The pathology of bowel cancer screening

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Gloucester & Cheltenham, UK

Rodger C Haggitt Memorial Lecture
Rodger C Haggitt Gastrointestinal Society
USCAP, Vancouver, March 18, 2018

Rodger C Haggitt

The pathology of bowel cancer screening

Even if you have never seen a specimen
from bowel cancer screening, and never will,
this lecture is still very relevant to you!!!

What gives me the right?

The UK, or more correctly England, in the vanguard?!?

The first (large) country to roll out full population screening for colorectal cancer in the world

Cancer screening: what's it all about?

Cervical cancer	detection of pre-malignant change	cervical smear
	detection of high risk patients	HPV testing
Breast cancer	detection of early stage cancer	mammography
	detection of pre-malignant change	mammography
Colorectal cancer	detection of early stage cancer	FOB, FIT, endoscopy, etc
	detection of pre-malignant change	FOB, FIT, endoscopy, etc

Table 1 Test performance per screening test in asymptomatic, average-risk adults

	gFOBT	FIT	FS	CTC	Colonoscopy
Sensitivity (%) for detecting advanced neoplasia	9 to 24[43–48]	32 to 53[43 44 47 49]	90 to 92*[50]	88[35] to 97[43]	88 to 98[51]
Sensitivity (%) for detecting CRC	13 to 50[44–46]	79 [52]	90 to 92*[50]	100†[53]	92 to 99[50]
Reduction in CRC incidence (%) intention-to-screen	No‡[19 54]	Unknown	18[54]	Unknown	69§[55]
Reduction in CRC mortality (%) intention-to-screen	14 to 16[19]	22¶[25]	28[54]	Unknown	68§[55]

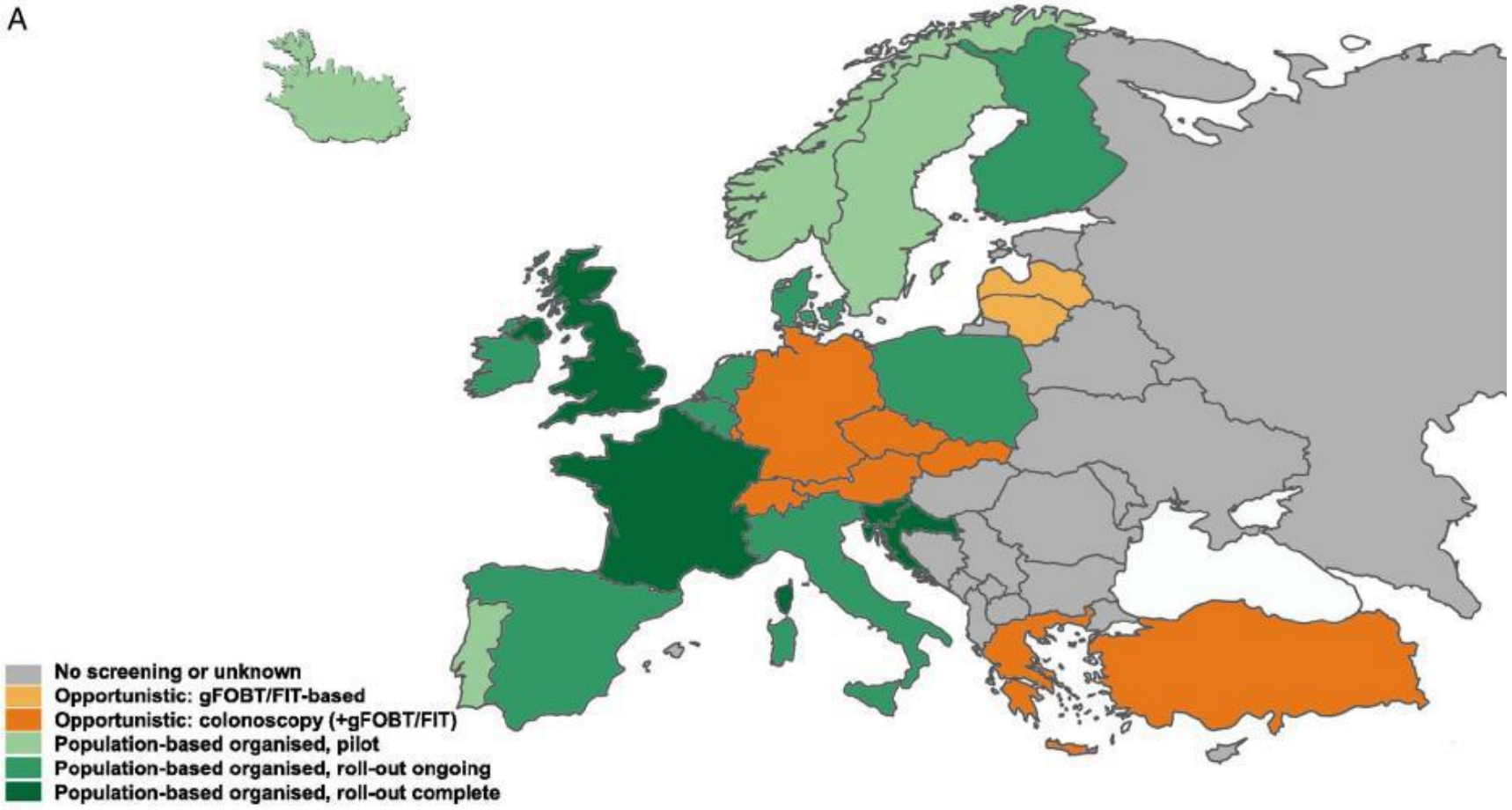
*Sensitivity is given for the distal colon.
†No CRCs were missed by CTC in six screening trials.
‡No reduction in incidence was found in three of four RCTs included in meta-analysis.
§ Meta-analysis of observational studies, more results expected.
¶ Ecological study.
CRC, colorectal cancer; CTC, CT colonography; FIT, faecal immunochemical test for haemoglobin; FS, flexible sigmoidoscopy; gFOBT, guaiac faecal occult blood test; RCT, randomised controlled trial.

Colorectal cancer screening: a global overview of existing programmes

Eline H Schreuders,[1] Arlinda Ruco,[2] Linda Rabeneck,[3,4,5,6,7] Robert E Schoen,[8] Joseph J Y Sung,[9] Graeme P Young,[10] Ernst J Kuipers[1]

Gut 2015; 64: 1637-49.

