Incidental finding of a malignant polyp

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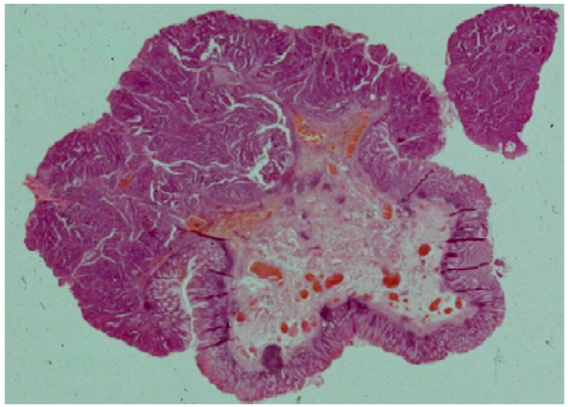
Plan

1. What is a polyp malignant ?
2. Role of the pathologist and the endoscopist
3. Quantitative and qualitative risk assessment
4. How to decide what to do?

Malignant or not?



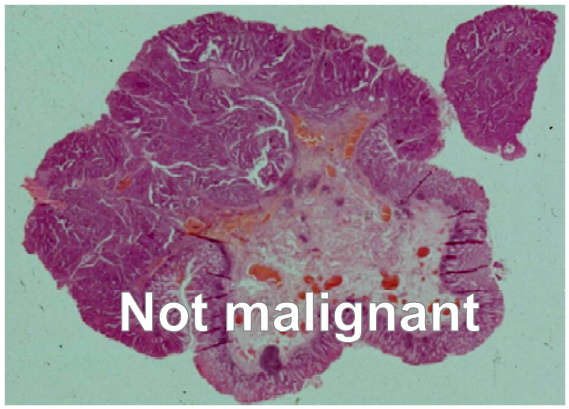
What is a malignant polyp?

- A **malignant** (pedunculated, sessile or flat) **polyp** is defined as a lesion that endoscopically appears like an adenoma but histologically contains invasive adenocarcinoma extended into but **not beyond the submucosa**
- We use the term of **adenocarcinoma** when the neoplasm has invaded the submucosa
- A **desmoplastic stromal** reaction is virtually always present
- Capable of **metastasis**

In contrast:

- An **intra-mucosal carcinoma** breaks the basal membrane and invades the lamina propria but does not reach the muscularis mucosae (pTis)
- **Metastasis** has **never** been reported from colonic intra-mucosal carcinoma
- Therefore, intra-mucosal carcinomas should not be regarded as malignant polyps

Malignant or not?



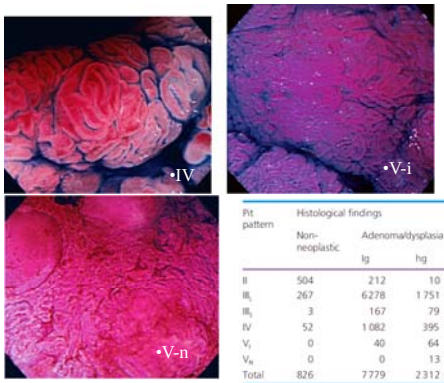
The role of the pathologist:

- Not only to propose a **correct diagnosis**
- But also provide crucial information for the therapy:
  - Is the lesion completely excised?
  - What is the risk for lymph nodes metastasis?

