Corso di Self-Assessment e Retraining

LA COLONSCOPIA
DI SCREENING

ISTOPATOLOGIA DELLE LESIONI NEOPLASTICHE ALLA LUCE DELLE NUOVE linee guida EUROPEE

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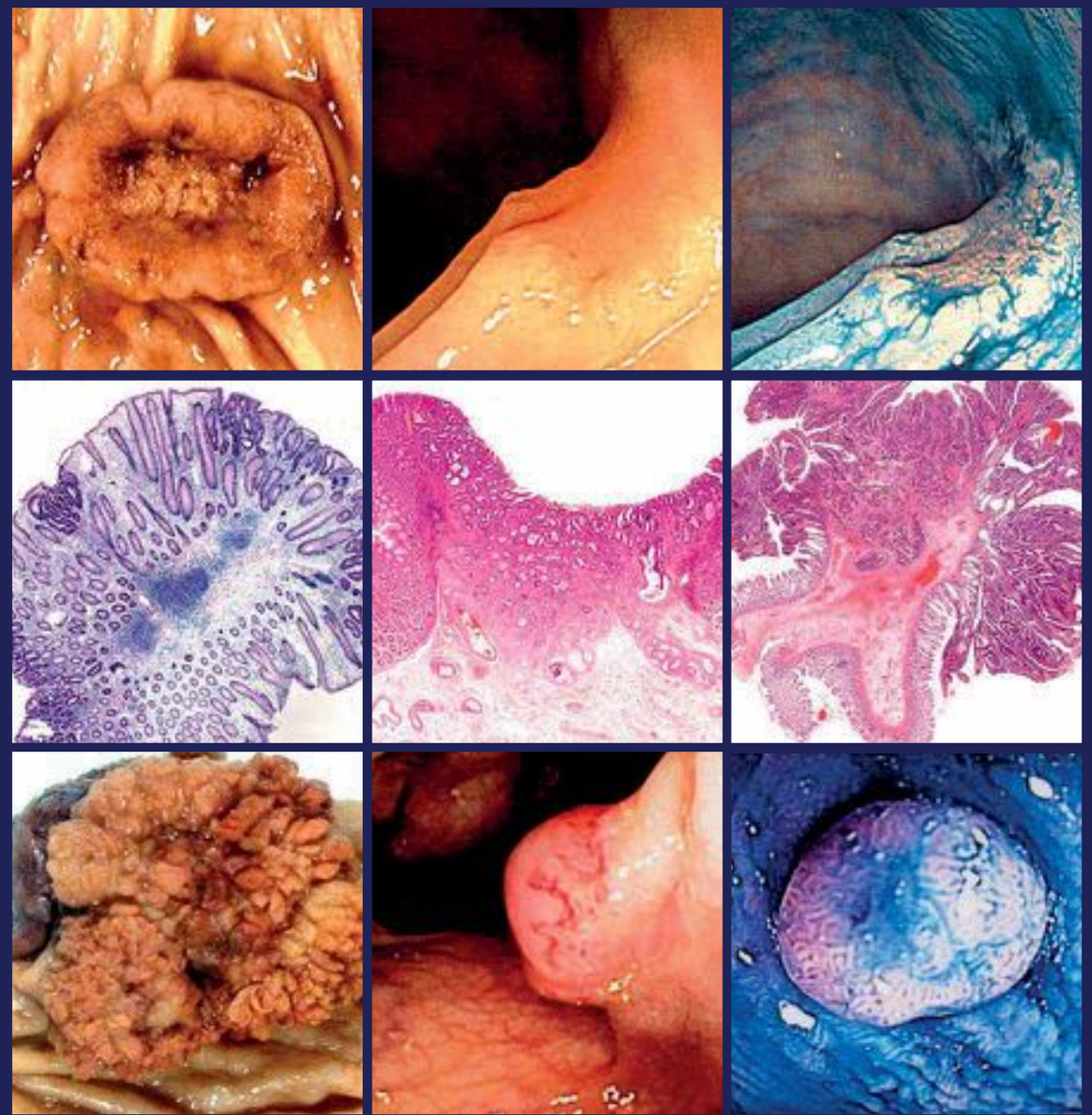
European Union 2010



European guidelines for quality assurance in colorectal cancer screening and diagnosis *First Edition*

European Commission

Lo screening dei carcinomi colorettali mira a identificare precocemente le forme tumorali invasive, ma anche a individuare e rimuovere possibili precursori.

Una peculiarità dei programmi di Screening è quella di stabilire linee guida condivise ed in modo da generare percorsi diagnostico-terapeutici omogenei

Il GISCoR, Gruppo Italiano Screening ColoRettale, seguendo quanto è stato fatto in altri paesi Europei, ha emanato già nel 2005 delle linee guida sia per quanto riguarda il 1° livello sia per la refertazione AP

Diagnosi anatomo-patologica negli screening del carcinoma colo-rettale: indicazioni. Documento del gruppo di lavoro dei patologi del GISCoR approvato nel convegno nazionale di Stra (Verona), giugno 2005.

7

Quality assurance in pathology in colorectal cancer screening and diagnosis

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Annex

Annotations of colorectal lesions

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European guidelines for quality assurance in colorectal cancer screening and diagnosis
First Edition

- The pathology service plays a very important role in colorectal cancer screening since the management of participants in the programme depends on the quality and accuracy of the diagnosis.
- Pathologists working within a colorectal cancer screening programme require **full training** in the histopathology of gastrointestinal disease with specific emphasis on colorectal cancer.

•These pathologists should be skilled in the following areas:

1. The preparation and histological interpretation of endoscopic polypectomy specimens;
2. The preparation and histological interpretation of surgical resection specimens.
3. The interpretation of biopsies taken from benign and malignant tumours of the colon and rectum

7.6.1 Submission of specimens

It is recommended to place specimens in separate containers, one for each lesion, to avoid confusion about exact location; if lesions are small, individual cassettes or multicassettes can be used.
Biopsies from the same lesion can be placed in the same container.
For endoscopic resections it is helpful to pin out specimens by inserting pins through the periphery of the specimen onto cork or thick paper.
Too much tension on the specimen could result in artificially thinned lesions. Needles should not be placed directly through a lesion but at the margin.
Besides patient data, an exact description on location should be provided (e.g. cms from anocutanous line), as well as size and morphology (stalked polyp, non-polypoid Paris classification, etc.).
Additional information about central depression or focal erosion or ulceration or coexistent chronic inflammatory bowel disease can be useful.
Endoscopic pictures can also be submitted with the specimen(s).

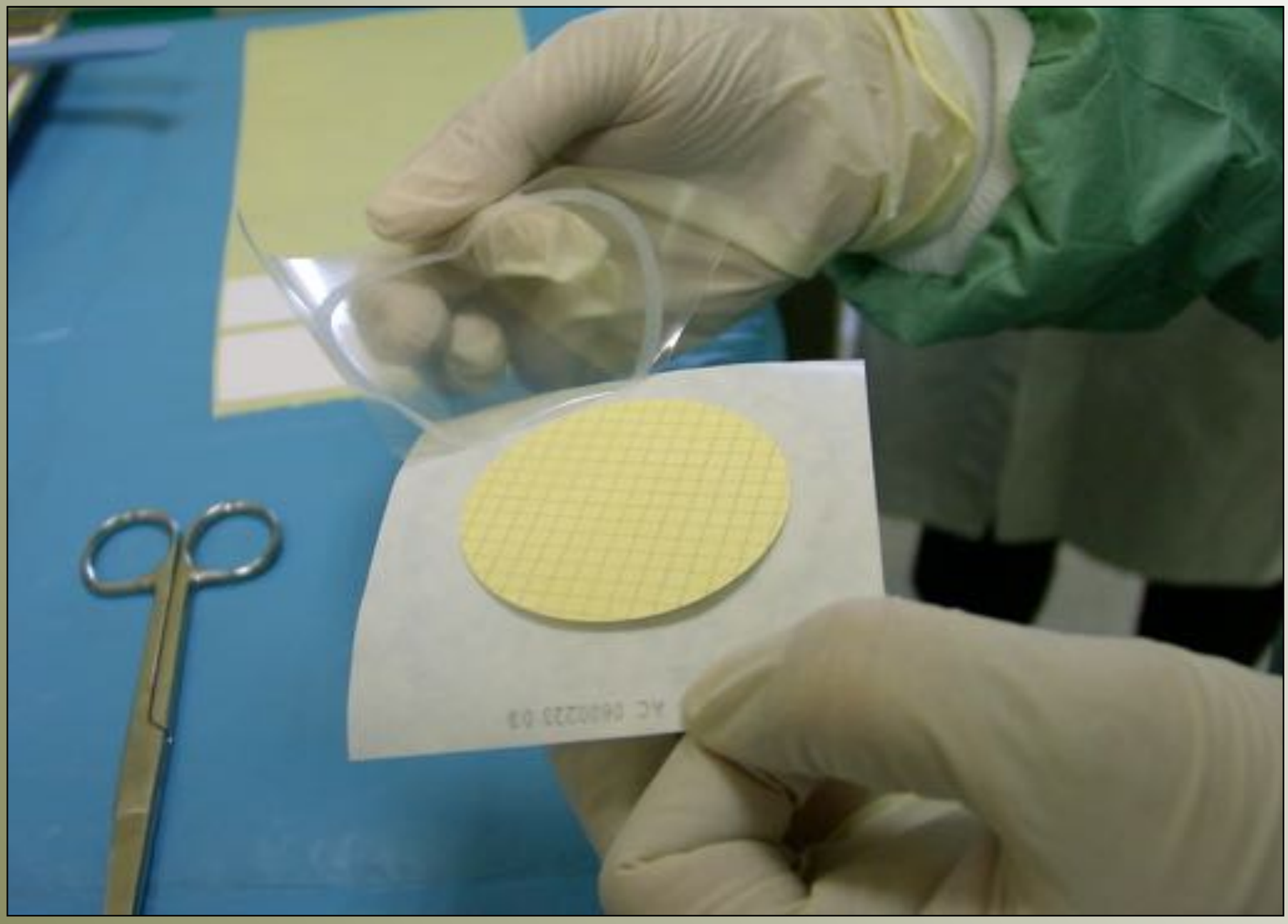
7.6.2 Fixation

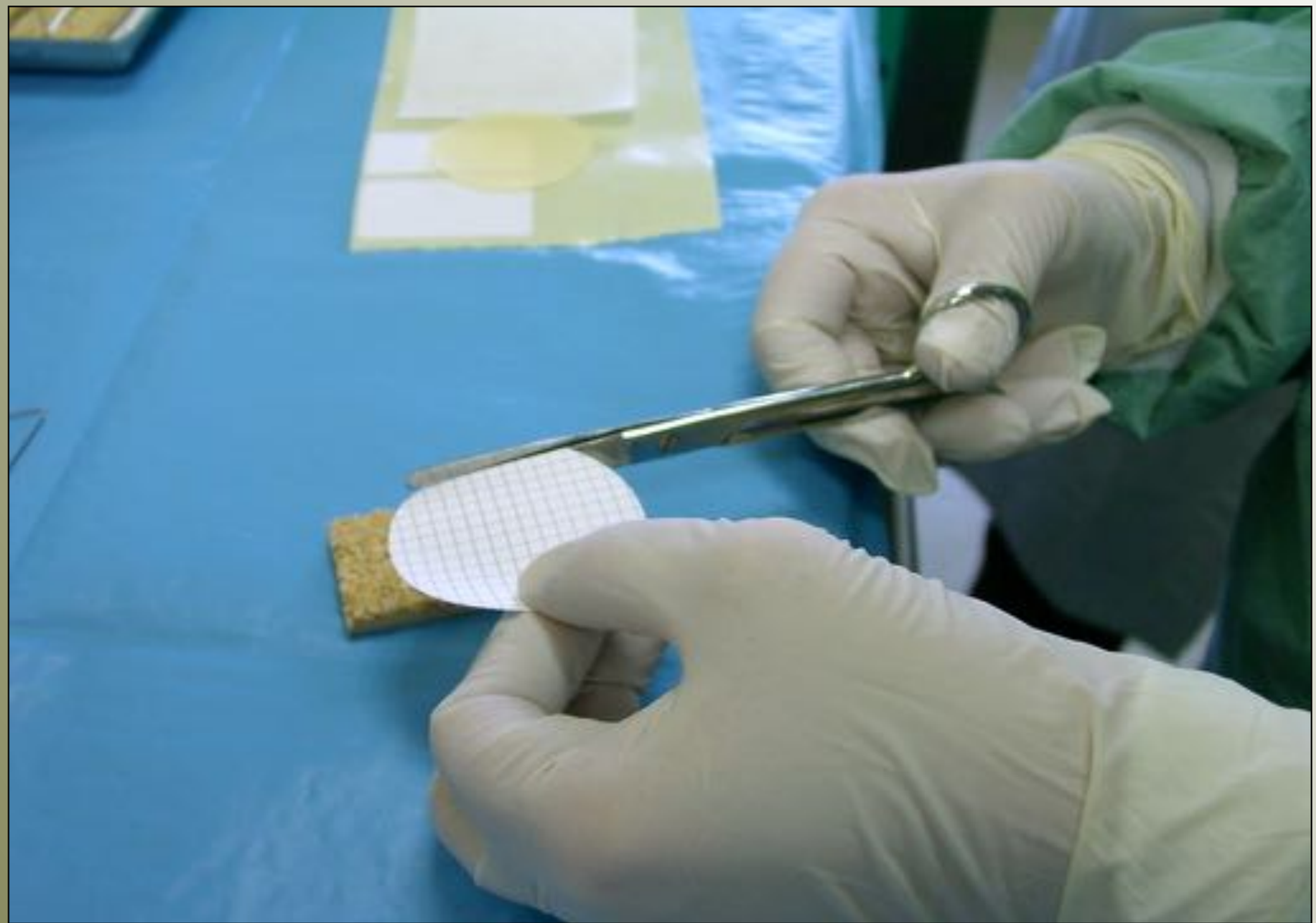
- Fixation should be by buffered 10% formalin; this equals a roughly 4% paraformaldehyde concentration, as formalin is 30–40% paraformaldehyde.
- Specimen(s) can shrink due to formalin fixation, therefore measurements taken after fixation can differ from those prior to fixation.
- Fixation in alcohol is not recommended and if any other fixatives are used a comparative study of size of adenomas after fixation should be performed prior to use to avoid excessive shrinkage of adenomas to avoid under treatment.

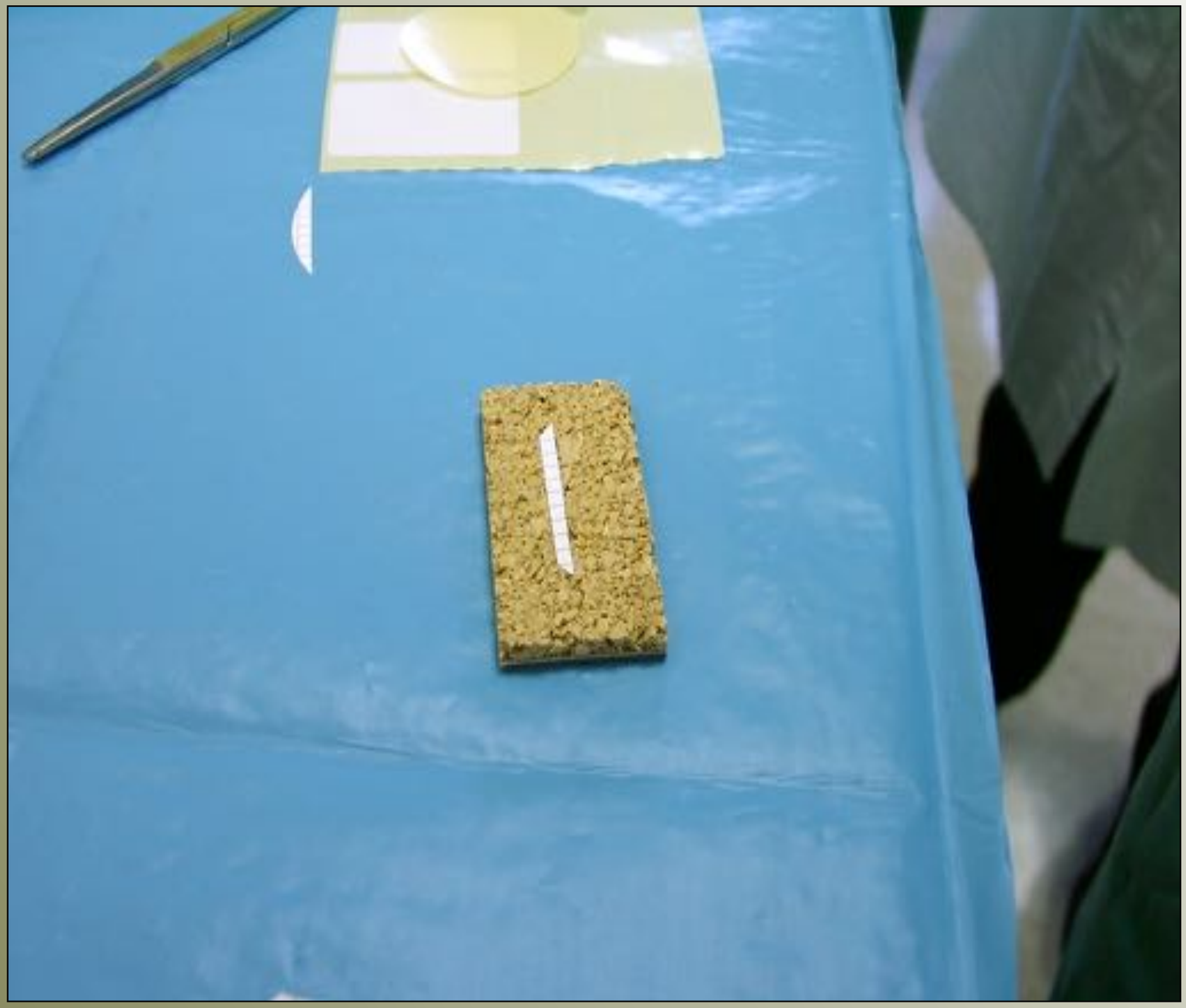
Trattamento dei reperti e modalità di invio del materiale

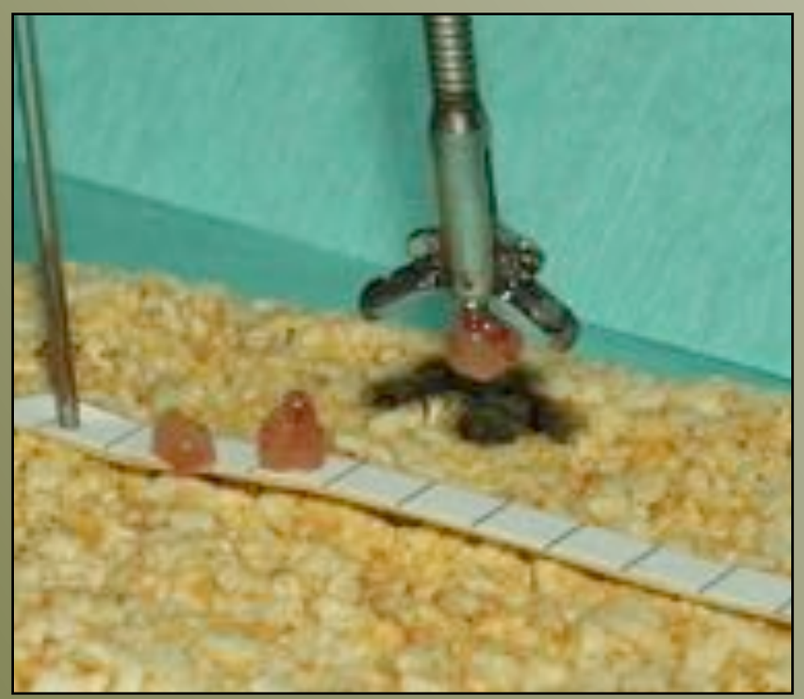
- Il materiale deve essere inviato integro, senza tagli e dissezioni preliminari che possano alterare il corretto campionamento della lesione.
- Il materiale deve essere inviato al Servizio in formalina tamponata al 10%.
- Le formazioni polipose <0,5 cm devono essere preventivamente appoggiate su supporto rigido con la faccia corrispondente alla superficie di exeresi.
- La fissazione deve essere rapida, ed immediata per i prelievi bioptici di piccole dimensioni.
- Il volume del fissativo deve essere circa 10 volte quello del campione prelevato.
- La capacità del contenitore deve essere tale da accogliere il prelievo e l'adeguata quantità di fissativo, al fine di evitarne le deformazioni.
- Il contenitore deve essere a chiusura ermetica, per evitare la dispersione di liquidi e materiale.
- I polipi peduncolati o comunque "orientabili" devono essere appesi per il peduncolo o per la base mediante infissione con uno spillo ad un supporto galleggiante (polistirolo, sughero) e messi in un contenitore sufficientemente grande da permettere la distensione del polipo per gravità prima del fissaggio.
- Lo staff di endoscopia seleziona tra i polipi >0,5 cm quelli con caratteristiche (polipi semipeduncolati, peduncolati con peduncolo <0,3 cm, ecc.) che presumibilmente rendono difficile la identificazione della base di resezione dopo fissazione e provvede alla marcatura della stessa mediante trasmissione con idoneo repere o con inchiostro di china.
- Le dimensioni del polipo vengono definite dal maggior diametro e,se significativi, dai due diametri minori, escludendo dalle misurazioni i segmenti pertinenti al peduncolo senza approssimazione a 0.5-1 mm.
- Un prelievo para-centrale (comprensivo del piano medio-sagittale del polipo) con separazione delle due calotte laterali dalla parte centrale garantisce la valutazione su ampia superficie della interfaccia tra tessuto epiteliale ed asse vasculo-stromale comprensivo della sottomucosa.
- La settorializzazione della sezione para-centrale è prevista per polipi di dimensioni tali da non potere essere compresi in un'unica inclusione.
- Ulteriori prelievi paralleli a quello para-centrale ogni 2 mm (sezioni paramediane) progressivamente contrassegnate) con inclusione finale del tessuto residuo delle calotte laterali.

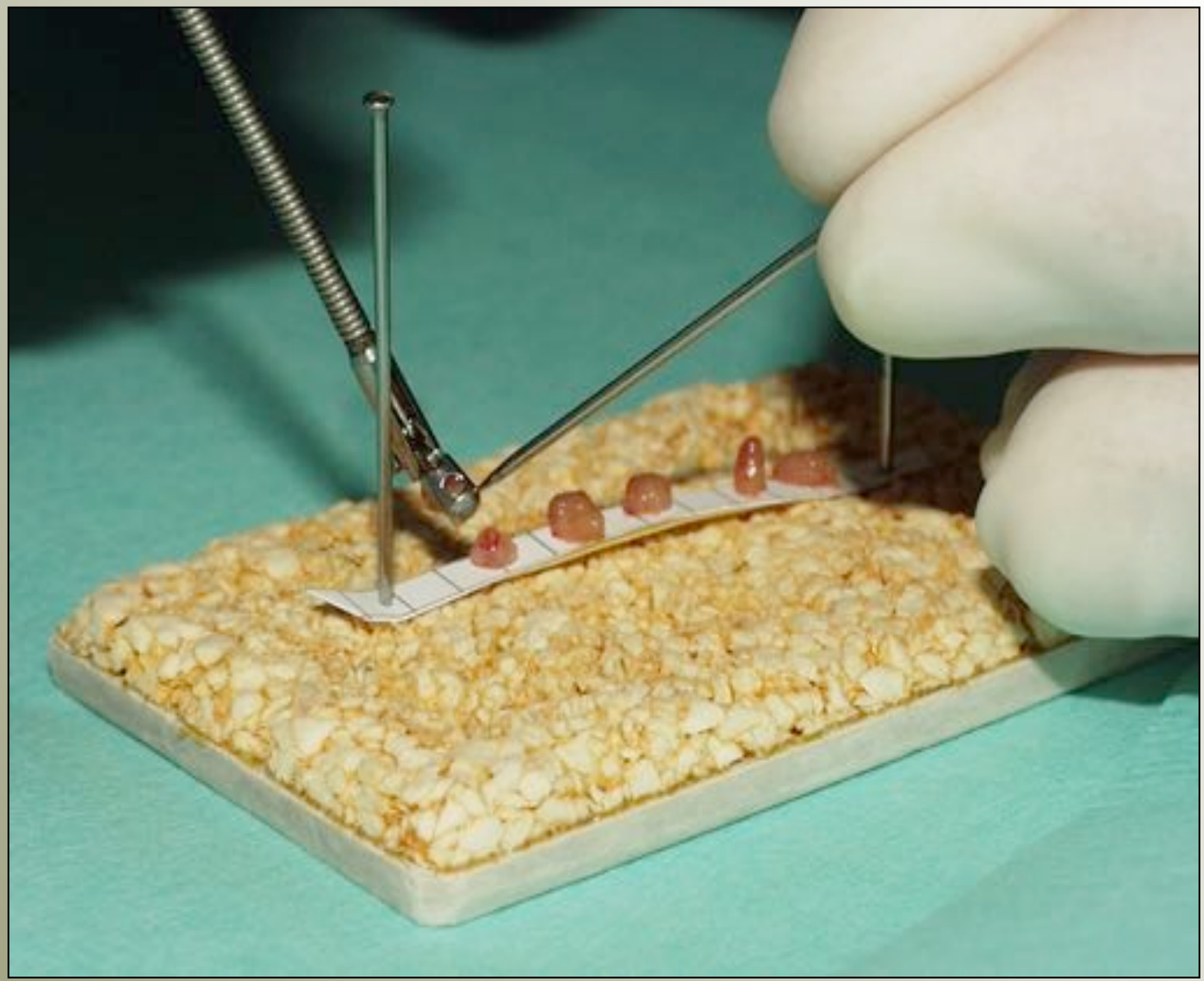
GISCOR 2005

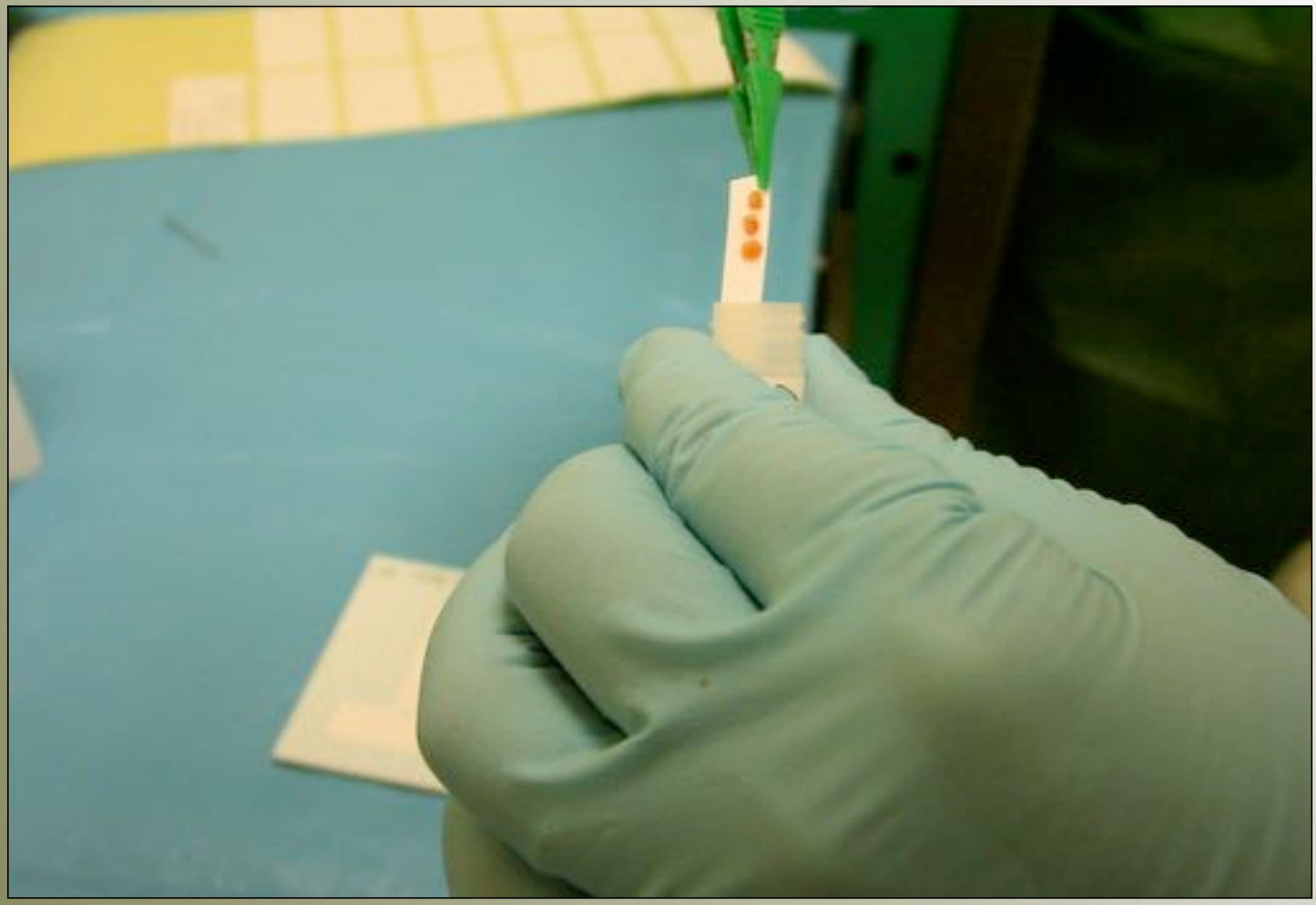


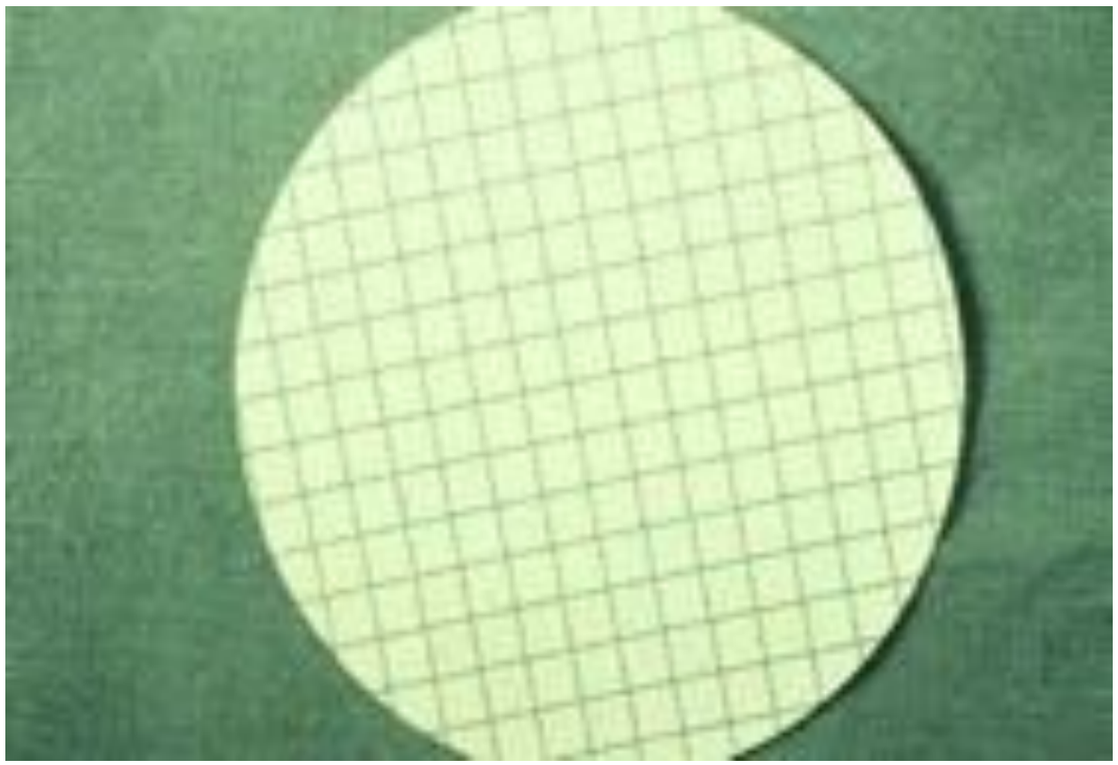


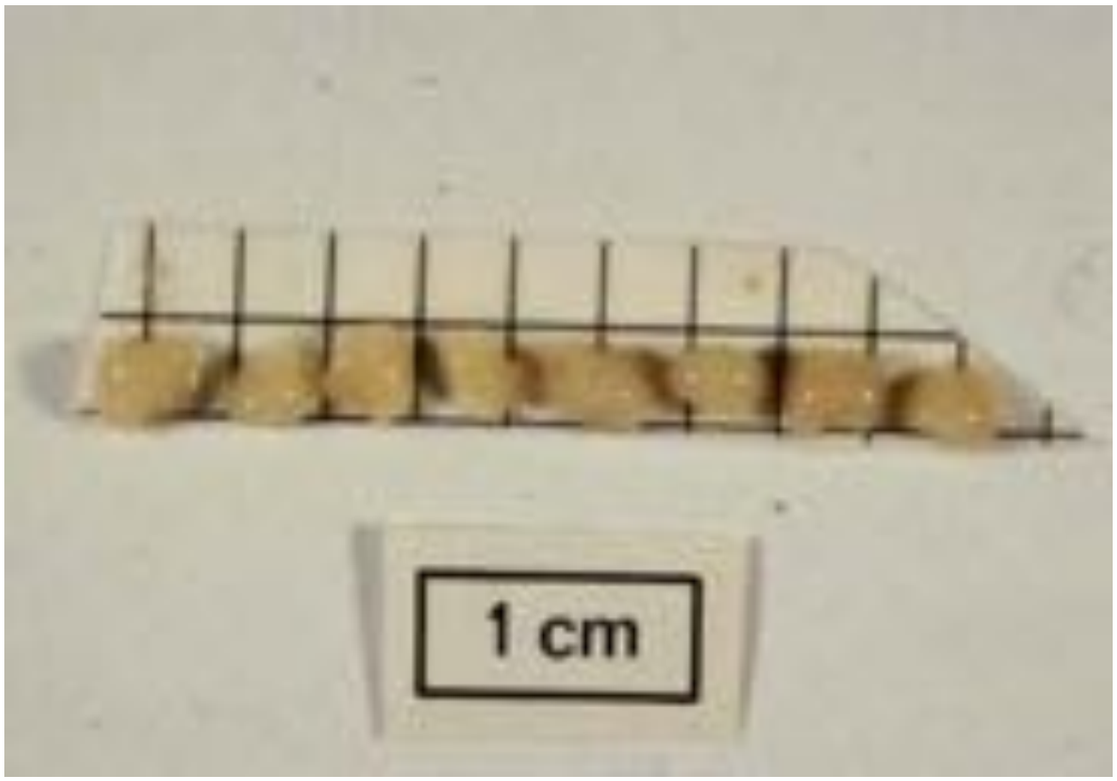


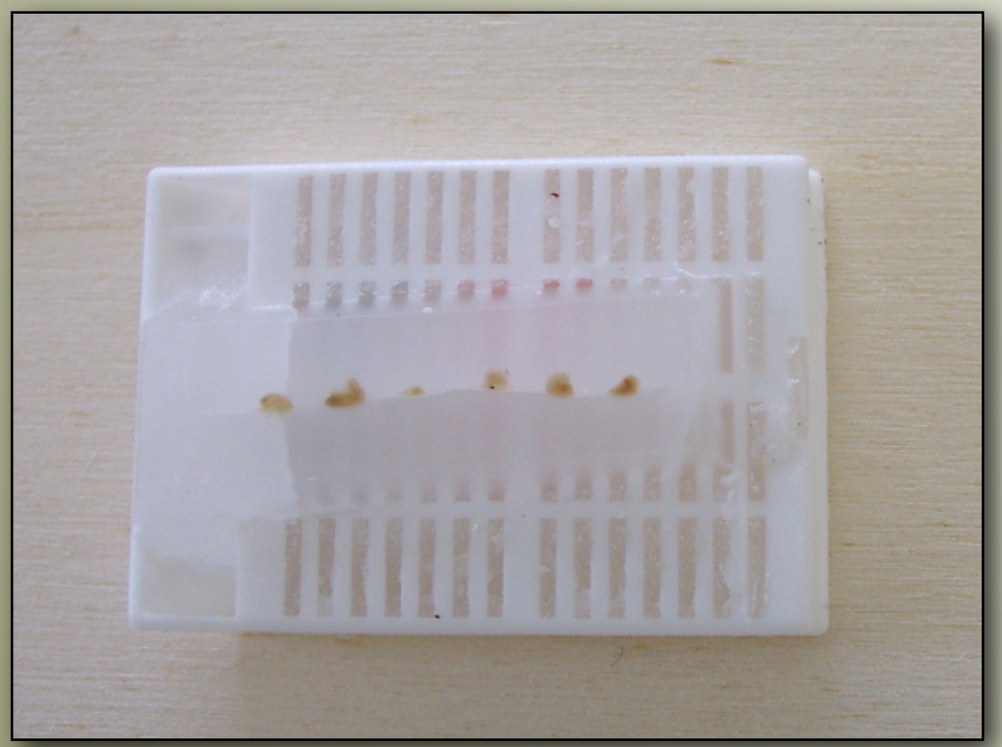




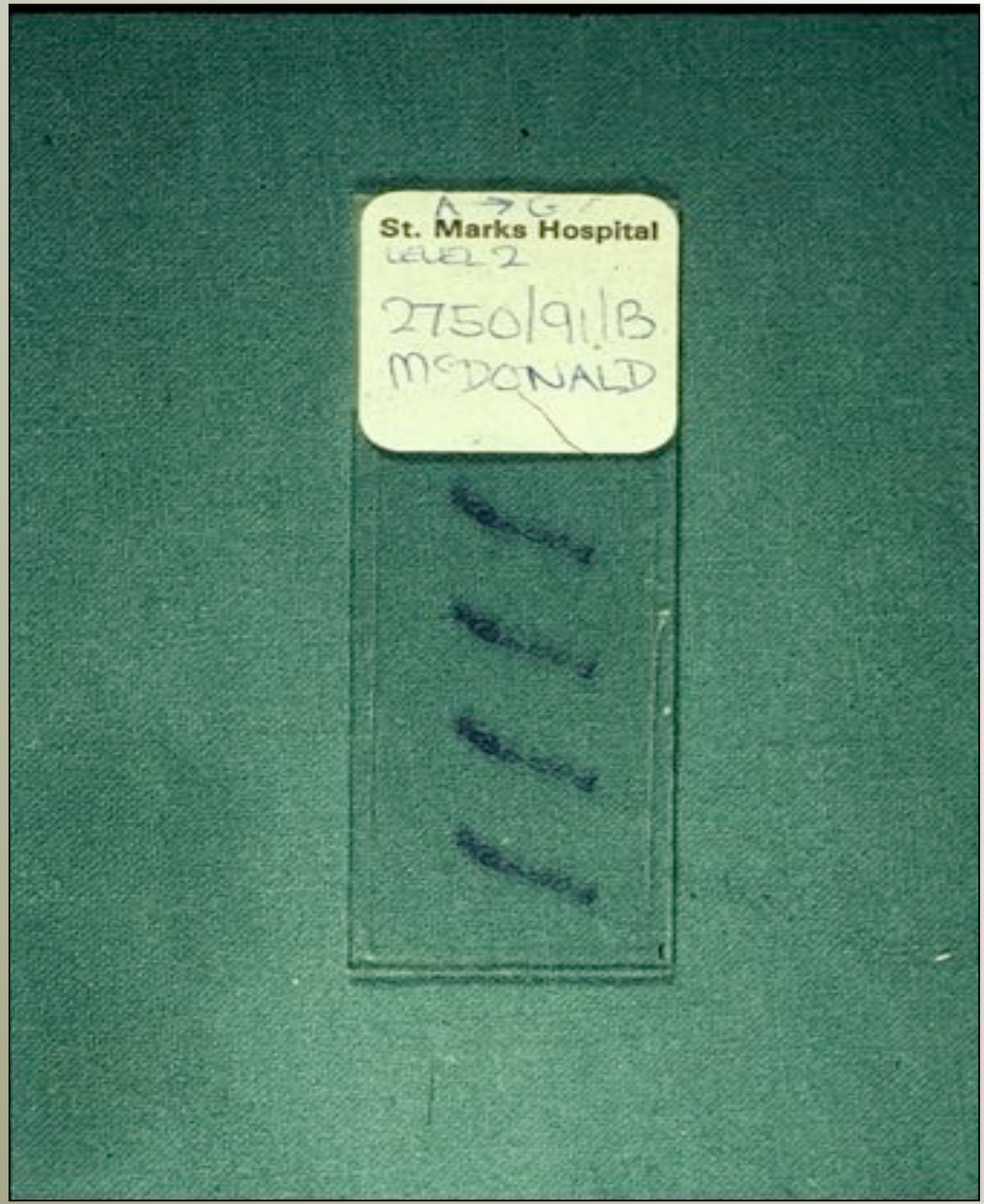




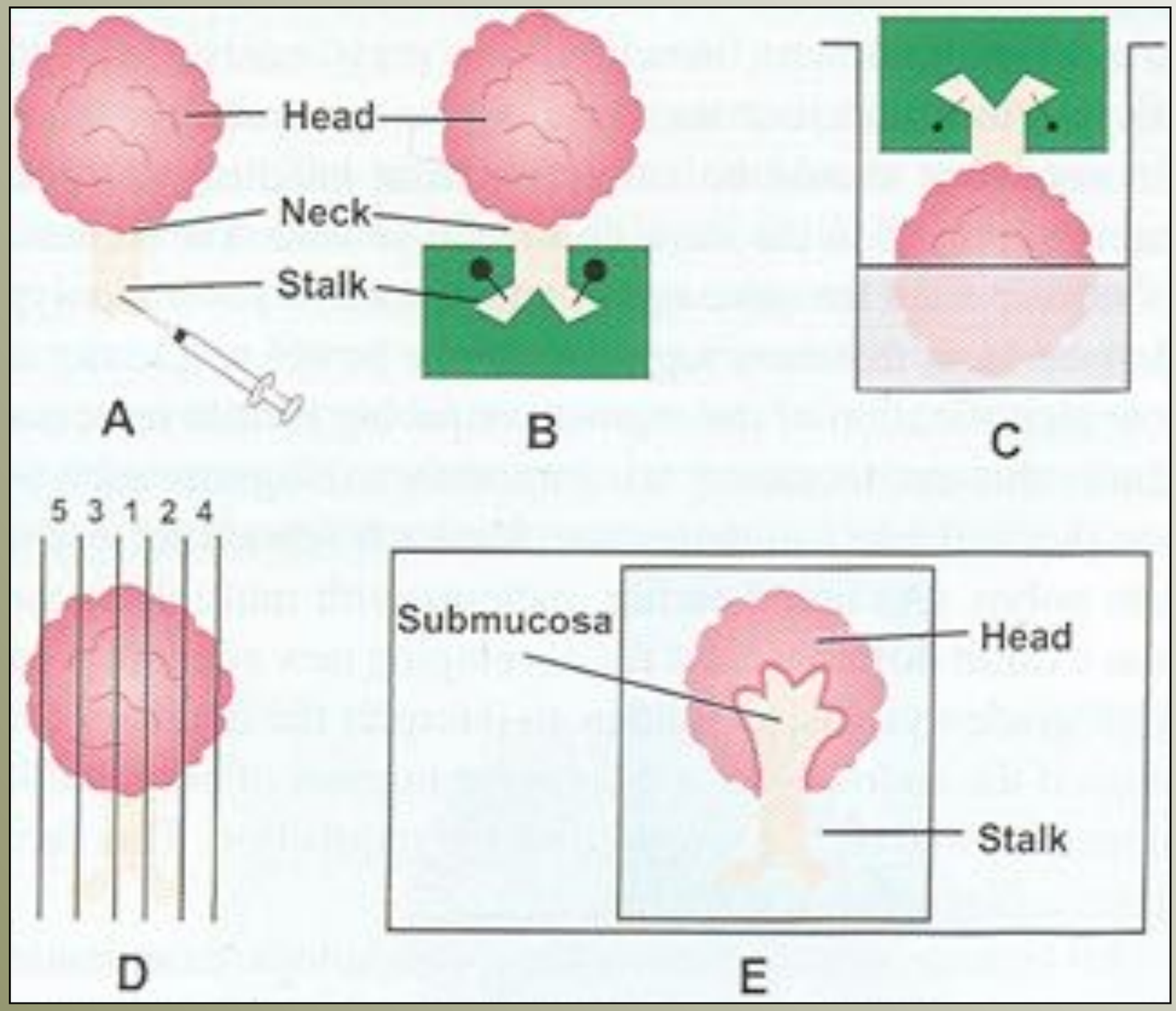

1 cm



L'immagine del vetrino è in onore del St.Mark's Hospital dove il Prof. Williams per primo propose il metodo