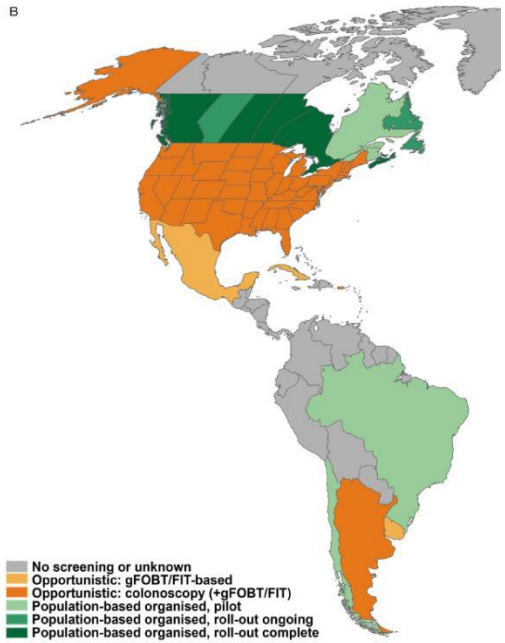
Bowel cancer screening in Europe, 2015



Colorectal screening in North America

Canada

- National Colorectal Cancer Screening Network in place since 2007
- population-based screening organised by province
- FIT is the recommended test
- rapid roll-out
- seeing the same issues as UK



USA

- too large a population to organise on national basis
- lots of opportunistic screening, by colonoscopy +/- FOB/FIT
- driven by American Cancer Society & 2008 AGA guidelines

Thanks to David Driman,
London, Ontario

Thanks to Kay Washington,
Nashville, Tennessee

Colorectal Cancer Screening Program Availability

Colorectal cancer screening program availability over time

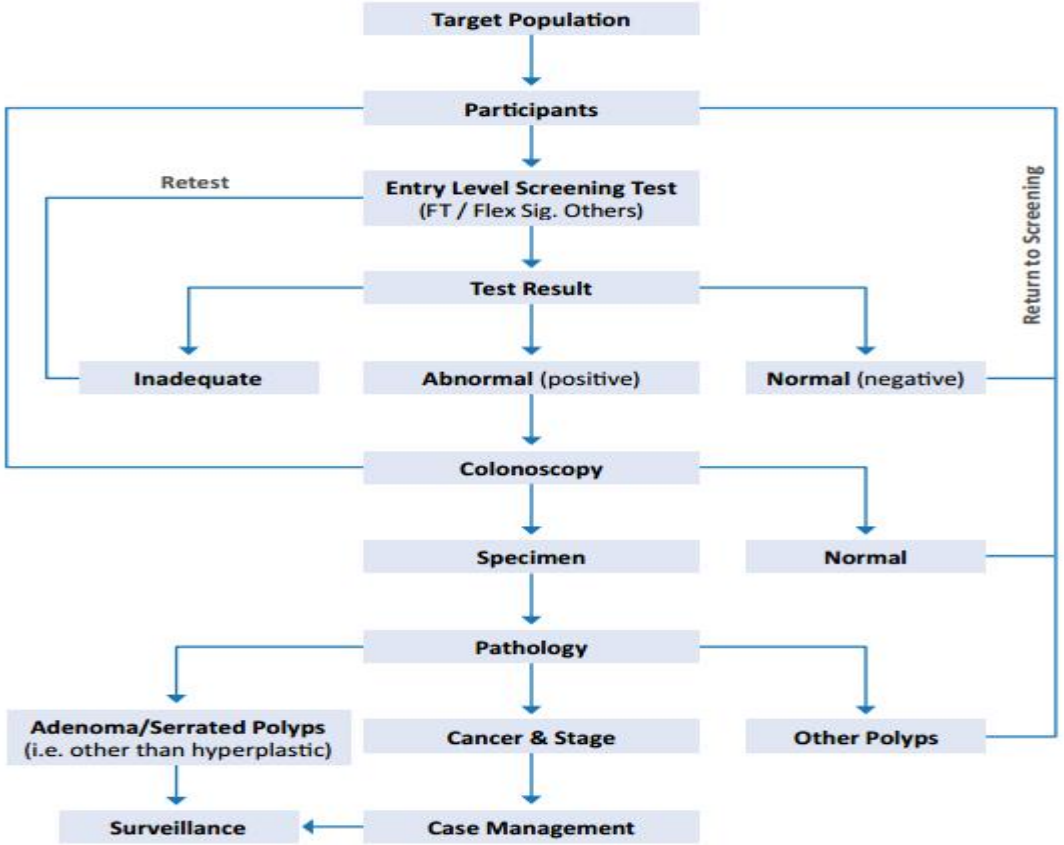
% of the population for whom organized CRC programs were available

- No organized program
- Reviewing feasibility
- Announced or planning
- 1–9%
- 10–49%
- 50–99%
- 100%

July 2016

Data source: Colorectal Cancer Screening Guidelines Across Canada: Environmental Scan, March 2013; Colorectal Cancer Screening Guidelines Across Canada: Environmental Scan, August 2014; National Colorectal Cancer Screening Network Report Survey; July 2016.

Colorectal Cancer Screening Pathway



Adapted from: Canadian Partnership Against Cancer. Colorectal Cancer Screening in Canada: Program Performance Results Report, January 2009– December 2011. Toronto: Canadian Partnership Against Cancer; December 2013

Colorectal Cancer Screening Fecal Testing Information - Highlights

Entry Level Test: Fecal Test Guaiac (FTg) Sampling Details (refer to slide #21)

- There are only two provinces (Manitoba and Ontario) which currently offer fecal test guaiac (FTg) as a screening test for colorectal cancer. FTg is offered to eligible individuals every two years. In Canada, the number of labs processing the results ranges from one lab (Manitoba) to six labs (Ontario). The FTg brands include Hemoccult II SENSA (Manitoba) and Hema-screen (Ontario).

Entry Level Test: Fecal Immunochemical Testing (FIT) Sampling Details (refer to slide #22-23)

- Eight provinces and two territories offer fecal immunochemical testing (FIT) up to every two years as a primary screening test for colorectal cancer. The most common brand for FIT in Canada is Alere (four provinces/one territory) and Polymedco (three provinces). Most provinces/territories require a single sample collection method for the FIT, whereas, one province and one territory collects two samples. The FIT cut-off value varies across Canada and ranges from 75 ng/ml (NWT) to ≥175 ng/ml (QC). The number of labs processing the FIT results ranges from one lab (six provinces/one territory) to five labs (one province).

In the UK, it's not just England's BCSP…..