The role of the endoscopist:

- Not to resect lesions that have **high probability of (deep) submucosal invasion**.
- In case of large or suspicious lesions to provide the pathologist with an **optimal specimen**:
  - If possible, complete en bloc resection
  - Adequate orientation of the polyp

Pitt pattern

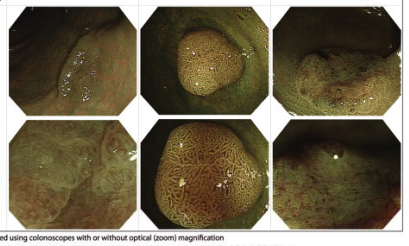


Pit pattern	Histological findings					
	Non-neoplastic	Adenoma/dysplasia		Carcinoma		Total
		lg	hg	m	sm	
II	504	212	10	0	0	726
III_L	267	6278	1751	365	0	8661
III_S	3	167	79	25	11	285
IV	52	1082	395	369	73	1971
V_I	0	40	64	106	56	266
V_N	0	0	13	54	128	195
Total	826	7779	2312	919	268	12104

Kudo, Endoscopy 2001

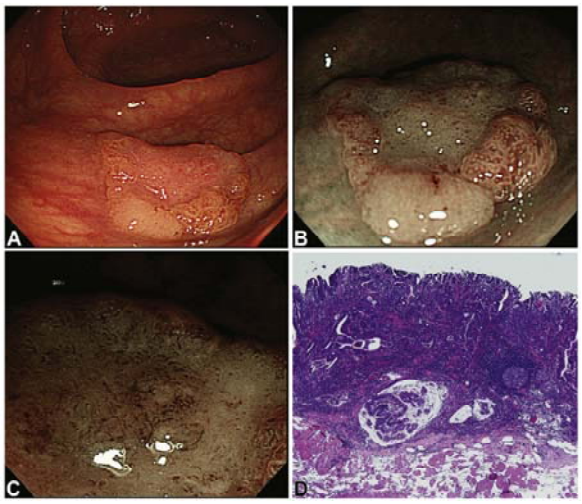
NICE

NBI International Colorectal Endoscopic (NICE) Classification*

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels coursing across the lesion	Brown vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface Pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular or branched white structure surrounded by brown vessels**	Amorphous or absent surface pattern
Most likely pathology	**Hyperplastic**	**Adenoma*** **	**Deep submucosal invasive cancer**
Examples			

* Can be applied using colonoscopes with or without optical (zoom) magnification
** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.
*** Type 2 consists of Vienna classification types 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area).

Hayashi, Gastrointest Endosc 2013



Technical issues

Incomplete Polyp Resection During Colonoscopy—Results of the Complete Adenoma Resection (CARE) Study

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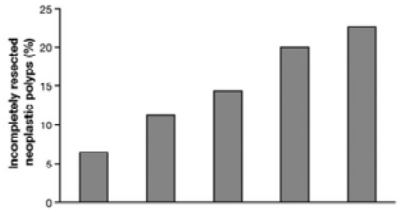
Table 3. Polyp Characteristics Associated With Incomplete Resection of Neoplastic Polyps

	Neoplastic polyps		Relative risk (95% CI)	
Polyp characteristics	All (N = 346), n	Incompletely resected (n = 35) (10.1%), n (%)	Univariate	Multivariate[a]
Size, mm				
5–7	172	10 (5.8)	1.00 (reference)	1.00 (reference)
8–9	64	6 (9.4)	1.61 (0.61–4.26)	1.66 (0.62–4.46)
10–14	67	9 (13.4)	2.34 (0.98–5.43)	1.95 (0.87–4.37)
15–20	43	10 (23.3)	4.00 (1.78–9.00)	3.21 (1.41–7.31)
Location in the colon				
Left colon	135	11(8.1)	1.00 (reference)	
Right colon	211	24 (11.4)	1.40 (0.71–2.76)	Not applicable[b]
Location at fold				
Between/on a fold	271	25 (9.2)	1.00 (reference)	
Behind a fold	67	6 (9.0)	0.97 (0.41–2.27)	Not applicable[b]
Morphology				
Nonflat	158	11 (7.0)	1.00 (reference)	1.00 (reference)
Flat	153	19 (12.4)	1.78 (0.88–3.62)	1.45 (0.73–2.91)
Histology				
Adenoma[c]	304	22 (7.2)	1.00 (reference)	1.00 (reference)
SSA/P	42	13 (31.0)	4.28 (2.34–7.83)	3.74 (2.04–6.84)
Resection				
En bloc	286	24 (8.4)	1.00 (reference)	1.00 (reference)
Piecemeal	54	11 (20.4)	2.43 (1.27–4.66)	1.41 (0.66–2.98)
Ease of resection				
Easy	222	17 (7.7)	1.00 (reference)	1.00 (reference)
Moderately difficult	75	10 (13.3)	1.74 (0.83–3.63)	1.56 (0.75–3.24)
Difficult	45	8 (17.8)	2.32 (1.07–5.05)	1.71 (0.67–4.44)