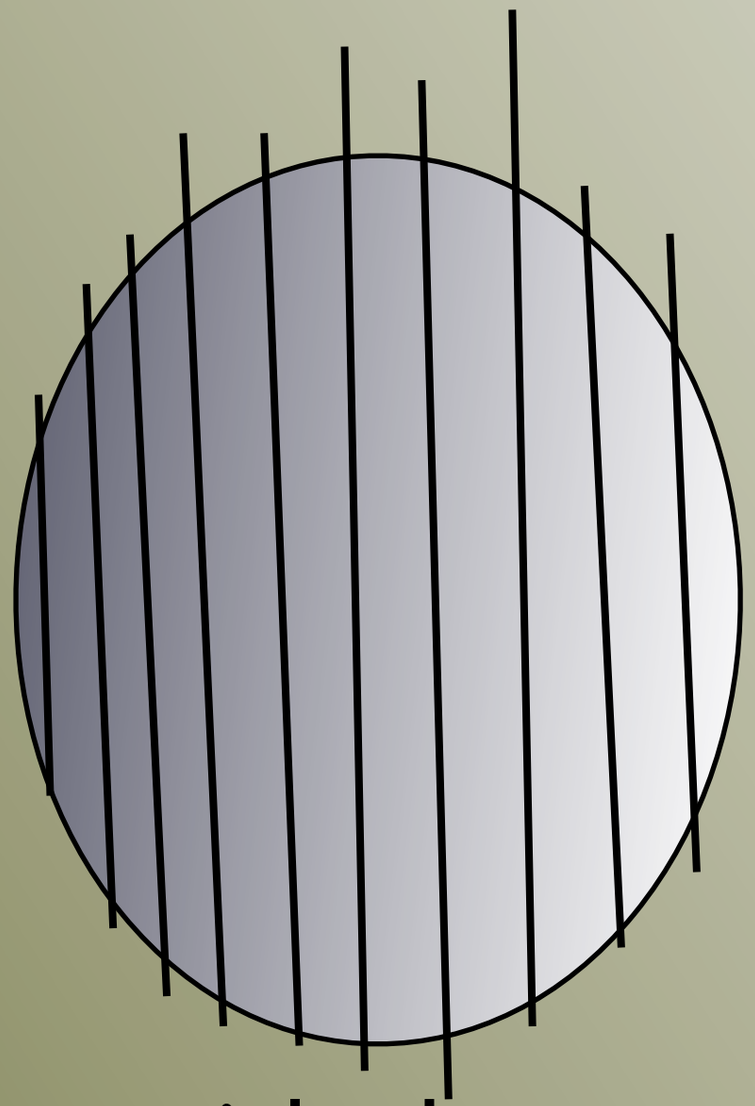
Polipo peduncolato : Modalità di prelievo



Fenoglio-Preiser "Gastro-Intestinal Pathology" 1999 pg 964

MUCOSECTOMIA

A

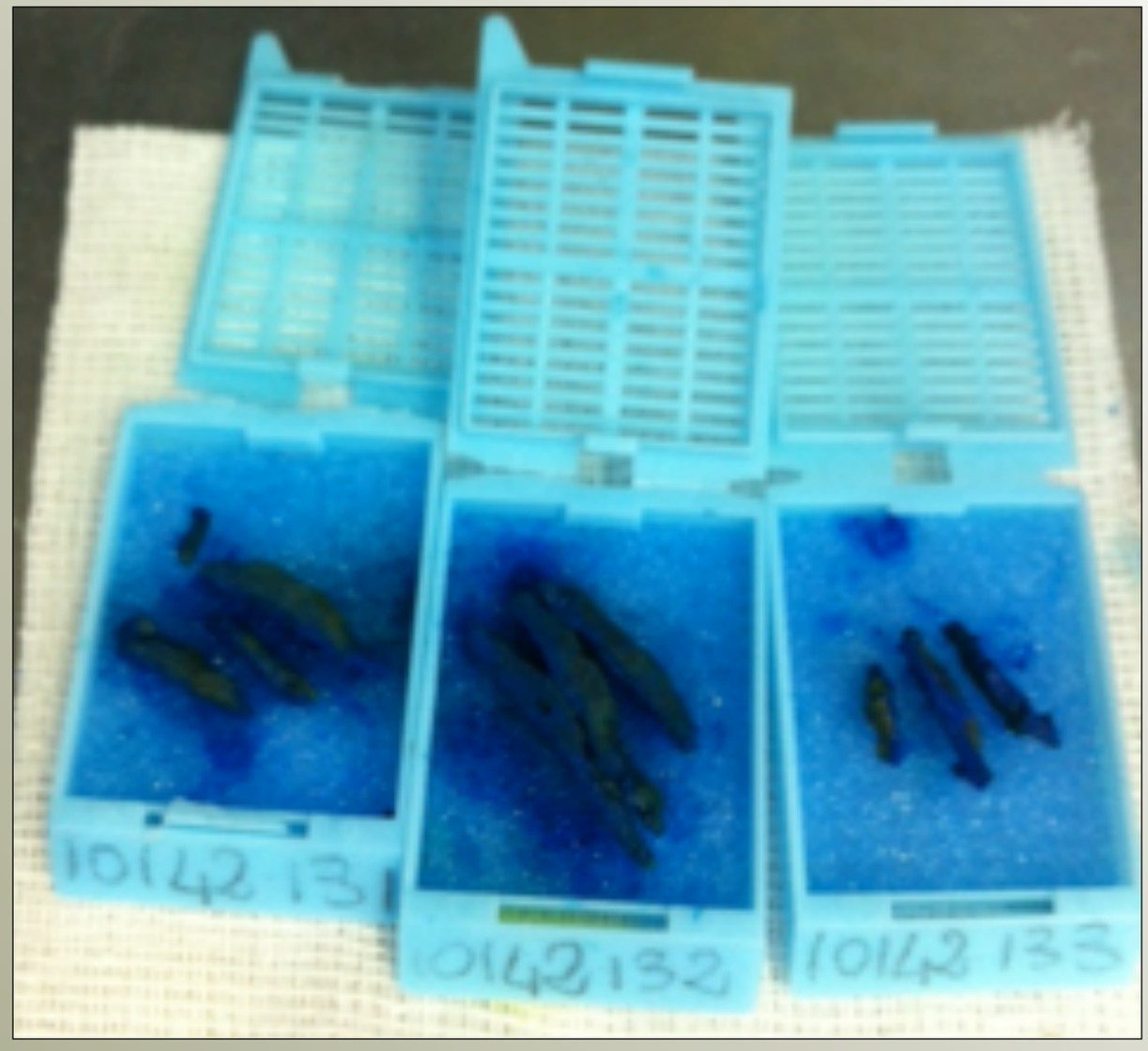


B

Il materiale da mucosectomia andrebbe fissato su un supporto in modo da evitare la coartazione del tessuto e permettere un corretto orientamento dei prelievi:

A longitudinali; B a “torta”

Mucosectomia con tagli longitudinali



Measurement of size of adenomas

Size (largest diameter) is an important objective measurement best performed by the pathologist (Schoen, Gerber & Margulies 1997) **from the slide**, as is recommended in the EU Guidelines for breast cancer screening (EC Working Group on Breast Screening Pathology 2006).

If the lesion is too large for the maximum dimension to be measured by this method, because it cannot be represented on a single slide, the measurements taken at the time of specimen dissection should be used.

If a biopsy is received or the specimen is fragmented it should be stated that it cannot be accurately assessed for size by the pathologist and the endoscopy measurements should be used.

Measurements should exclude the stalk if it is composed of normal mucosa however the distance to the excision margin should be noted.

TIPI PRINCIPALI DI ADENOMI

Introduction

Classification of lesions in the adenoma- carcinoma sequence

- A colorectal adenoma is defined as a lesion in the colon or rectum containing unequivocal epithelial neoplasia.

- Classification of adenomas should include grading of neoplasia according to the revised Vienna classification that has been modified for the European Guidelines to obtain a two-tiered system of low-grade and high-grade neoplasia

- This modified grading system aims to minimise intra- and inter-observer variation and facilitate management of endoscopically detected lesions by improving correlation between histopathology of biopsies and resection specimens (Tominaga et al. 2009)

- The two-tiered grading of mucosal colorectal neoplasia recommended in the European Guidelinesis based on the revised Vienna Classification that has improved diagnostic reproducibility, particularly for non-polypoid lesions

(Schlemper et al. 2000; Schlemper, Kato & Stolte 2001; Dixon 2002; Stolte 2003; Suzuki et al. 2006)

Classification of lesions in adenoma-carcinoma sequence

Classically, adenomas are divided into :

- tubular,
- villous
- tubulo-villous types and demarcation between the three is based on the relative proportions of tubular and villous components, according to the "20% rule" described in the WHO classification of tumours in the digestive tract

- Non polypoid adenomas: lesions referred as "flat adenoma", included in Paris classification and measuring less than mm 3 in height

(WHO 2000)

Non Polypoid Adenomas

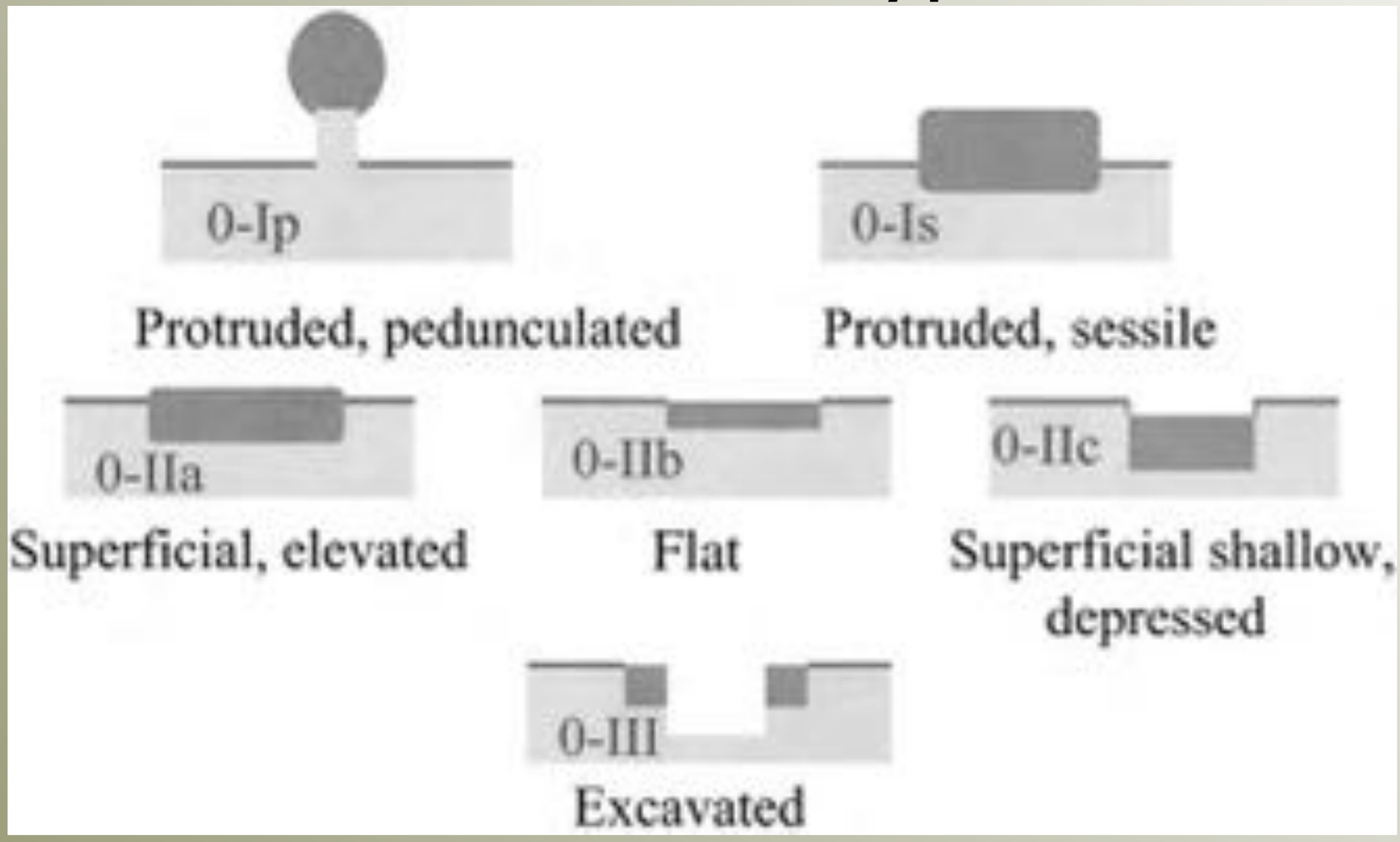
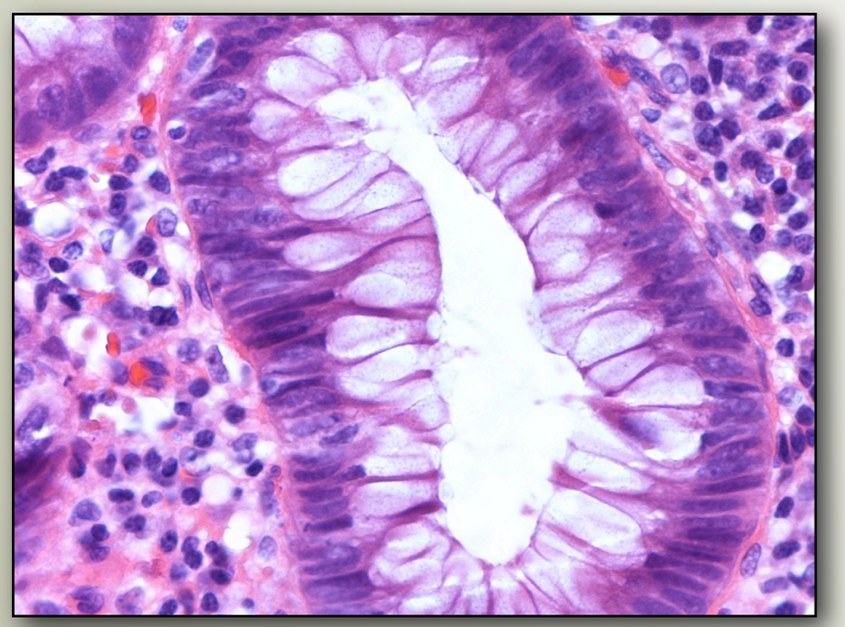


Diagram 1. Schematic representation of the major variants of *type 0* neoplastic lesions of the digestive tract: polypoid *(Ip and Is)*, non-polypoid *(IIa, IIb, and II c)*, non-polypoid and excavated *(III)*. Terminology as proposed in a consensus macroscopic description of superficial neoplastic lesions.[15]

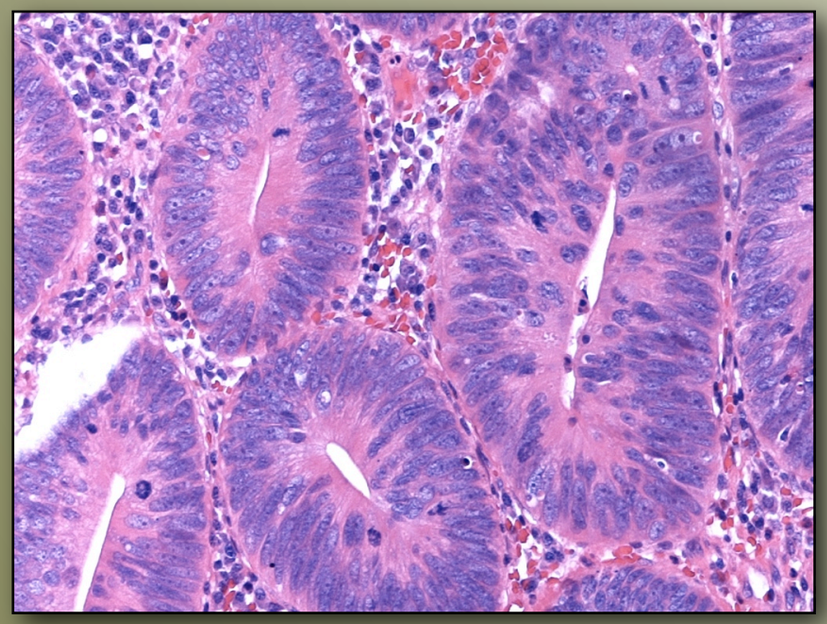
The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon
November 30 to December 1 , 2002

VOLUME 58, NO. 6 (SUPPL), 2003 GASTROINTESTINAL ENDOSCOPY

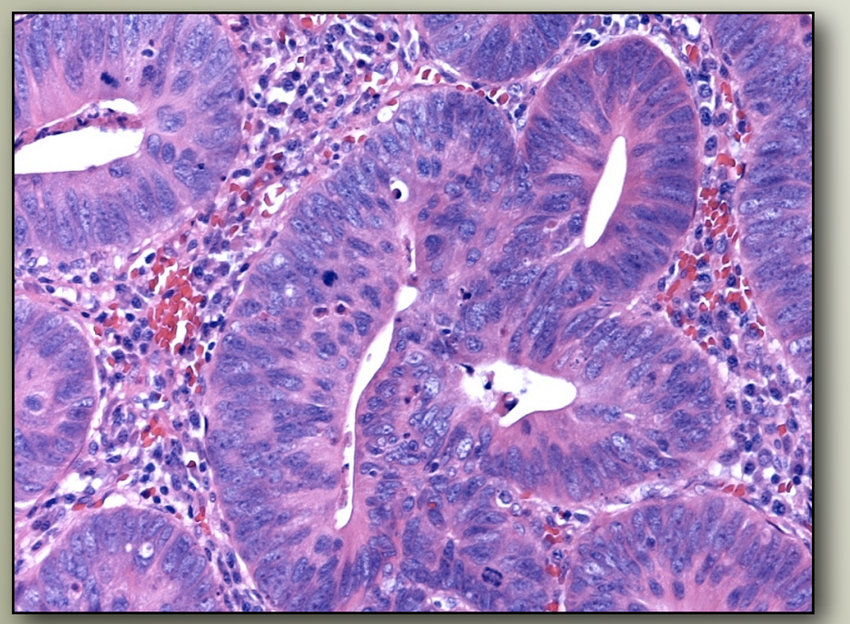
Tubular adenoma



Displasia Lieve

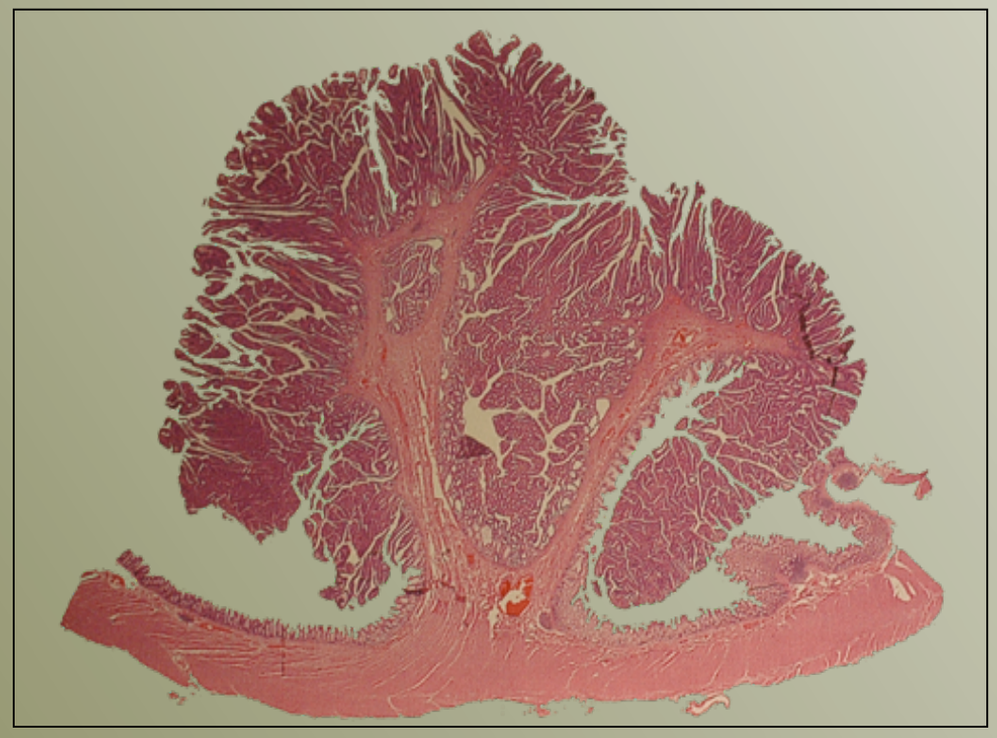


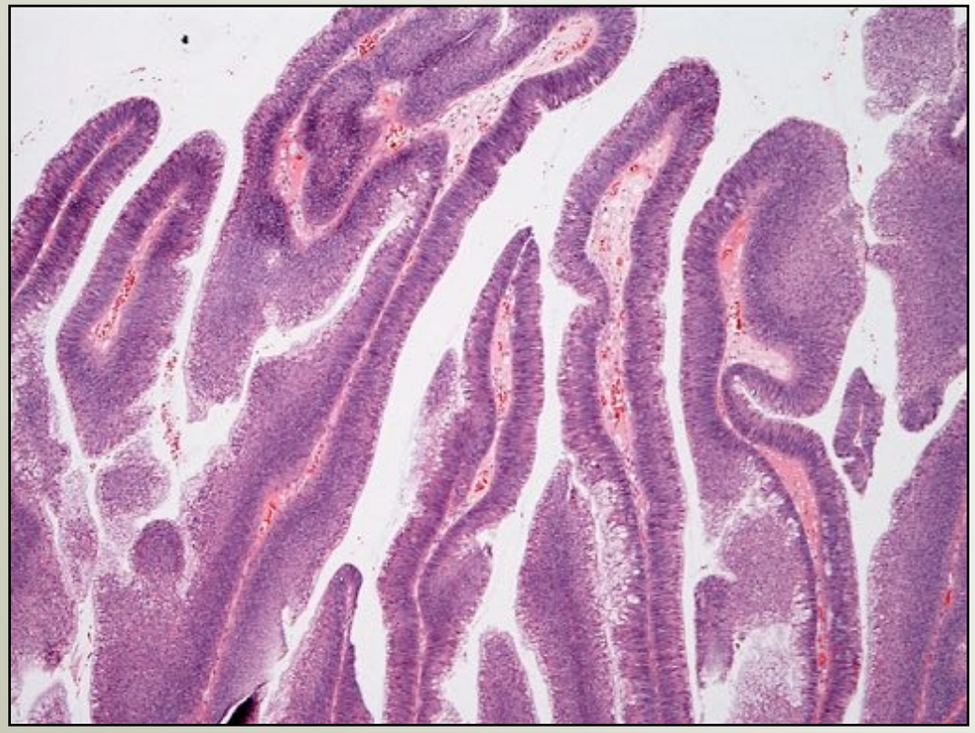
Displasia moderata



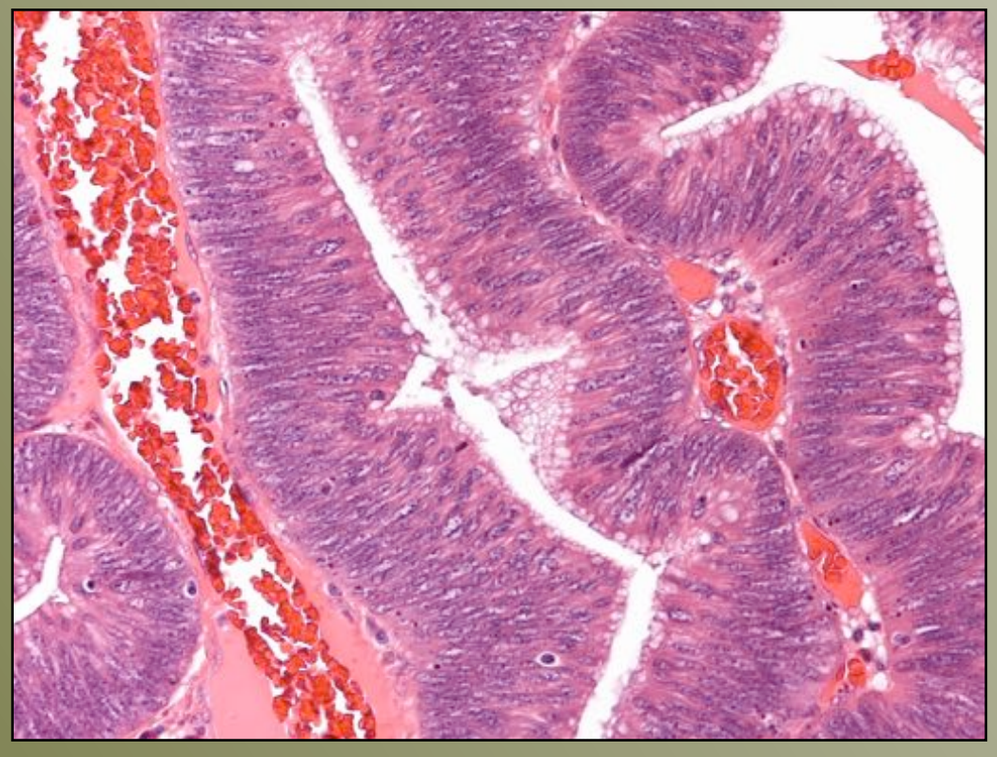
Displasia grave

Villous Adenoma

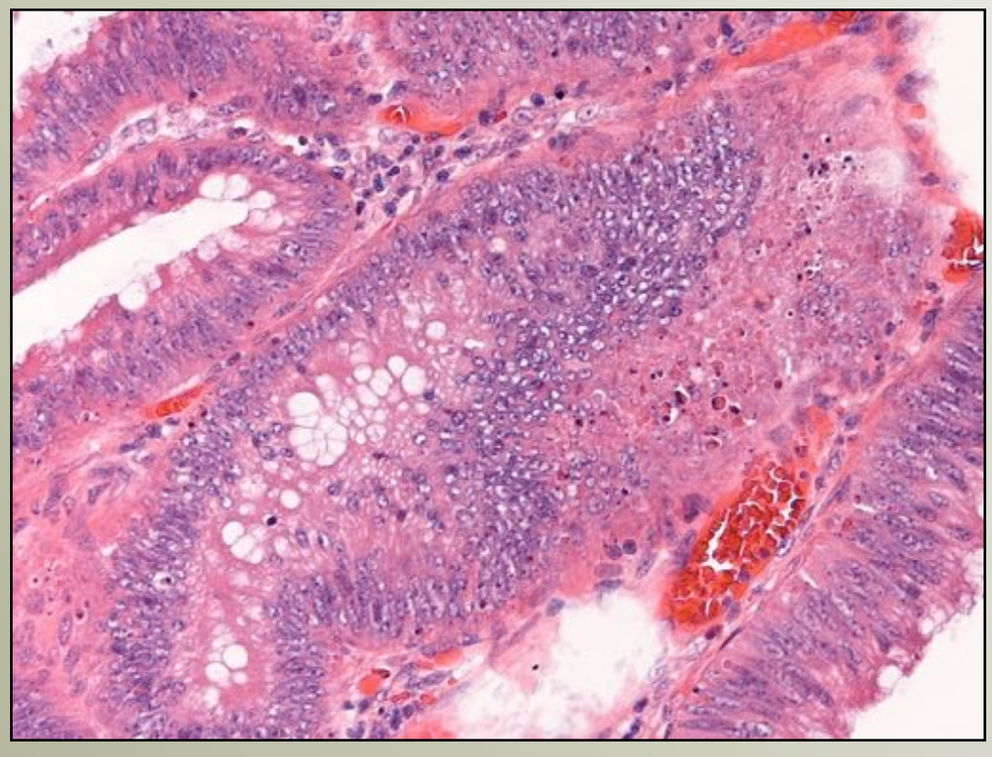




Low grade

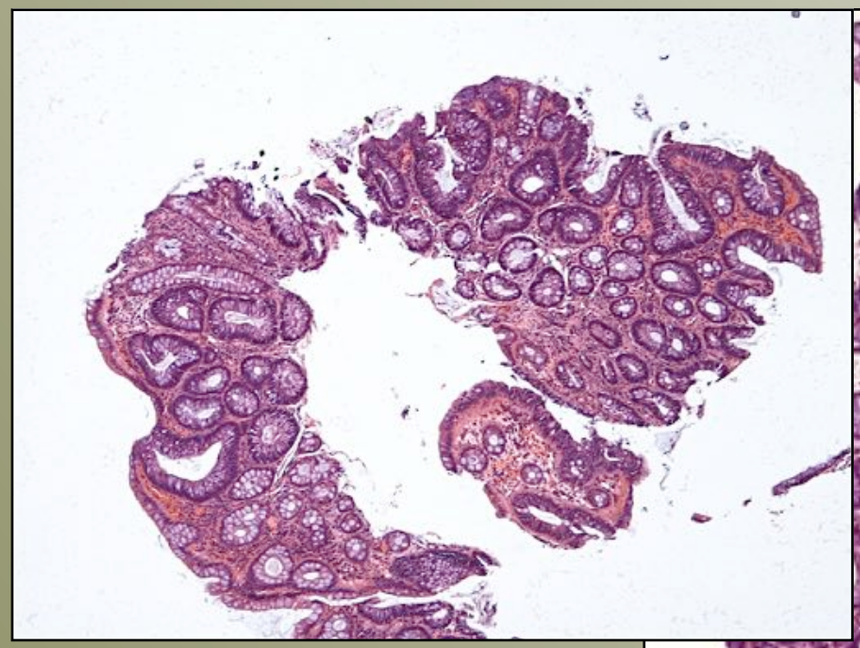


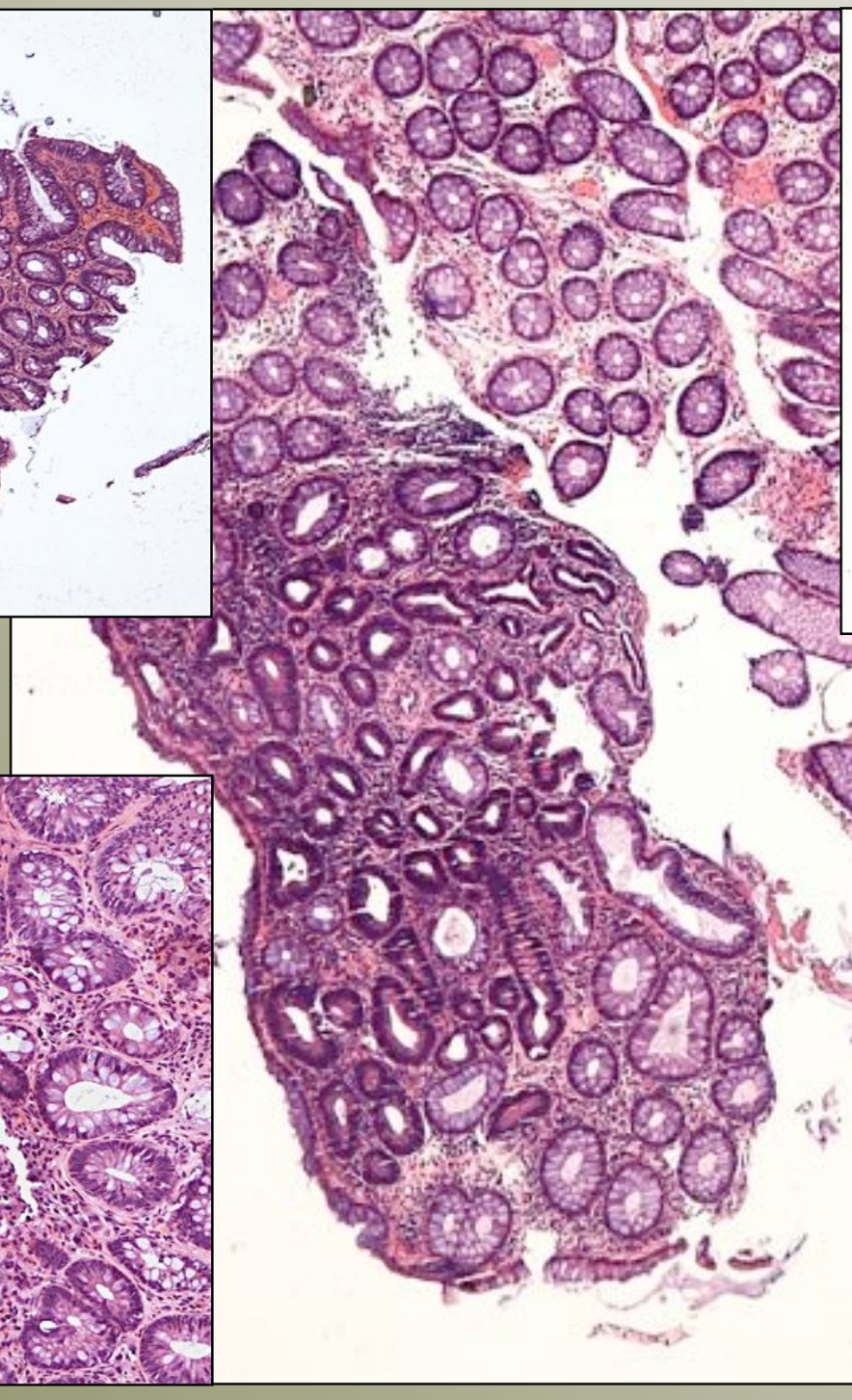
Low grade

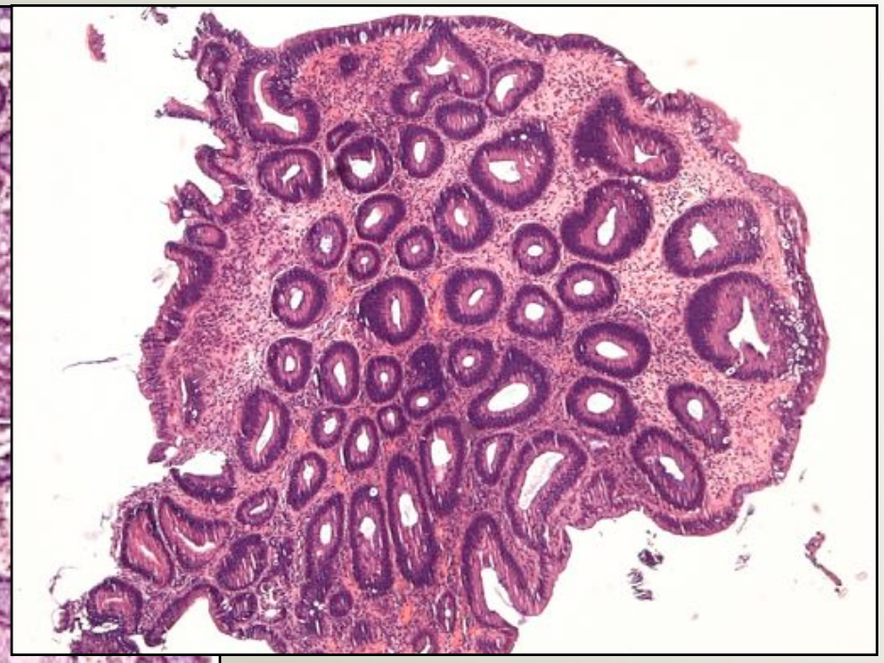


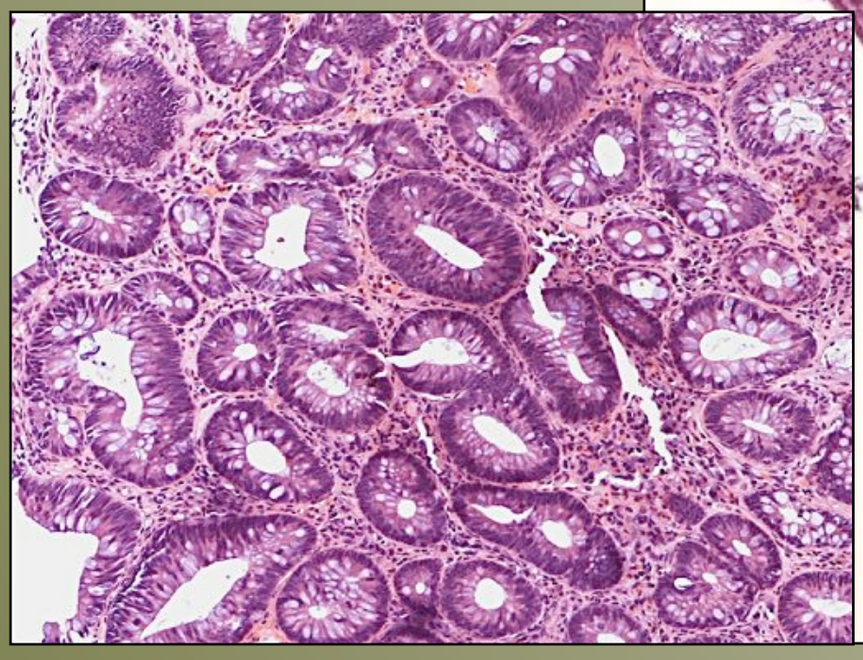
High grade

Non Polypoid (micro)Adenoma









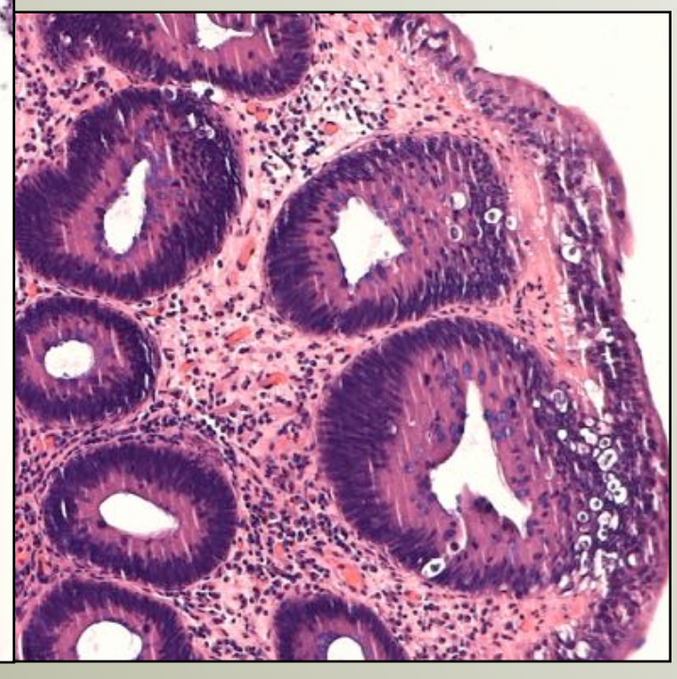


Table 1 Vienna classification of gastrointestinal epithelial neoplasia

Category 1	Negative for neoplasia/dysplasia
Category 2	Indefinite for neoplasia/dysplasia
Category 3	Non-invasive low grade neoplasia (low grade adenoma/dysplasia)
Category 4	Non-invasive high grade neoplasia
	4.1 High grade adenoma/dysplasia
	4.2 Non-invasive carcinoma (carcinoma in situ)*
	4.3 Suspicion of invasive carcinoma
Category 5	Invasive neoplasia
	5.1 Intramucosal carcinoma†
	5.2 Submucosal carcinoma or beyond

*Non-invasive indicates absence of evident invasion.
†Intramucosal indicates invasion into the lamina propria or muscularis mucosae.

Gut 2000;47:251–255

Table 7.1: Adaptation of the revised Vienna classification[1] for colorectal cancer screening

1. NO NEOPLASIA:[2]
Vienna Category 1 (Negative for neoplasia)

2. MUCOSAL LOW GRADE NEOPLASIA:
Vienna Category 3 (Mucosal low-grade neoplasia
Low-grade adenoma
Low-grade dysplasia);
Other common terminology
mild and moderate dysplasia;
WHO: low-grade intra-epithelial neoplasia

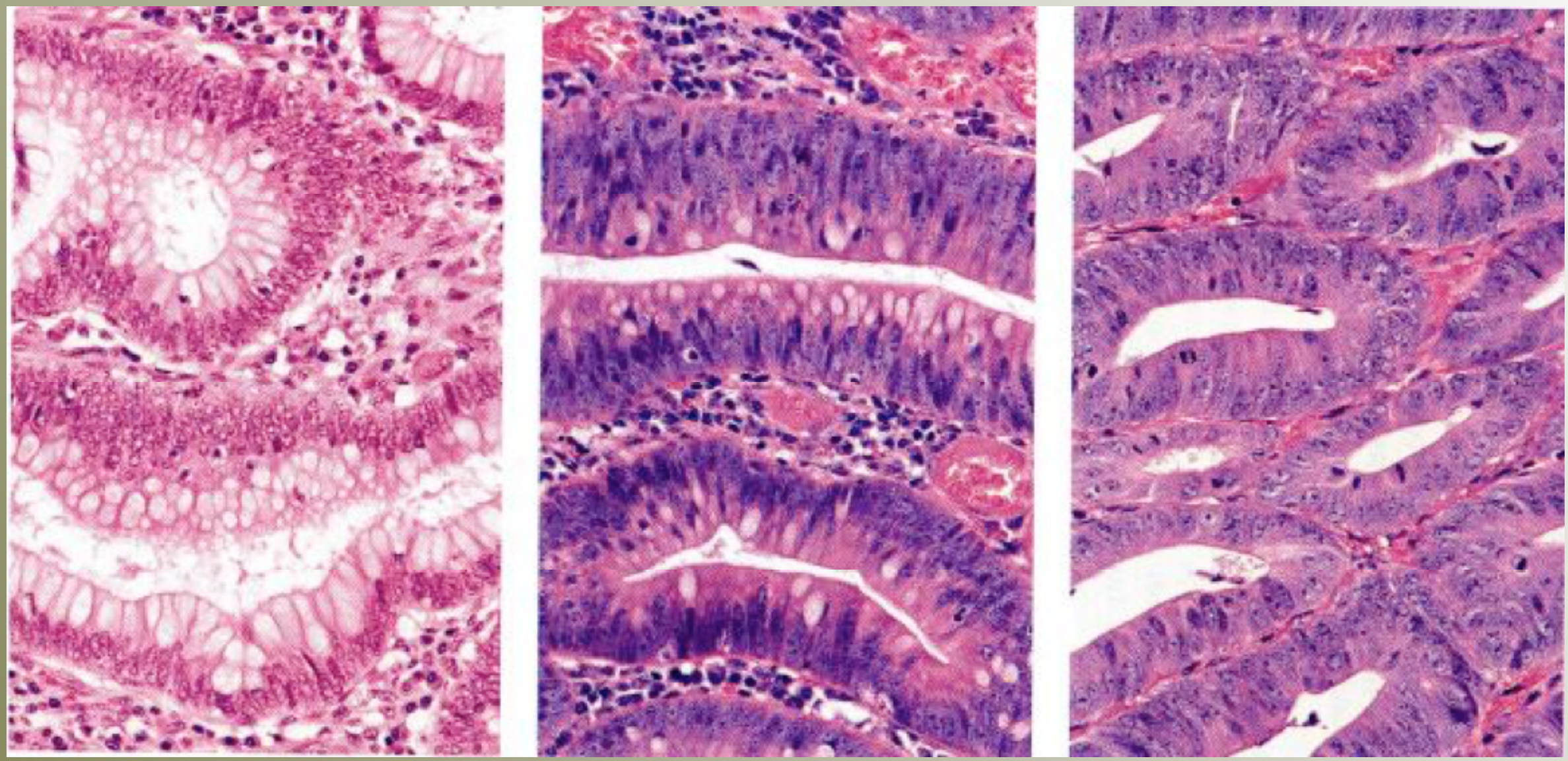
3. MUCOSAL HIGH GRADE NEOPLASIA:
Vienna: Category 4.1–4.4 (Mucosal high grade neoplasia
High-grade adenoma/dysplasia
Non-invasive carcinoma (carcinoma *in situ*)
Suspicious for invasive carcinoma
Intramucosal carcinoma);
Other common terminology
severe dysplasia;
high-grade intraepithelial neoplasia;
WHO: high-grade intraepithelial neoplasia
TNM: pTis

4. CARCINOMA invading the submucosa or beyond:
4a. Carcinoma confined to submucosa
Vienna: Category 5 (Submucosal invasion by carcinoma);
TNM: pT1
4b. Carcinoma beyond submucosa
TNM: pT2-T4

[1] For revised Vienna classification see Dixon (2002), for WHO classification see WHO (2000), for TNM see (TNM classification of malignant tumours, 5th edition 1997; TNM Classification of malignant tumours, 6th edition 2002; TNM Classification of Malignant Tumours, 7th edition 2009).