NHS
Cancer Screening Programmes

Bowel Screening Wales
Sgrinio Coluddion Cymru

Bowel Screening:
Scottish Bowel Screening Programme

NICaN
Northern Ireland Cancer Network

Bowel cancer screening in England

- universal screening (60-70) by FOB first introduced in 2006
- then age extension to 75
- then one-off sigmoidoscopy screening at age 55 introduced independent of FOB screening and initiated in 2013
- now conversion from FOB to FIT


immunostics, inc.
hema-screen™
SLIDE TEST FOR FAECAL OCCULT BLOOD
WITH ON-SLIDE CONTROLS
000007400420-H
DATE
TEAR BACK FOR INSTRUCTIONS
1
Tab
immunostics, inc.
hema-screen™
SLIDE TEST FOR FAECAL OCCULT BLOOD
WITH ON-SLIDE CONTROLS
454 198 1653
000007400420-H
DATE
TEAR BACK FOR INSTRUCTIONS
2
Tab
CAUTION: PROTECT FROM HEAT AND LIGHT
I
II

Faecal immunochemical test (FIT)

- due to be introduced in England in 2018
  - introduction in Scotland on 30.11.17
- single sample only
- kit is ‘more scientific-looking’ to participants
- only detects human (haemo)globin
- increased sensitivity e.g. for advanced adenomas

OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL OFF PEEL

Participant Name

Please make sure
The sample bottle is in the box
You write your sample date on the bottle
You peel off the tape to seal the box
Please post as soon as possible!

This is your test kit for NHS Bowel Cancer Screening. Using it takes only a few minutes.
The test helps to detect bowel cancer early. The earlier bowel cancer is found, the easier it is to treat.

Instructions on using the kit are on the box (below) and on the additional information sheet enclosed.
The kit has been specifically designed to be safe to send in the post.

Please make sure you have read the leaflet about bowel cancer screening that we sent to you.
The leaflet tells you about screening, and its benefits and risks. The information is to help you decide whether or not you want to have bowel cancer screening. You can see a copy of the leaflet at http://www.cancerscreening.nhs.uk/bowel/publications/the-facts.html.

For more information about screening, or about using the test kit, call us on 0800 707 60 60. Calls are free from UK landlines.
Or visit our website at http://www.cancerscreening.nhs.uk

Instructions

1

- Write the date on the sample bottle.
- Use layers of toilet paper to catch your poo.
- Twist cap to open sample bottle.

2

- Collect sample by scraping the green stick along the poo until all grooves are covered.

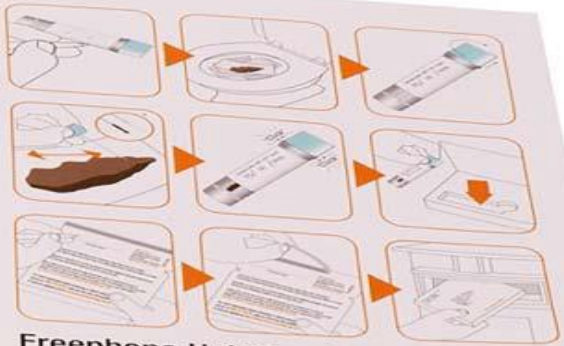
3

- Put stick back in bottle and 'click' the green cap to close it.
- Do not repeat the collection.
- Wash hands after use.

4

- Put the sample bottle back into the box.
- Write your name on the box in the space provided.
- Peel off the tape, close and seal the box.

NHS



Freephone Helpline 0800 707 60 60
Calls are free from UK landlines.
Or visit our website at http://www.cancerscreening.nhs.uk

Increased uptake and improved outcomes of bowel cancer screening with a faecal immunochemical test: results from a pilot study within the national screening programme in England

Sue Moss,[1] Christopher Mathews,[1] T J Day,[2] Steve Smith,[3] Helen E Seaman,[4] Julia Snowball,[4] Stephen P Halloran[4,5]

[1]Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK
[2]NHS Cancer Screening Programmes, Sheffield, UK
[3]NHS Bowel Cancer Screening Midlands and North West Programme Hub, Rugby, UK
[4]NHS Bowel Cancer Screening Southern Programme Hub, Guildford, UK

ABSTRACT

Background The National Health Service Bowel Cancer Screening Programme (BCSP) in England uses a guaiac-based faecal occult blood test (gFOBt). A quantitative faecal immunochemical test (FIT) for haemoglobin (Hb) has many advantages, including being specific for *human* blood, detecting Hb at a much lower concentration with a single faecal sample and improved uptake.

Methods In 2014, a large comparative pilot study was performed within BCSP to establish the acceptability and

Significance of this study

What is already known on this subject?

- Guaiac-based faecal occult blood test (gFOBt) screening for bowel cancer reduces bowel cancer mortality in those screened by 25%.
- Uptake of gFOBt in the National Health Service (NHS) Bowel Cancer Screening Programme (BCSP) was 58.2% in the fiscal year 2014/2015

Gut 2017; 66: 1631-44.

FIT workload implications: the triple whammy for pathologists

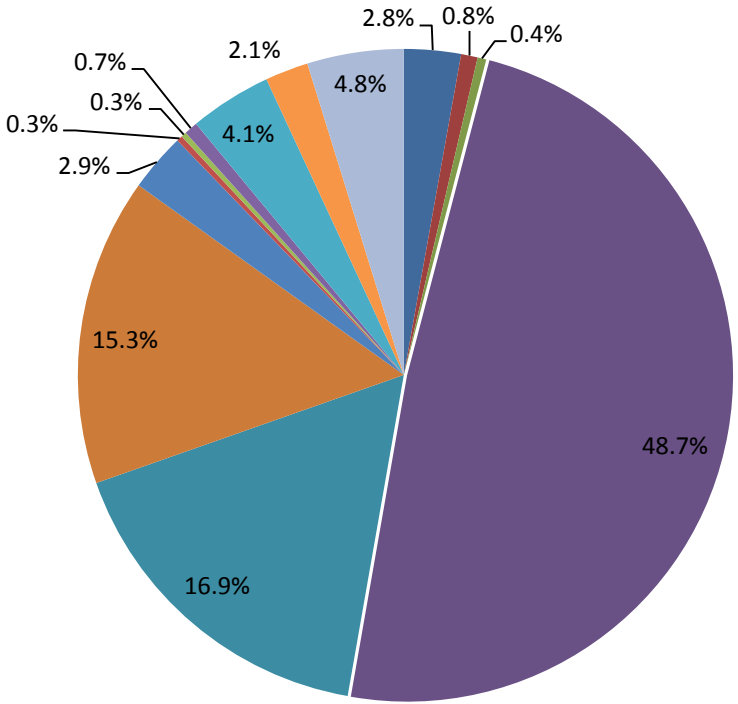
- in England platform and cut-off for FIT not determined yet
- If ‘FIT 120’ chosen, potential increase in pathology workload could be:
  - increased uptake: 66% for FIT v 59% for FOB
  - increased positivity rate: 2.12 (‘FIT 120’) v 1.71 (2016 FOB positivity rate)
  - enhanced sensitivity for advanced adenomas: 2.0 for FIT v 1.5 for FOB

82% increase in pathology workload

Bowel cancer screening: the subconscious musings of a Gloucestershire pathologist, circa 2006

- most of it will be a pathological doddle
- 130 extra polyps a year – mainly adenomas and HPs – piffle!
- a few more cancer resections but lots of easy Dukes A/stage 1
- and the BCSP Director is going to give us a whole wad of dosh to do it…..