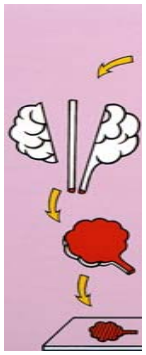
Pohl, Gastroenterology 2013

Importance of technique and operator!

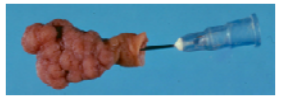


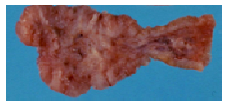
Endoscopist	A	B	C	D	E
Polyps resected, n = 418	241 (57.7%)	28 (6.7%)	29 (6.9%)	24 (5.7%)	26 (6.2%)
Neoplastic polyps resected, n = 346	201 (58.1%)	18 (5.2%)	28 (8.1%)	20 (5.8%)	22 (6.4%)
Incompletely resected neoplastic polyps, n = 35	13 (6.5%)	2 (11.1%)	4 (14.3%)	4 (20.0%)	5 (22.7%)
Univariate analysis, RR (95% CI)	1.00 (referent)	1.72 (0.42-7.05)	2.21 (0.77-6.32)	3.09 (1.11-8.61)	3.51 (1.38-8.95)
Multivariate analysis, RR (95% CI)	1.00 (referent)	1.98 (0.51-7.75)	2.87 (1.02-8.03)	2.04 (0.71-5.93)	3.45 (1.35-8.81)

How to evaluate completeness of excision?

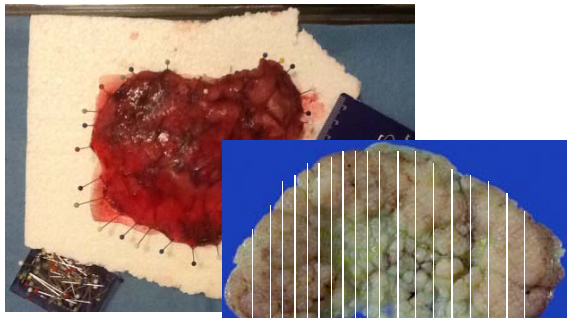


- Correct gross examination is crucial
- Importance of the orientation





The majority of polyps are sessile



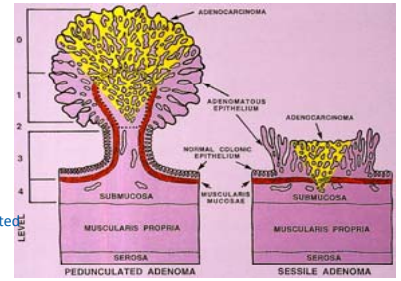
Haggitt classification: levels of submucosal invasion

Level 1: submucosal invasion (head)

Level 2: submucosal invasion (neck):
low risk of lymph node mets (<3%)

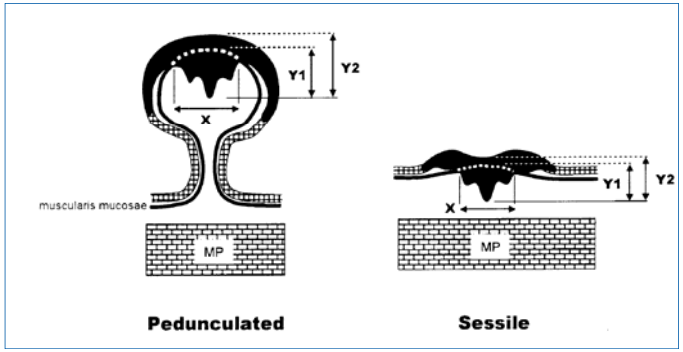
Level 3: submucosal invasion (stalk)