[2] Category 2 of the Vienna Classification (indefinite) is not recommended for screening.

Aspetto istologico della displasia (sec. Morson)



lieve moderata grave

Basso grado sec. WHO Alto grado sec. WHO

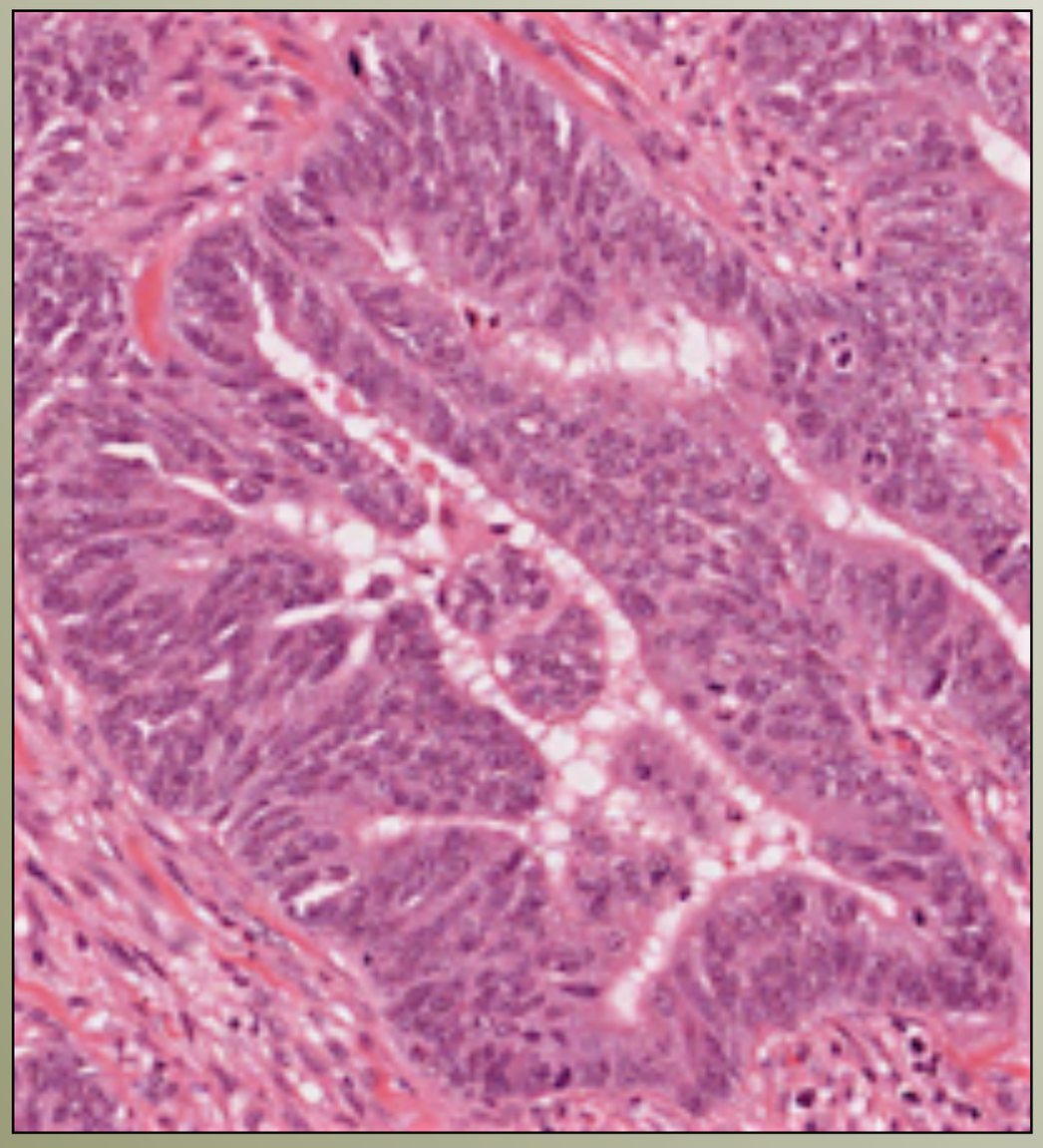
High grade /Carcinoma in situ

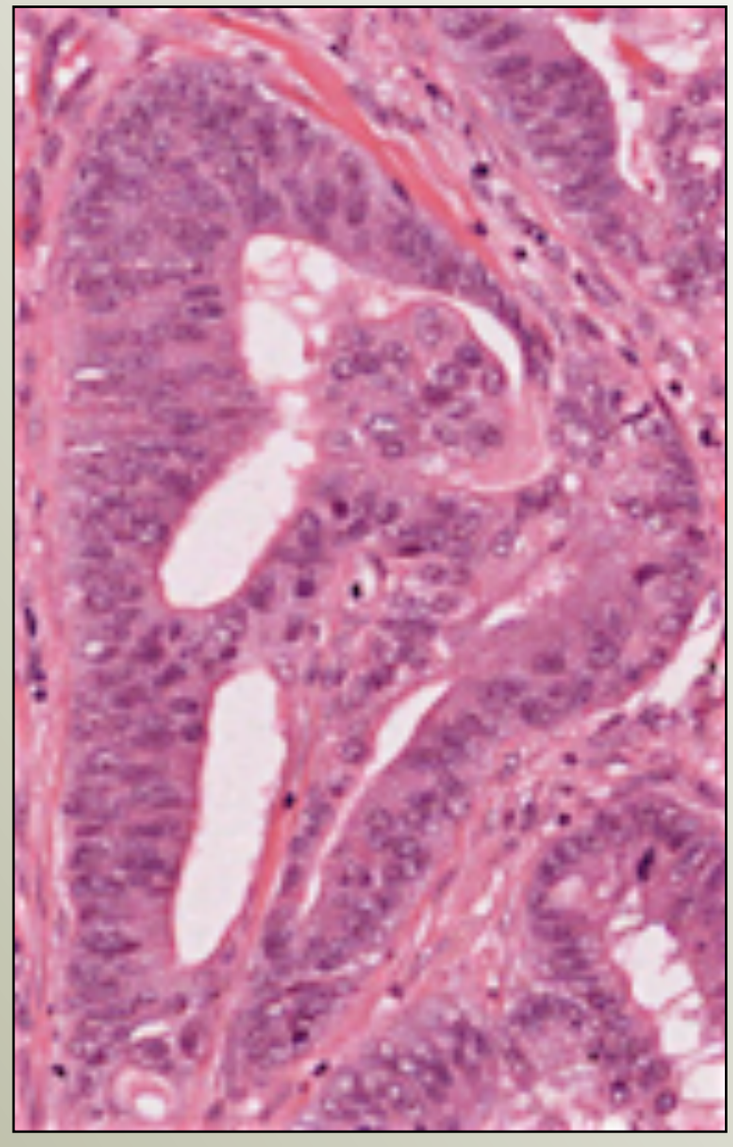
The changes of high-grade neoplasia should involve more than just one or two glands

Caution should be exercised in over-interpreting isolated surface changes that may be due to trauma, erosion or prolapse.

Structural features:

- Complex glandular crowding
- Cribriform appearance and "back to back" glands
- prominent intraluminal papillary tufting
- Prominent glandular budding





LESIONI SERRATE

- These lesions have in common a serrated morphology, but depending on other characteristics, the potential to develop into invasive adenocarcinoma differs considerably. **In the last ten years this lesion received much focus and its role in serrated neoplasia pathway(s) is well established ***

1. **hyperplastic polyp**, which although relatively common, has no implications for the screening programme unless very numerous, proximally located or of a large size (<10 mm)
2. **sessile serrated lesions** (sometimes referred to as sessile serrated polyps/**sessile serrated adenomas**)

3.traditional serrated adenomas

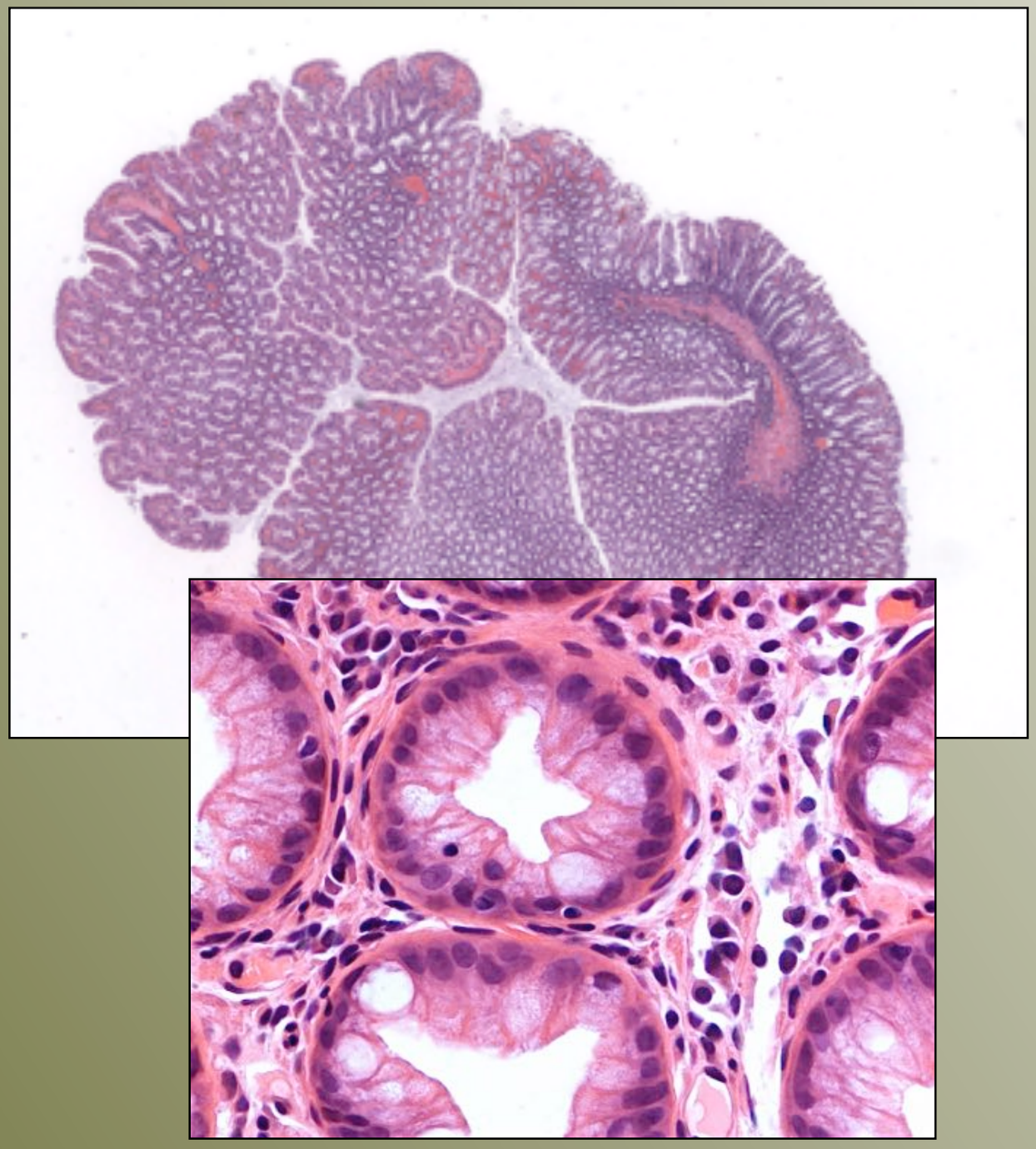
4.mixed lesions/mixed polyps

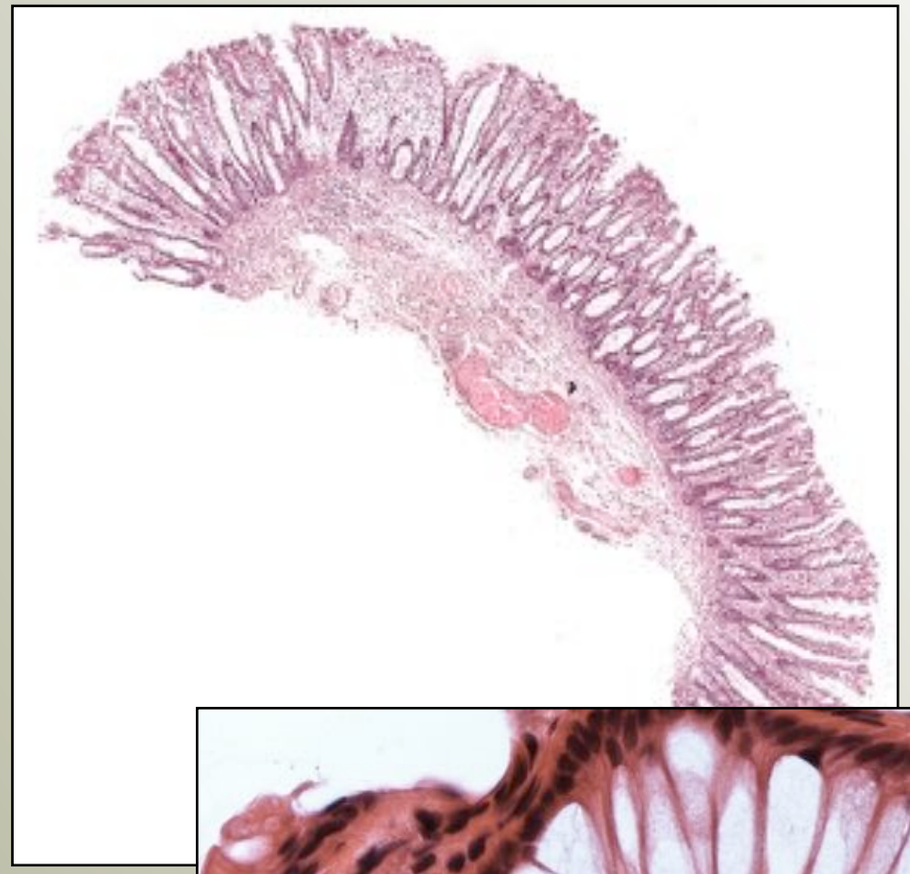
*** Pathol Res Pract 2011 207(7) 410-6**

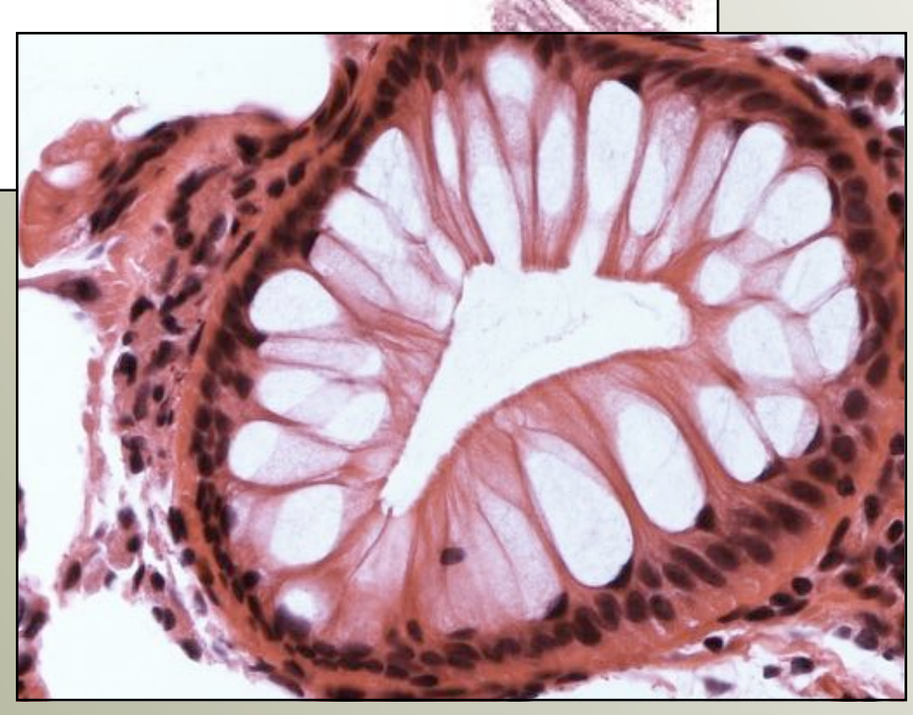
1. Hyperplastic (metaplastic) polyp

- Hyperplastic polyps (HPs) are often small lesions (<5 mm in diameter), frequently found in the left (distal) colon.
- Hyperplastic polyps comprise about 90% of all polyps and are benign protrusions. They are usually less than 0.5 cm in diameter. Hyperplastic polyps most commonly occur in the rectosigmoid region during adulthood.
- They are composed of simple elongated crypts with a serrated structure in the upper half.
- These polyps usually show some proliferation in the basal (non-serrated) part of the crypts (regular proliferation).
- Nuclei are small, regular and basally orientated. There is no hyperchromasia, and stratification of the upper half of the crypts has a serrated appearance without cytological atypia.
- Hyperplastic polyposis should be excluded in cases with giant hyperplastic polyps (>10 mm), or multiple hyperplastic polyps in the right colon, or in first-degree relatives of individuals with hyperplastic polyposis.
- MUC-6 negative respect Traditional Serrated Adenoma
- Three histological sub-types: microvescicular; goblet cell; mucin poor

Polipo iperplastico

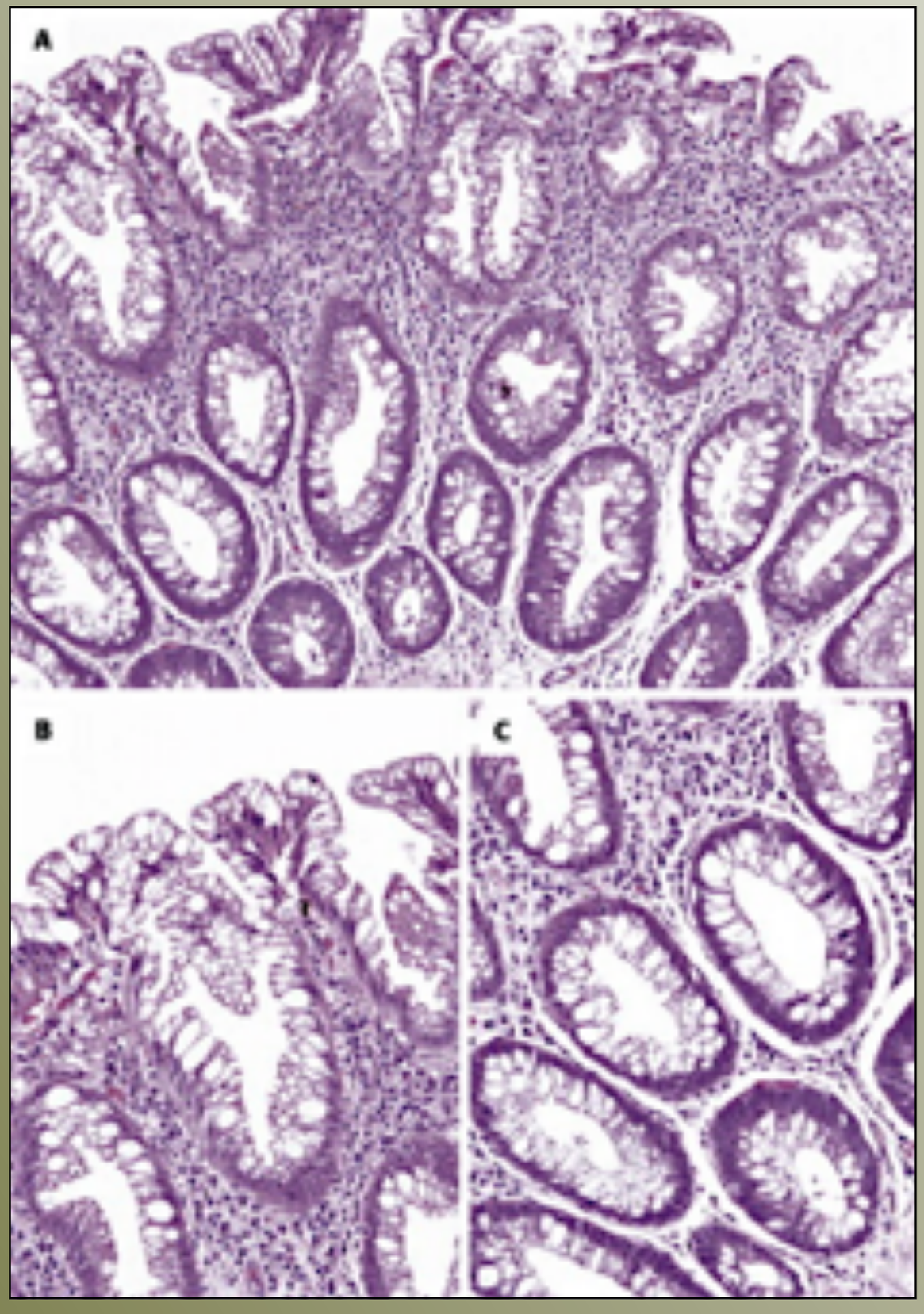




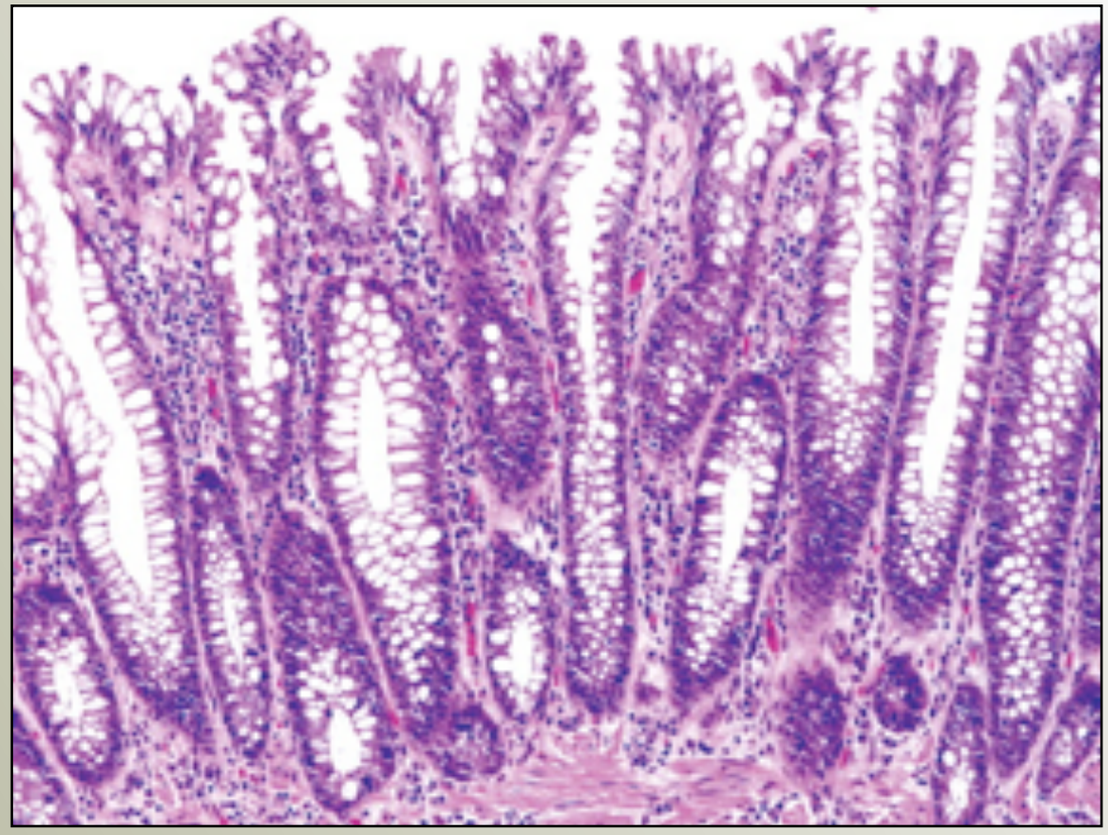


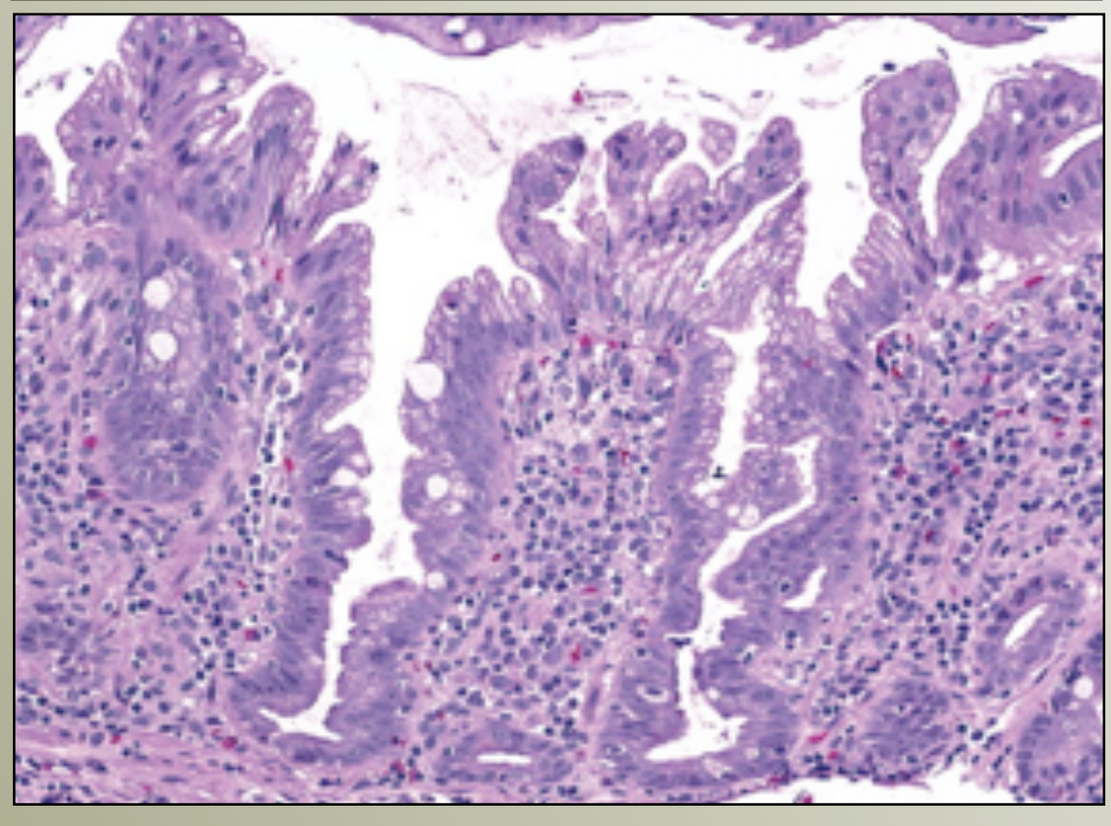
Aspetto a dente di sega; citoplasma eosinofilo; evidenza di orletto a spazzola; nuclei esenti da atipia

Polipo serrato microvescicolare



Polipo serrato goblet cell

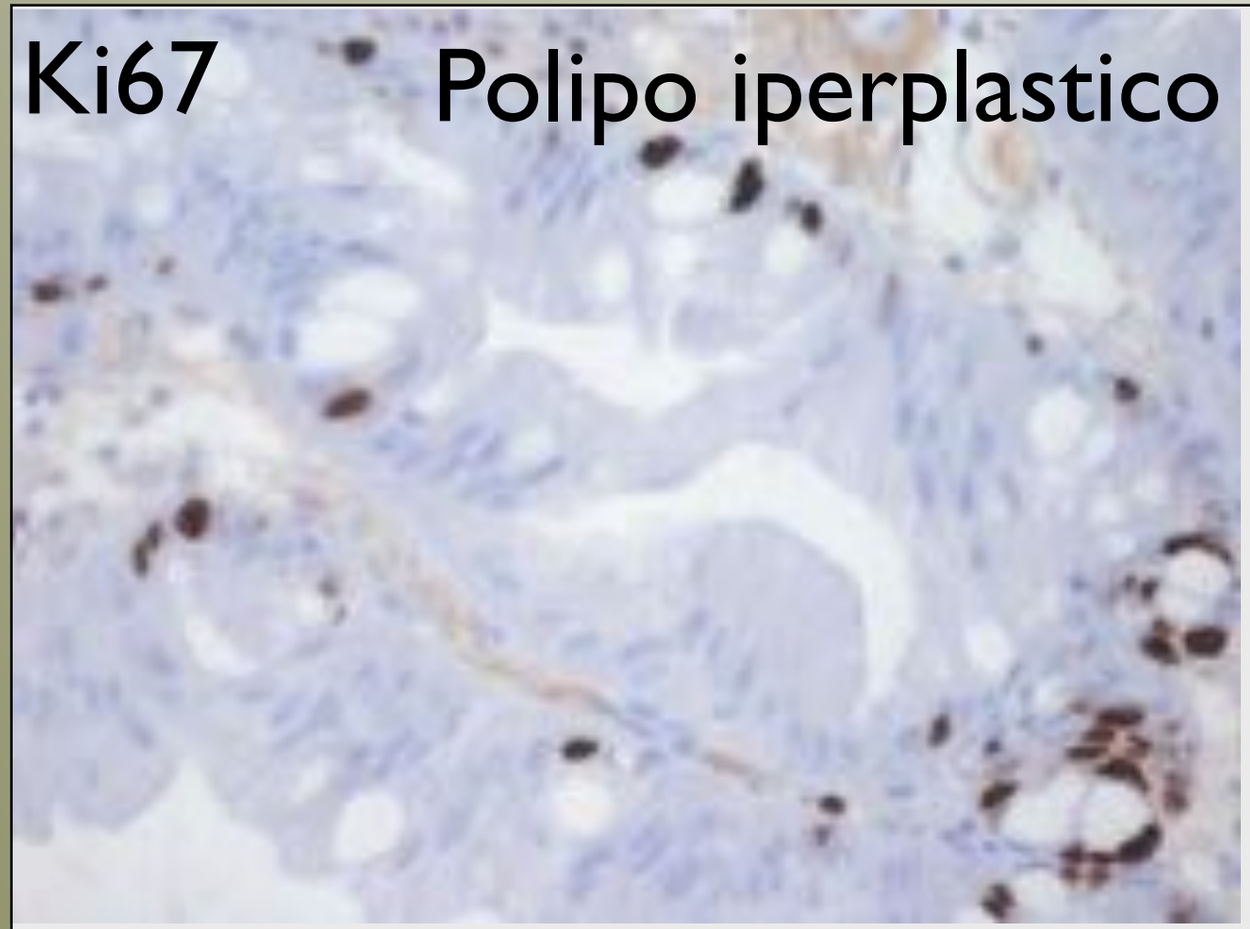




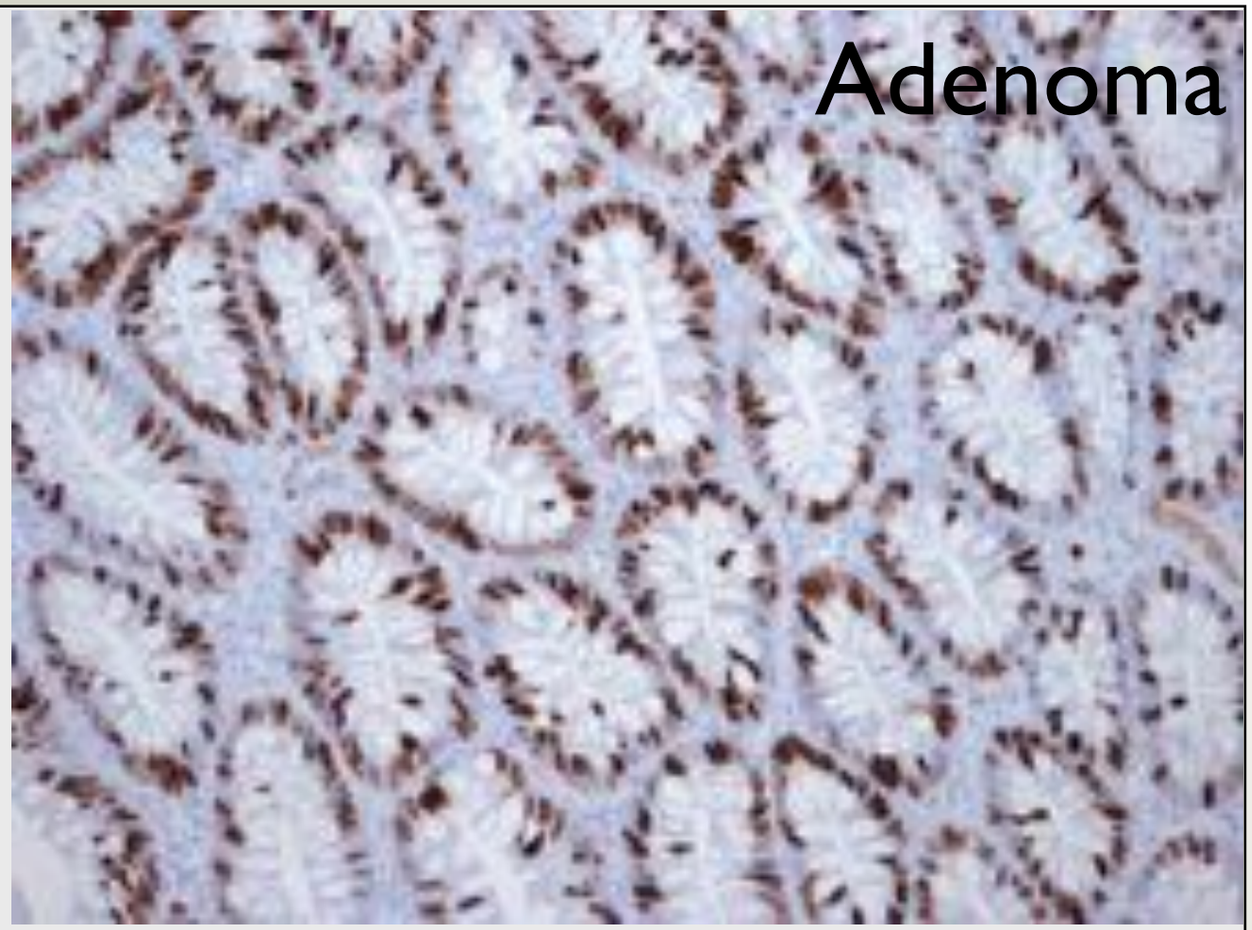
Polipo serrato mucin poor

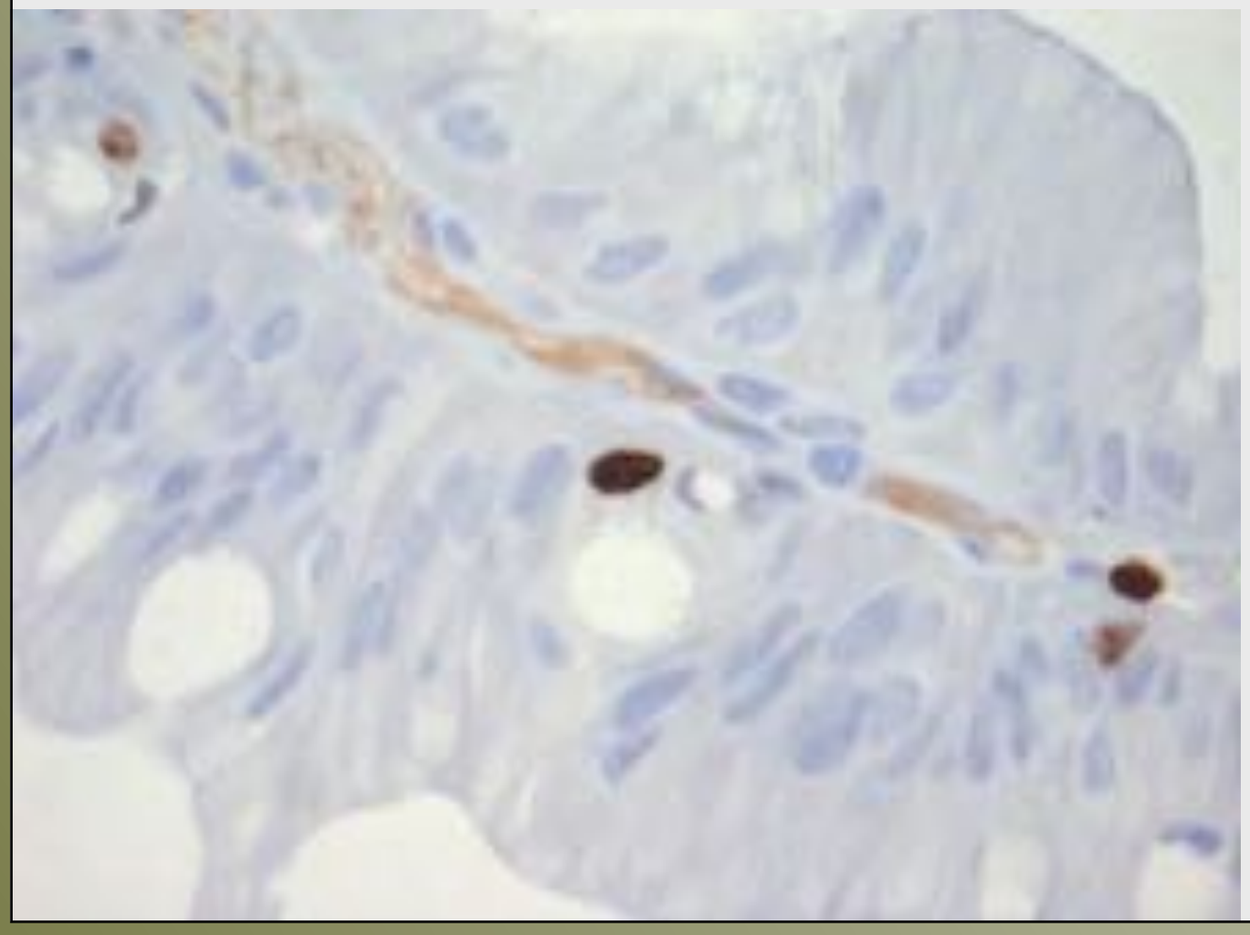
Ki67

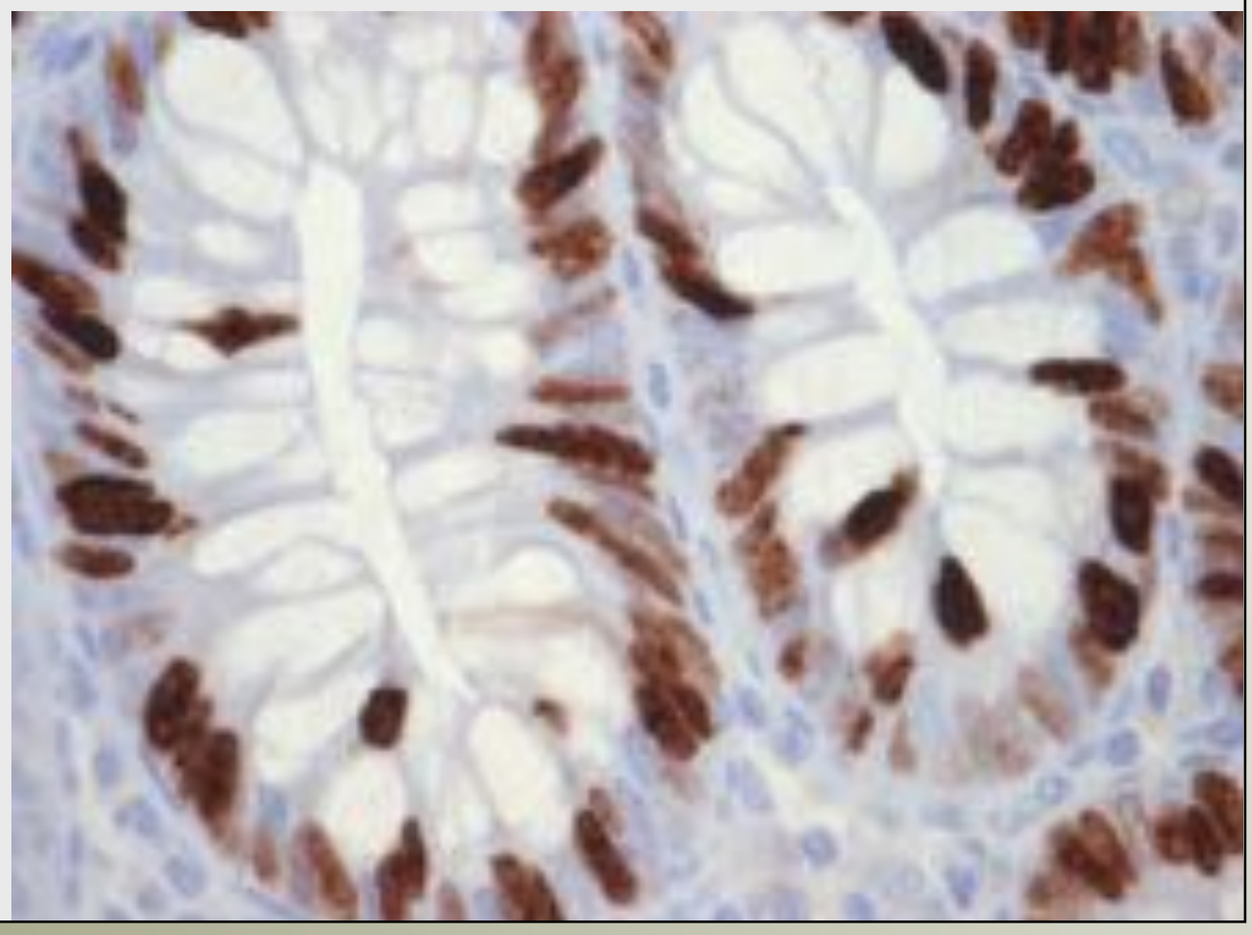
Polipo iperplastico



Adenoma







SESSILE SERRATED LESION

Sessile serrated lesions are described in the literature as "**sessile serrated adenoma**" and are often found in the right colon. This is a **misnomer since sessile serrated lesions do not contain adenomatous changes** (Higuchi & Jass 2004; Kudo et al. 2008; Lambert et al. 2009).

To date, four synonymously used terms exist for these lesions: sessile serrated adenoma (Torlakovic & Snover 1996), superficial serrated adenoma (Oka et al. 2004), Type 1 serrated adenoma (Jaramillo, Tamura & Mitomi 2005), and serrated polyp with abnormal proliferation (Torlakovic et al. 2003).

We recommend using only the term sessile serrated lesion and avoiding use of any other terms for this entity. This recommendation is given in full awareness that sessile serrated lesions do not show histological signs of an adenoma, but, like adenomas, they should be excised if detected during an endoscopic examination. Currently even in the hands of expert GI pathologists the agreement on the sub-types of serrated lesions is only moderate (Wong et al. 2009).

The vast majority of SSLs will **not** progress to adenocarcinoma. Histological criteria of these sessile, usually larger lesions include an abnormal proliferation zone with structural distortion, usually most pronounced in dilatation of the crypts, particularly near the base. Abundant mucus production is usually also observed as pools of mucin in the lumen of the crypts and on the surface of the mucosa.

SSLs are found mainly in the right colon and may be misdiagnosed as hyperplastic polyps.

Clues to the correct diagnosis include location (right colon)and large size (>3cm).

Cytological signs of "neoplasia" are lacking, but structural abnormalities are present, i.e. glandular branching (Higuchi & Jass 2004).In about 5,8% near cancer are serrated lesions.

Sessile serrated lesions have an elevated serration index and serration in the basal half of crypts with basal dilation of crypts.

There is crypt branching with horizontal growth (above muscularis mucosae; e.g. T- and L-shaped glands) and often pseudoinvasion into the submucosal layer, rectangular dilation of whole crypts with and without presence of mucus, increased number of goblet cells at the base of the crypts, vesicular nuclei with prominent nucleoli and proliferation zone in the middle of the crypts.