The first 10,000 Northern Ireland BCSP specimens



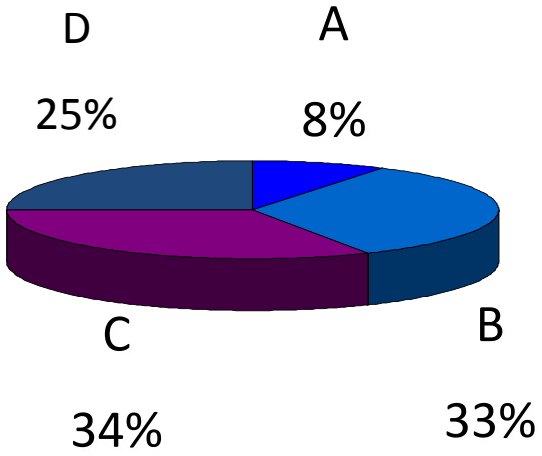
Diagnosis	Total
Adenocarcinoma	2.8%
Adenocarcinoma (in polyp)	0.8%
Suspicion of malignancy	0.4%
Tubular adenoma	48.7%
Tubulovillous adenoma	16.9%
Hyperplastic polyp	15.3%
Sessile serrated lesion	2.9%
Traditional serrated adenoma	0.3%
Villous adenoma	0.3%
Inflammatory polyp	0.7%
Inflammation	4.1%
Other	2.1%
Normal	4.8%
Grand Total	100%

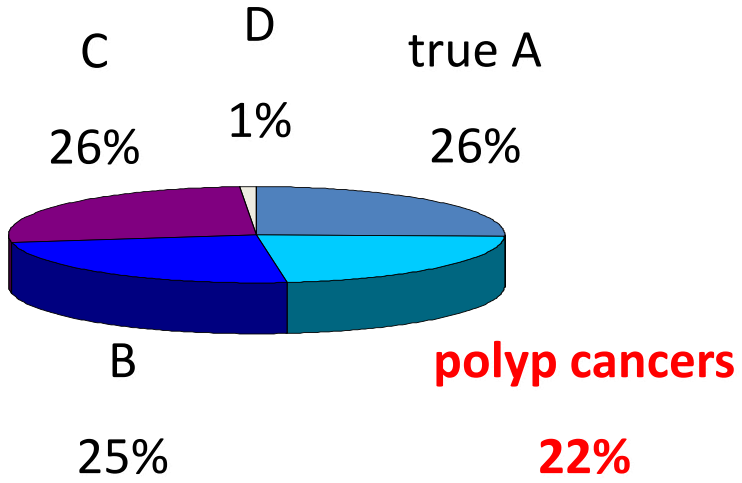
Table 1. Frequencies of common histopathological diagnoses from 240,842 non-invasive lesions detected during screening colonoscopy since inception of the English Bowel Cancer Screening Programme

Tubular adenoma	**57%**
Tubulovillous adenoma	18%
Villous adenoma	1%
Hyperplastic polyp	21%
Sessile serrated lesion	1%
Other	2%
Total	100%

What colorectal cancer screening is all about….