Level 4: same submucosal invasion pedunculated or sessile: high risk



Robert, Clin Gastroenterol Hepatol 2007; Haggitt Gastroenterology 1985

Pedunculated vs. flat lesions



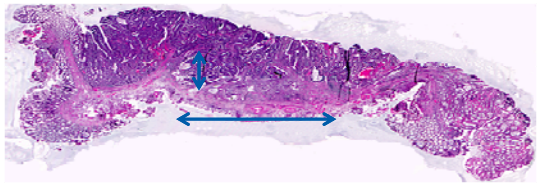
Ueno, Gastroenterology 2004

Quantitative risk assessment

- Grade of vertical submucosal invasion (depth -Y)
  - Sm1 = less than 0.5mm from the mm, superficial third
  - Sm 2= 0.5 to 1mm , middle third
  - Sm3= over 1mm, deepest third

  sm3 : high risk for metastases Ueno : > 2000µm 17.1 %
- Grade of horizontal submucosal invasion (width-X)
  - < 2mm of the tumoral width
  - 2 –3mm of the tumoral width
  - > 4 mm of the tumoral width

  > 4mm high risk for metastases Ueno : > 4mm 18.2 %



Kikuchi R Dis Colon Rectum 1995
Ueno, Gastroenterology 2004

Qualitative measures

- Tumour differentiation
  - Well- or moderately differentiated: favourable
  - Poorly differentiated or mucinous: unfavourable
- Margin
  - Negative: favourable (but until which distance ?)
  - Positive including in cautery: unfavourable
- Lymphatic invasion: unfavourable
- Tumour budding, cribriform features: unfavourable

Relation between margin and recurrence

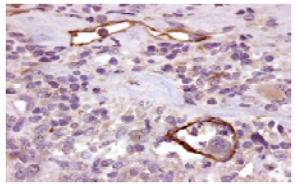
Table 8. Correlation Between Resection Margin and Intramural Residual and Intramural Local Recurrence

		Tumors with endoscopic excision followed by laparotomy (n = 68)		Tumors with endoscopic excision alone (n = 35)	
Location of tumor front	Circumferential excision margin	Number of tumors	Residual tumor in the submucosa	Number of tumors	Intramural local recurrence
Within the coagulation region	<1 mm	31	4 (12.9%)	2	1 (50.0%)
	1 mm ≤ margin <2 mm	1	0	1	0
Outside the coagulation region	<1 mm	19	0	14	0
	1 mm ≤ margin <2 mm	10	0	7	0
	≥2 mm	7	0	11	0

Ueno, Gastroenterology 2004

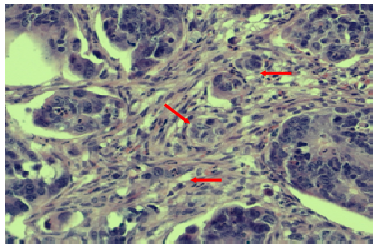
Lymphatic invasion

- Not commonly seen
- Inter-observer variability : retraction artefact can mimic lymphatic invasion
- Lymphatic invasion without other unfavourable pathologic features : rare
- Immunohistochemistry : D2-40 increases detection (more than 2-fold)