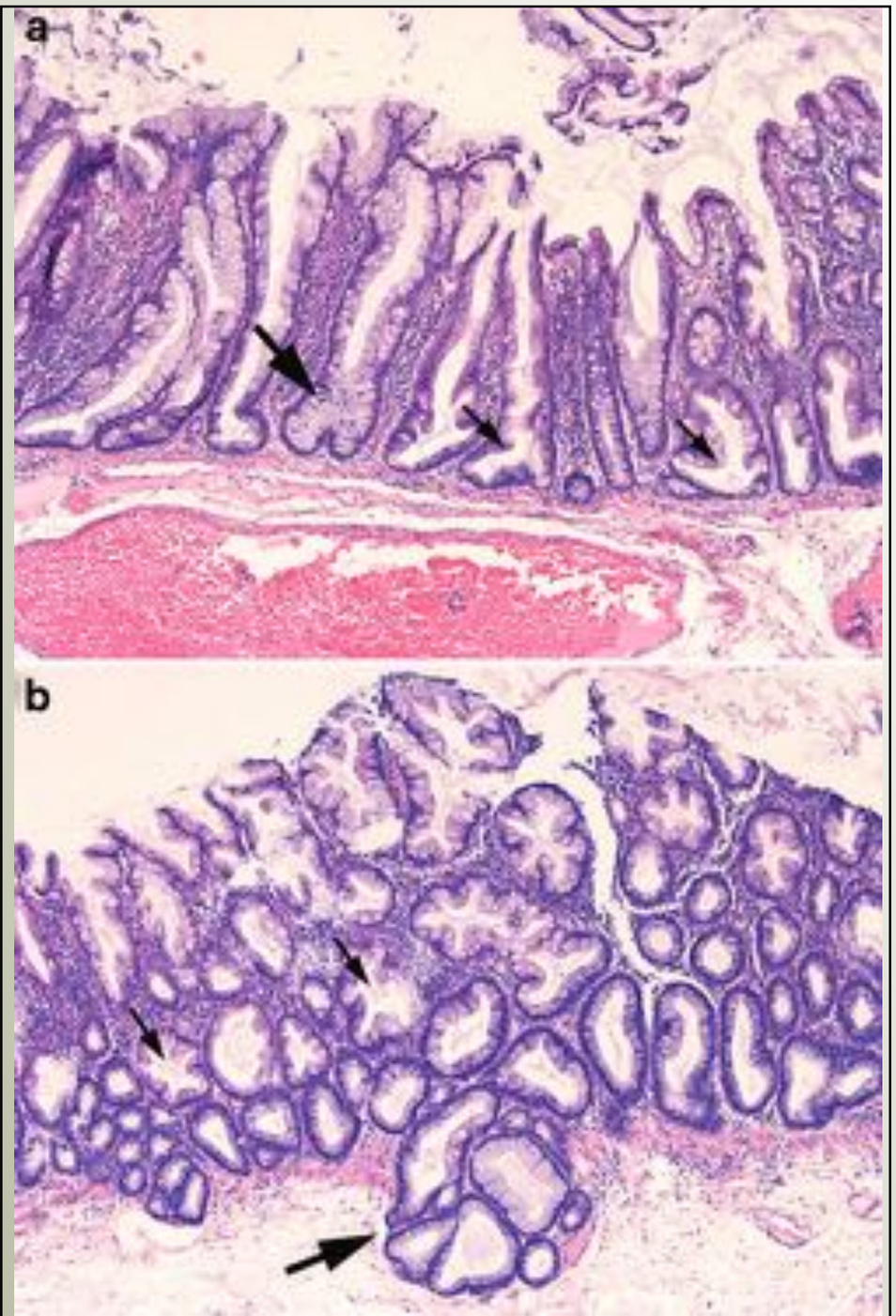
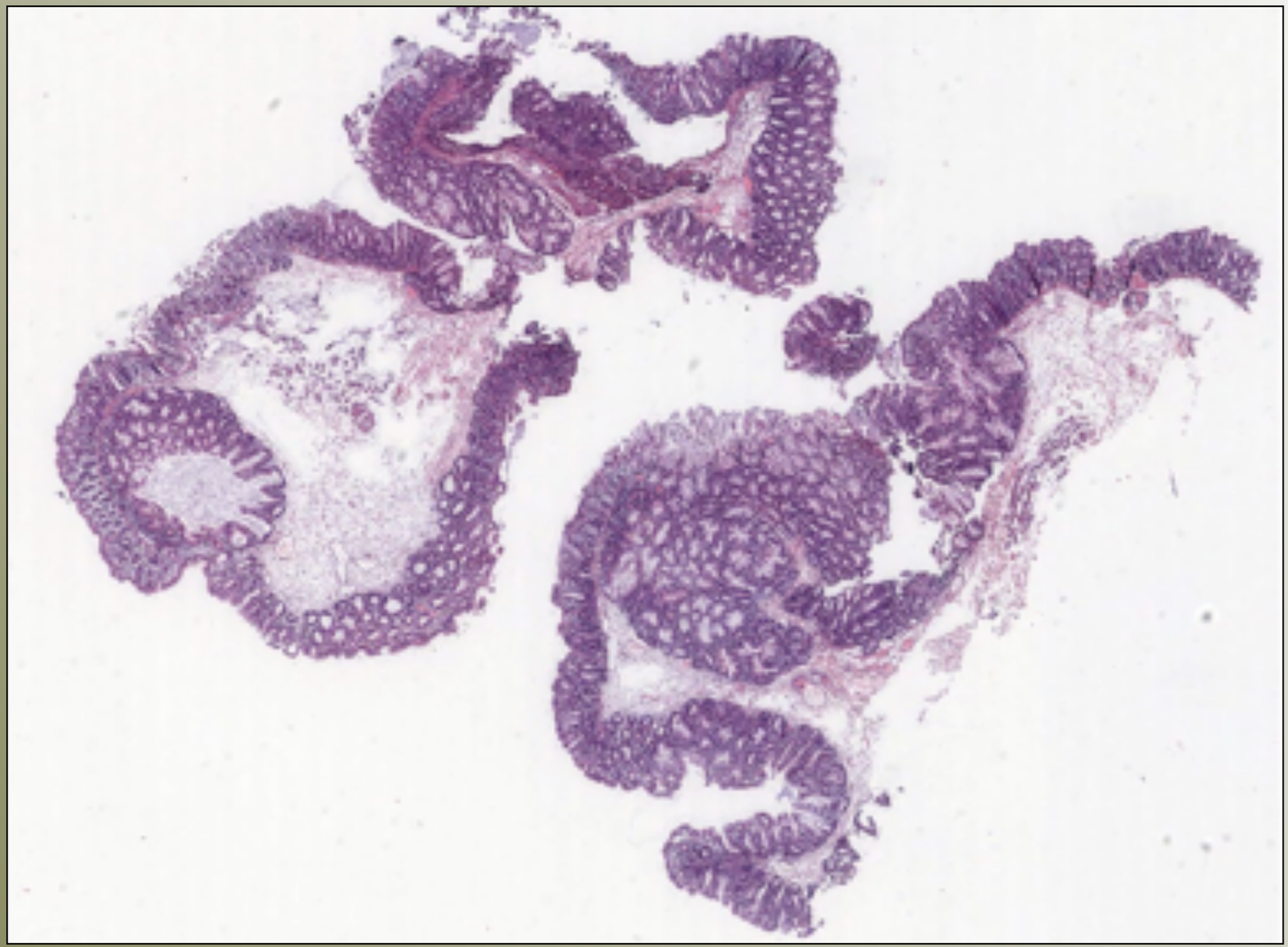


Fig. 3 Sessile serrated adenoma. **a** Branched crypts (*bold arrow*), T- and L-shaped bases of the crypts (*thin arrows*) and columnar dilatation of the crypts (×2.5); **b** serration reaching to the lower third of the crypts (*thin arrows*), inverted crypts below the muscularis mucosae (*bold arrow*) (×2.5) (with permission from PD. Dr. M. Vieth)

Serrated polyps of the colon and rectum (hyperplastic polyps, sessile serrated adenomas, traditional serrated adenomas, and mixed polyps)—proposal for diagnostic criteriaDaniela E. Aust & Gustavo B. Baretton & Members of the Working Group GI-Pathology of the German Society of Pathology Virchows Arch (2010) 457:291–297

Sessile Serrated Adenoma : pseudoinvasione



Traditional serrated (true) adenomas

If the lesion shows a serrated morphology as well as mucosal neoplasia (cytological abnormalities), it is considered to be a traditional serrated adenoma (TSA) (Longacre & Fenoglio-Preiser 1990).

It should be reported as such (TSA) and treatment and surveillance should be the same as for adenomas.

This pragmatic recommendation recognises the neoplastic nature of these lesions.

The non-serrated features found in such lesions (e.g. size and grade of neoplasia) and any co-existing pathology (e.g. number of neoplastic lesions) should be taken into account in selecting an appropriate surveillance protocol

A well-oriented polypectomy is mandatory for the identification of such histological features. Correct assessment of the deepest portions of the mucosa is impossible in superficial or tangentially cut lesions (O'Brien 2007; O'Brien et al. 2008).

Often mild cytological atypia (slightly enlarged vesicular nuclei, nucleoli) is found without clear signs of neoplasia (dysplasia).

BRAF-Mutations depend on the type and location of lesion with prevalence in proximal location

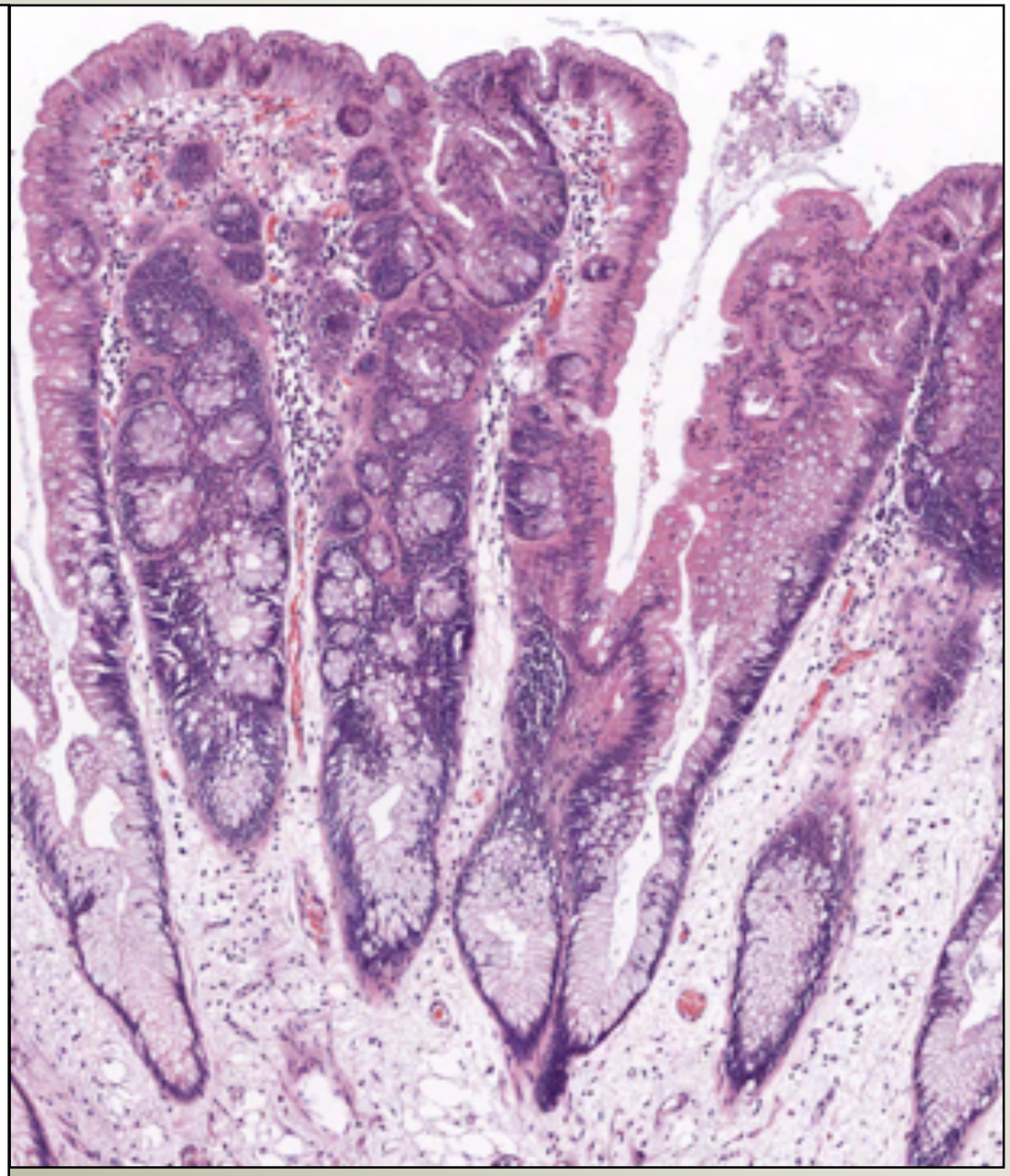
Other abnormalities include:

- The majority of SSL and TSA show CIMP and promoter methylation of hMLH1
- BRAF mutations in 8–10% of all CRC (27–76% of CIMP and sporadic MSI-H CRC)
- BRAF mutations in the majority of SSL and TSA (also microvesicular variant of HP, especially proximal), but rarely (0–5%) in adenoma.

(Toyota et al. 1999; Toyota et al. 2000; Ogino et al. 2006; Jass 2007; Samowitz et al. 2007; Ogino et al. 2007; Shen et al. 2007; Grady & Carethers 2008; Kawasaki et al. 2008; Ogino & Goel 2008; Suehiro et al. 2008; Ogino et al. 2009).

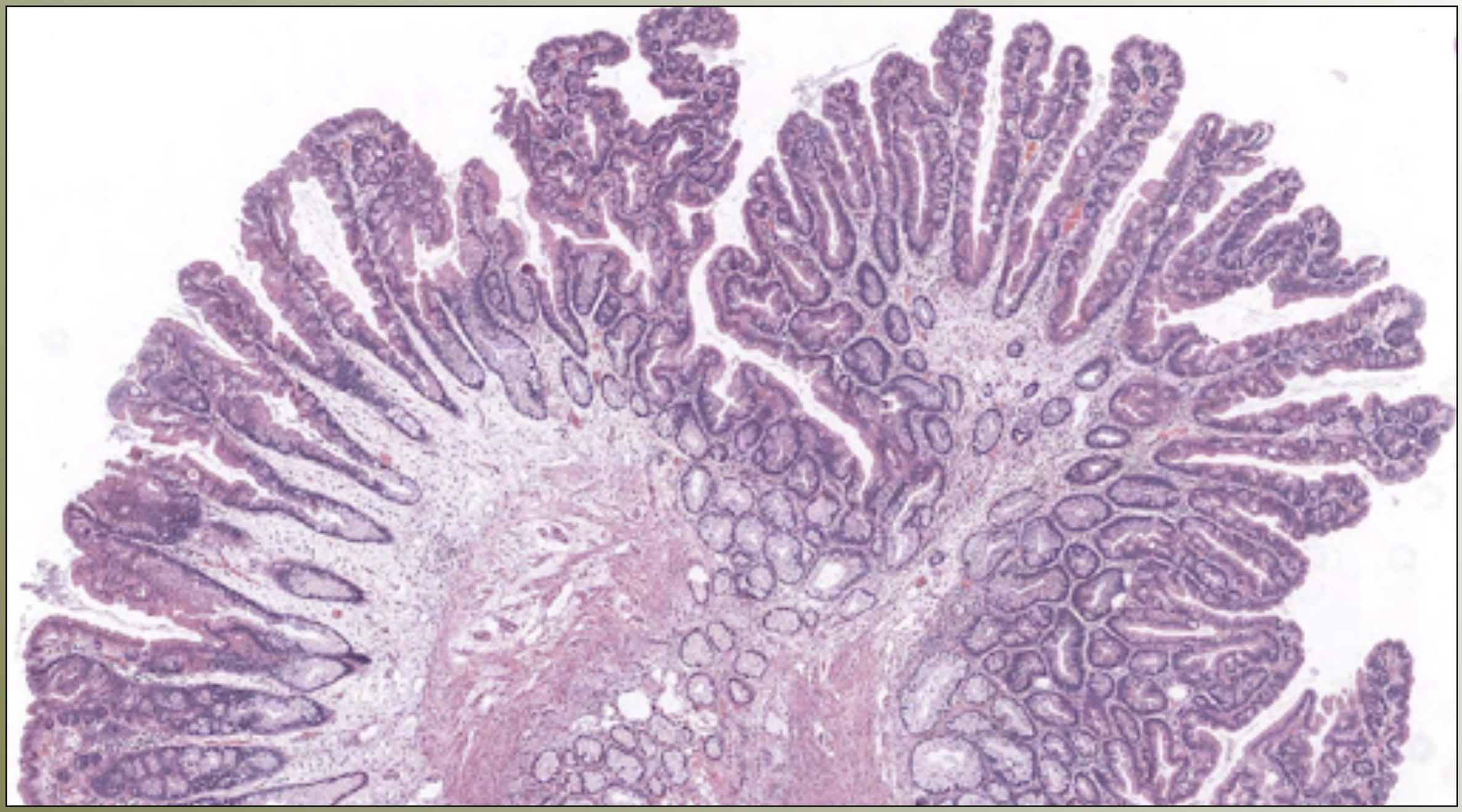
Traditional serrated adenomas

- This is the rarest variant of serrated lesions (1-6%)
- Known since 1990 by the term "serrated adenoma" as rare variant of adenoma
- Grossly, TSA are peduncolated or villous polyps, more common in the left side (60%)
- More frequent in mostly elderly
- By definition TSA microscopically shows IEN (90% LG and 10% HG)
- Prominent serration with diffuse cytoplasmic eosinophilia
- Ectopic Crypt Formation (ECF): small budding aberrant crypts which loss their orientation towards the muscolaris mucosa

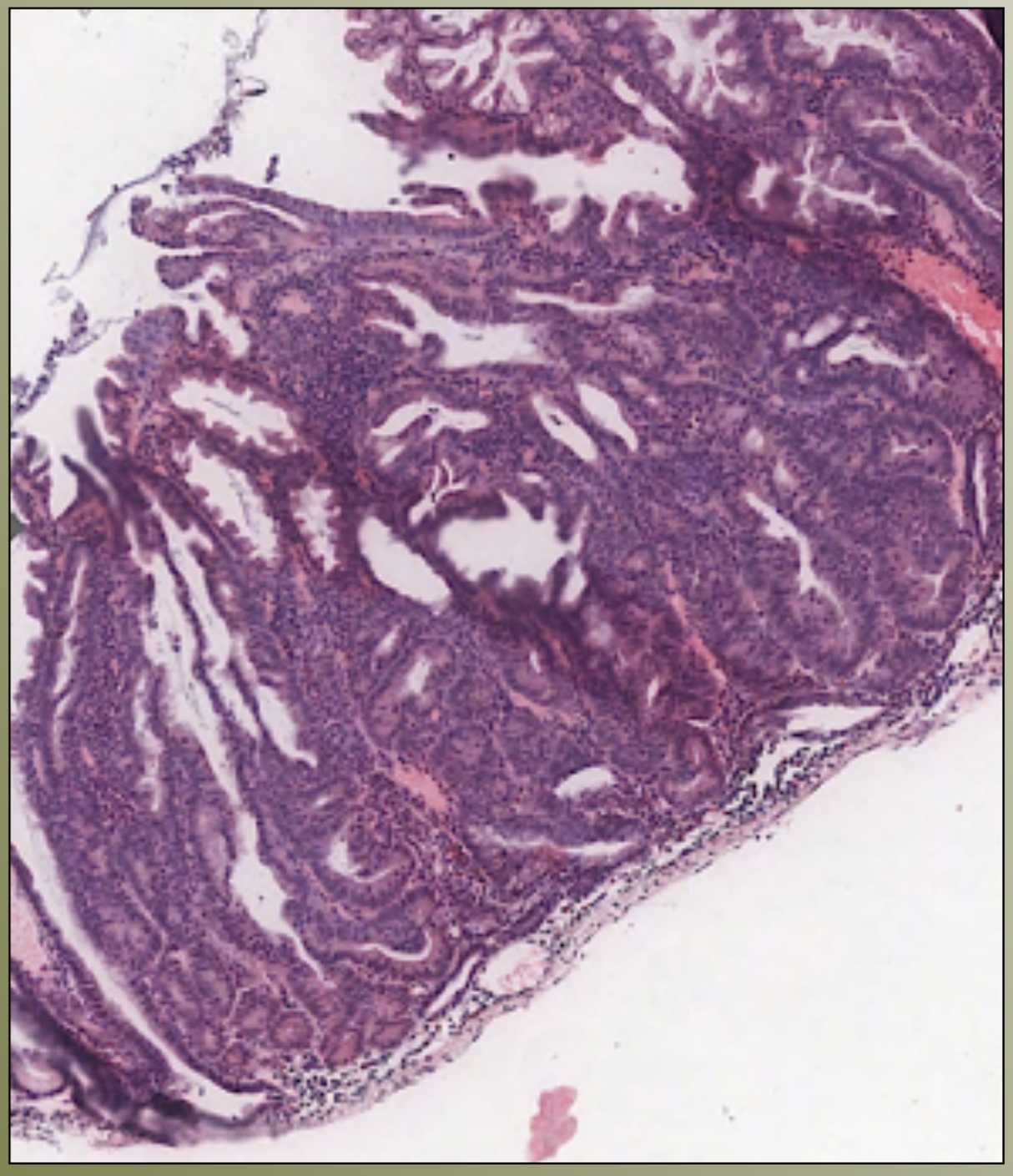


Serrated polyps of the colon and rectum (hyperplastic polyps, sessile serrated adenomas, traditional serrated adenomas, and mixed polyps)—proposal for diagnostic criteria Daniela E. Aust & Gustavo B. Baretton & Members of the Working Group GI-Pathology of the German Society of Pathology Virchows Arch (2010) 457:291–297

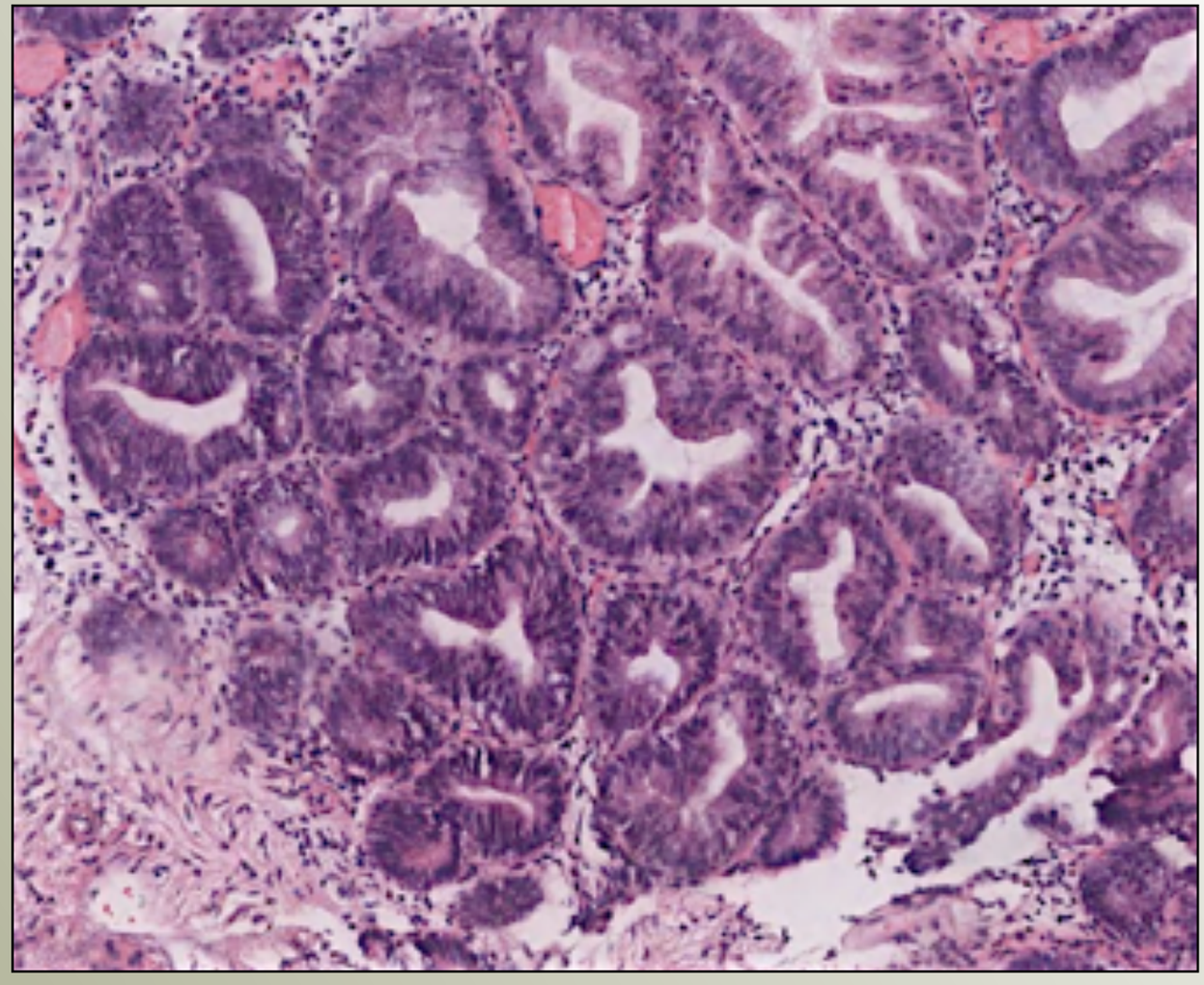
Traditional Serrated Adenoma



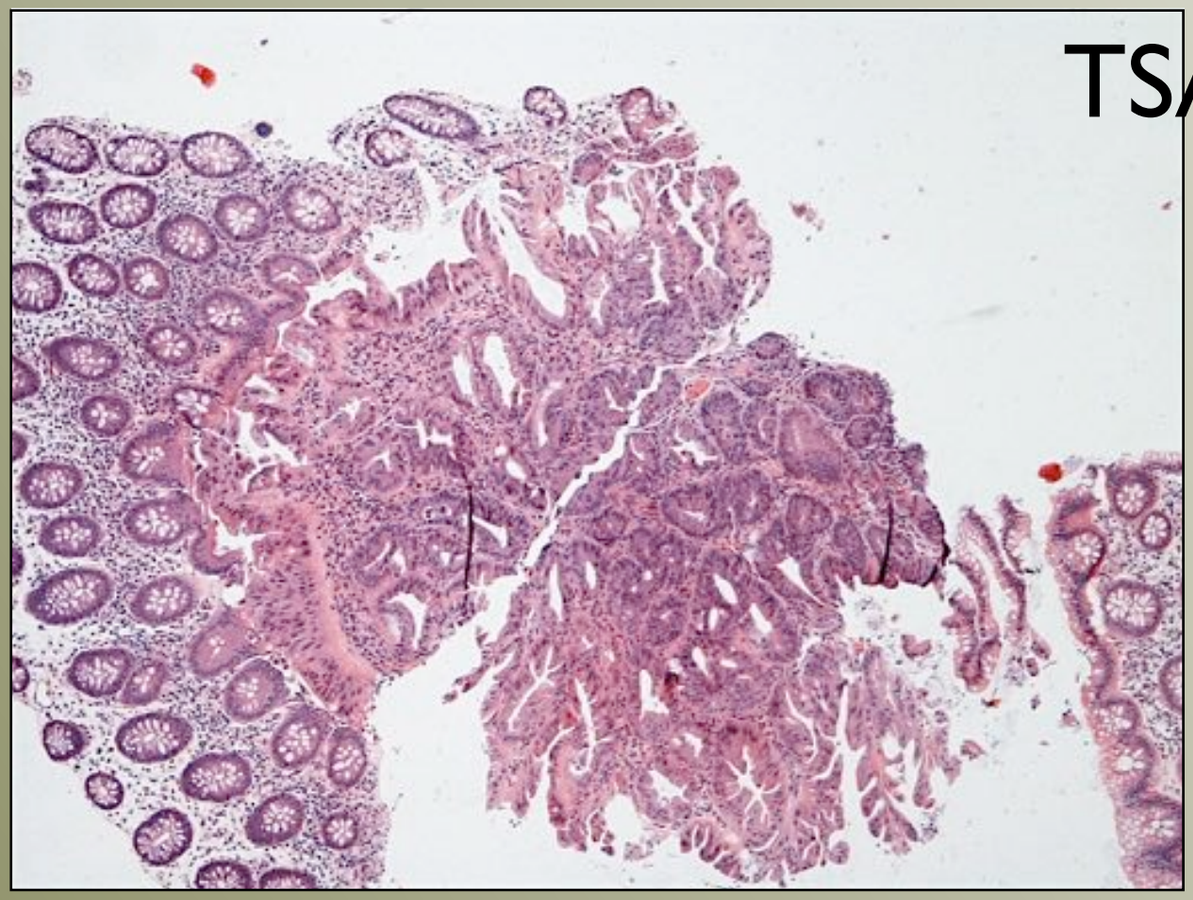
Traditional Serrated Adenoma IEN



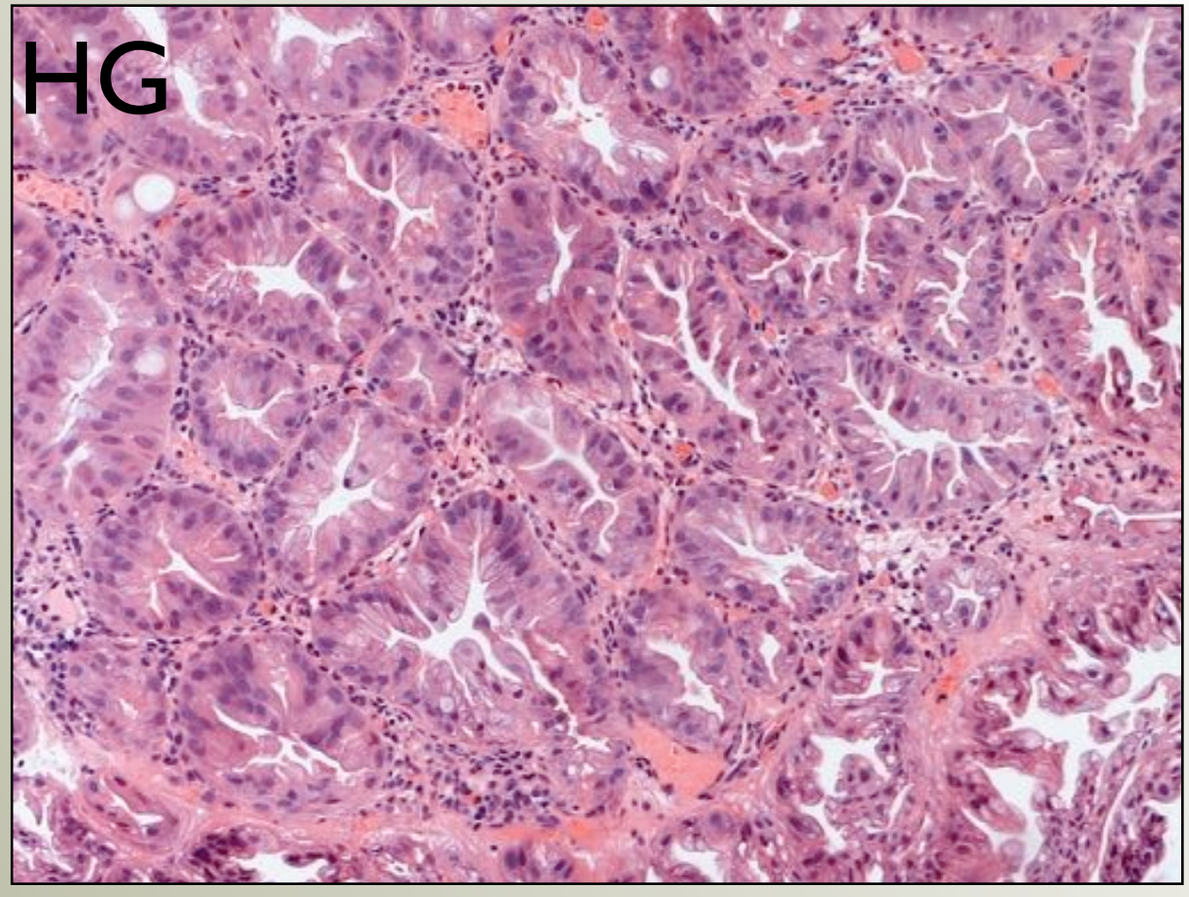
LG

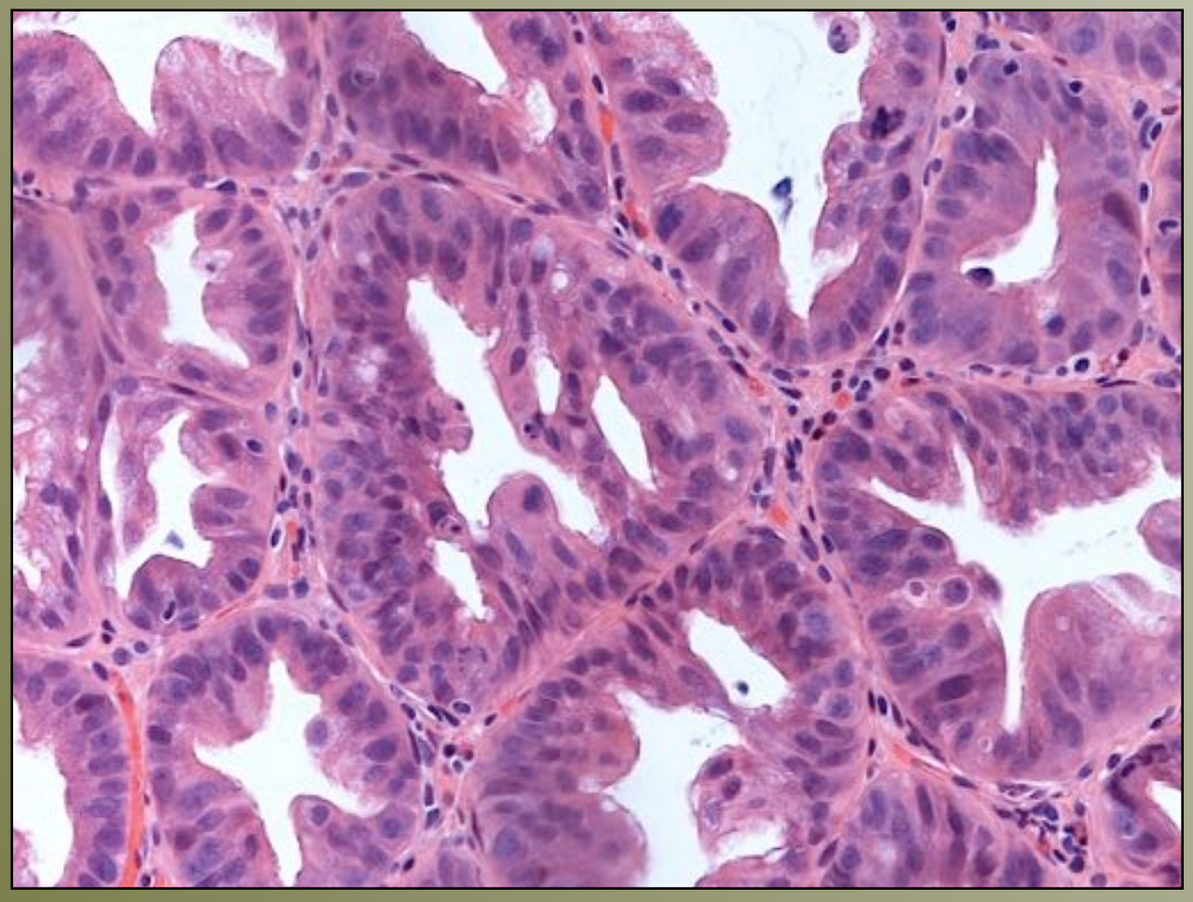


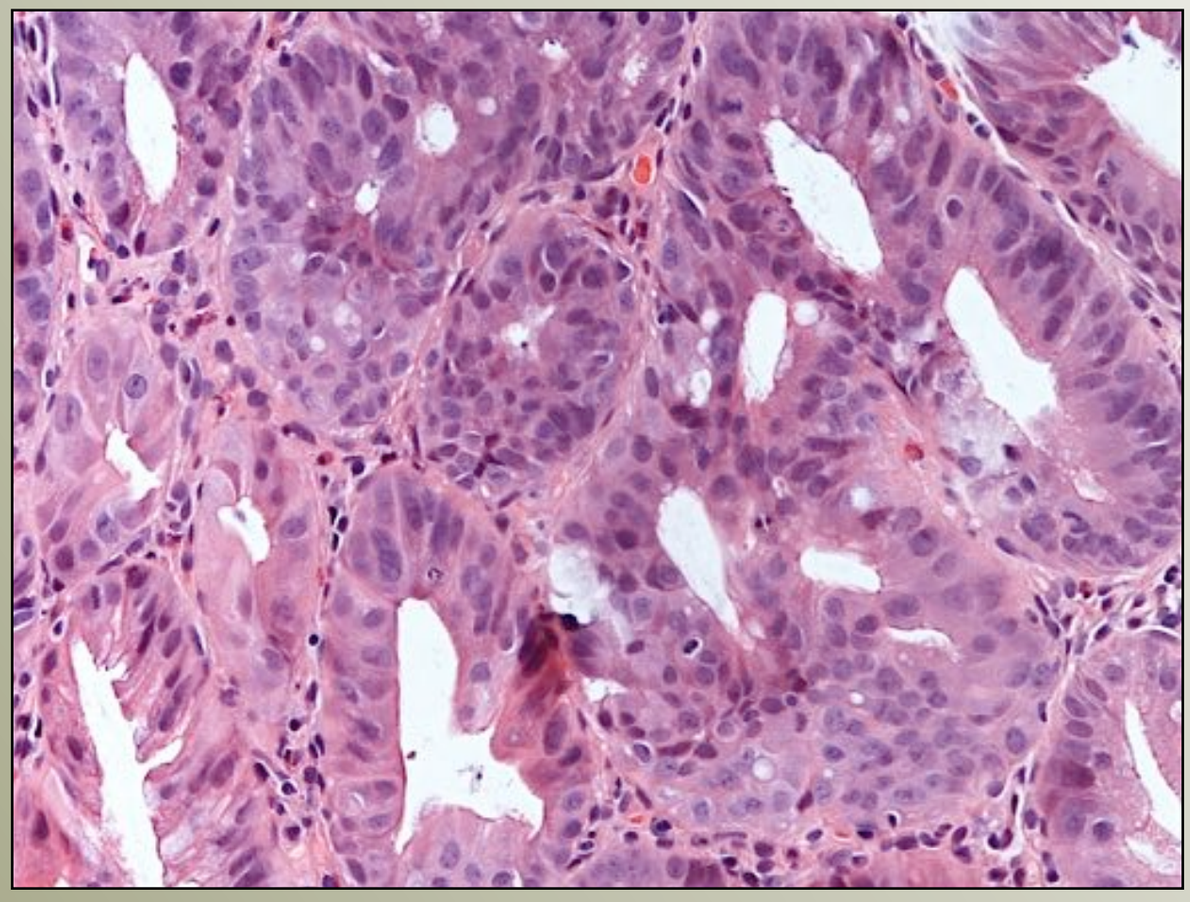
HG



TSA HG







Mixed Polyp

Combination of conventional adenomas (tubular, tubulovillous and villous) with different grades of IEN and serrated lesion

In the past considered collision tumors

Is recommended to first describe the component of the polyp and then include the term mixed polyp

Three different forms:
1.SSA and TSA
2.SSA and conventional adenoma
3.TSA and conventional adenoma

Rare combination: HP and conventional adenoma

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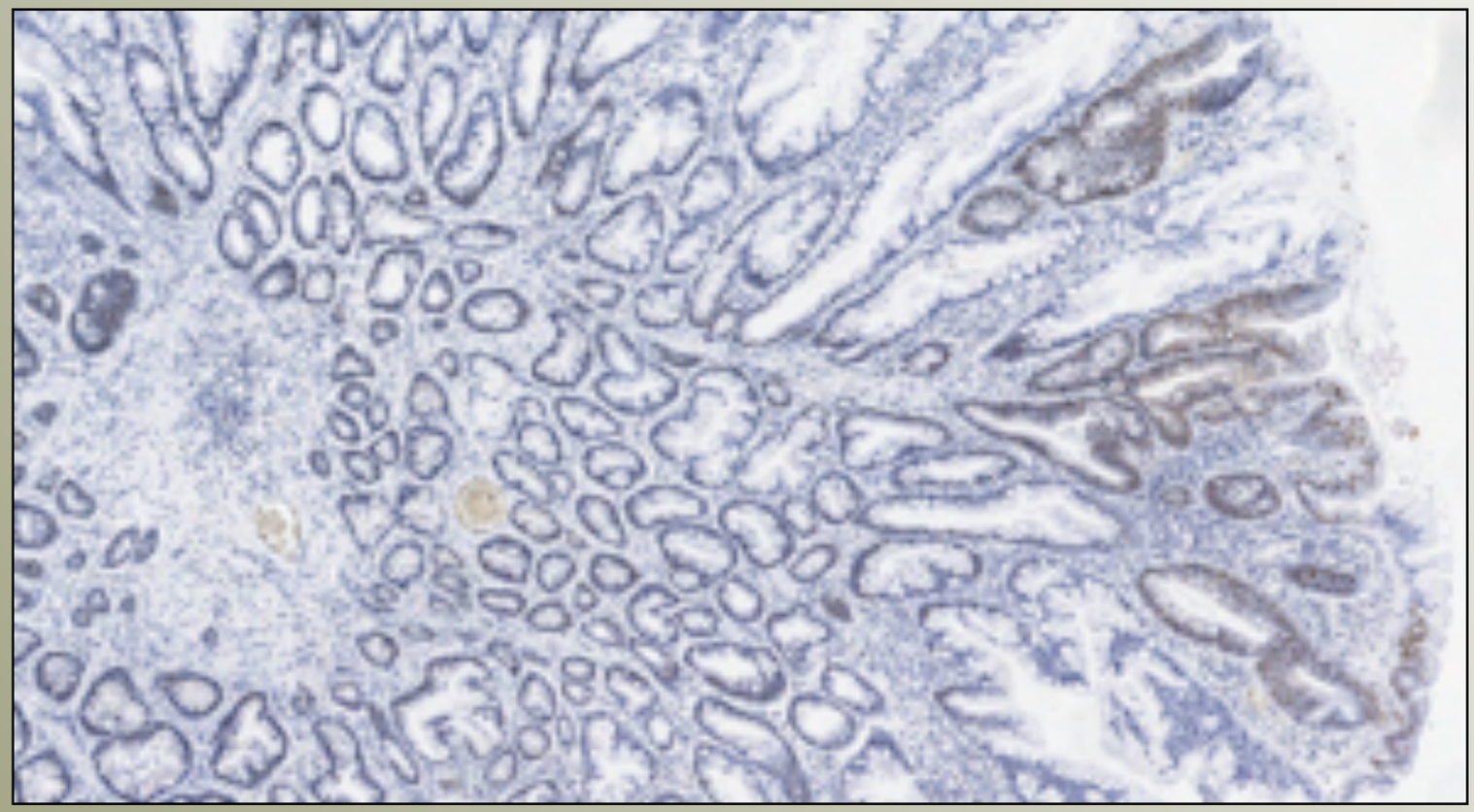
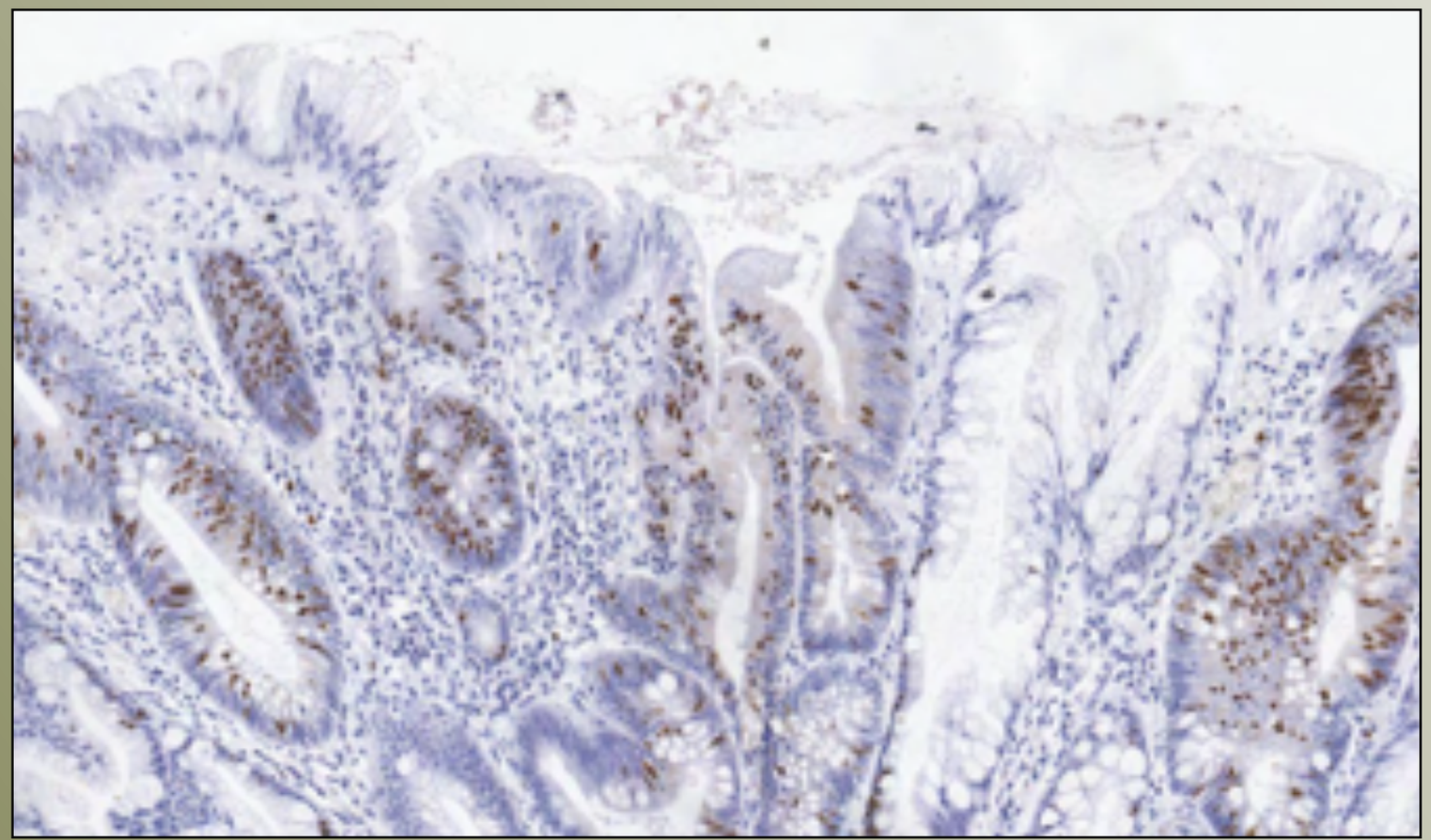
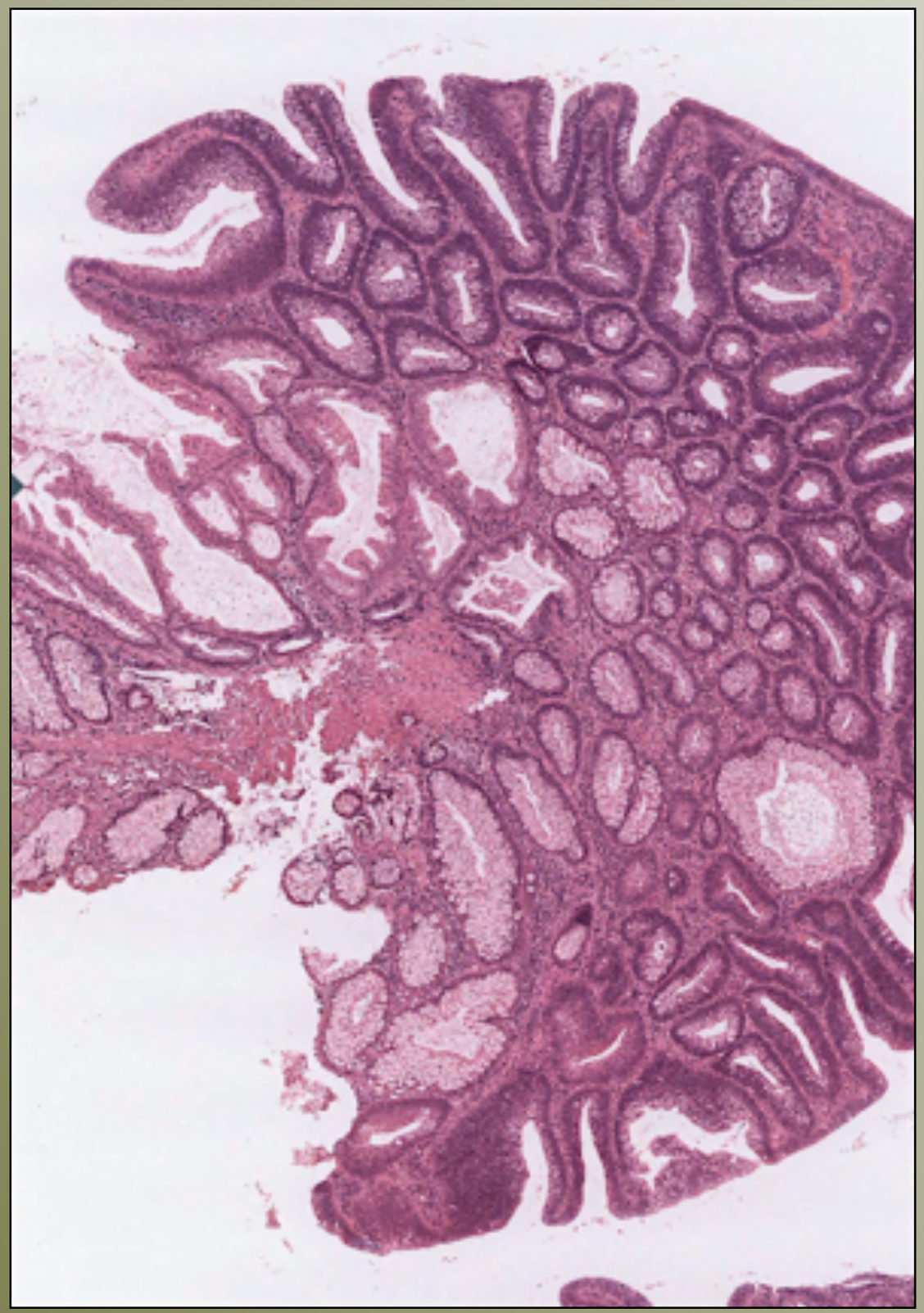
p53