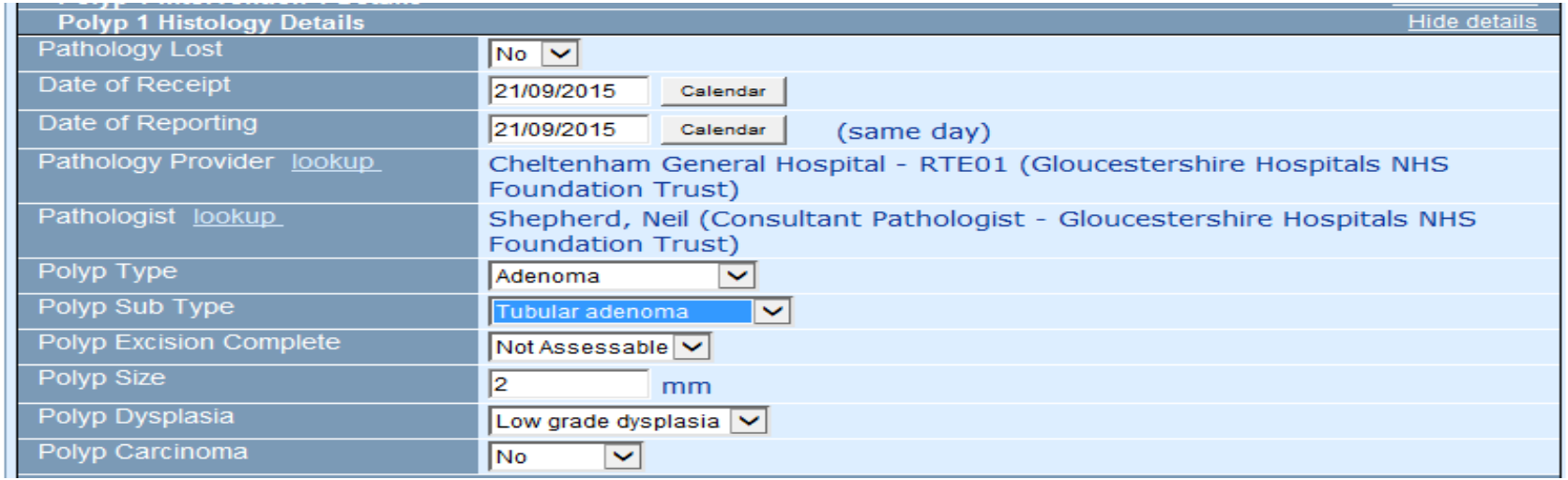
- **detecting early stage cancer**



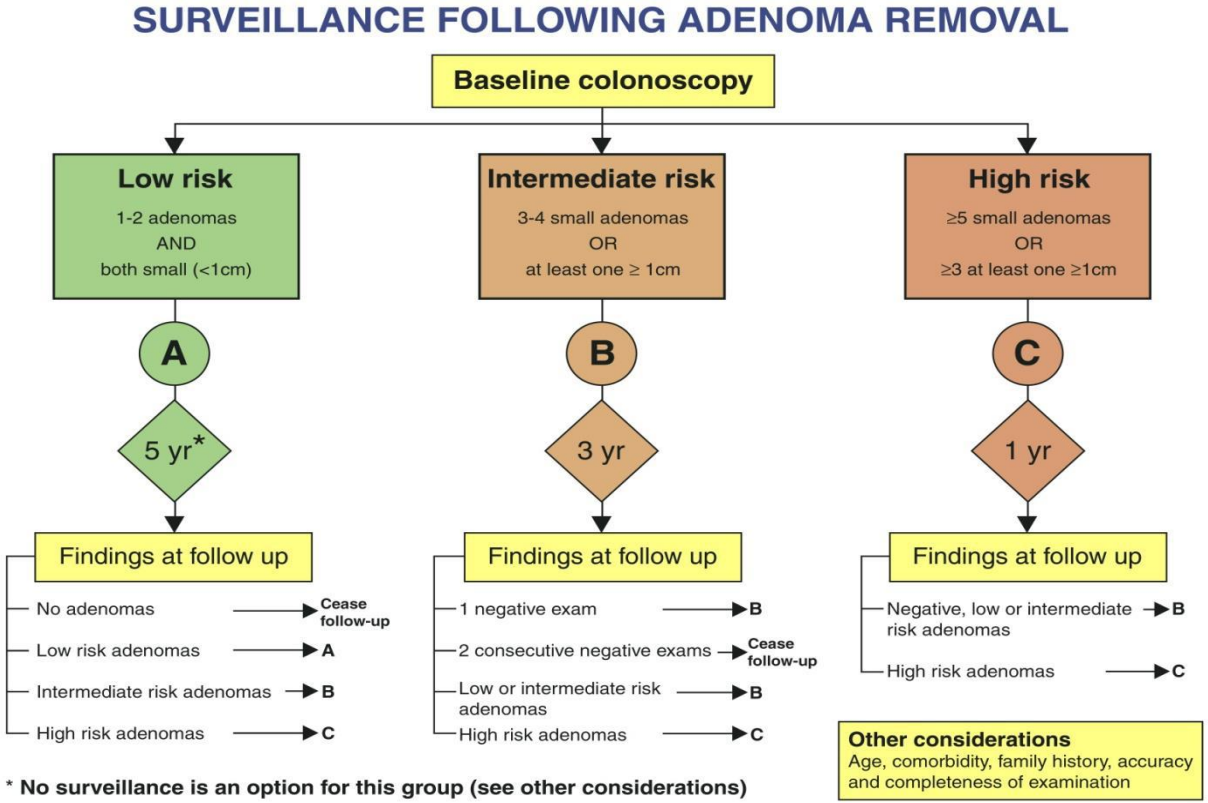


Dukes staging for symptomatic CRC versus screen-detected CRC in the English BCSP

BCSS polyp pathology screenshot



Polyp 1 Histology Details	Hide details
Pathology Lost	No
Date of Receipt	21/09/2015 Calendar
Date of Reporting	21/09/2015 Calendar (same day)
Pathology Provider lookup	Cheltenham General Hospital - RTE01 (Gloucestershire Hospitals NHS Foundation Trust)
Pathologist lookup	Shepherd, Neil (Consultant Pathologist - Gloucestershire Hospitals NHS Foundation Trust)
Polyp Type	Adenoma
Polyp Sub Type	Tubular adenoma
Polyp Excision Complete	Not Assessable
Polyp Size	2 mm
Polyp Dysplasia	Low grade dysplasia
Polyp Carcinoma	No



Cairns SR, et al; BSG guidelines 2010 (after Atkin WS, Saunders BP; Gut 2002)

Reliability of pathological assessment of villosity and dysplasia grade

Vol. 11, 660–663, July 2002 Cancer Epidemiology, Biomarkers & Prevention

Histopathology 2013, 62, 916–924. DOI: 10.1111/his.12110

Interobserver variability in assessing dysplasia and architecture in colorectal adenomas: a multicentre Canadian study

Allison Osmond,[1] Hector Li-Chang,[2,3] Richard Kirsch,[3] Dimitrios Divaris,[4] Vincent Falck,[5] Dong Feng Liu,[6] Celia Marginean,[7] Ken Newell,[8] Jeremy Parfitt,[1] Brian Rudrick,[8] Heidi Sapp,[9] Sharyn Smith,[10] Joanna Walsh,[1] Fasahat Wasty,[11] David K Driman[1]

Histopathology, University Hospital Llandough, [4]Department of Primary Care and Public Health, Cardiff University School of Medicine, and [5]Institute of Cancer and Genetics, Cardiff University School of Medicine, Cardiff, UK

New York 10032; South Carolina Cancer Center, University of South Carolina, Columbia, South Carolina 29203 [R. M. B.]; Cancer Prevention Research, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109 [J. D. P.]; Department of Preventive Medicine, University of Southern California/Norris Comprehensive Cancer Center, Los Angeles, California 90033 [R. W. H.]; and Department of Pathology and Laboratory Medicine, College of Medicine, University of Cincinnati, Cincinnati, Ohio 45267-0529 [C. F-P.]

Introduction

Although most colorectal carcinomas are thought to arise from colorectal adenomas (1–3), most adenomas, which are quite common, do not progress to invasive carcinoma (3, 4). Therefore, the study of advanced adenomas (those with severe dysplasia, CIS,[2] and intramucosal carcinoma), which have a

Reliability of pathological assessment

Reproducib … High-grade
Dy … m

*Dipti Mahaj… , MD, PhD,**
*Deepa T. P… lesec, MD,**
*Osca… MD**

TABLE 2. κ Indices for Interobserver Agreement

Feature	κ	*P*	95% CI	Interobserver Agreement*
Preconsensus diagnosis				
A-VC	0.21	< 0.001	0.15-0.27	Poor
HGD	0.26	< 0.001	0.20-0.32	Poor
AA	0.29	< 0.001	0.23-0.35	Poor
Postconsensus diagnosis				
A-VC	0.37	< 0.001	0.31-0.43	Poor
HGD	0.31	< 0.001	0.25-0.37	Poor
AA	0.34	< 0.001	0.28-0.40	Poor

Improvement in κ (1-sided *z*-test): A-VC, $P = 0.038$; HGD, $P = 0.11$; AA, $P = 0.14$.

*Agreement beyond chance; poor: $\kappa < 0.40$; moderate: $0.40 \leq \kappa \leq 0.75$; excellent: $\kappa > 0.75$.