Budding

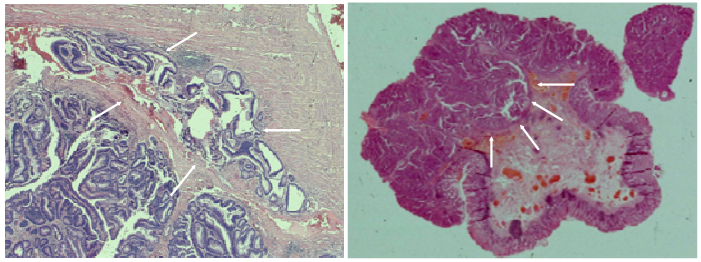
- Tumour budding is defined as an isolated single cancer cell or a cluster composed of fewer than 5 cancer cells
- Independent predictor of lymph node metastasis*



Choi, Dis Colon Rectum 2009

Pseudo-invasion

- Glands arranged in a smooth rounded nest or « bolus » lobular configuration
- Displaced glands have rounded contours and lobular configuration
- Herniated neoplastic tubules surrounded by lamina propria
- Glands invested by lamina propria with inflammatory cells , sometimes hemosiderin



Summary of unfavourable features

- Incomplete resection
- Submucosal invasion
- Tumour less than 1 mm from the deep cauterized margin
- Differentiation : Grade III (poorly differentiated)
- Presence of lympho-vascular invasion

Combination of qualitative and quantitative risk factors for nodal metastases

Table 5. Combination of Qualitative and Quantitative Risk Factors and the Incidence of Nodal Involvement

	Qualitative risk factors 1–3[a]		Qualitative risk factors 1–3[a] plus Haggitt's level 3–4		Qualitative risk factors 1–3[a] plus width ≥4000 μm		Qualitative risk factors 1–3[a] plus depth ≥2000 μm	
Number of risk factors	Nodal involvement	Micrometastasis	Nodal involvement	Micrometastasis	Nodal involvement	Micrometastasis	Nodal involvement	Micrometastasis
None	0.7% (1/138)[b]	6.8% (4/59)[c]	0.0% (0/27)[d]	15.4% (2/13)[c]	0.0% (0/62)[e]	0.0% (0/26)[f]	0.0% (0/56)[d]	0.0% (0/19)[c]
1	20.7% (12/58)	14.3% (3/21)	0.8% (1/118)	4.3% (2/47)	2.3% (2/87)	10.8% (4/37)	3.3% (3/92)	8.9% (4/45)
2 or more	36.4% (20/55)	16.7% (3/18)	30.2% (32/106)	15.8% (6/38)	30.4% (31/102)	17.1% (6/35)	29.1% (30/103)	17.6% (6/34)

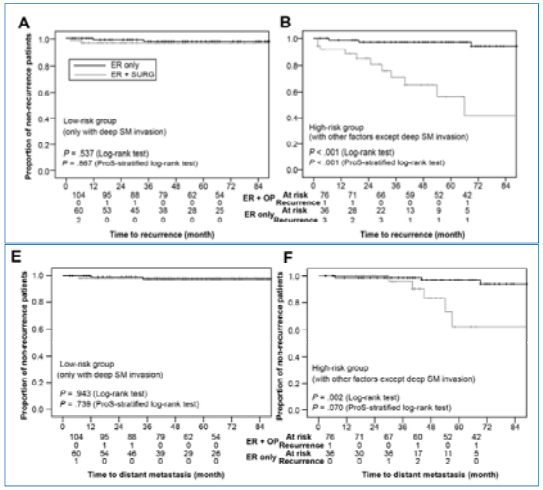
NOTE. Nodal involvement was based on the conventional examination.
[a]Risk factors: 1, unfavorable grade; 2, vascular invasion; 3, tumor budding. [b]$P < 0.0001$; [c]$P > 0.1$; [d]$P = 0.031$ (Fisher exact test); [e]$P = 0.0004$; [f]$P = 0.058$ (Fisher exact test); [d]$P = 0.0010$.