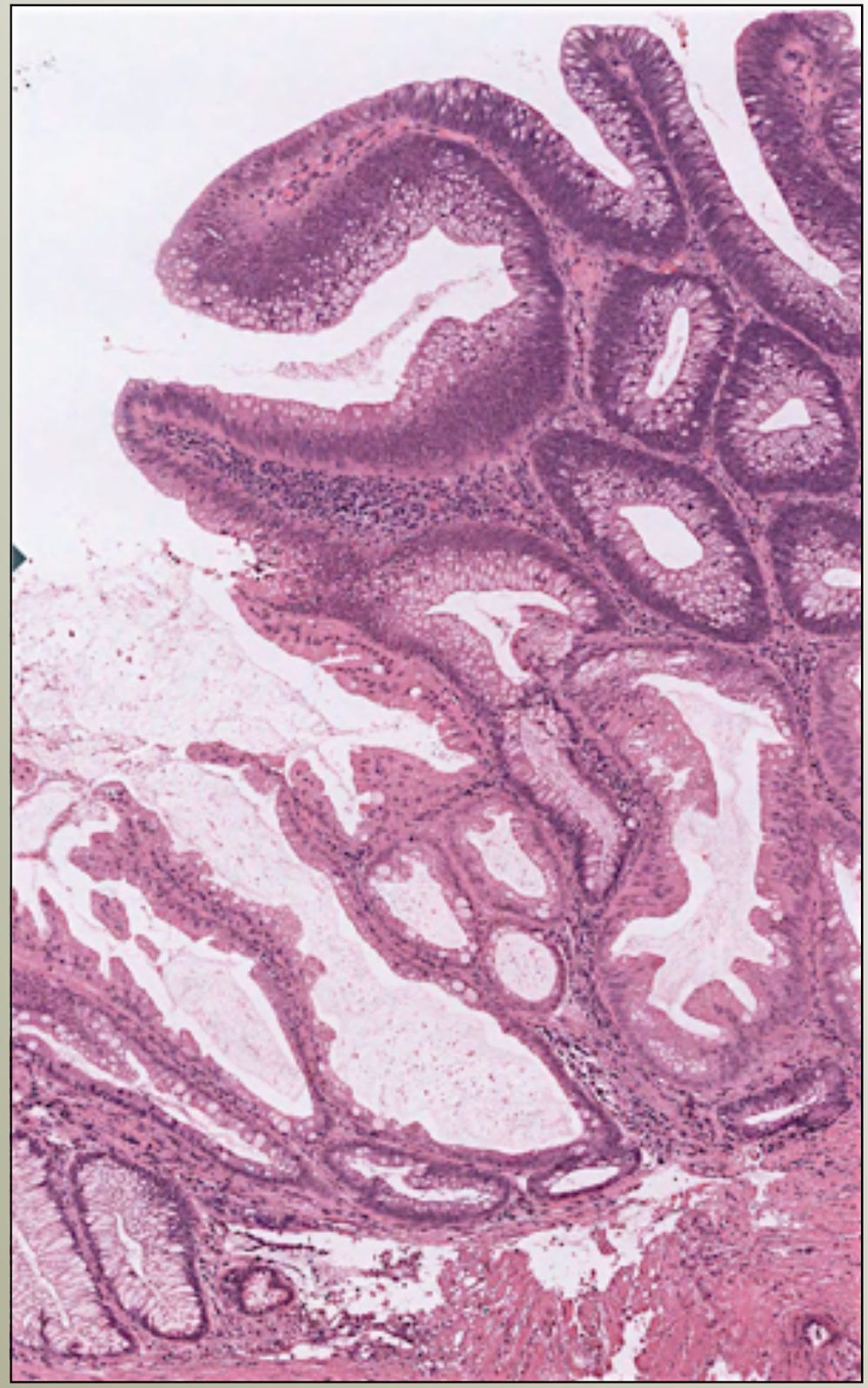


Ki67

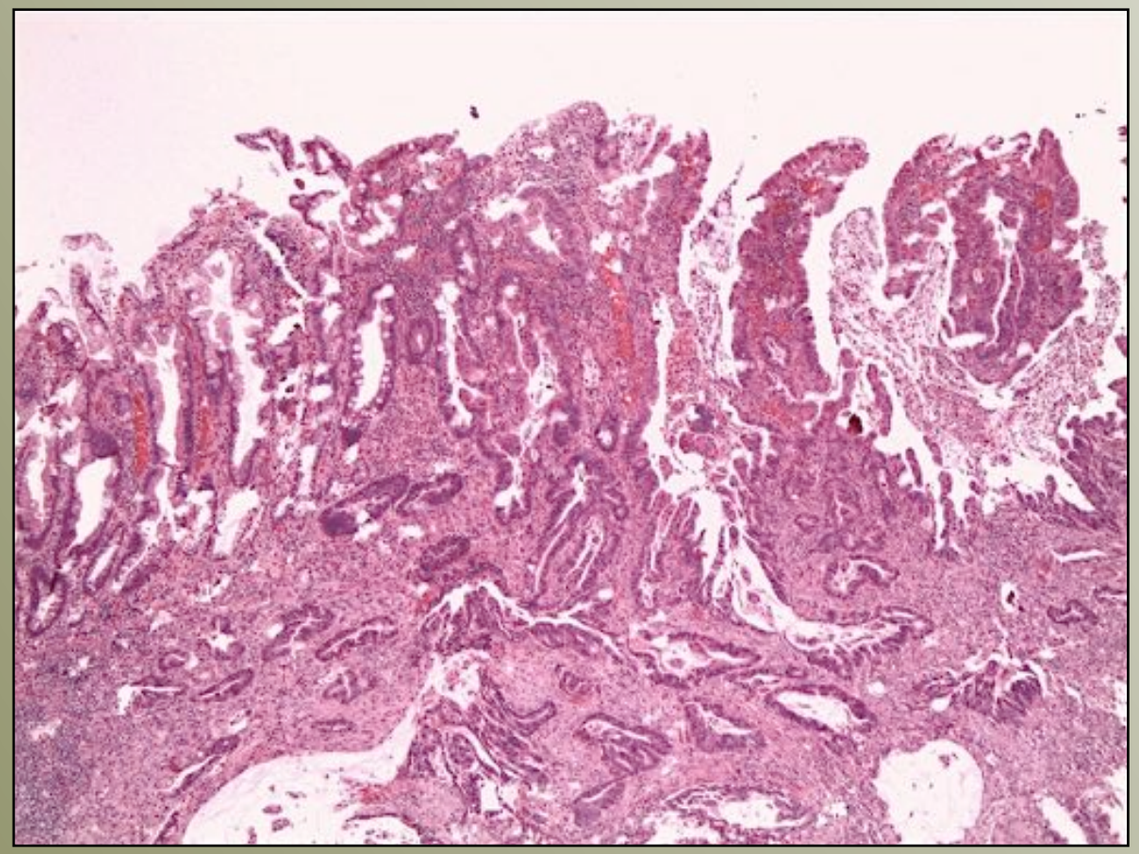


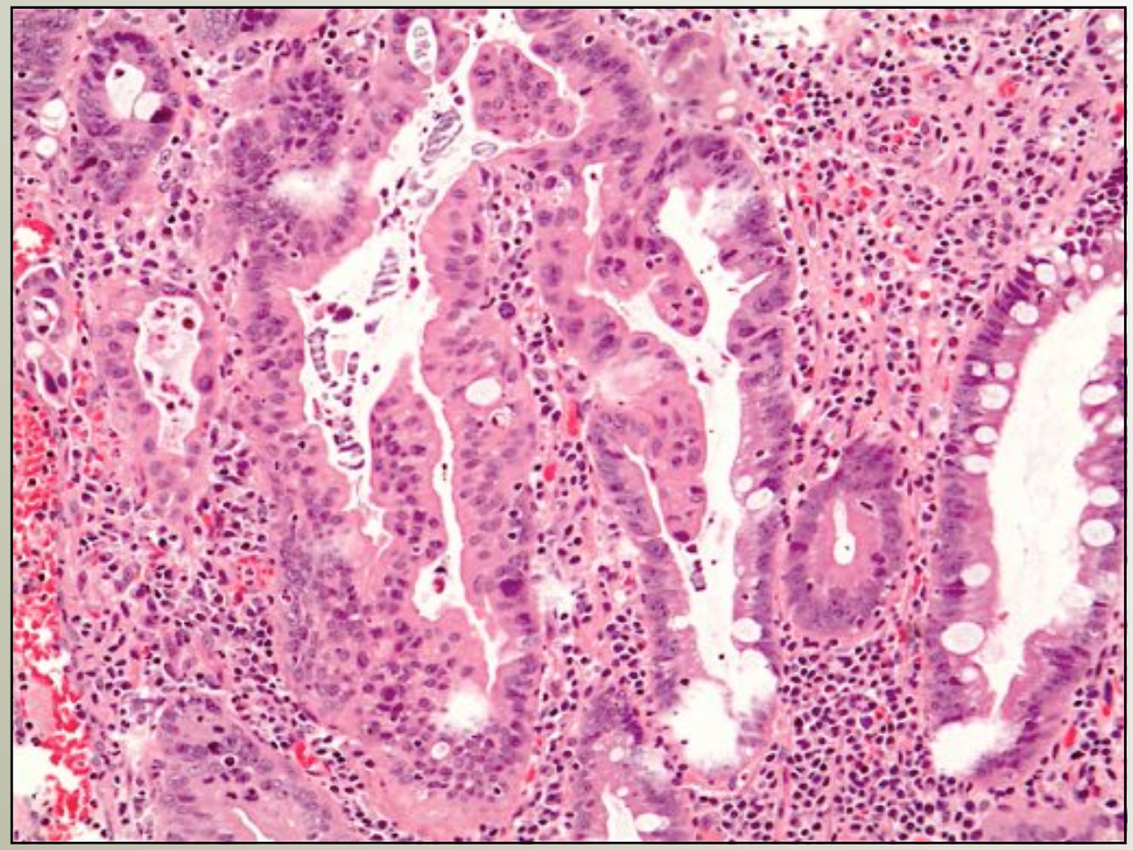
Adenoma misto, serrato/tubulare (TSA + CA IEN LG)

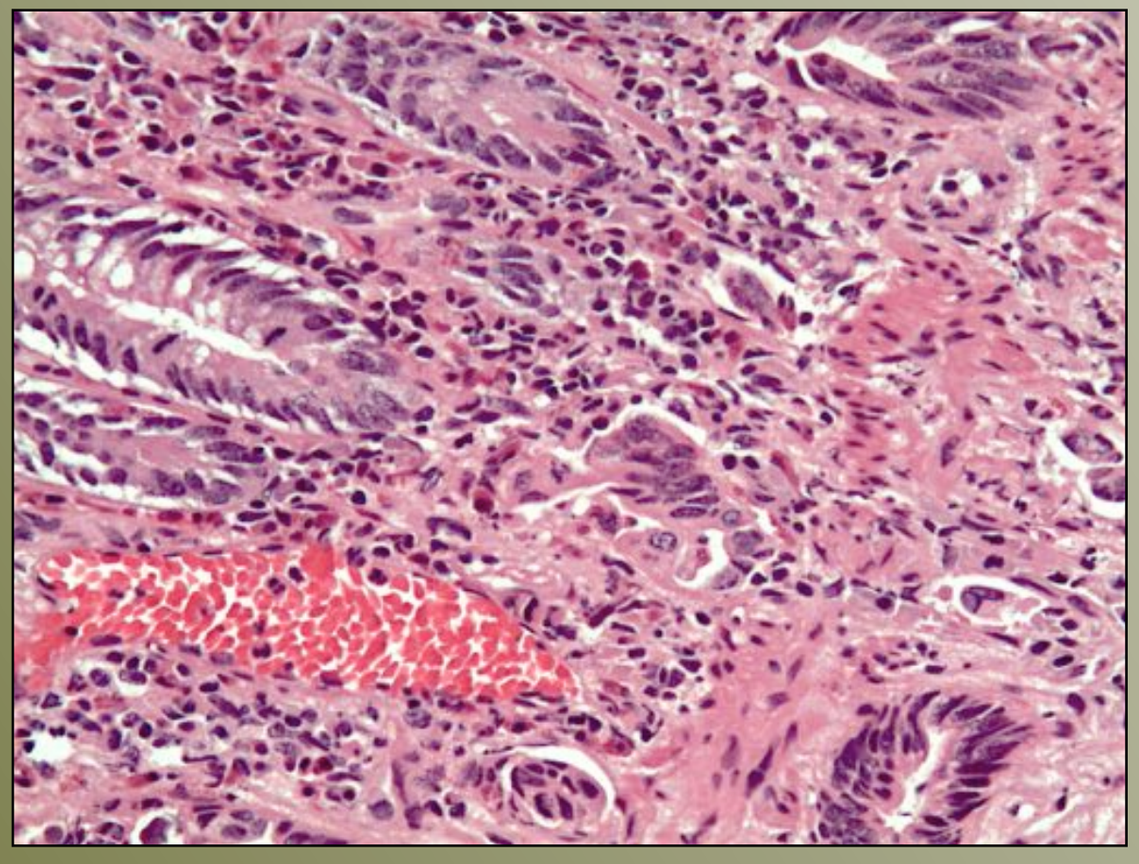


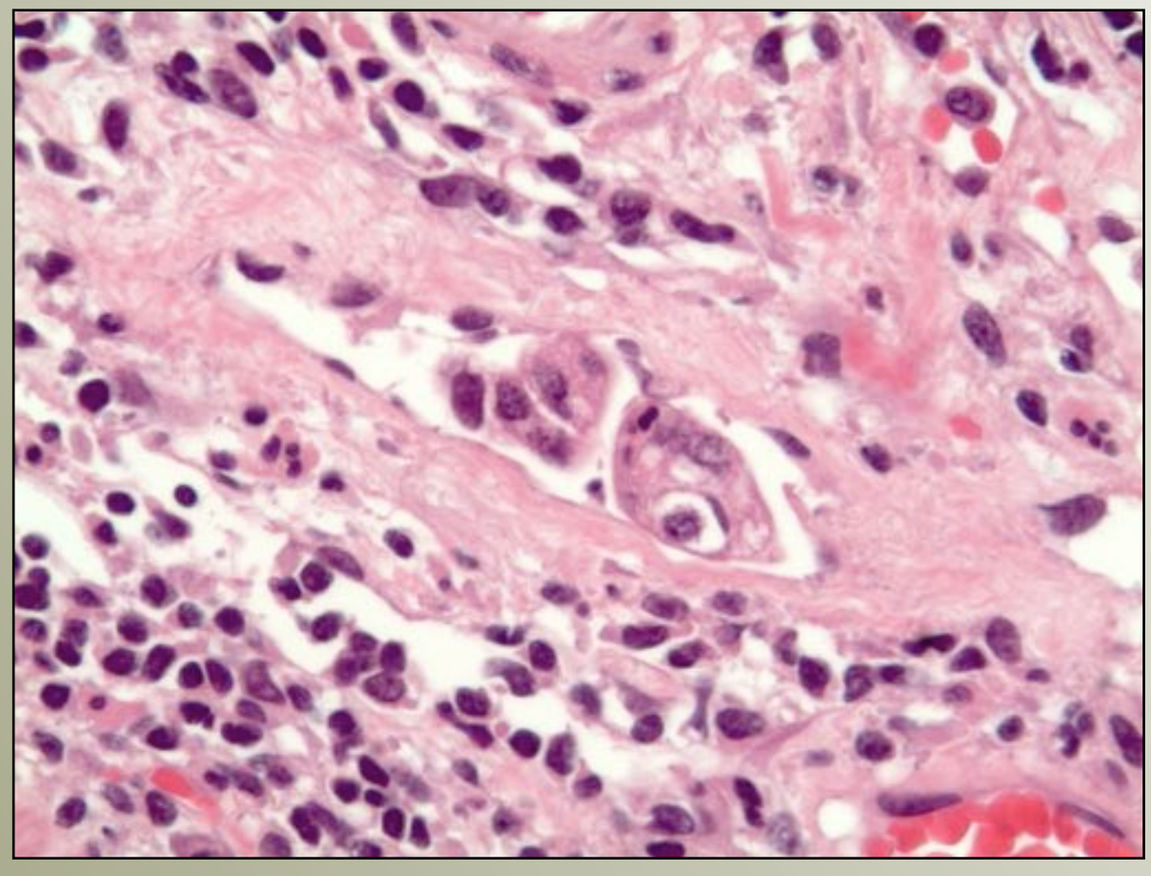


Sequenza lesione serrata-adenocarcinoma serrato









Assessment of the degree of invasion of pT1 colorectal cancer and prognostic index

1. Definition of invasion
2. Epithelial misplacement
3. High risk pT1 adenocarcinoma
4. Sub-staging pT1
5. Tumour grade in pT1 lesions
6. Lymphovascular invasion in pT1 adenocarcinomas
7. Margin involvement in pT1 adenocarcinomas
8. Tumour cell budding in pT1 adenocarcinomas

1. Definition of invasion

pT1 cancers are those showing invasion through the muscularis mucosae into the submucosa but not into the muscularis propria.

We recommend the use of the WHO definition (WHO 1989; WHO 2000) of an adenocarcinoma as **an invasion of neoplastic cells through the muscularis mucosae into the submucosa**

The term intramucosal carcinoma should be substituted by mucosal high-grade neoplasia according to the WHO classification and the modified classification of neoplasia recommended in the European Guidelines based on the revised Vienna classification

Definition of Carcinoma of the colon and rectum (WHO 2000)

A malignant epithelial tumour of the colon or rectum.
Only tumours that have penetrated through muscularis mucosae into submucosa are considered malignant at this site.
The presence of scattered Paneth cells, neuroendocrine cells or small foci of squamous cell differentiation is compatible with the diagnosis of adenocarcinoma.

1. Definition of invasion

Lesions with the morphological characteristics of adenocarcinoma that are confined to the epithelium or invade the lamina propria alone and lack invasion through the muscularis mucosae into the submucosa have virtually **no risk** of metastasis.

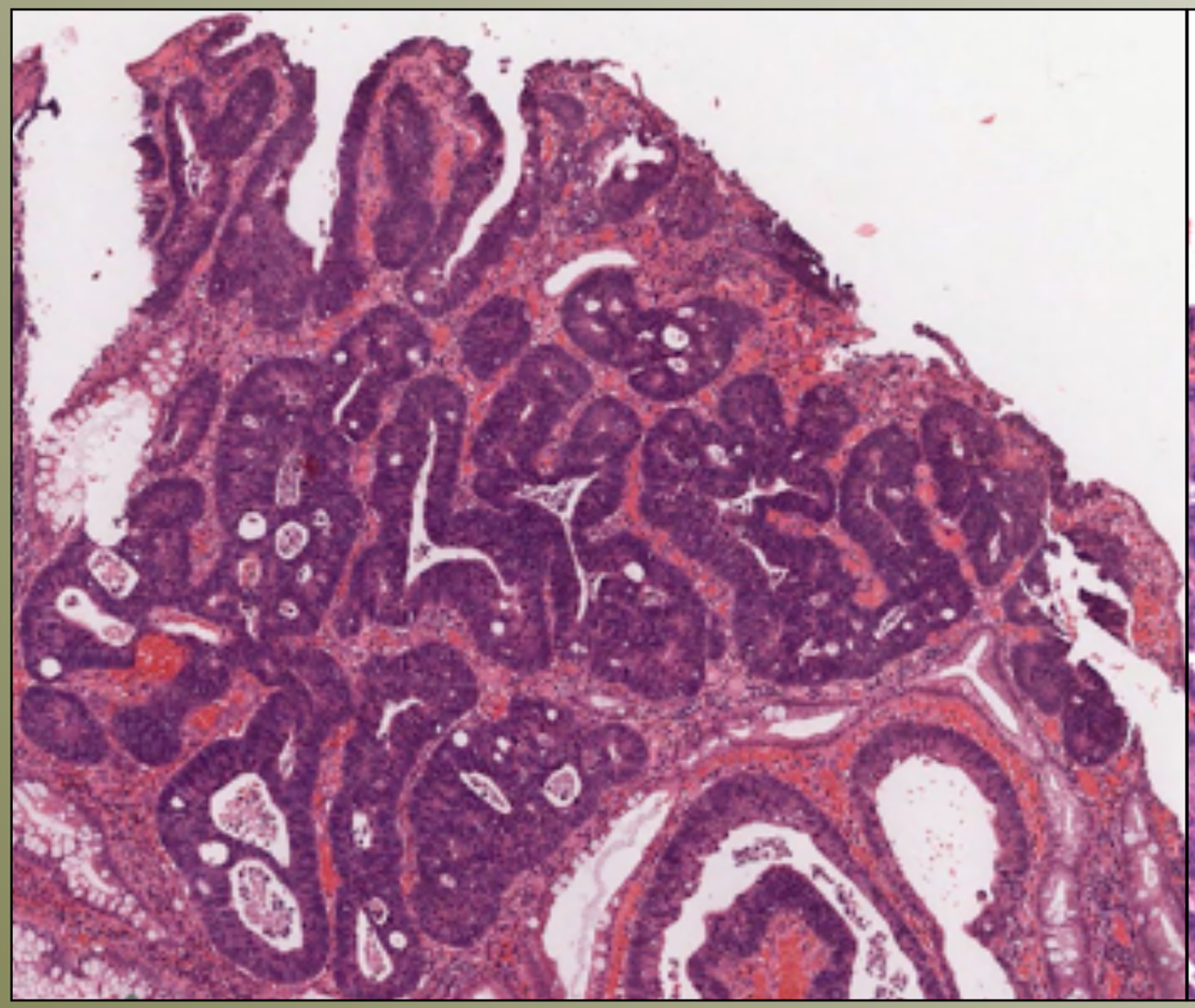
Therefore, ‘high-grade intraepithelial neoplasia’ is a more appropriate term than ‘adenocarcinoma in situ’, and ‘intramucosal neoplasia’ is more appropriate than ‘intramucosal adenocarcinoma’.

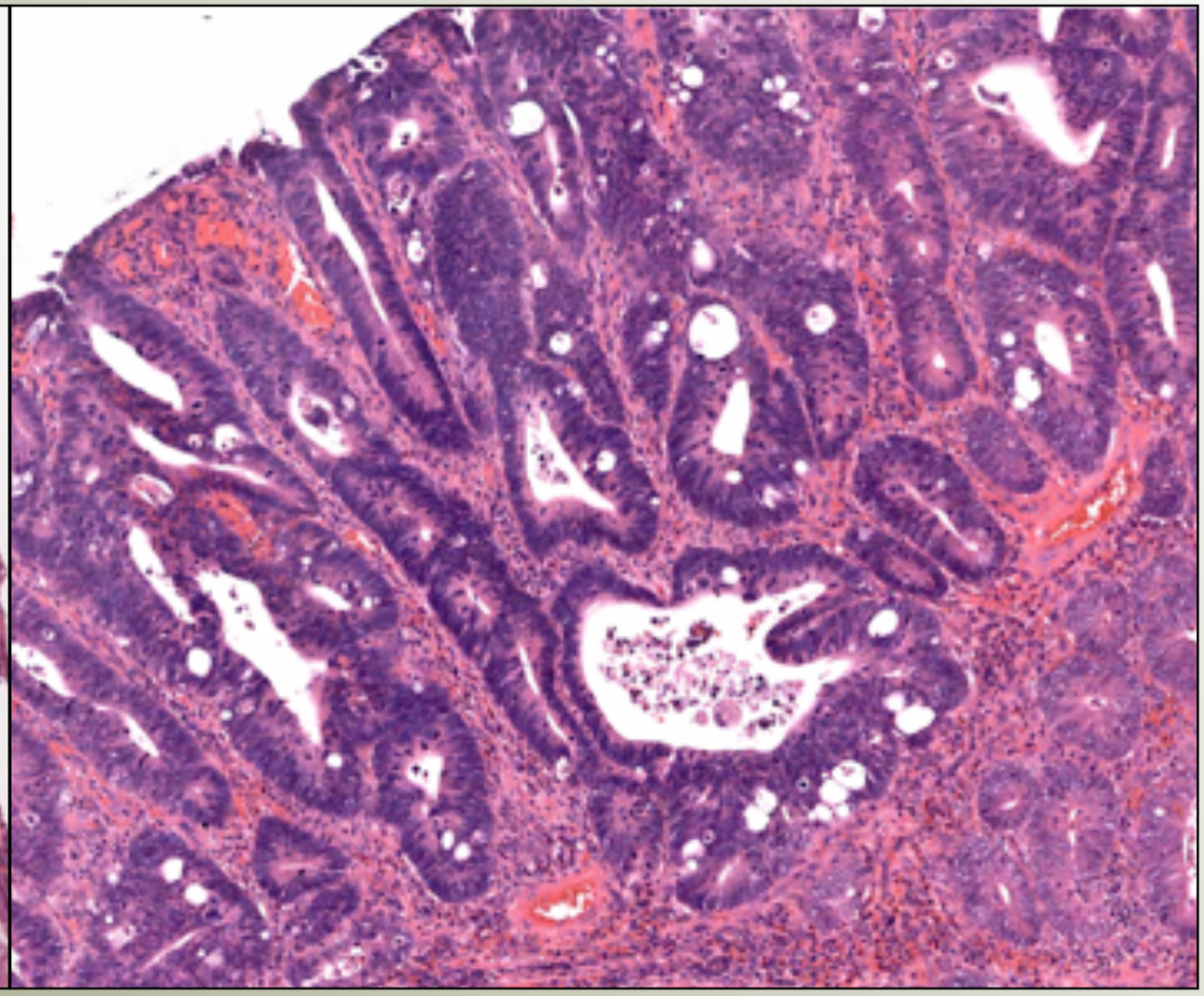
Use of these proposed terms helps to avoid overtreatment.

WHO 2000

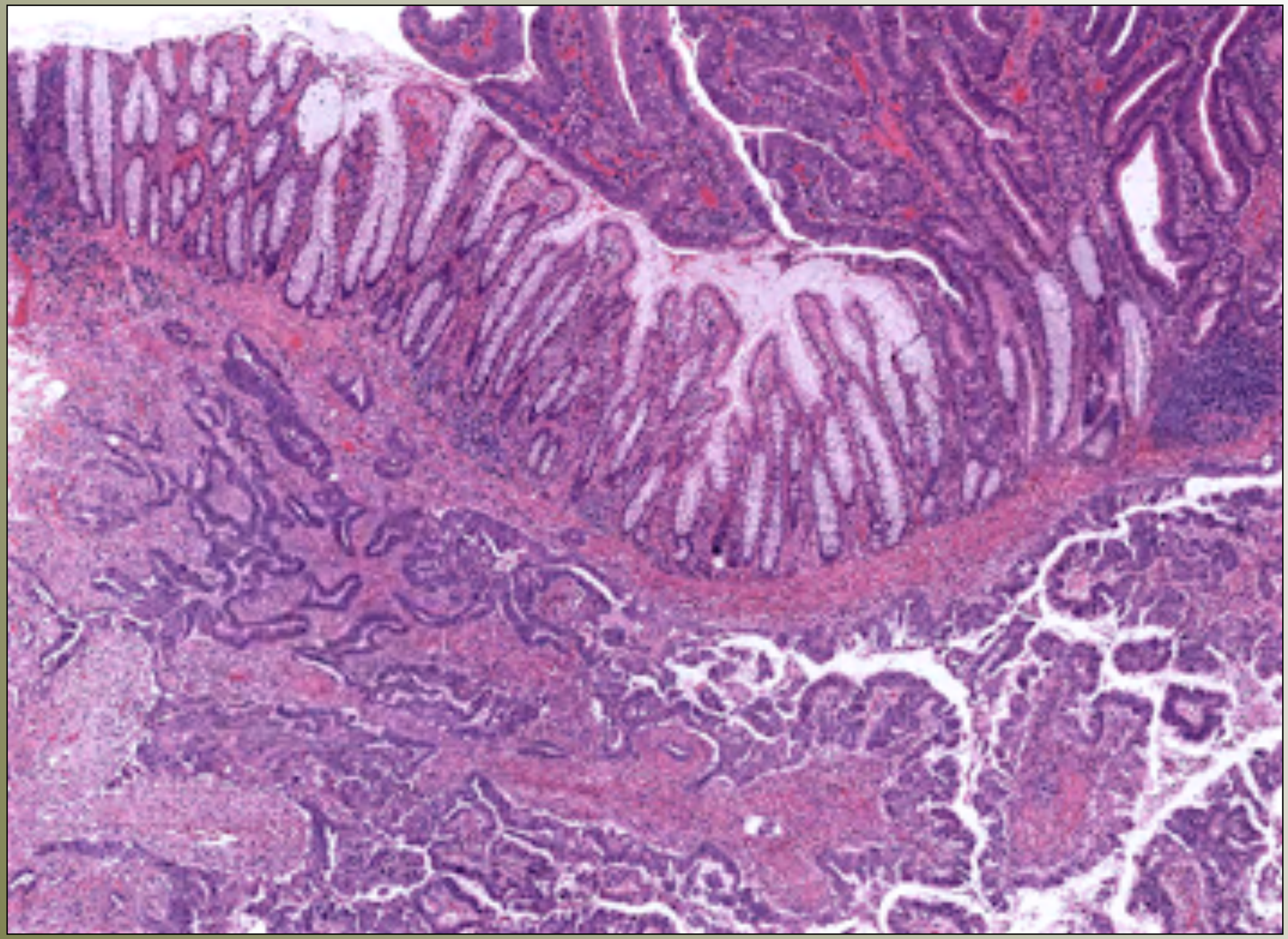
The WHO definition of adenocarcinoma in use when the EU Guidelines were developed excluded diagnosis of intramucosal carcinoma in the colon or rectum, in contrast to the accepted WHO definitions for the stomach, oesophagus and small bowel.

Displasia di HG - Carcinoma in situ





Carcinoma invasivo



Epithelial misplacement (pseudo-invasion)

- Well recognized phenomenon

Pseudo-carcinomatous invasion in adenomatous polyps of the colon and rectum
T. Muto, H. J. R. Bussey, and B. C. Morson J Clin Pathol 1973 26(1):25-31

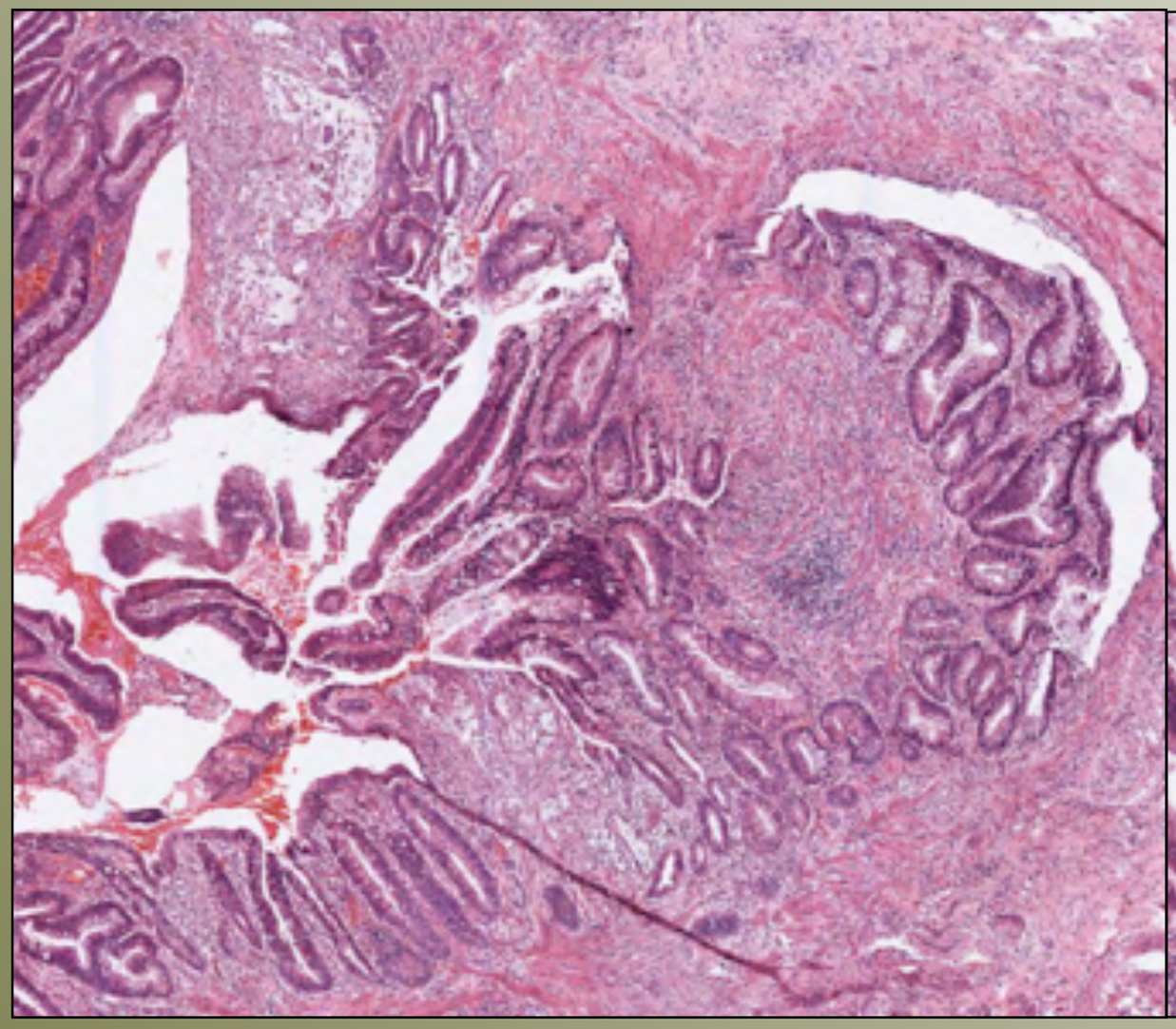
- It is commonly seen in prolapsing polyps in the sigmoid colon

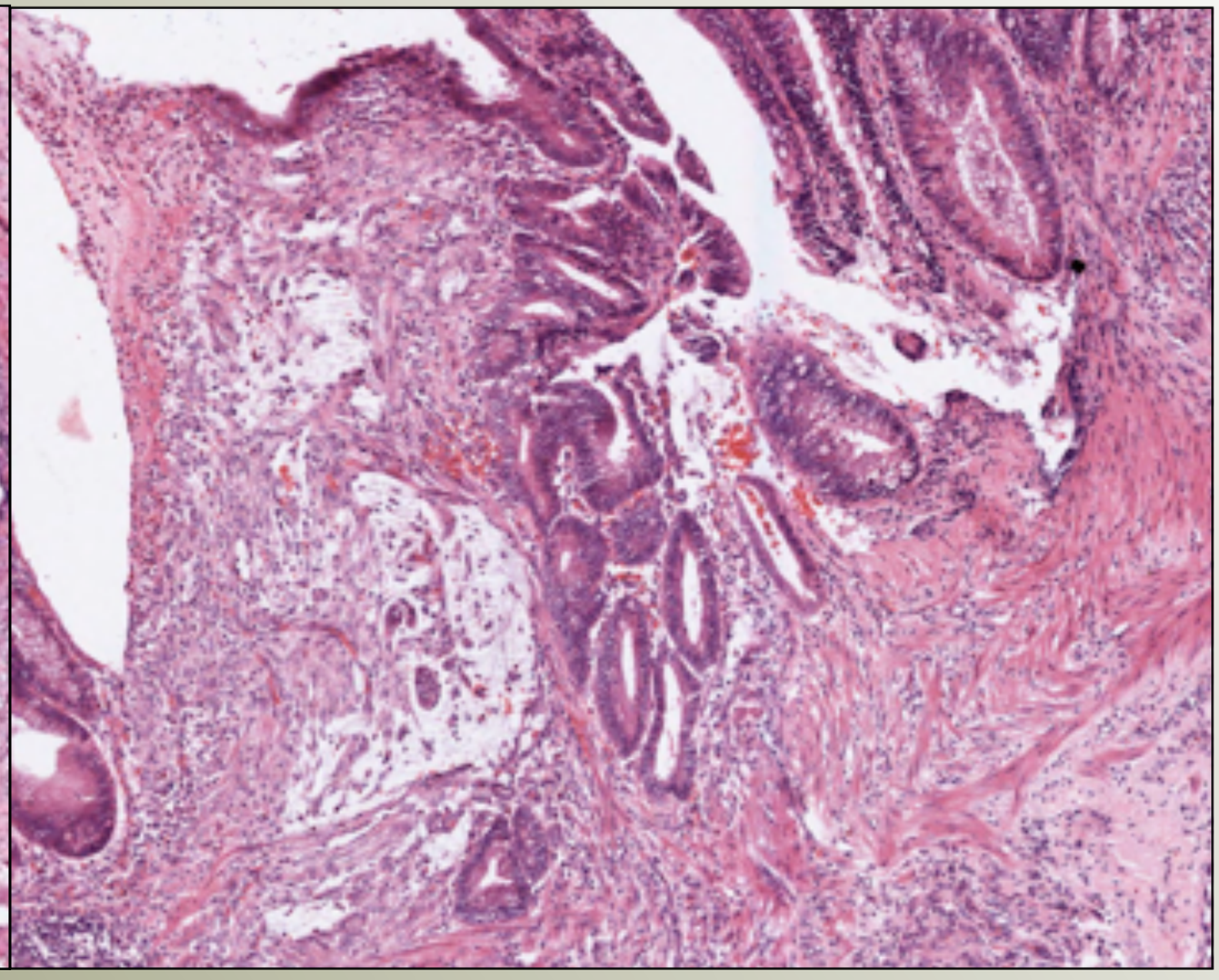
- Sigmoid colonic polyps are particularly prone to inflammation, a feature that tends to enhance the neoplastic changes present.

- In cases of epithelial misplacement, surrounding lamina propria and haemosiderin-laden macrophages are found.