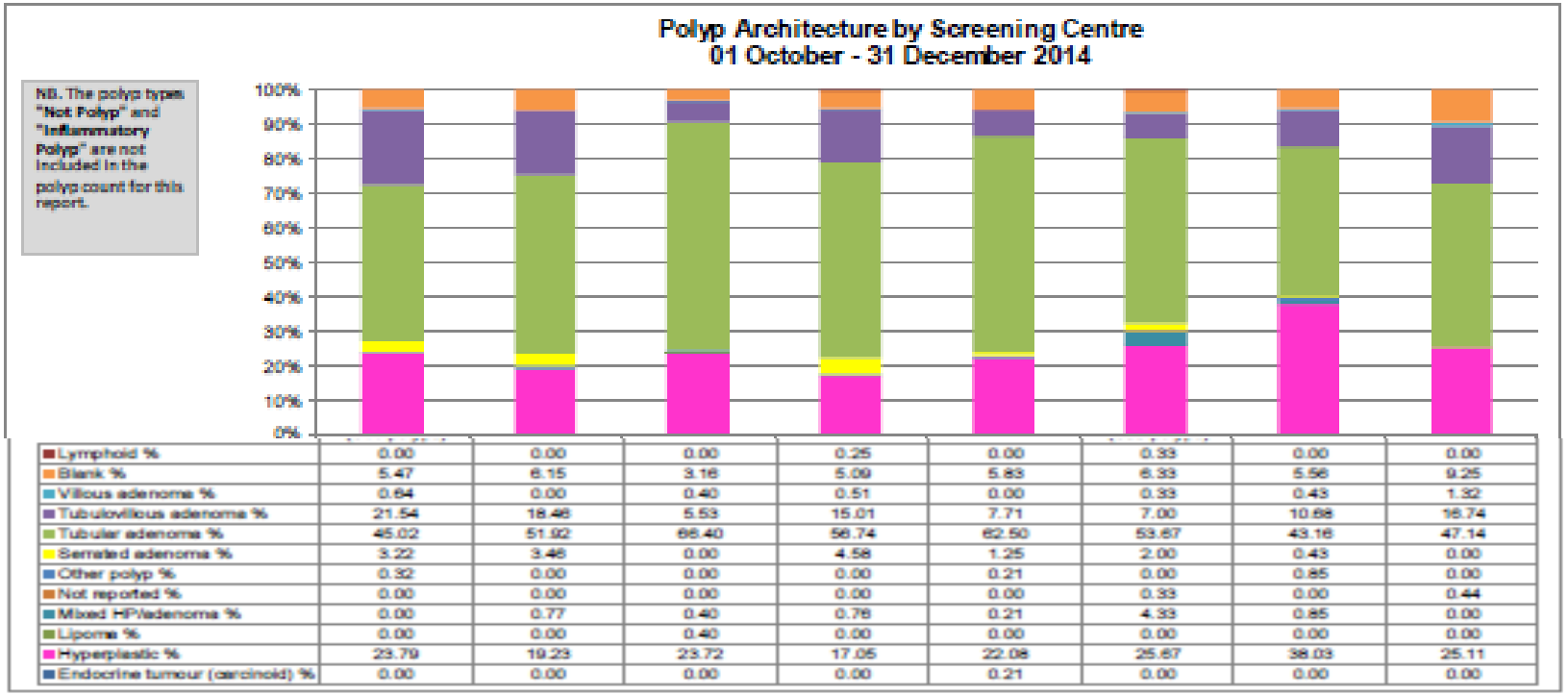
CI indicates confidence interval.

(*Am J Surg Pathol* 2013;37:427–433)

Variability in polyp type, BCSP South West

South West Bowel Cancer Screening Programme: Pathology Monitoring

3.2 Polyp Architecture



Lymphoid %	0.00	0.00	0.00	0.25	0.00	0.33	0.00	0.00
Blank %	5.47	6.15	3.16	5.09	5.83	6.33	5.56	9.25
Villous adenoma %	0.64	0.00	0.40	0.51	0.00	0.33	0.43	1.32
Tubulovillous adenoma %	21.54	18.46	5.53	15.01	7.71	7.00	10.68	16.74
Tubular adenoma %	45.02	51.92	66.40	56.74	62.50	53.67	43.16	47.14
Serrated adenoma %	3.22	3.46	0.00	4.58	1.25	2.00	0.43	0.00
Other polyp %	0.32	0.00	0.00	0.00	0.21	0.00	0.85	0.00
Not reported %	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.44
Mixed HP/adenoma %	0.00	0.77	0.40	0.76	0.21	4.33	0.85	0.00
Lipoma %	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00
Hyperplastic %	23.79	19.23	23.72	17.05	22.08	25.67	38.03	25.11
Endocrine tumour (carcinoid) %	0.00	0.00	0.00	0.00	0.21	0.00	0.00	0.00

So, our only useful role in the pathological assessment of the most common colorectal polyp is…….