Integration of clinical, endoscopic and pathologic features

Table 2. Associations Between Conventional Clinicopathologic Risk Factors and Recurrence

	ER only			ER + SURG		
	Recurrence			Recurrence		
Factors	No	Yes	HR[a] (95% CI)	No	Yes	HR[a] (95% CI)
Location						
Right colon	53	2	0.2 (0.4–1)	42	0	N/A
Left colon	90	6	0.3 (0.1–1.2)	138	3	0.2 (0.4–1.4)
Rectum	27	6	Reference	20	2	Reference
Configuration						
Pedunculated	53	1	Reference	58	1	Reference
Sessile	64	7	6.2 (0.8–50.2)	99	3	1.7 (0.2–16.8)
Flat elevated	44	5	6.5 (0.8–55.8)	26	0	N/A
Depressed	9	1	7.2 (0.5–116.1)	17	1	3.0 (0.2–48.2)
Resection method						
En bloc	145	7	Reference	155	5	Reference
Piecemeal	25	7	5.3 (1.9–15.2)	45	0	N/A
Vertical margin						
–	161	7	Reference	167	3	Reference
+	9	7	16 (5.5–46.6)	33	2	3.3 (0.5–19.6)
Submucosal invasion						
Superficial	94	3	Reference	34	0	Reference
Deep	76	11	4.3 (1.2–15.3)	166	5	N/A
Lymphatic invasion						
–	167	12	Reference	183	4	Reference
+	3	2	7.3 (1.6–33.2)	16	1	2.2 (0.2–20)
Venous invasion						
–	166	12	Reference	181	4	Reference
+	4	2	6.1 (1.3–27.6)	18	1	2.3 (0.3–22)
Histologic type						
well, mod	164	11	Reference	179	3	Reference
por, sig, muc	6	3	5.7 (1.6–20.6)	21	2	5.3 (0.9–31.5)
Tumor budding						
Low grade	161	12	Reference	185	4	Reference
High grade	9	2	3.8 (0.9–17.3)	15	1	3 (0.3–26.6)
Surgical indication (JSCCR, 2010)						
No	87	1	Reference	25	0	Reference
Yes	83	13	12.9 (1.7–98.5)	175	5	N/A
Total	170	14		200	5	

Yoshii, Clin Gastroenterol Hepatol 2014



To help you decide:

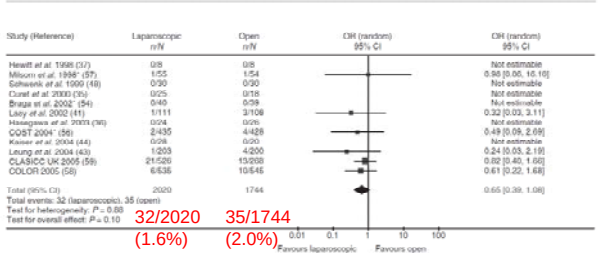


Figure 1 Mortality rate: laparoscopic *vs* open resection for colorectal cancer. *Studies including mixed cases of benign and malignant colorectal diseases.

Tjandra, Colorectal Dis 2006

What if you decide to operate?

- Ask you surgeon to perform an extensive lymphadenectomy!
- TME or even Abdomino-perineal resection if needed.

What if you decide not to operate?

- No evidence in the literature of the benefit of adjuvant (Radio-)chemotherapy in this setting
- Follow-up should focus on extra-mucosal disease:
  - CT
  - MRI
  - EUS

Conclusion

- Evaluate before it is too late:
  - Use the **endoscopic tools** (NBI, pit-pattern, lift sign, …) to determine before cutting if it is reasonable to do so!
- Do not cut if you are not sure to be able to remove the lesion **totally**
- If possible remove 'en-bloc' for **optimal pathological assessment**
- Important features in the pathology report for clinical decision-making:
  - Horizontal and vertical measure of submucosal infiltration in sessile polyp
  - Haggitt level and measure of distance between deepest infiltration and coagulated margin in pedunculated polyp
  - Lymphatic invasion
  - Venous invasion
  - Differentiation
  - Budding

Quirke, Endoscopy 2012