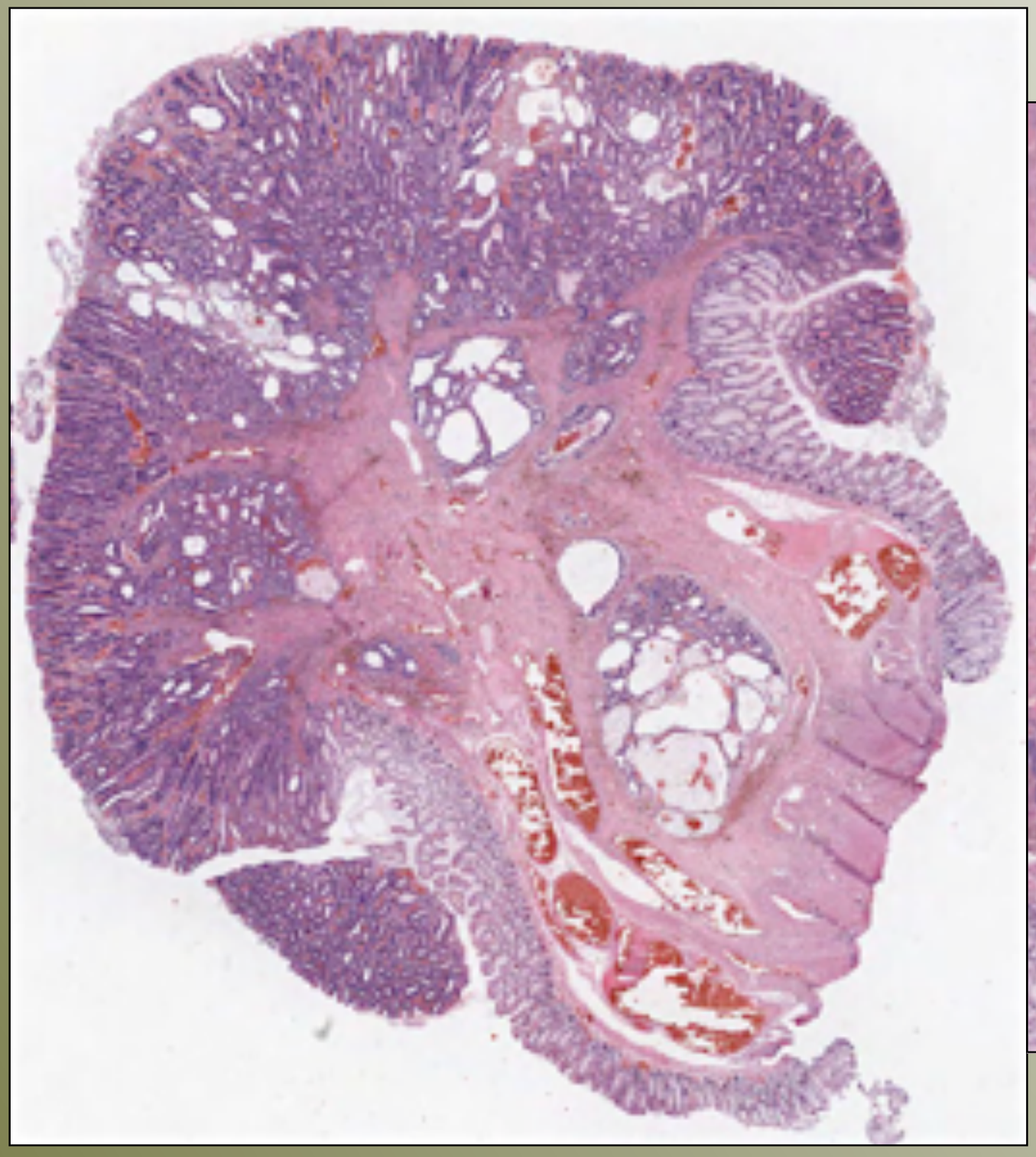
- Sub-mucosal mucinous lakes may be seen.

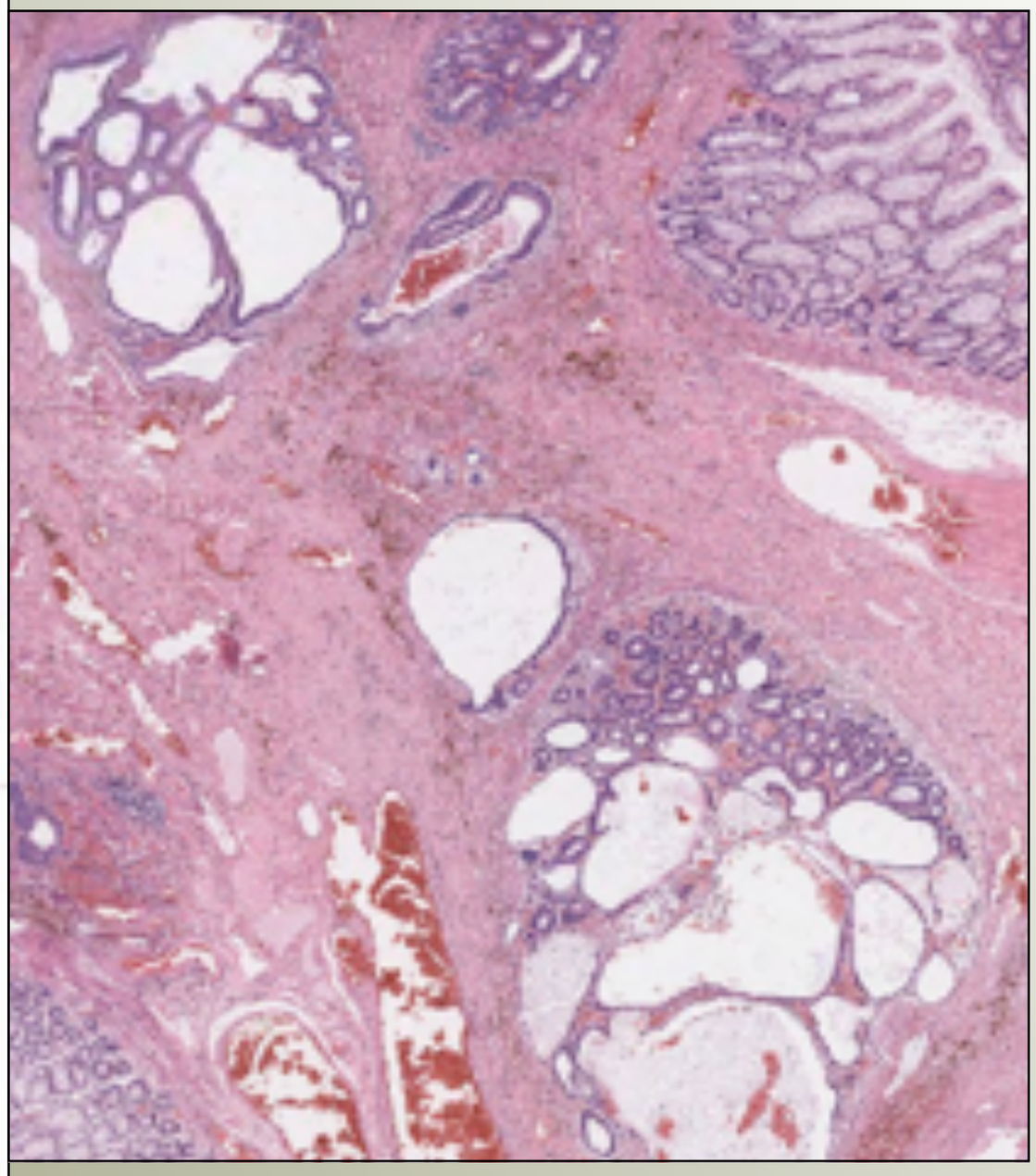
Pseudoinvasion



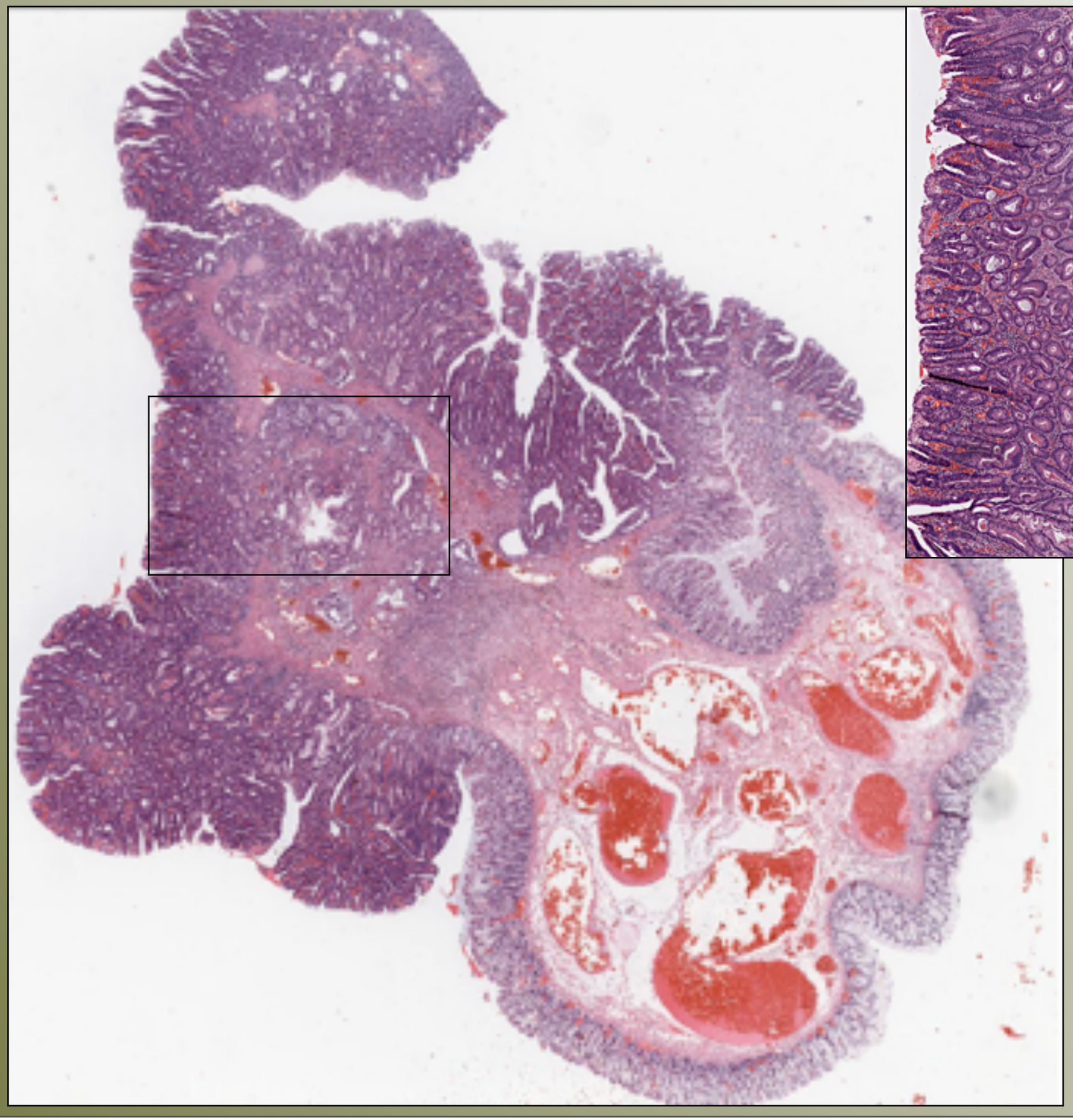


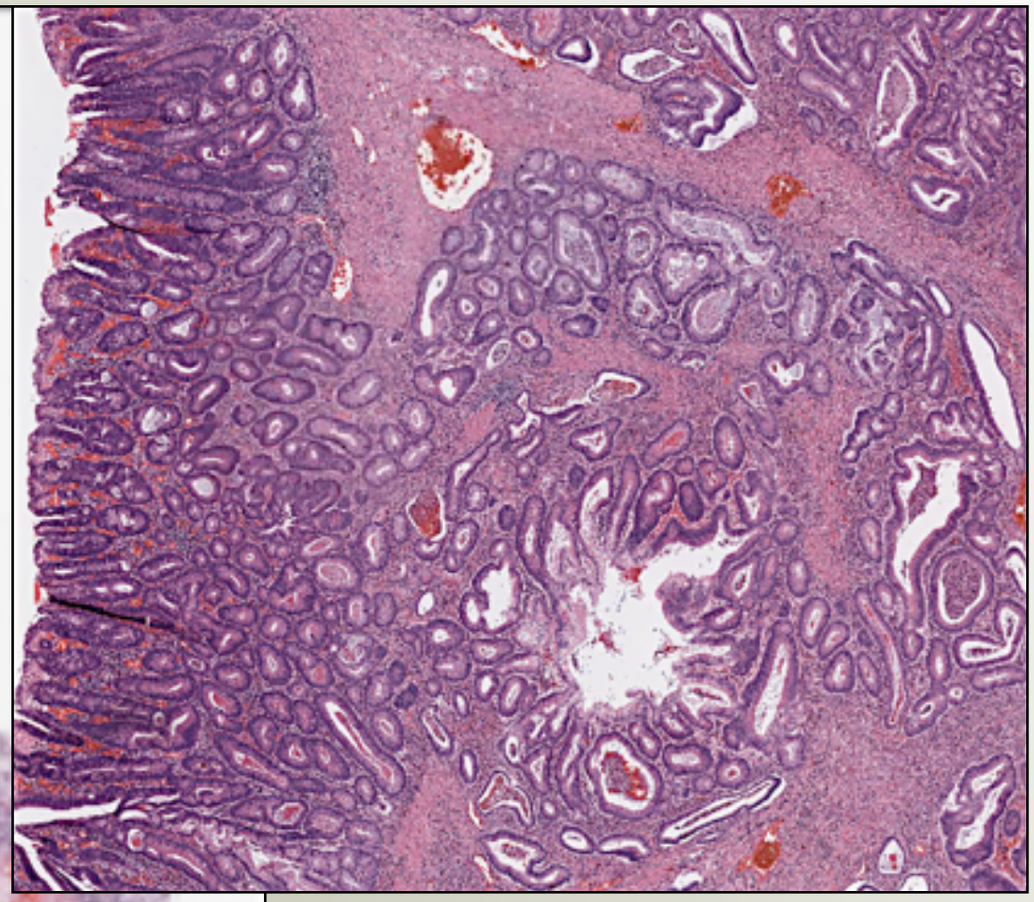
Pseudoinvasion





Pseudoinvasion





High risk pT1 adenocarcinoma

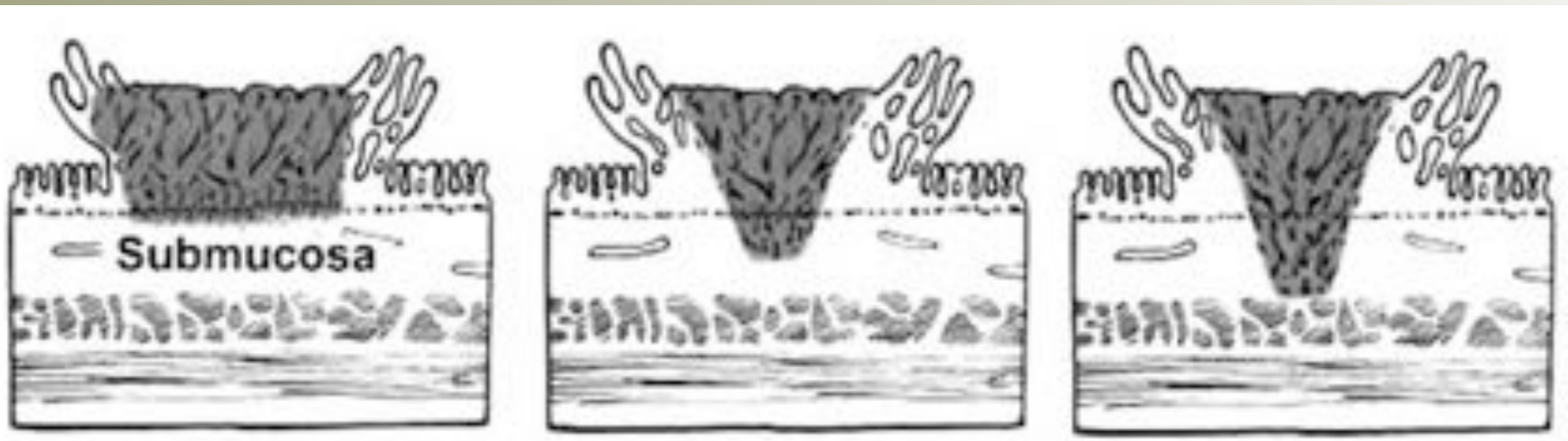
Many authors have searched regards about the correlation between clinical outcome and tumor pathology

(Coverlizza et al. 1989; Coo- per et al. 1995; Volk et al. 1995; Blumberg et al. 1999; Hassan et al. 2005)

Many factors:

1. Morphology of lesion and depth of invasion
2. Kikuchi levels
3. Haggit levels
4. Incomplete excision
5. Poor grade of histological differentiation
6. Venous and lymphatic invasion
7. Tumor budding
8. % neoplasia vs adenoma

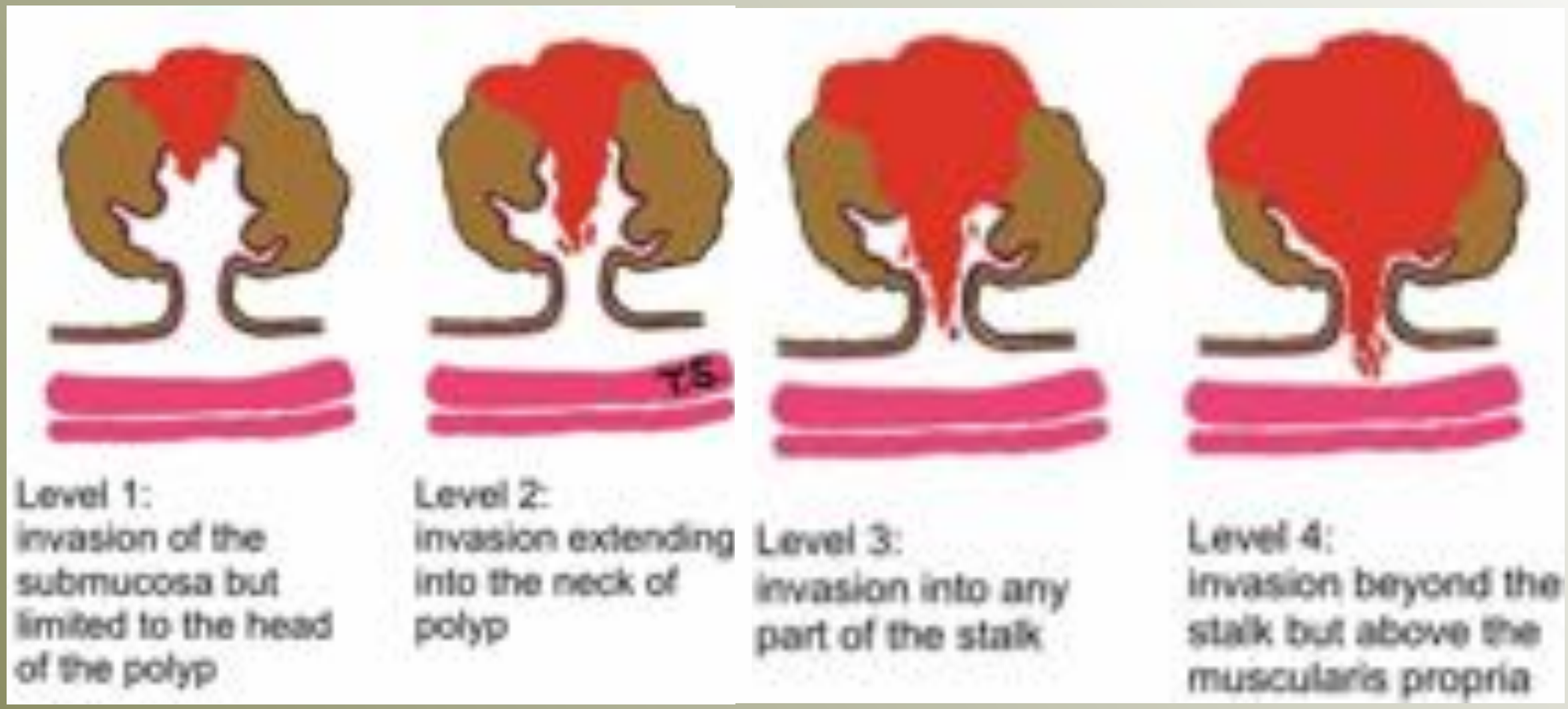
Kikuchi level for flat lesions



Sm1: mm	Sm2: intermediate	Sm3: muscle
200-300 µm	300-2000 µm	>2000 µm

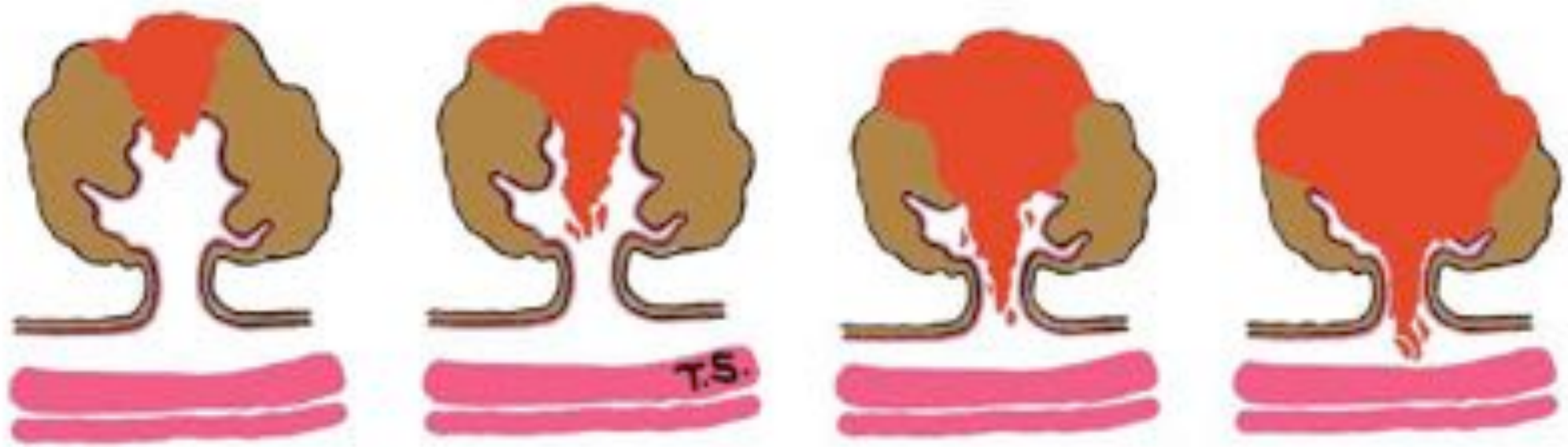
Kikuchi et al. 1995 Dis Colon Rectum 108:1657-65

Haggit levels



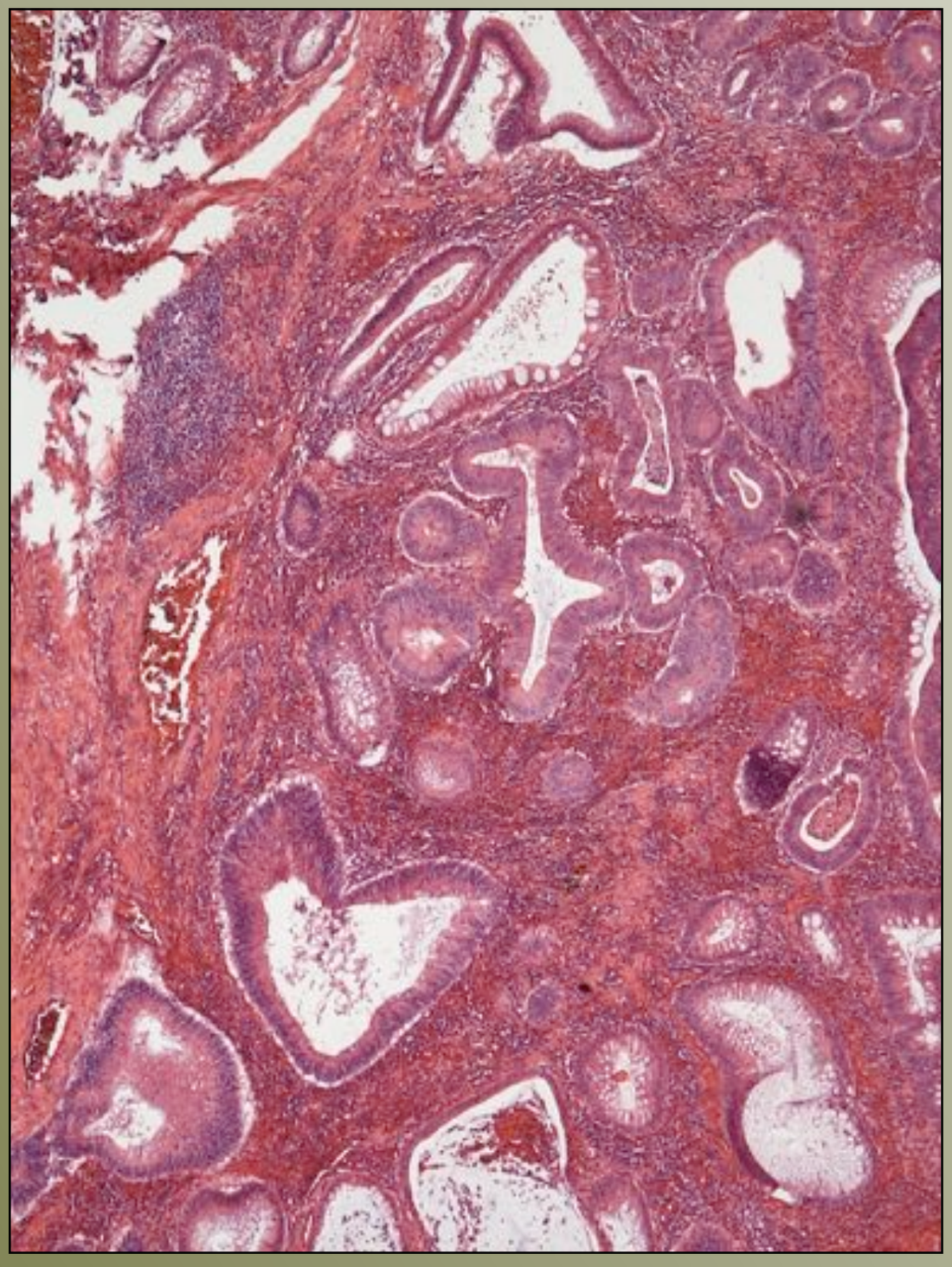
Measurement of width and deep of neoplasia are preferible.
Assesment of MM with actina.

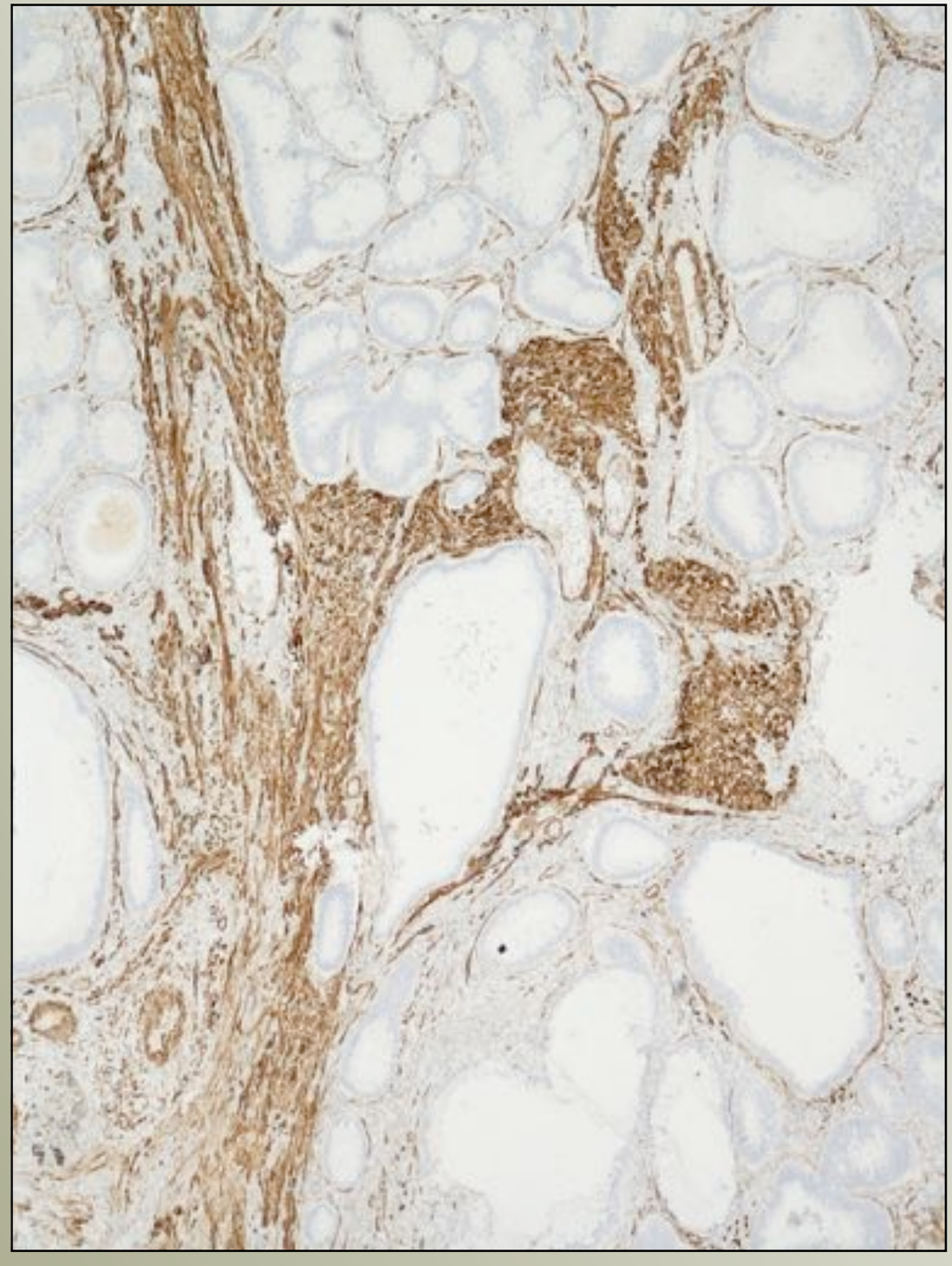
Kikuchi levels



Haggitt levels

Uso del test per Actina





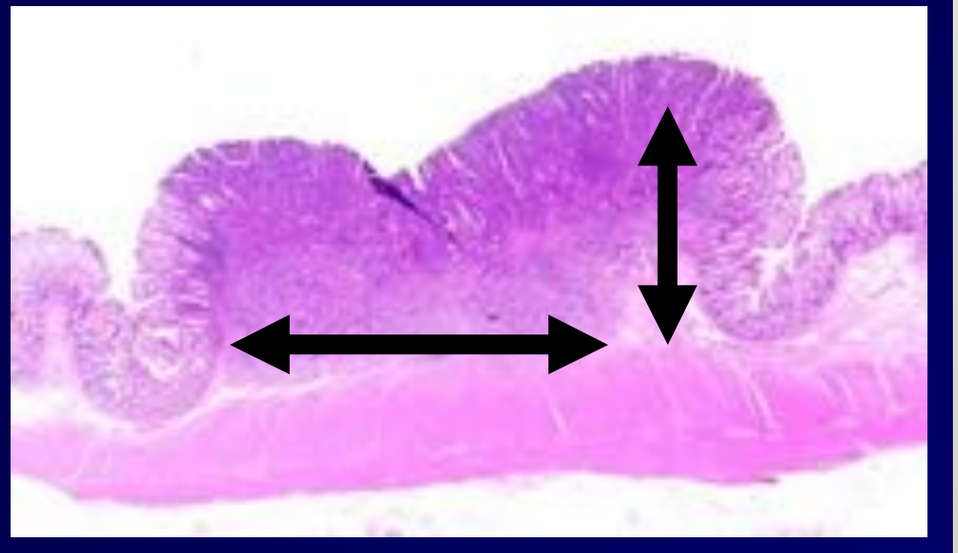
Substaging of pT1

•However, both the Kikuchi (for non-polypoid tumours) and the Haggitt (for pedunculated tumours) systems may be difficult to use in practice, especially if there is fragmentation or suboptimal orientation of the tissue, and only one study found lymph node metastases in 6/24 Haggitt level 3 lesions.
•Each classification has advantages and disadvantages:
•Kikuchi cannot be used in the absence of muscularis propria;
•Haggitt is not applicable in non-polypoid lesions, and measurement depends on a recognisable submucosa from which to measure.
•In view of the uncertainty and lack of consensus, a firm evidence-based recommendation for one method of assessing local invasion cannot yet be made.
•**At present we recommend :**
1.**the Kikuchi stage for nonpolypoid lesions** and
2.**Haggitt for pedunculated lesions.**
3.**More recently Ueno et al. (2004) have proposed use of the depth (>2000 µm) and width (>4000 µm) of invasion measured in microns beyond the muscularis mucosae provides a more objective assessment of lymph node metastatic potential (2.5% vs. 18.2% when submucosal invasion width is < or 4000 µm, respectively; and 3.9% vs. 17.1%, when submucosal invasion depth is < or 2000 µm, respectively; and this approach has been adopted in Japan.**

•All three approaches must be evaluated in further large series from multiple programmes to derive adequately evidence-based recommendations.

ADENOMI CANCERIZZATI: Volumetria del Carcinoma

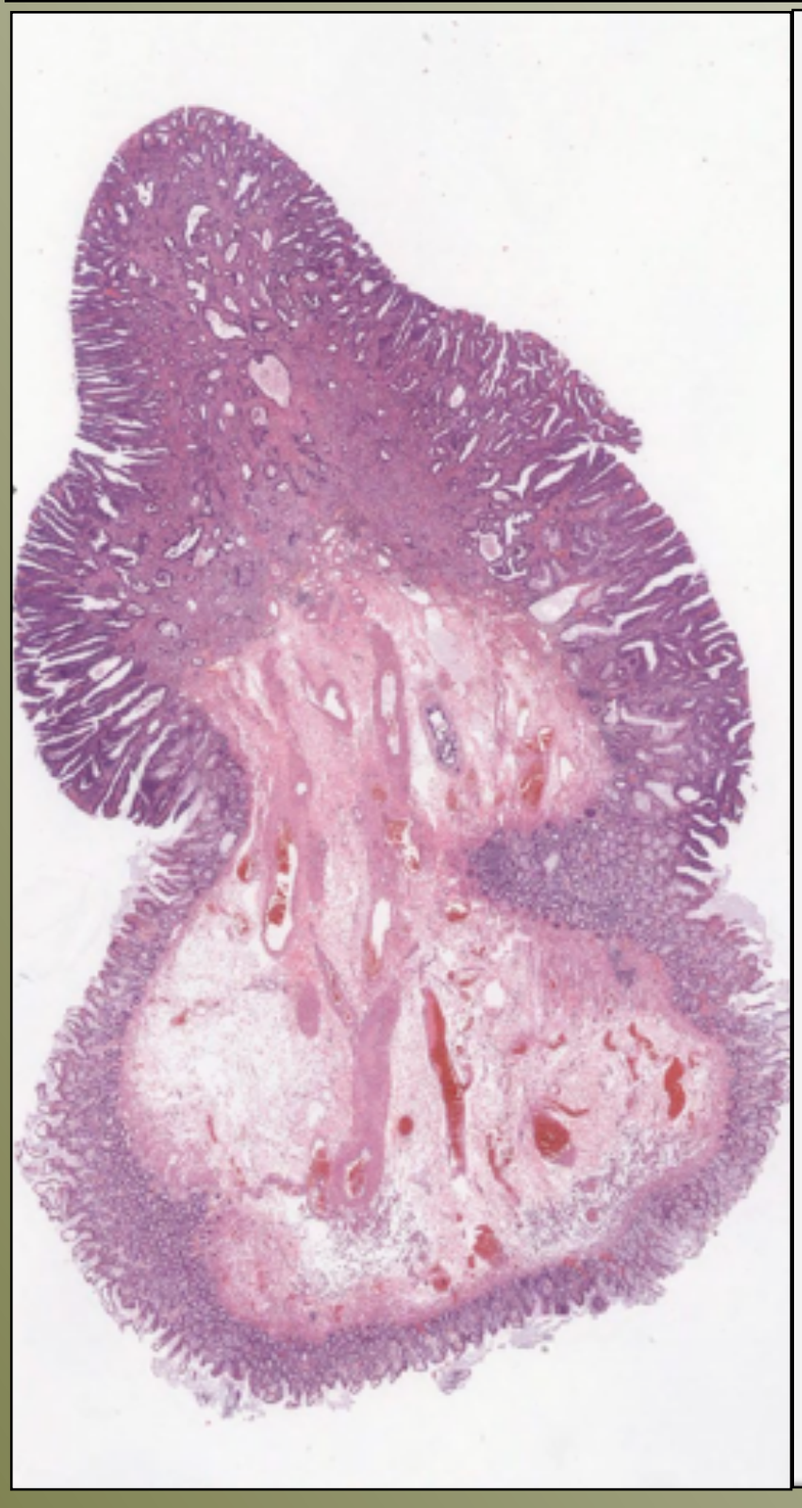
	Lymph Node Metastasis
Width sm < 4000 μm:	2.5%
Width sm > 4000 μm:	18.2%
Depth sm < 2000 μm:	3.9%
Depth sm > 2000 μm:	17.1%

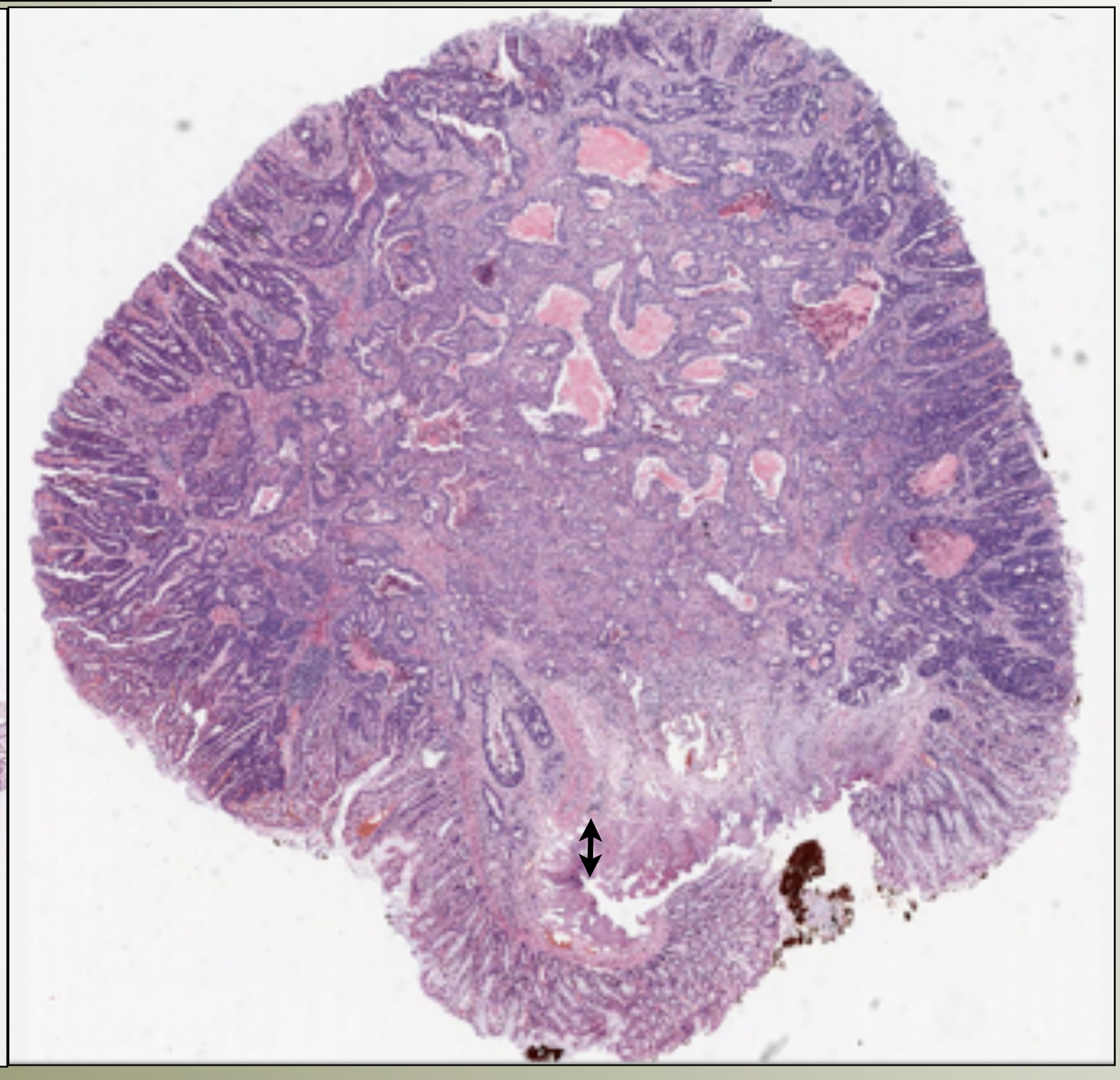


Ueno et al, Gastroenterology 2004

Margini: Stato del margine di resezione endoscopica:

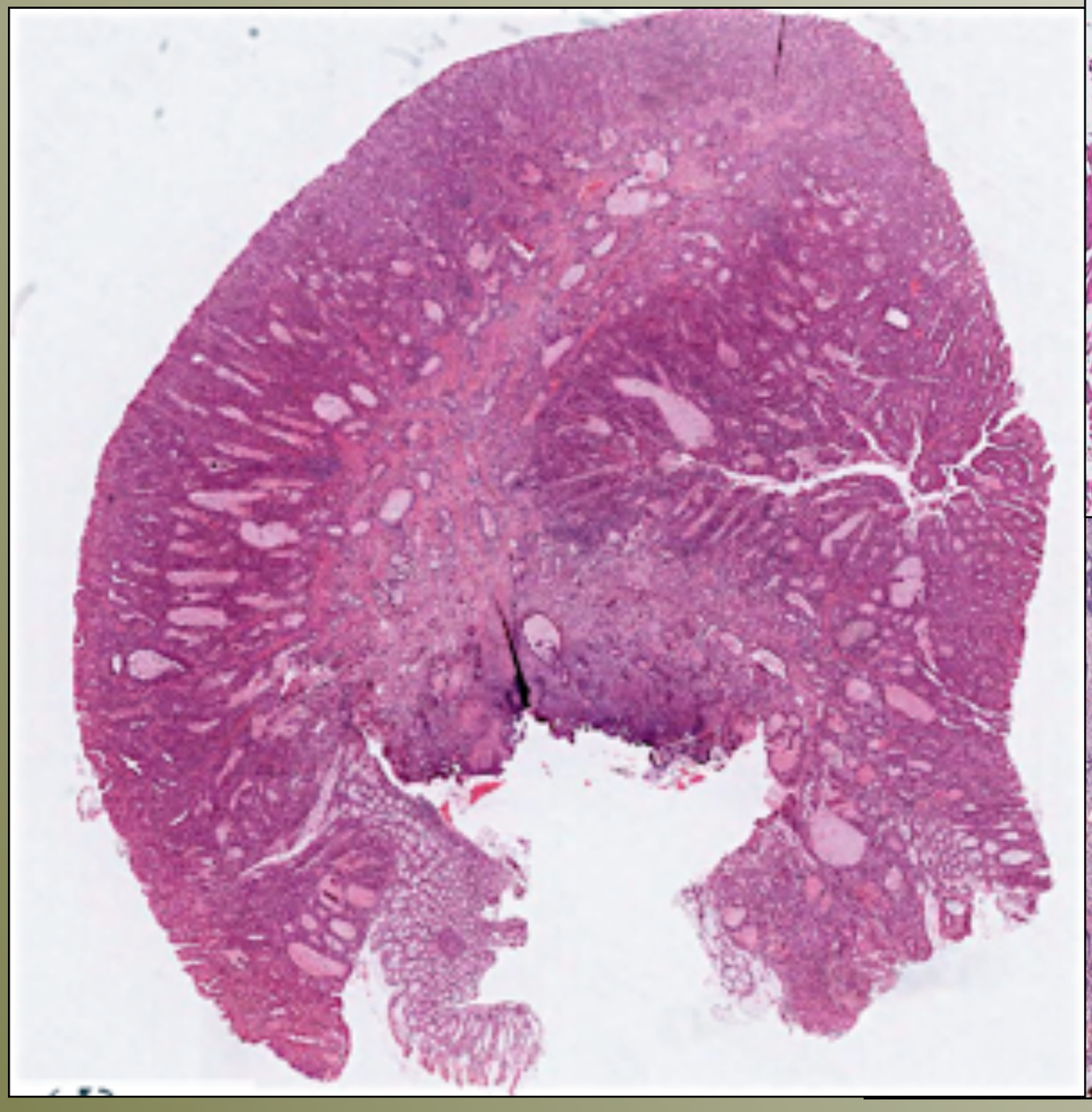
- **positivo quando si identifichino cellule di carcinoma a meno di 1 mm dal margine, o dentro la banda di diatermocoagulazione, o ancora entro un campo ad alto ingrandimento da essa**