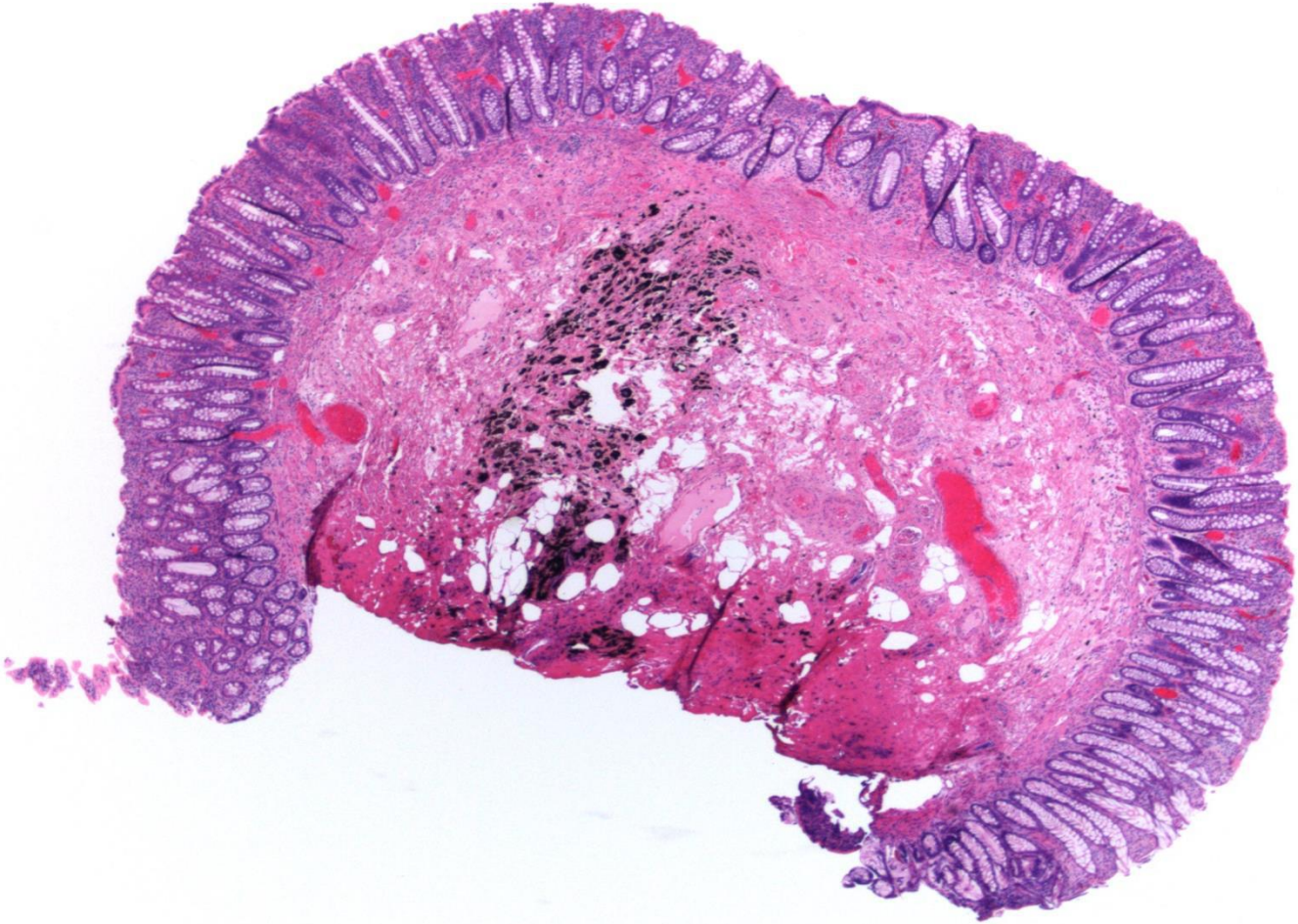
to confirm that it is an adenoma

we can’t agree on villosity/villousness

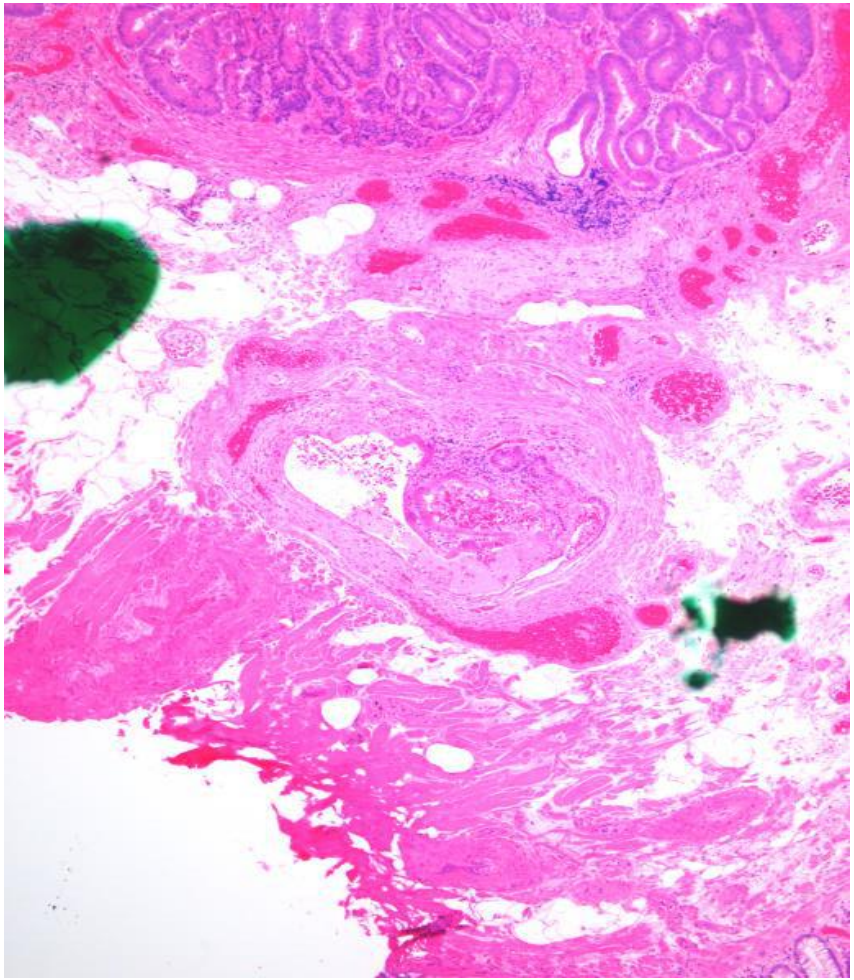
low or high grade dysplasia

until we do, we won’t be much use in determining further management in an important patient group

Some polyp curios in BCSP….



Is this vascular invasion?



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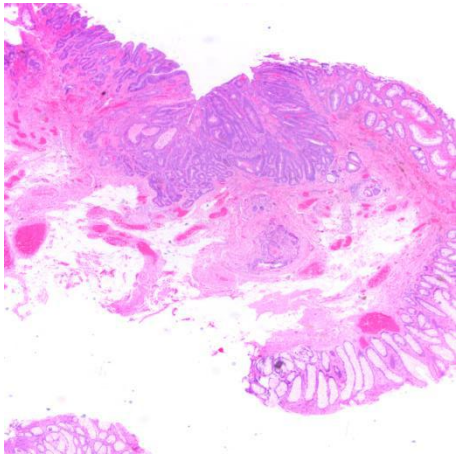
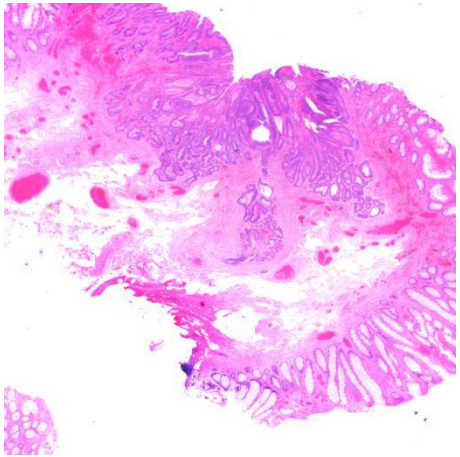
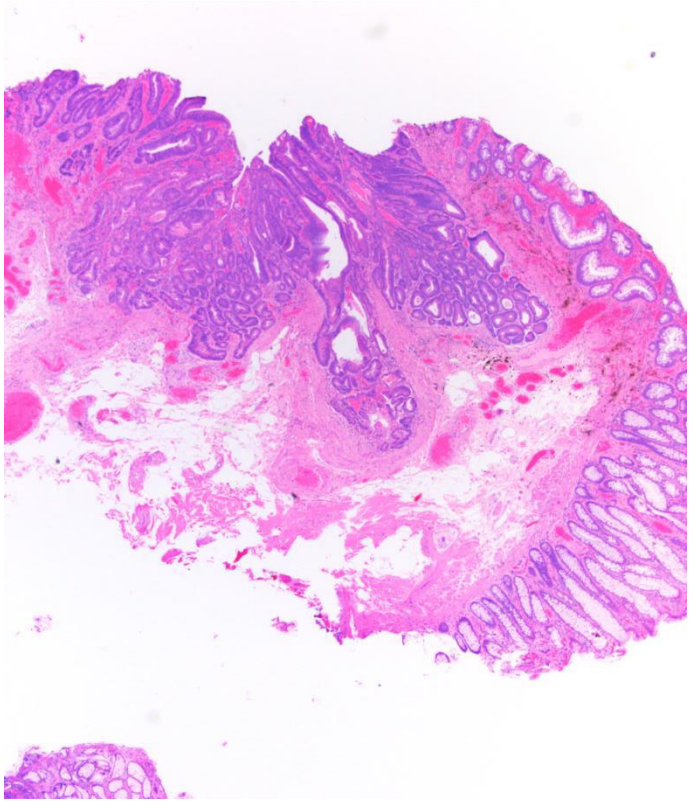






