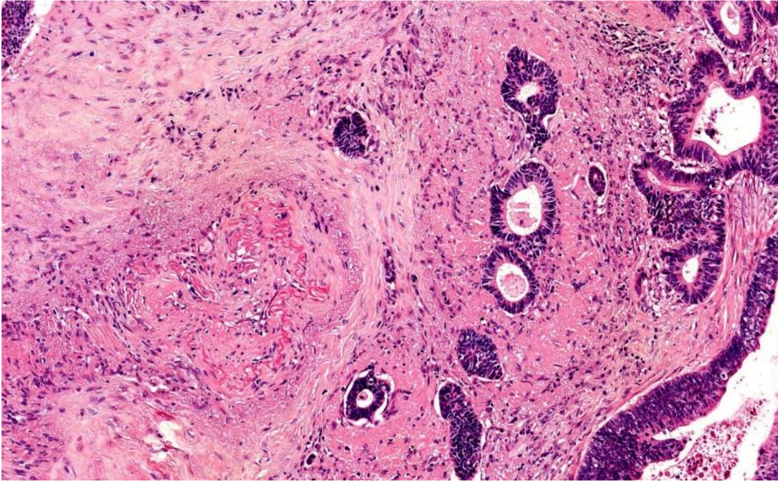
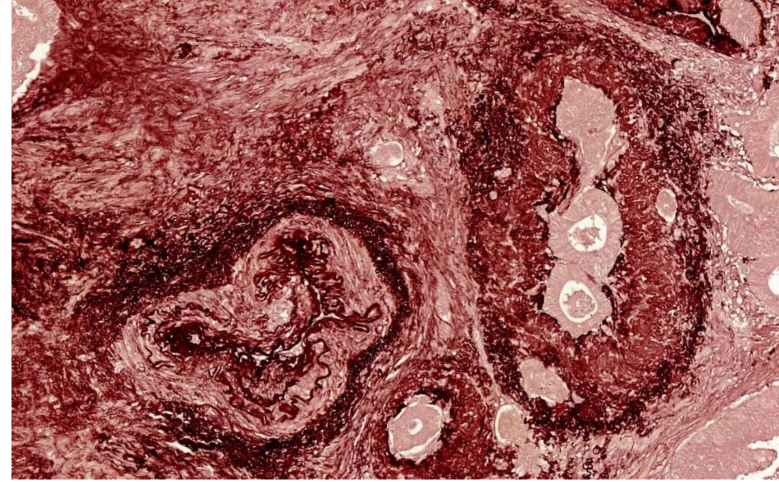
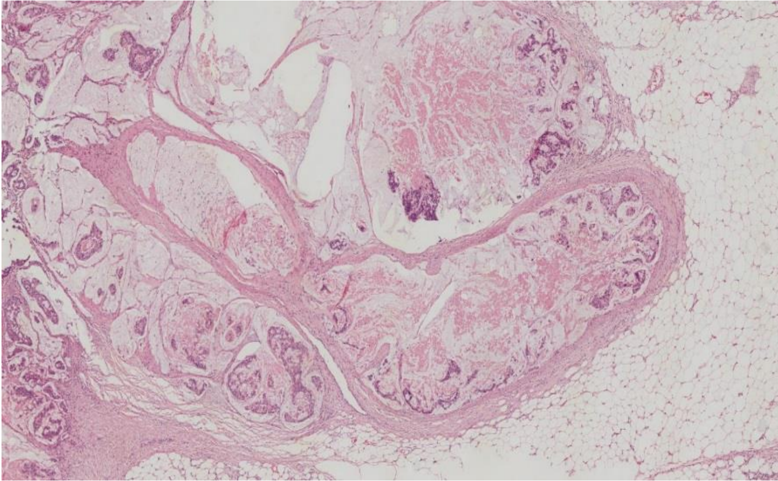
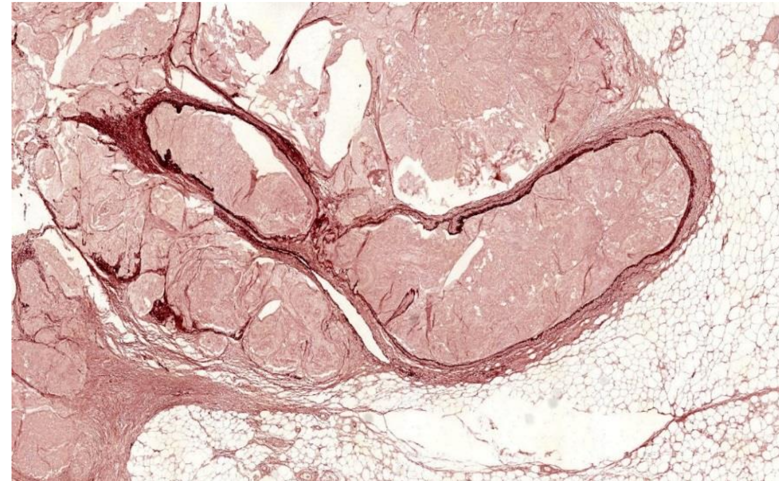
	PT1	Stadi 2
Bd 1 (0-4)		
Bd 2 (5-9)		
Bd 3 (≥ 10)		

Importanza delle invasioni venose

rischio metastatico e sopravvivenza



- Scopo:
  - migliorare l'individuazione delle I.V. nel CA del retto Stadio II con la colorazione speciale di Shikata.
- Risultati:
  - 15% con EE
  - 68% con colorazione di Shikata.
- **APPLICAZIONE:**
  - **utilizzo routinario della colorazione di Shikata in tutti i CA colo-rettali**

Take Home

Il referto perfetto verosimilmente non esiste….. ma se esiste è frutto di

COLLABORAZIONE

DISCUSSIONE ANATOMO-CLINICA

Grazie