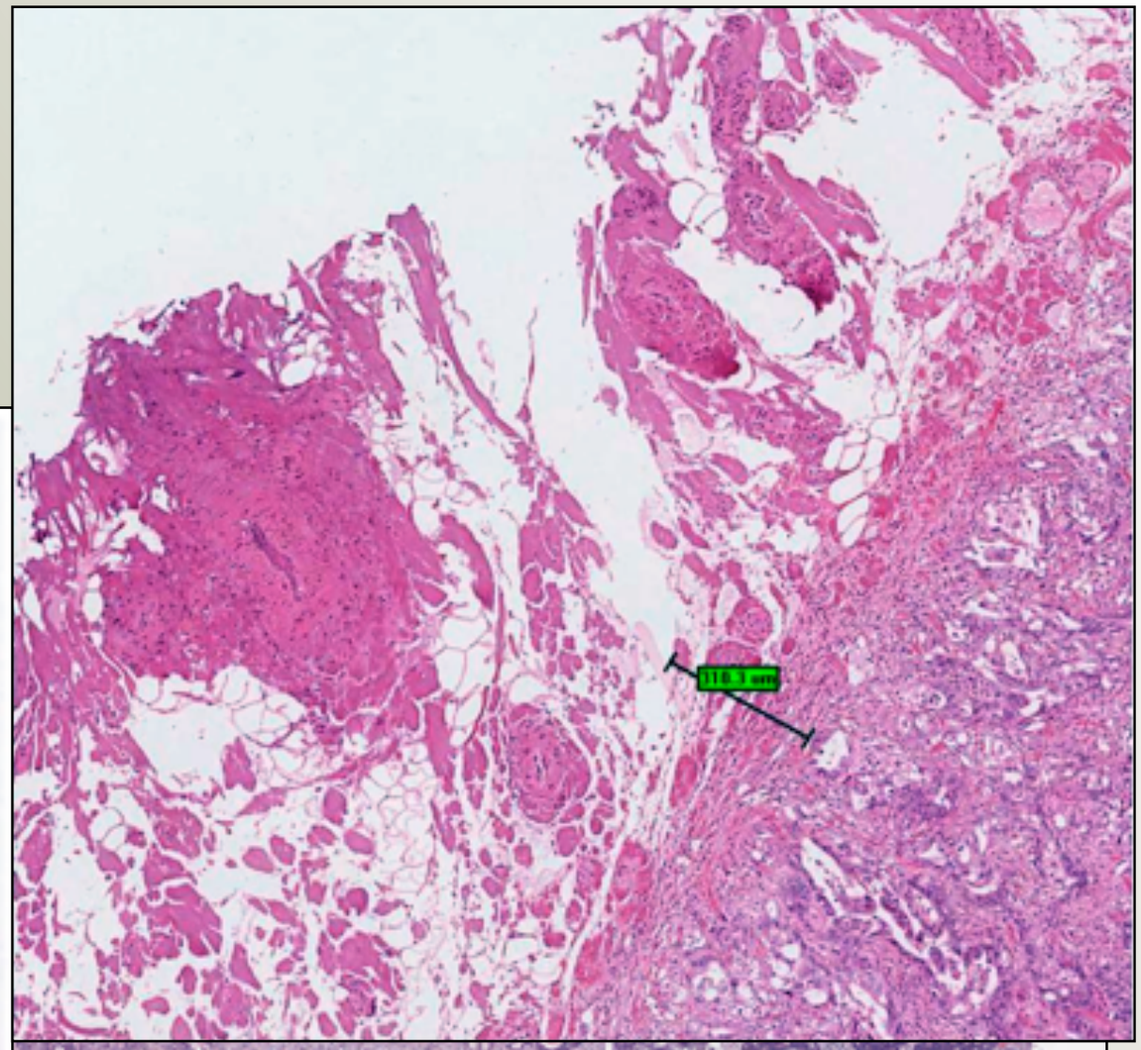


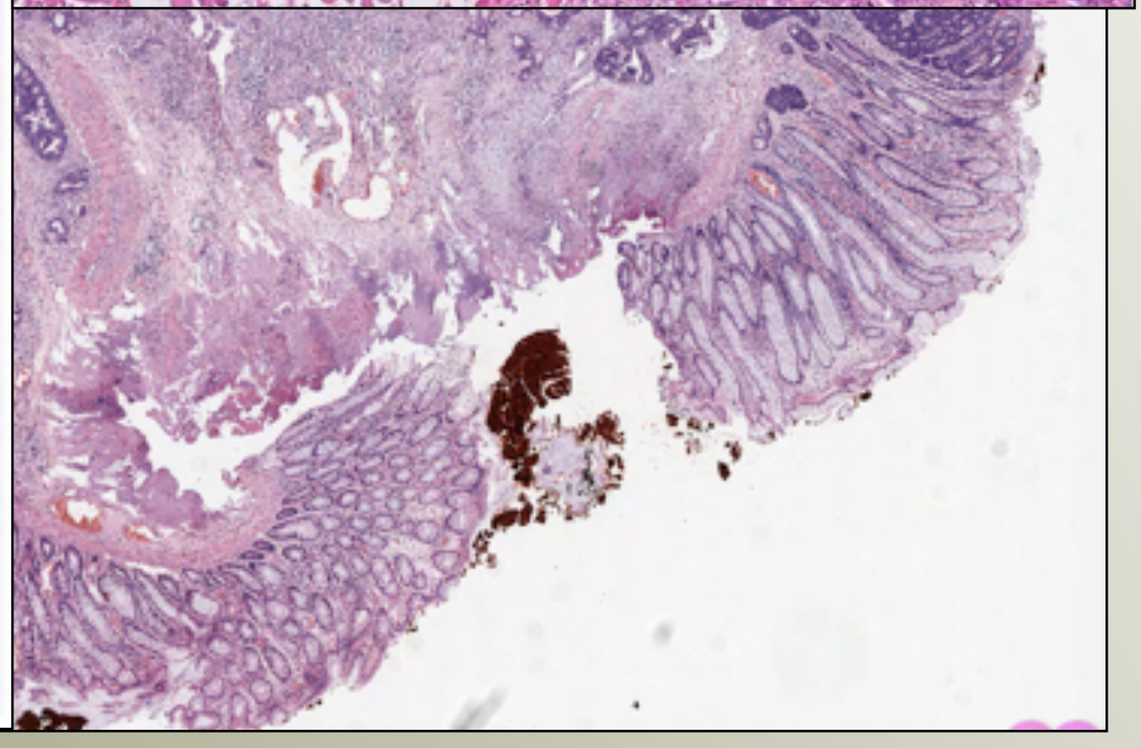


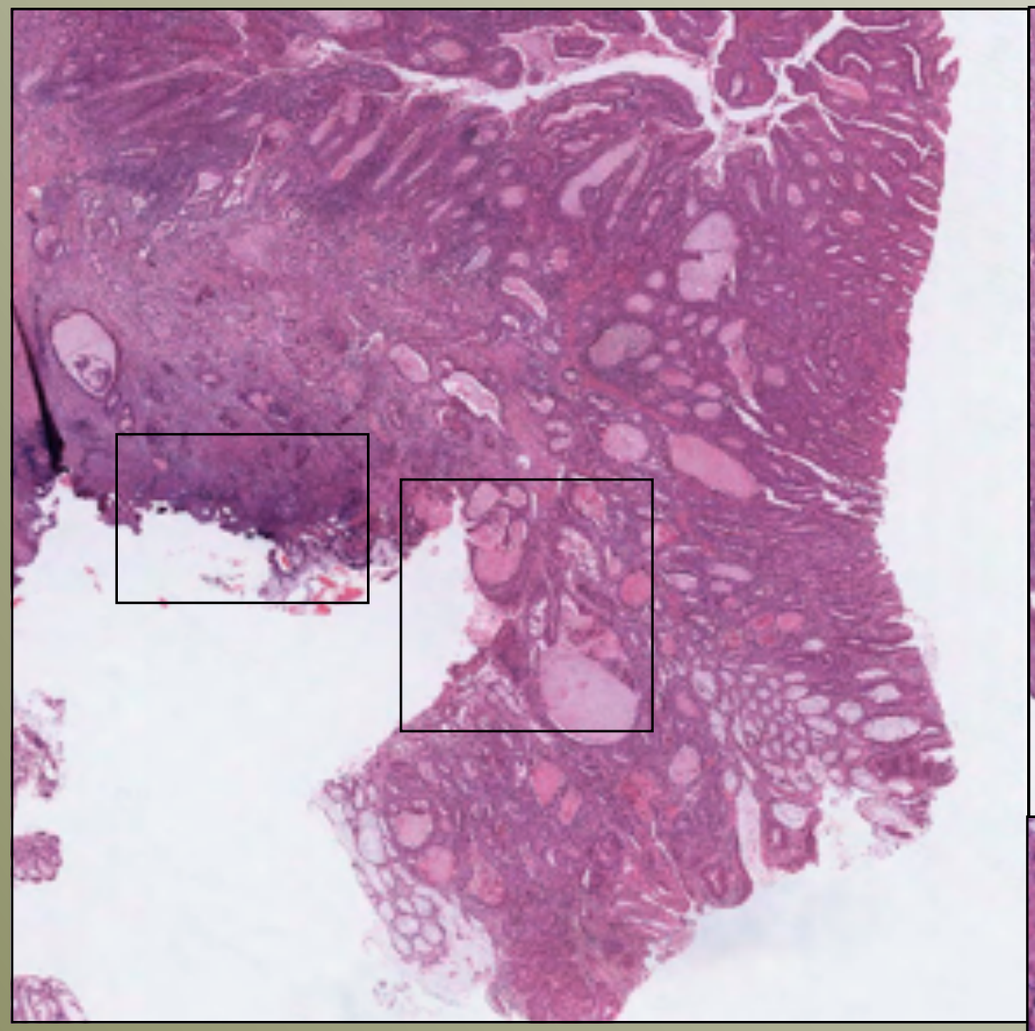
Margine preso

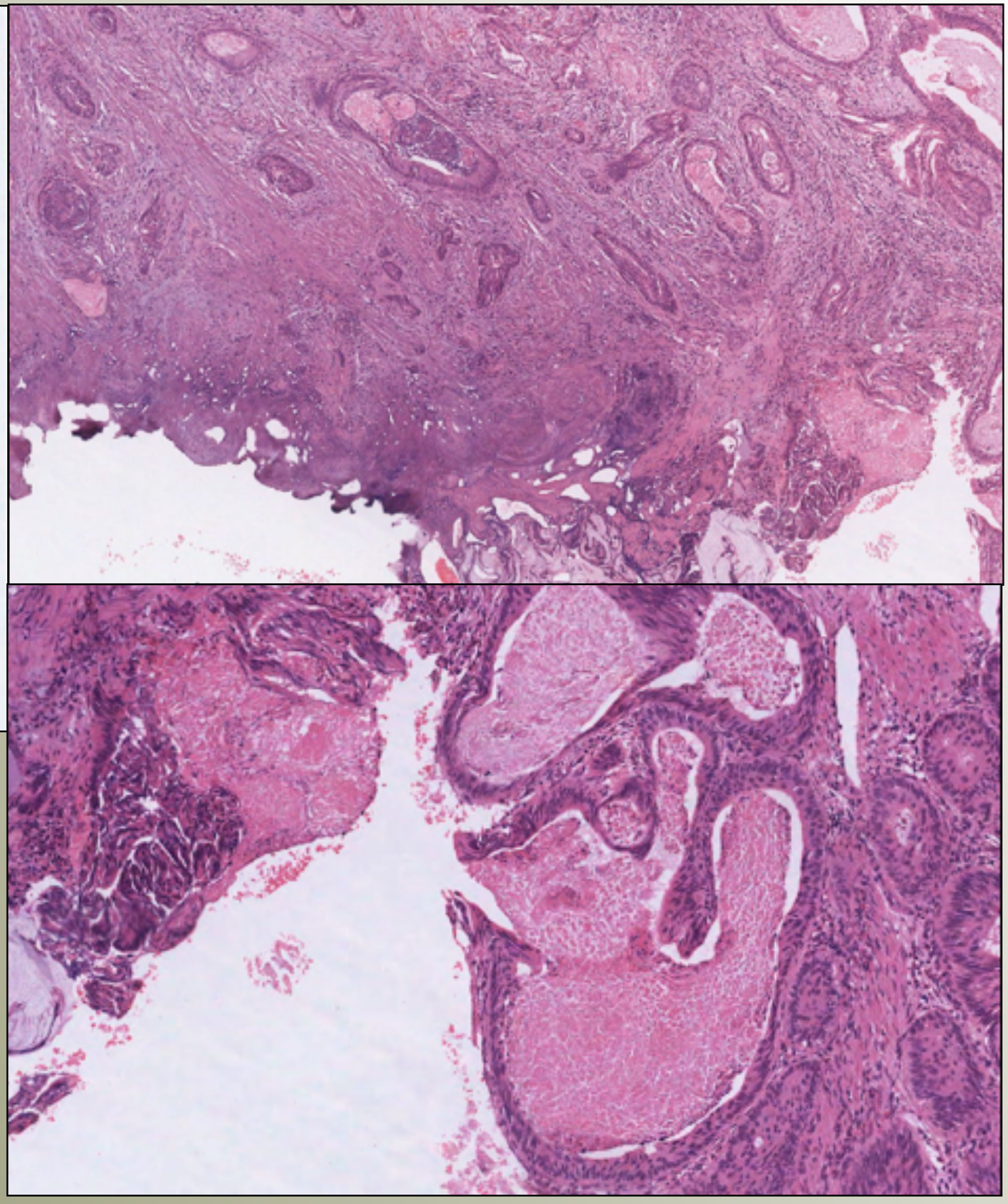
All would agree that a clearance of 0 mm, and most would agree that a clearance of <1 mm is an indication for further therapy, others would use <2 mm. We currently recommend that clearance of 1 mm or less indicates margin involvement . However, this may be handled by removal of any residual polyp endoscopically.











Margine preso

Budding

Tumour cell budding, i.e., the presence of small islands or single infiltrating tumour cells at the front of tumour invasion, has been described in the Japanese literature as an unfavourable prognostic factor if present in a marked degree.

Budding has been assessed either as slight, moderate or marked; or as present/ absent (Deinlein et al. 2003; Wang et al. 2005).

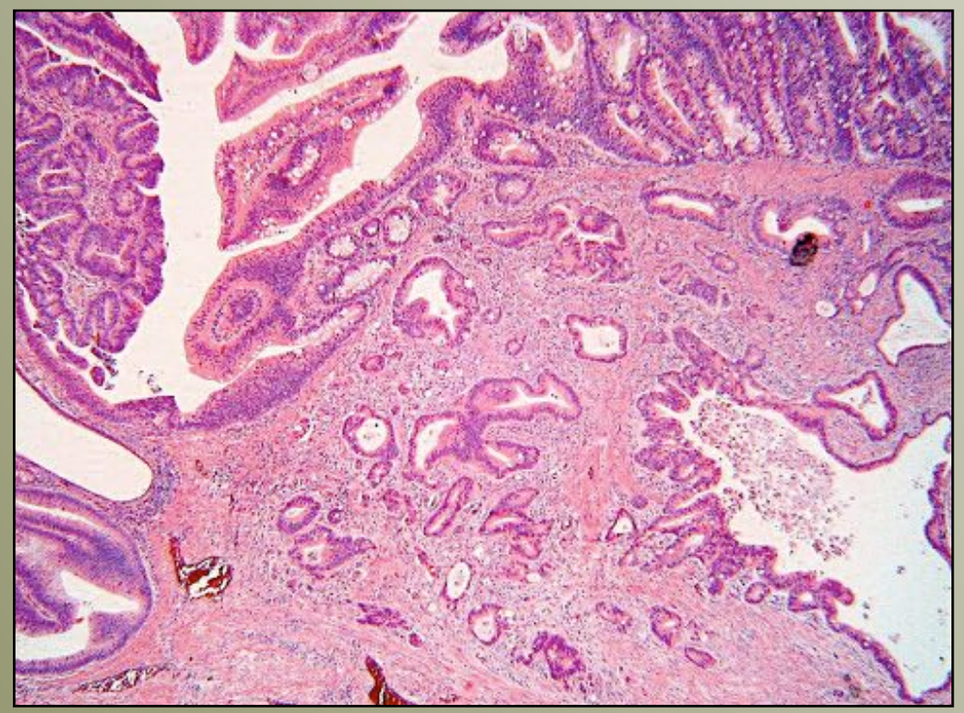
However, its reproducibility has been criticised, the diagnostic criteria vary (Prall 2007) and the ability to predict metastasis compared to the previously discussed factors is unproven.

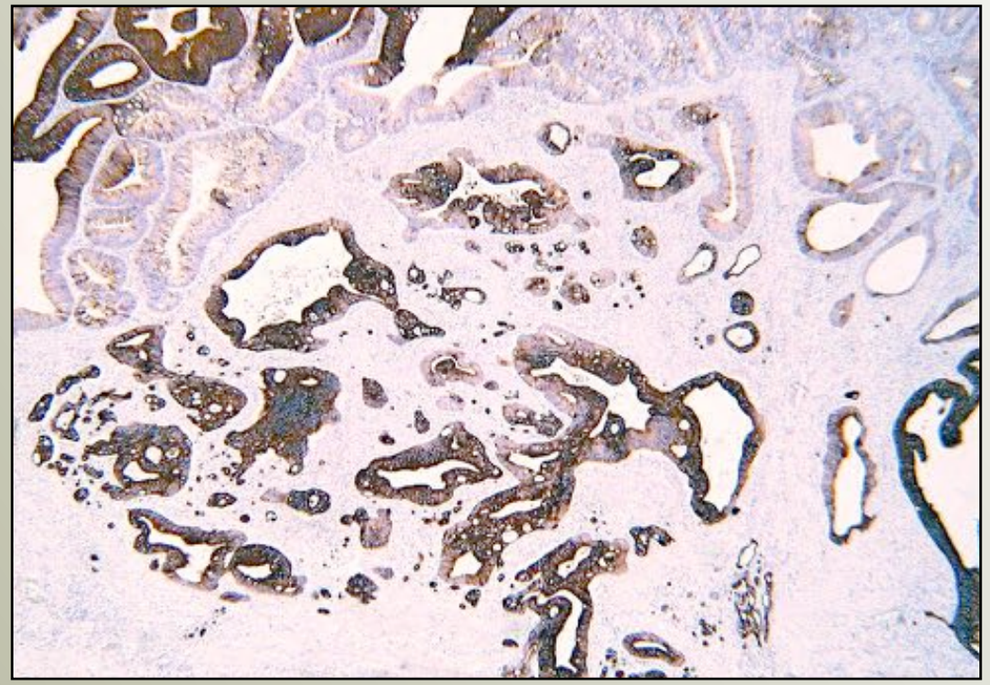
Further research is needed in this area to identify the optimum method and its reproducibility before tumour cell budding can be recommended for routine use as an indicator of metastasis.

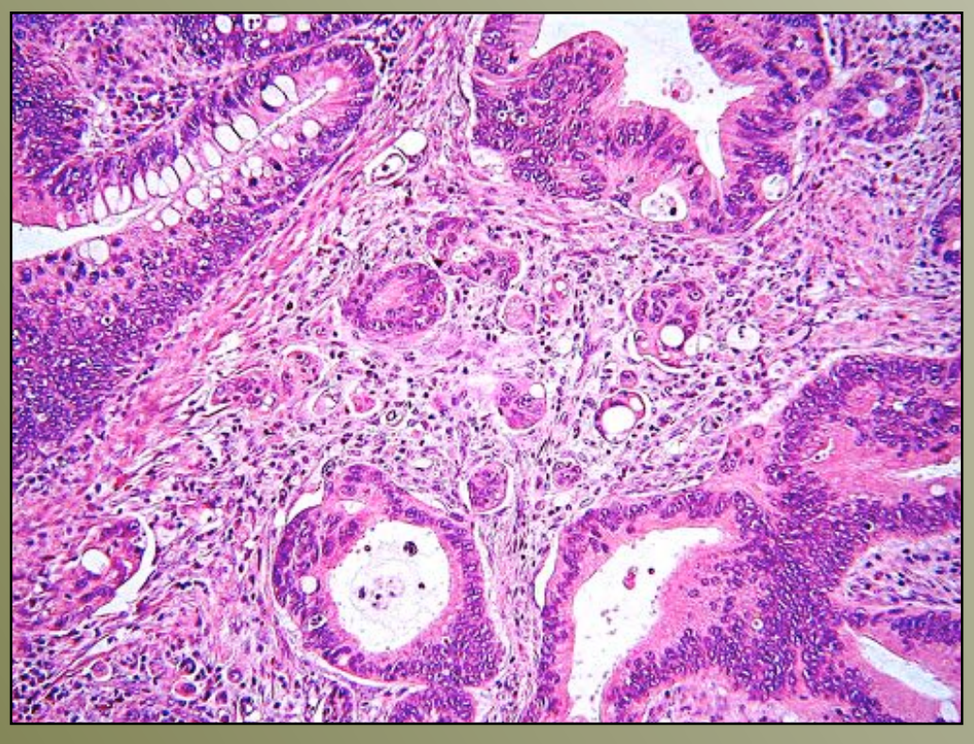
It is good practice but not mandatory to document the presence or absence of single tumour cells at the front of invasion, and we therefore recommend providing this additional information in the written report with an explanatory comment, as budding has been suggested as a prognostic factor in colorectal cancer

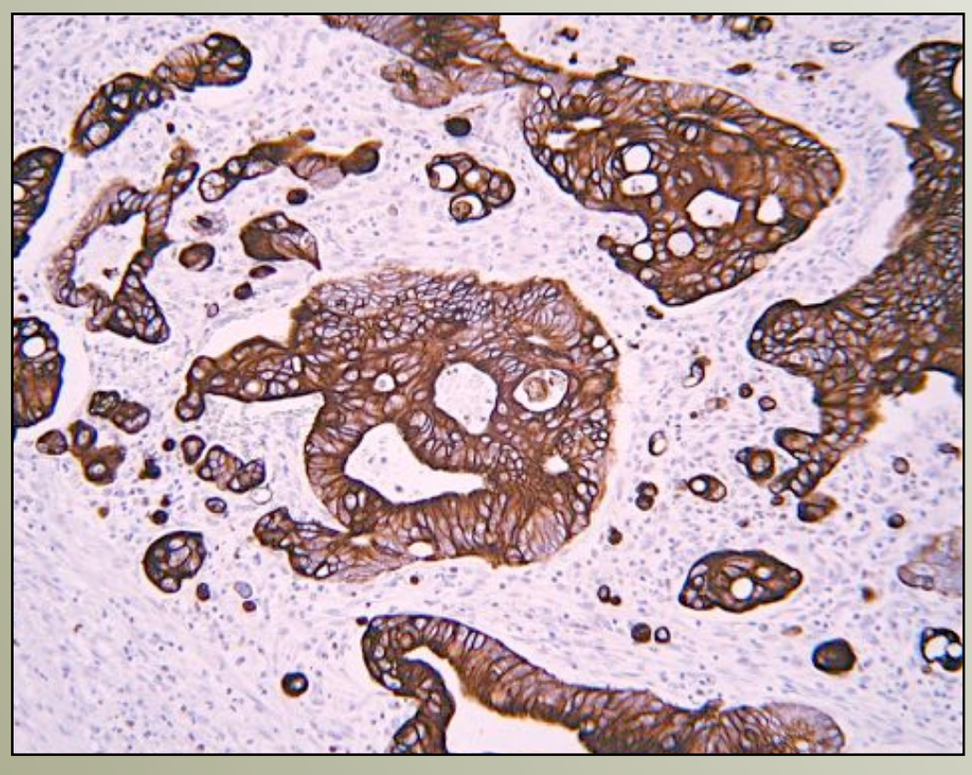
Tumour budding at the deepest invasive margin correlates with lymph node metastasis in submucosal colorectal cancer detected by anticytokeratin antibody CAM5.2
Kazama el al British Journal of Cancer (2006) 94, 293 – 298

Budding

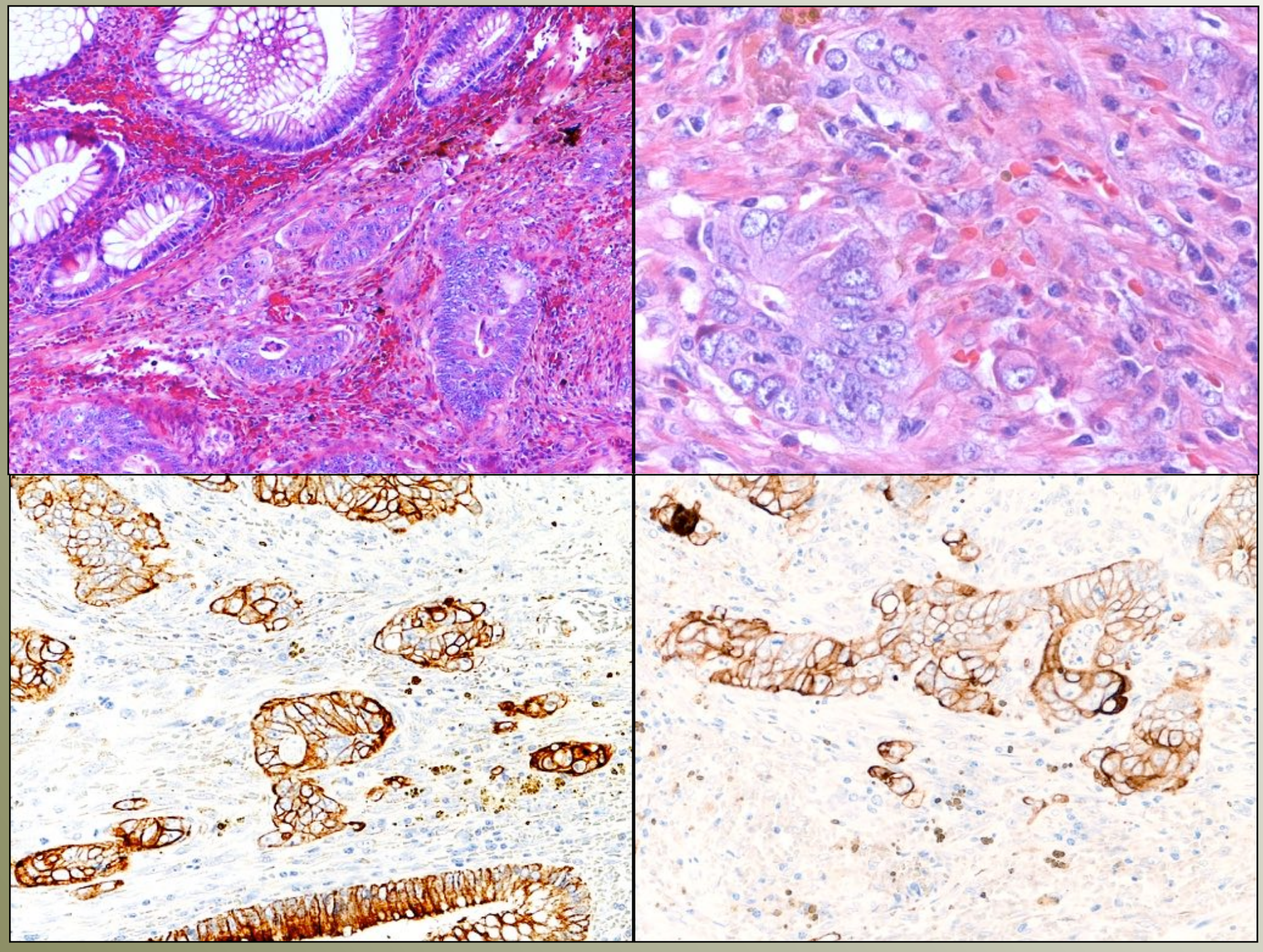








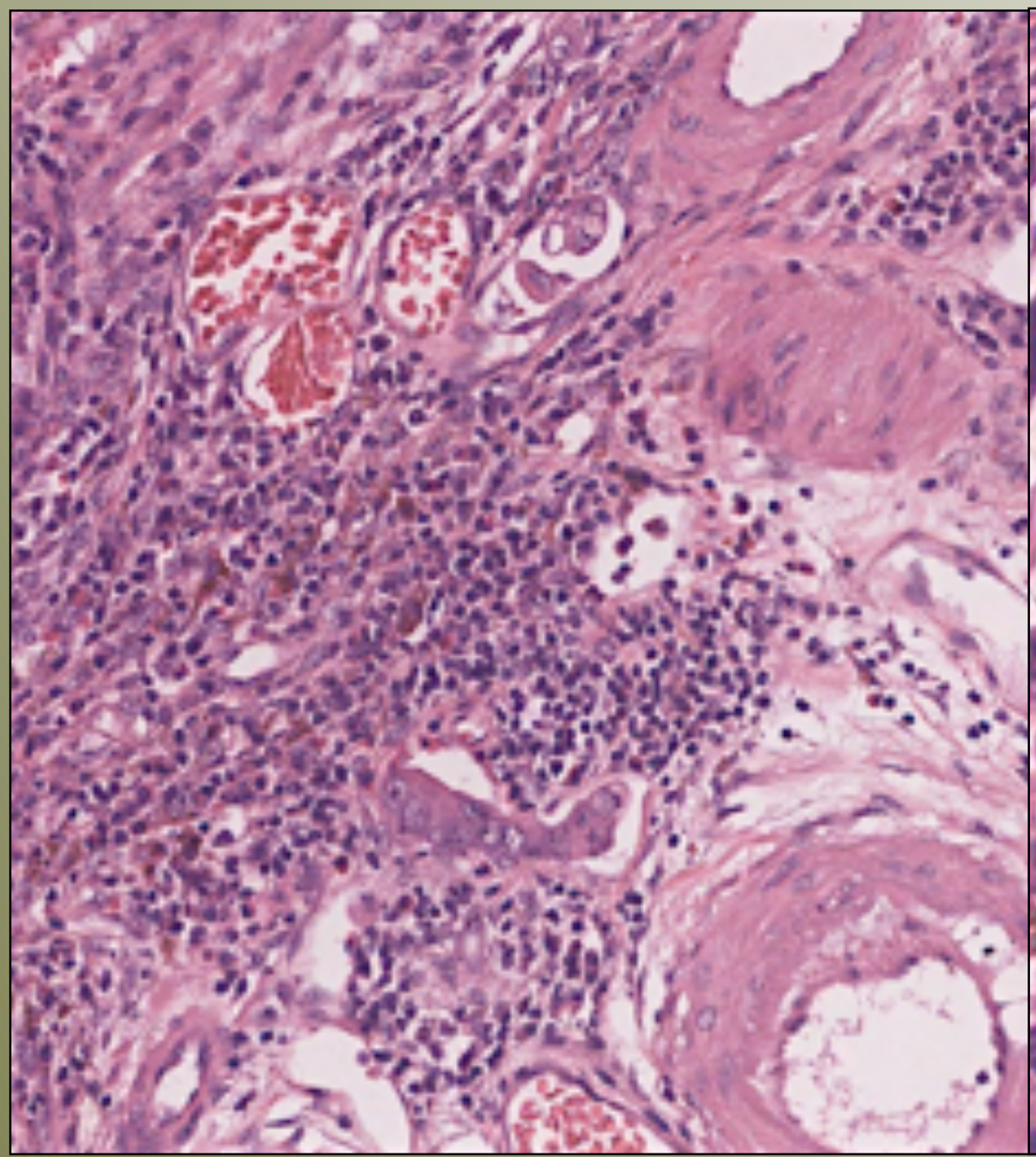
Budding

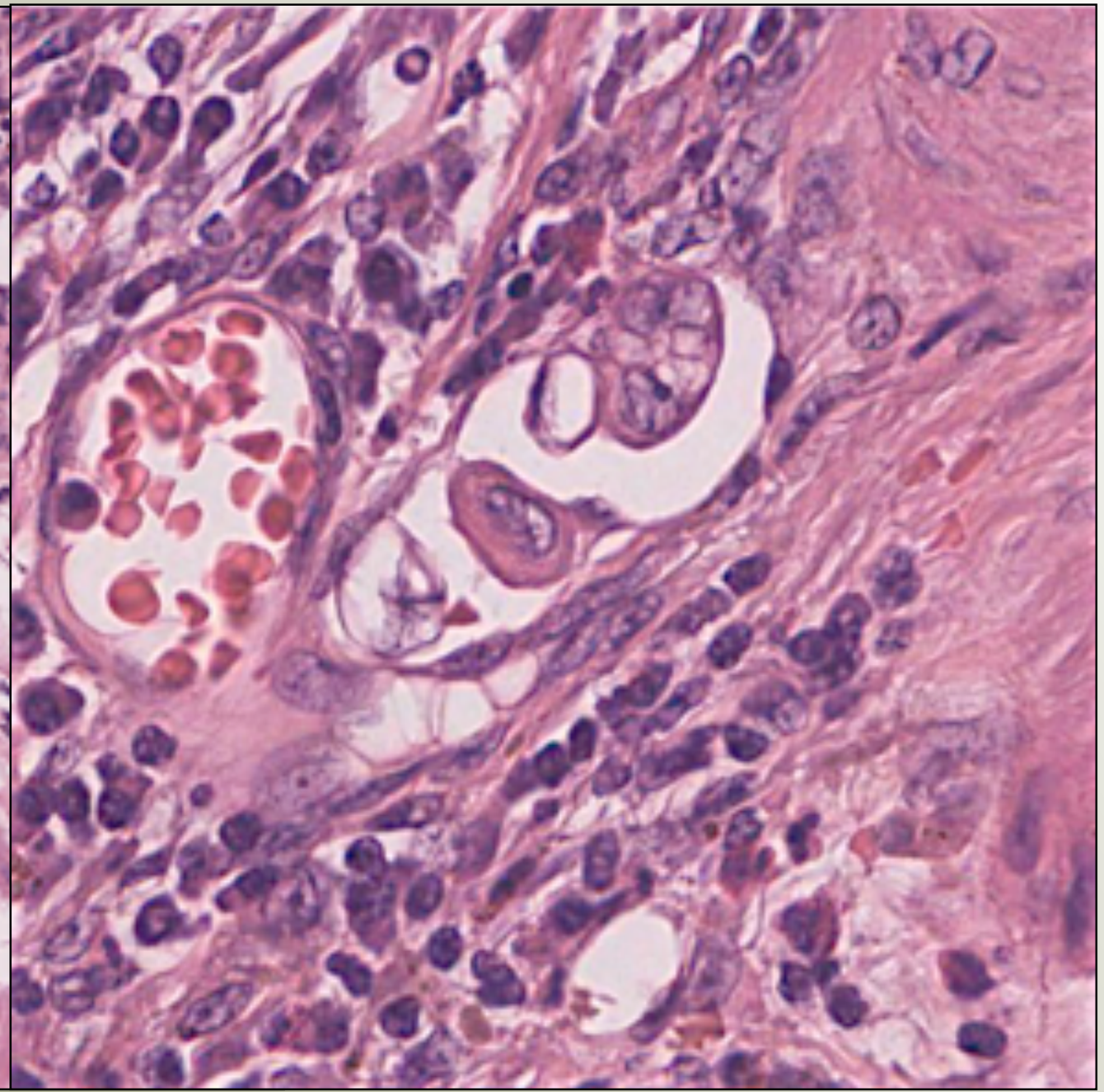


Vascular involvement

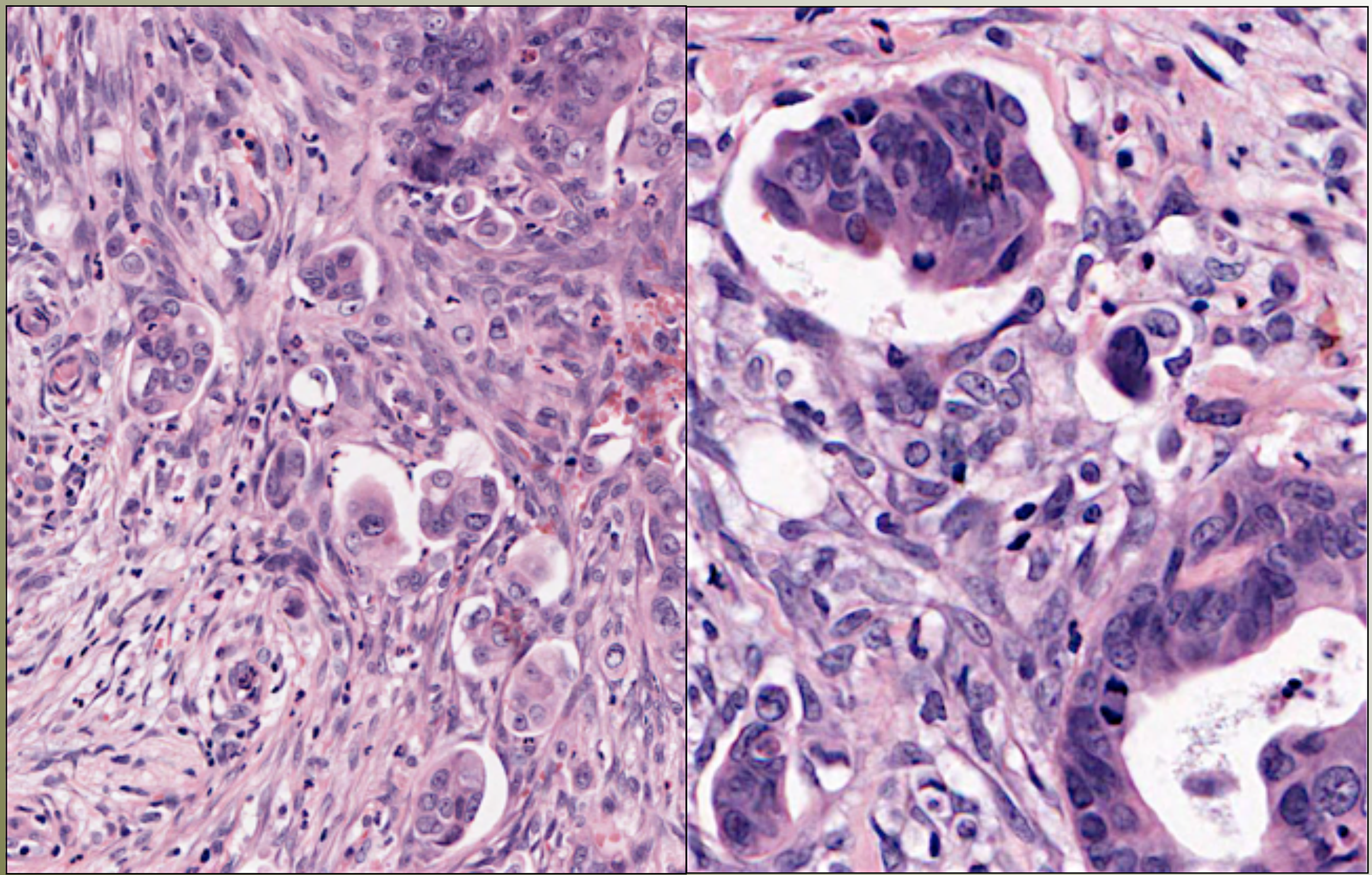
- La linfangite neoplastica è un fenomeno incostante e strettamente legato al budding.
- Se presente deve necessariamente essere segnalato
- L'infiltrazione vascolare e' considerata da alcuni un indicatore significativo (17,6% dei polipi maligni, Hassan e coll.,2005) ,ma altri (Mitchell e coll.,2007) ne sottolineano la difficile definizione ("artefatti da retrazione") mettendo in discussione anche l'uso delle comuni indagini immunoistochimiche
- At the moment there are no consistent data available on the additional use of immunohistochemistry, but this might be helpful in distinguishing retraction artefacts from lymphatic (e.g. LEM D 2-40) or capillary spread (e.g. CD 34).

Lymph vessel invasion

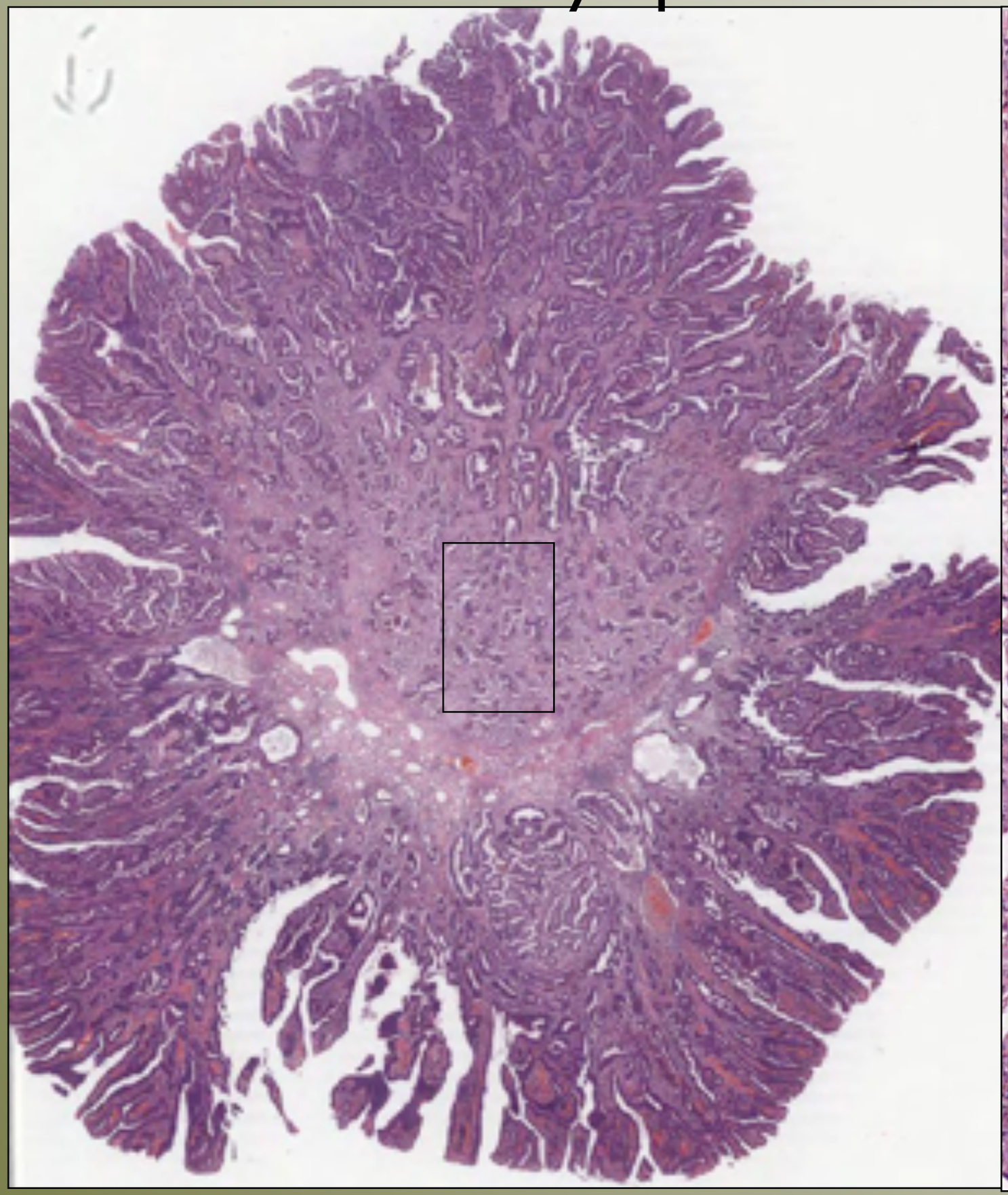


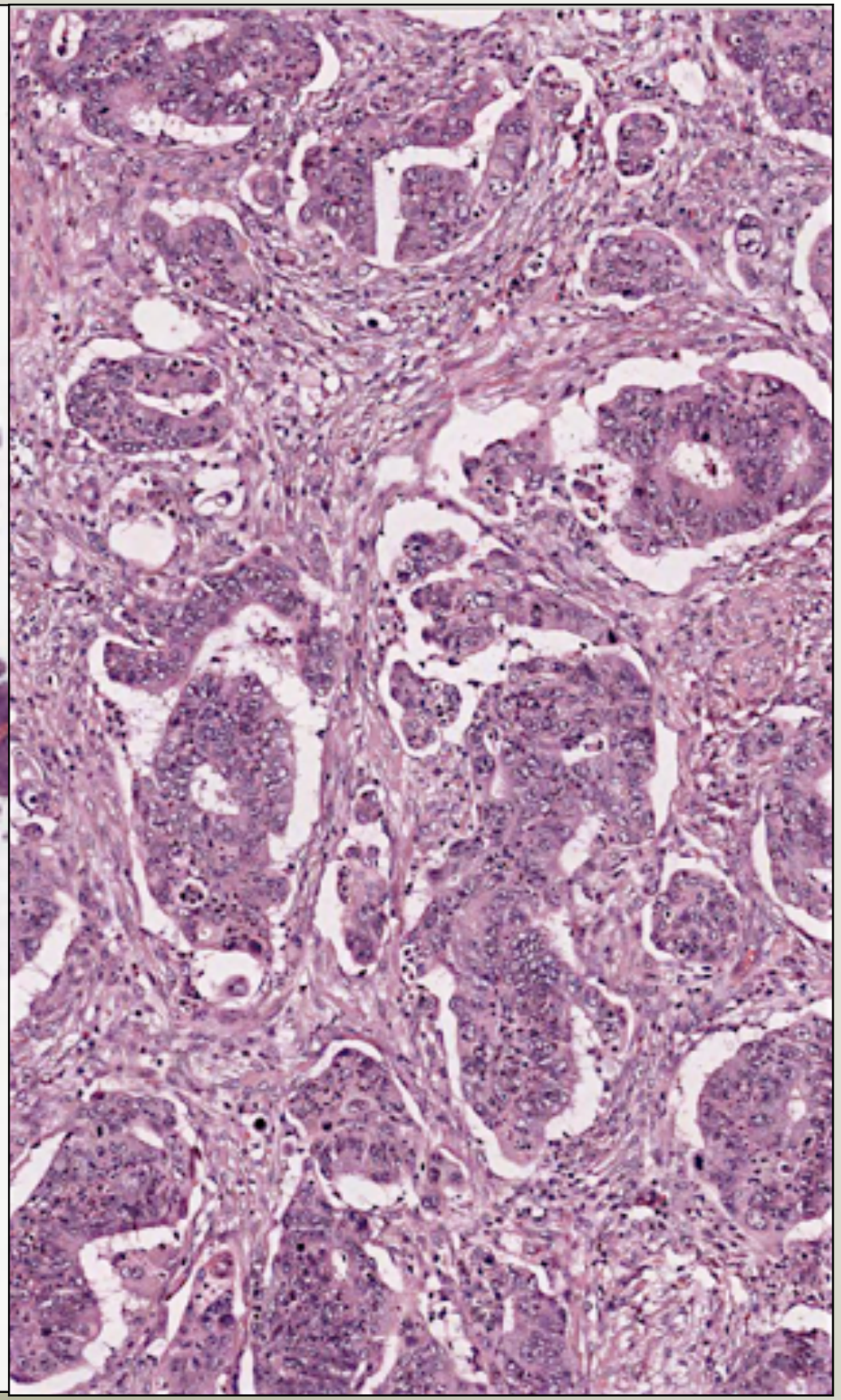


Lymph vessel invasion

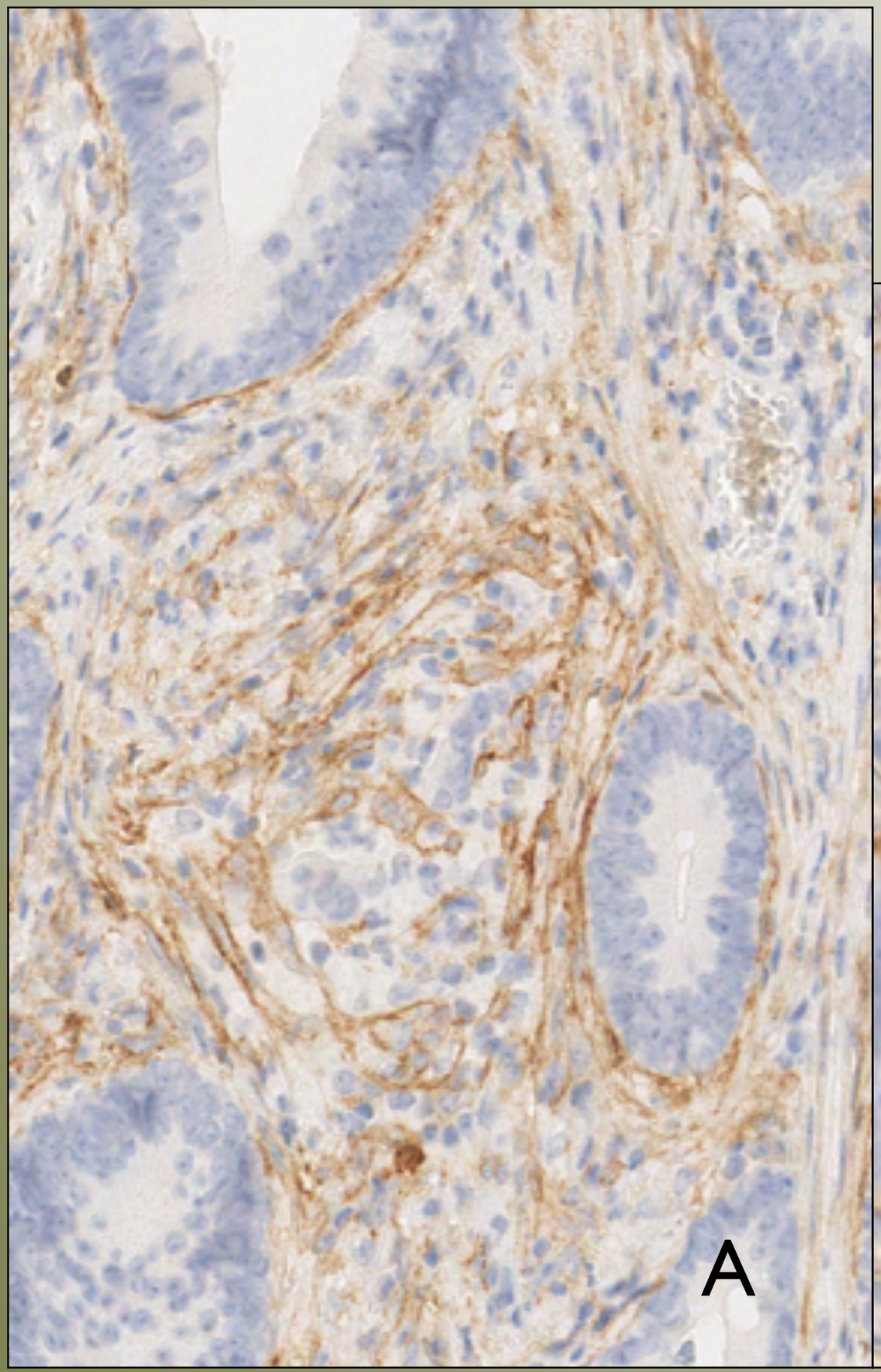


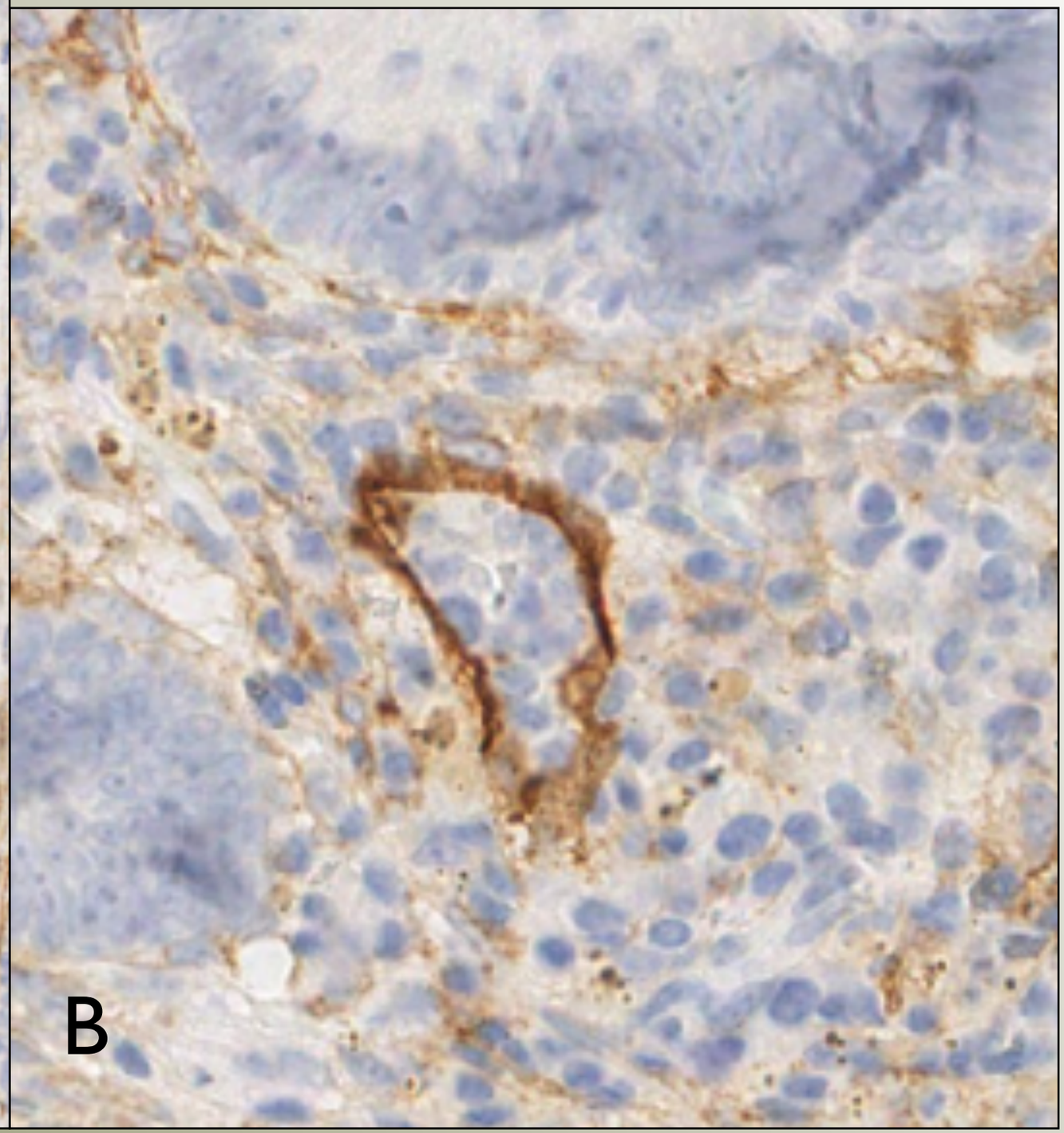
Lymph vessel invasion





Lymh vessel evidence with podoplanin
A: with budding
B: intravascular neoplastic cells

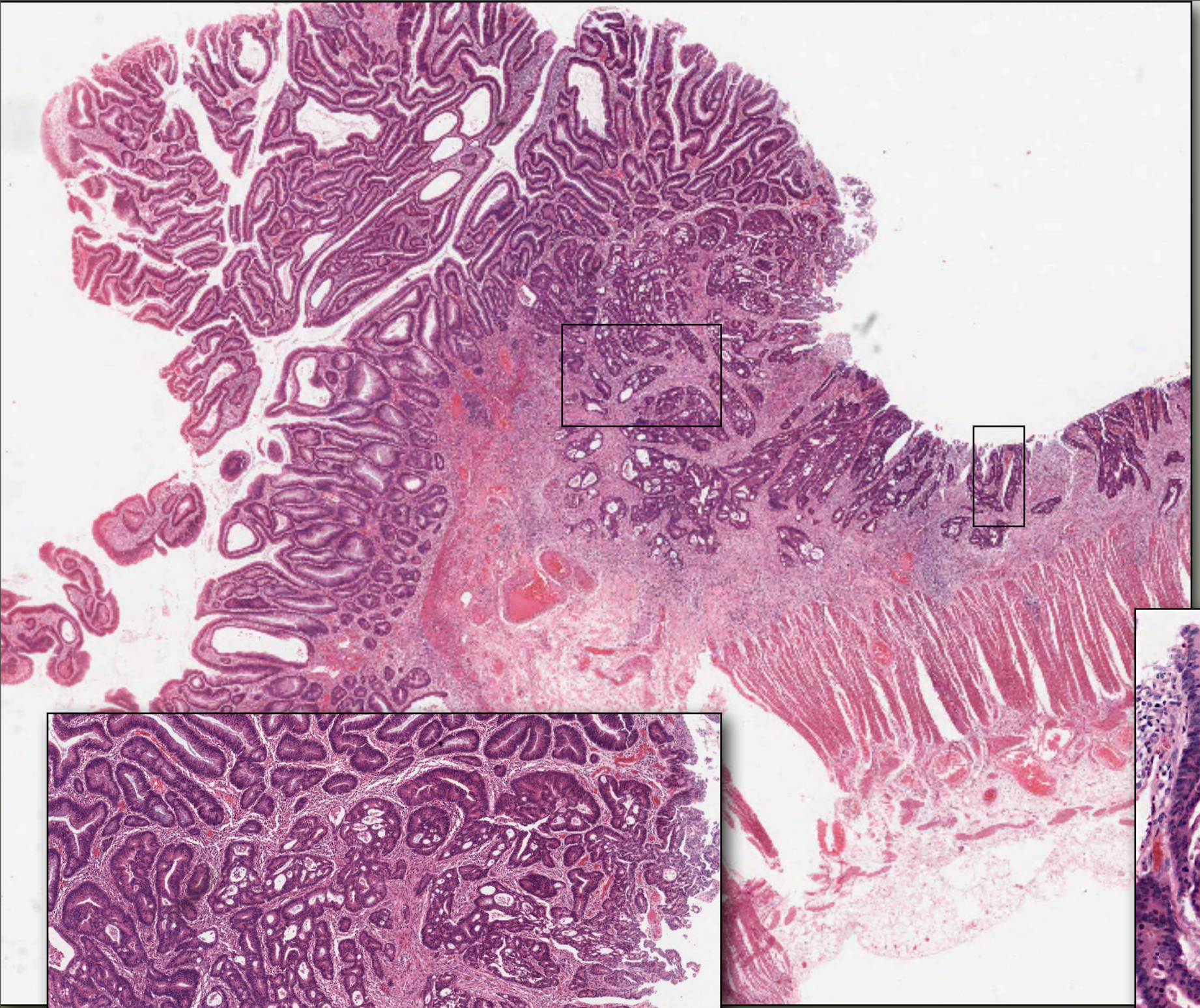


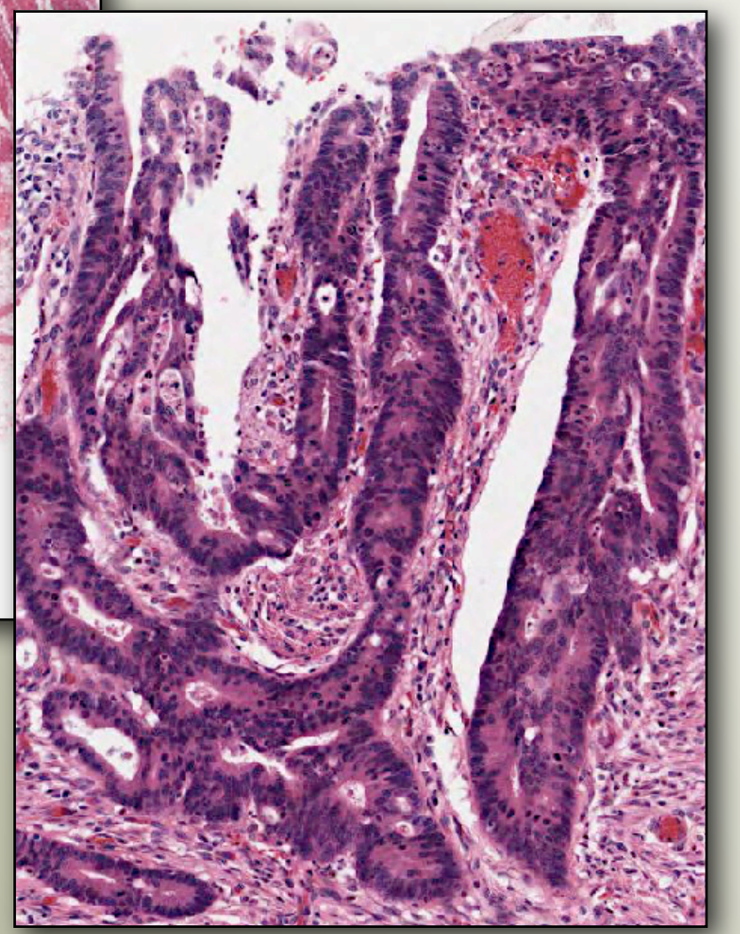


TUMOR GRADE

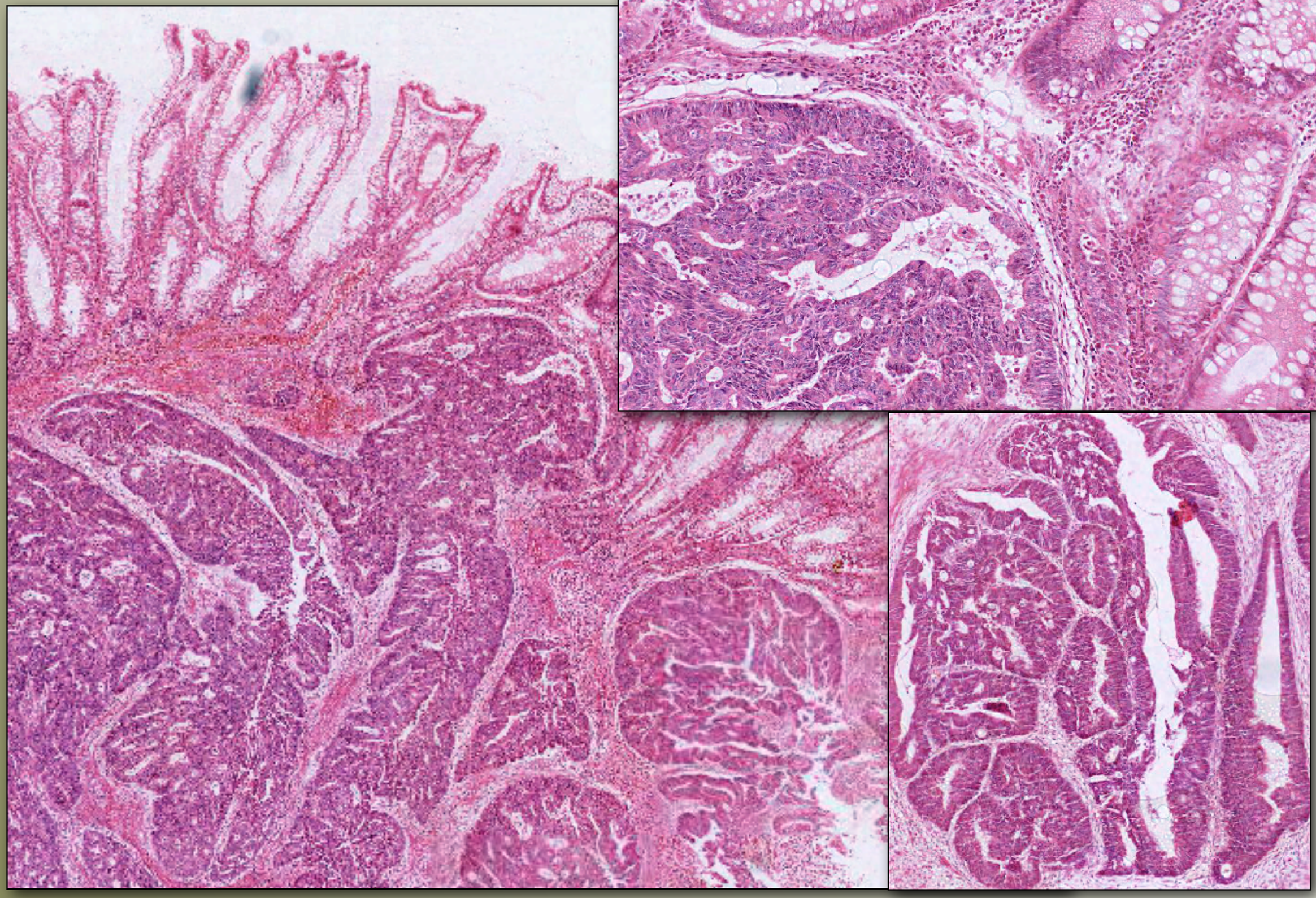
- Poorly differentiated carcinomas are identified by the presence of either irregularly folded, distorted and often small tubules, or the lack of any tubular formation and showing marked cytological pleomorphism.
- In the absence of good evidence, we recommend that a grade of poor differentiation should be applied in a pT1 cancer when **ANY** area of the lesion is considered to show poor differentiation.
- It should be noted that this is not in accordance with the WHO classification that recommends a certain proportion of lesion showing poor differentiation before diagnosing a lesion as G3.
- Poor differentiation includes undifferentiated and poorly differentiated as defined by the WHO classification (Washington et al. 2009).
- Signet ring carcinoma is graded G3

G1

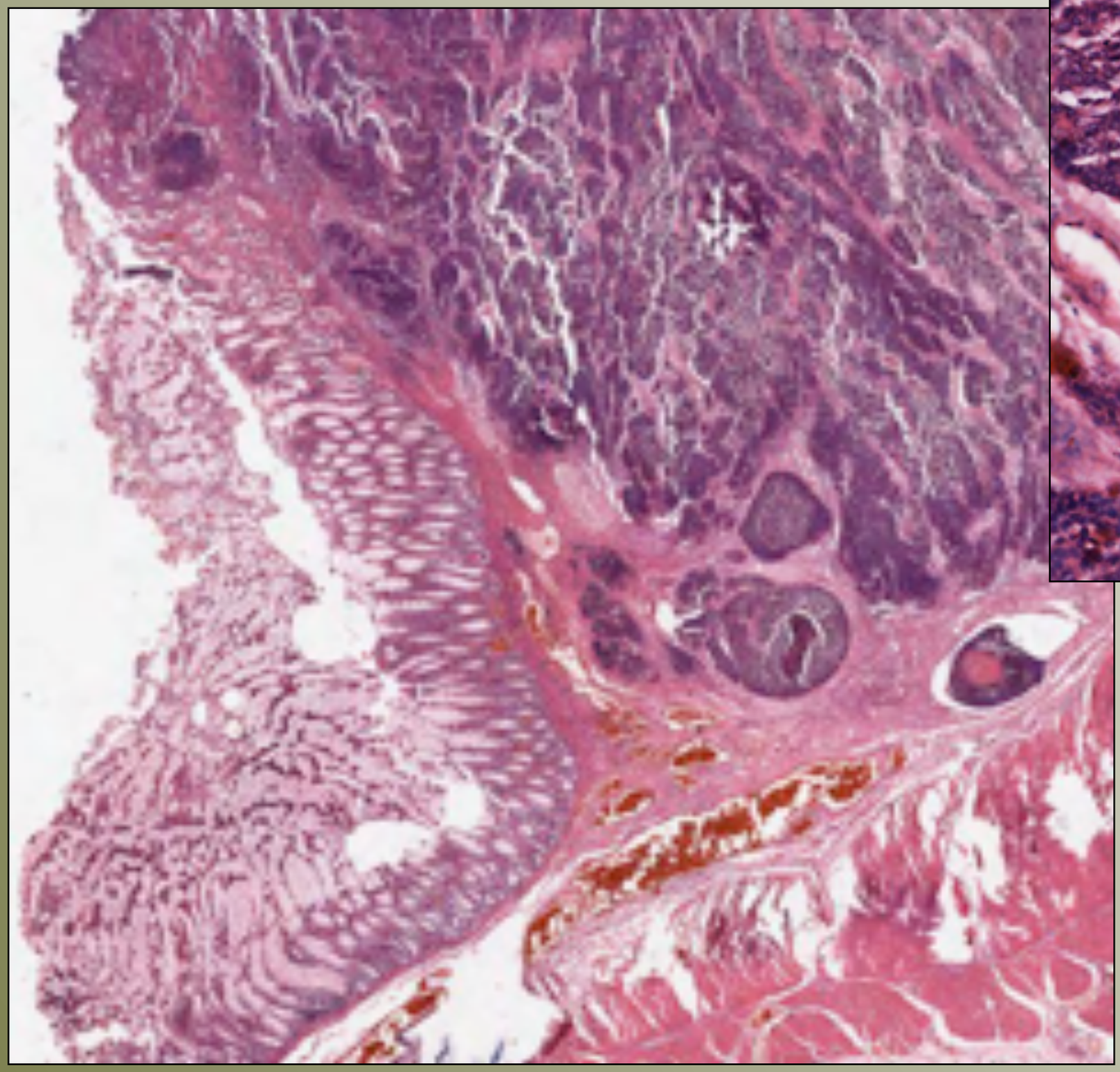


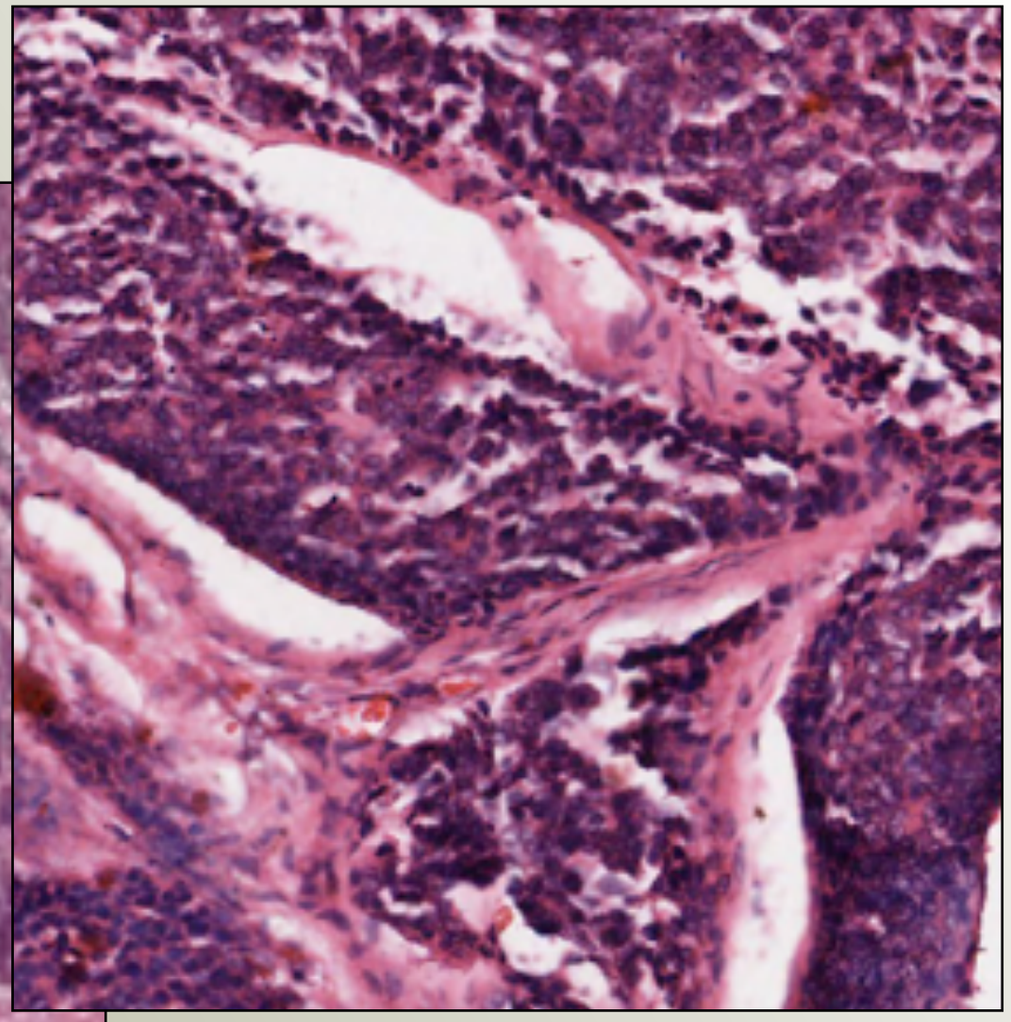


G2

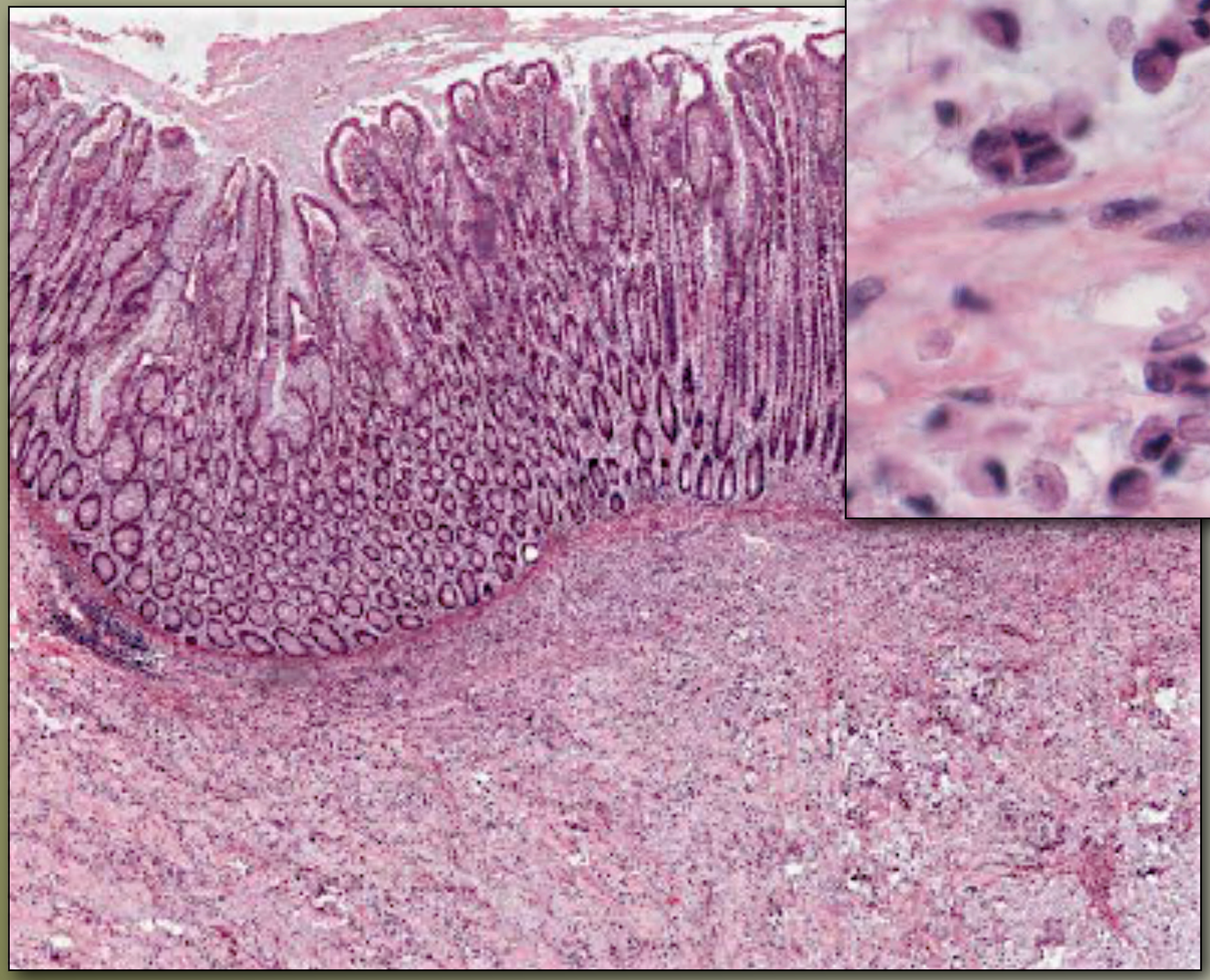


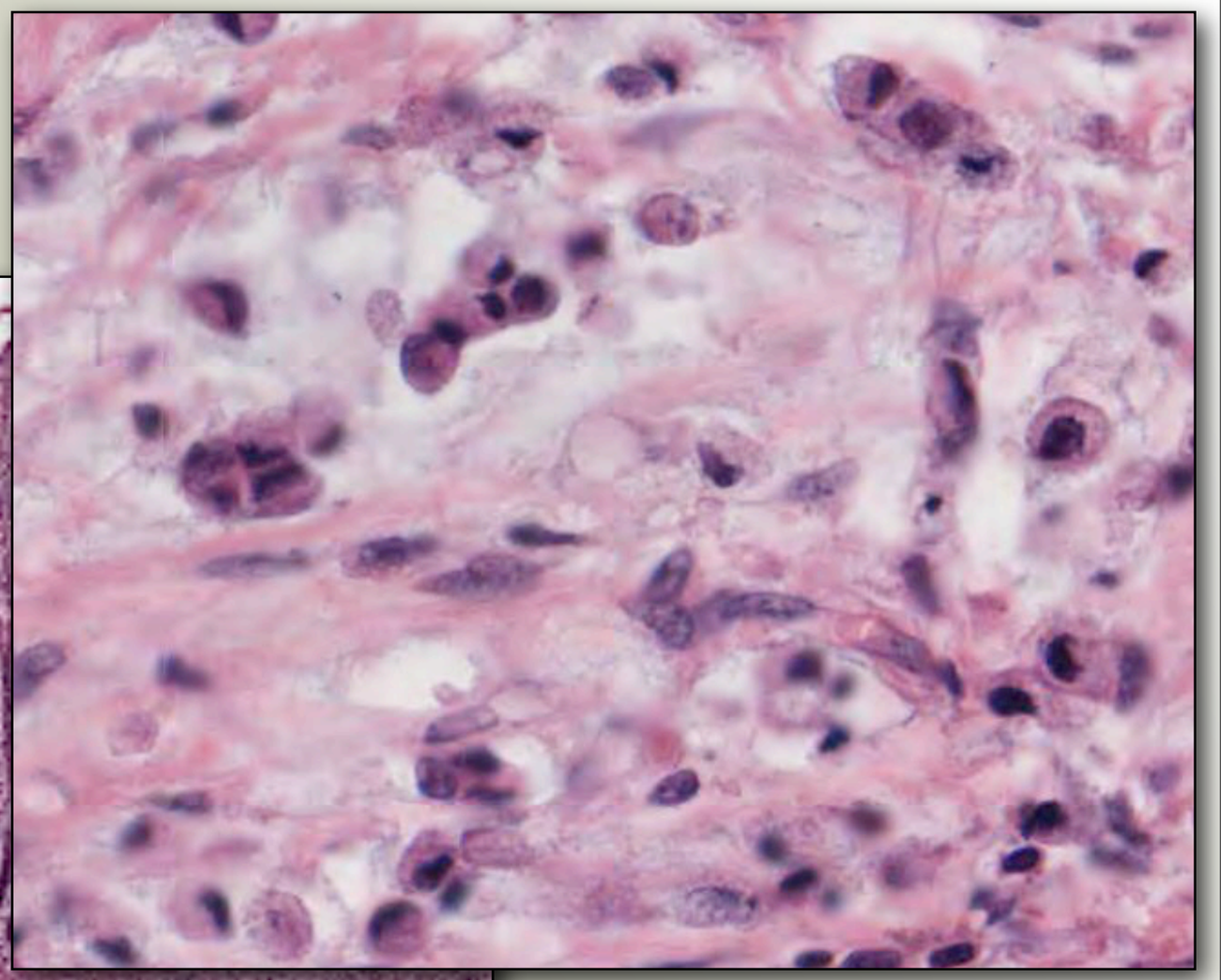
G3





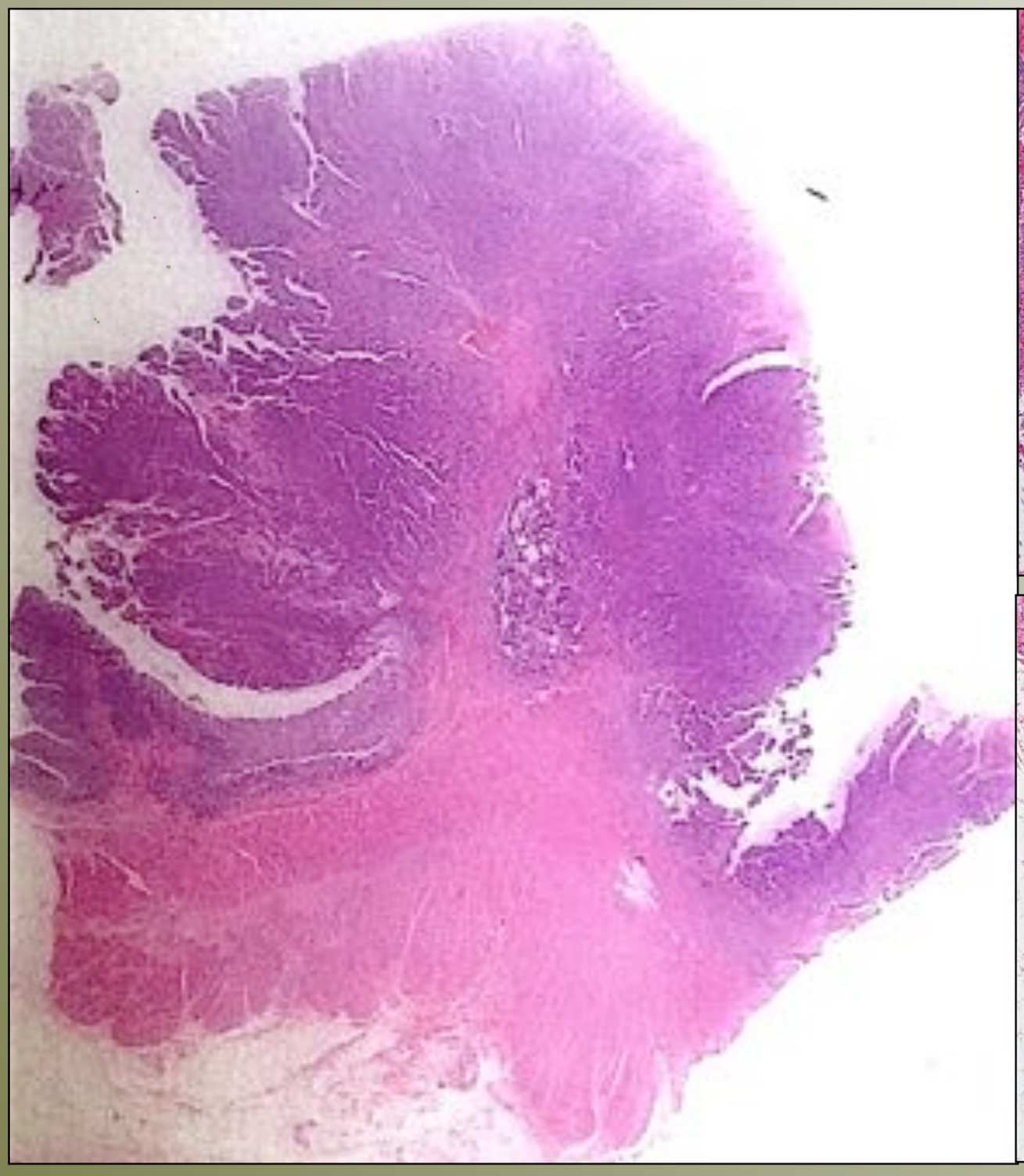
G3 Mucinoso

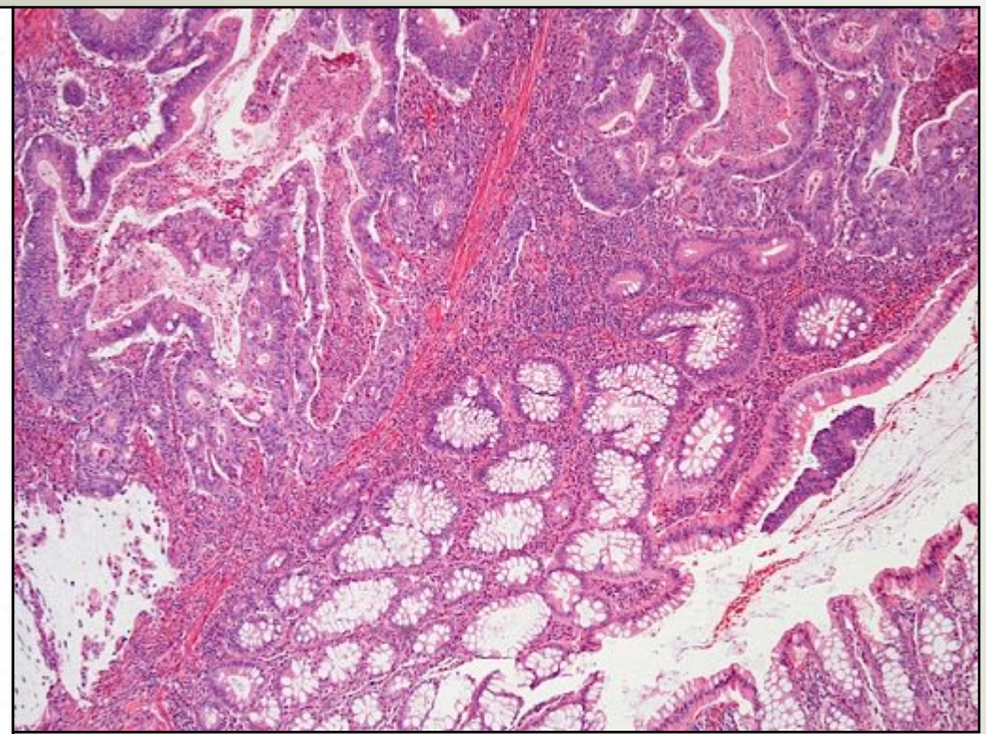


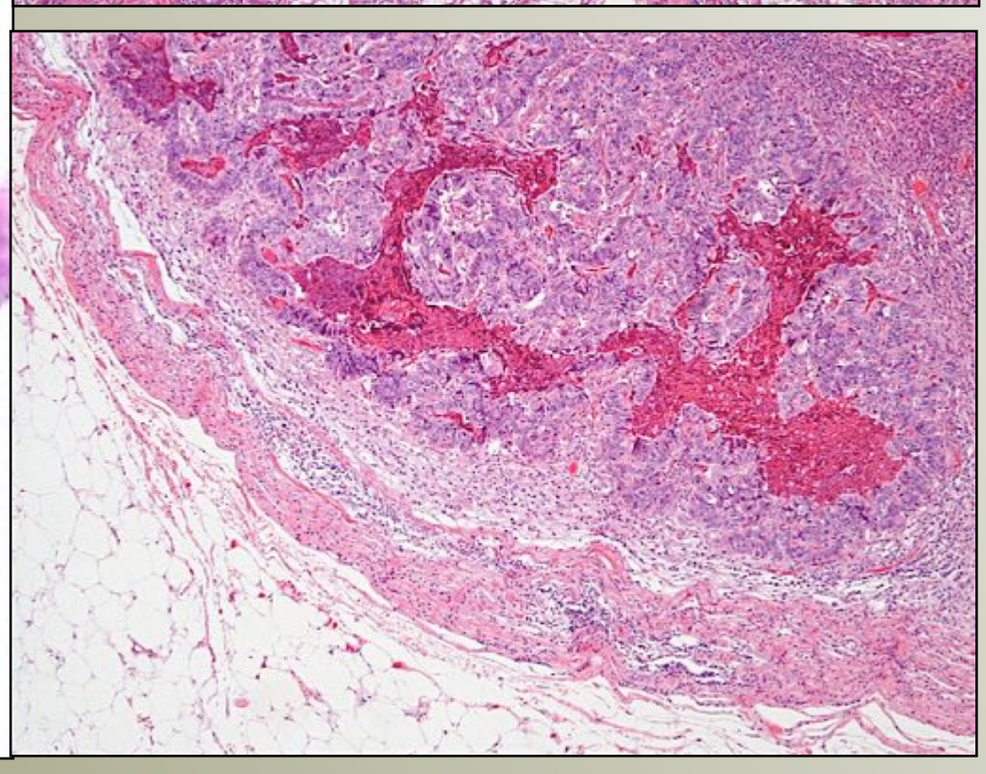


% TUMOR vs ADENOMA

G2 pT1 pN1; Haggitt 4 ; no Lymph; no budding; 90% tumoral mass







Compilazione del referto:

ADENOMA BENIGNO

1.Dati macroscopici : dimensioni, morfologia, presenza o meno di peduncolo, o se trattasi di polipectomia o biopsie
2.Dati microscopici: definizione di istotipo e architettura
3.Definizione di displasia
4.Stato dei margini

POLIPO CANCERIZZATO

1.Grado istologico di differenziazione del carcinoma, tumor budding, architettura, tipo di infiltrazione
2.Sede della neoplasia (testa; verso il peduncolo etc)
3.Dimensioni (ampiezza e profondità)
4.Rapporto con la muscolaris mucosae
- **Livelli di Haggitt**
- **Stadiazione sec. Kikuchi**
- **Microstadiazione sec. Ueno (rapporto percentuale tessuto adenomatoso/ Adenocarcinoma); alto rischio = W>4000 µm /D> 2000 µm**

5.Distanza dai margini
6.Angioinvasione

OTHER LESIONS

- Inflammatory polyps
- Juvenile polyps
- Serrated (hyperplastic) polyposis
- Cronkhite-Canada syndrome
- Neuroendocrine tumour

Non epithelial polyps

- Lipoma
- Leiomyoma of the muscularis mucosae
- Ganglioneuroma
- Gastrointestinal schwannoma
- Neurofibroma
- GIST
- Various forms of vascular tumour
- Perineurioma
- Fibroblastic polyp
- Epithelioid nerve sheath tumour
- Inflammatory fibroid polyp

Polipo Paul