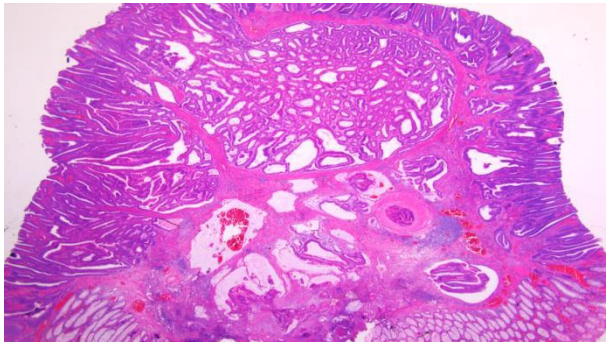
A bit of Sunday in Vancouver philosophy……

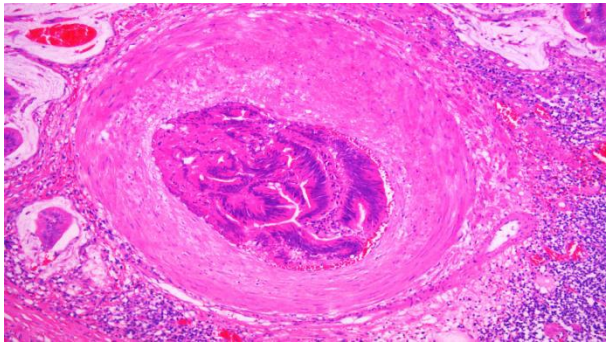
You can have all the fancy immunohistochemistry and molecular biology you like, but what are the two most important adjunctive tests we do in Histopathology?

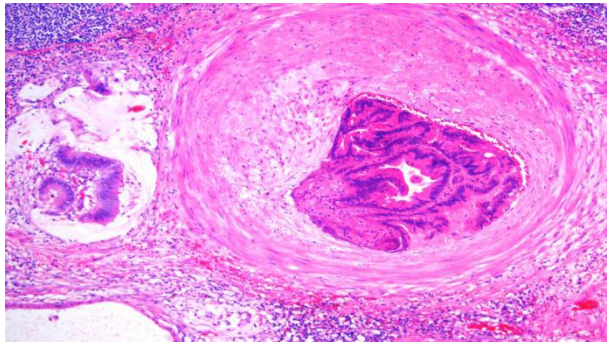
deeper levels

and the peer at the computer to get the patient's history…….

Is this vascular invasion?

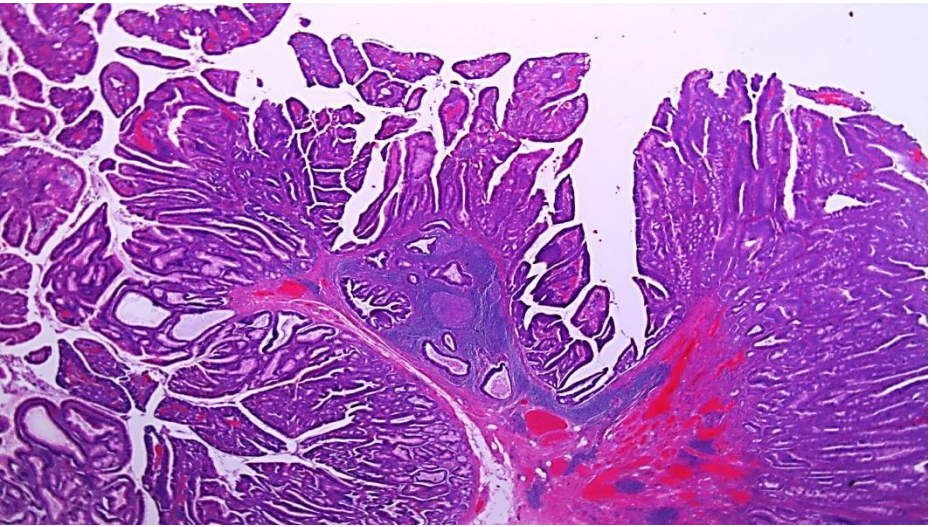


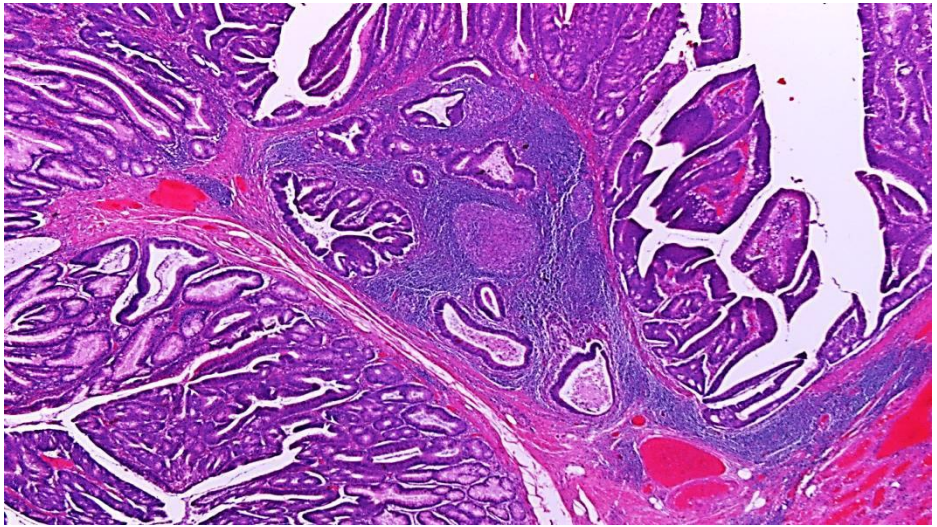




‘vascular intrusion’

Adenoma in a lympho-glandular complex: much commoner in the right colon





Four big issues in bowel cancer screening pathology (and all very relevant to routine colorectal pathology practice….)

- the diagnosis of colorectal cancer on biopsy
- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties
- polyp cancers (pT1 disease) & what we do about it – expected but not the management difficulties
- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties

Four big issues in bowel cancer screening pathology (and all very relevant to routine colorectal pathology practice….)

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- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties

The diagnosis of colorectal cancer on biopsy

- depends on definitions
- Japanese and Far East – cytological diagnosis
- North America and some of Europe – architectural features
- UK (and others) – definitive evidence of submucosal spread

Basil C Morson, doyen of GI pathologists, 1921-2016

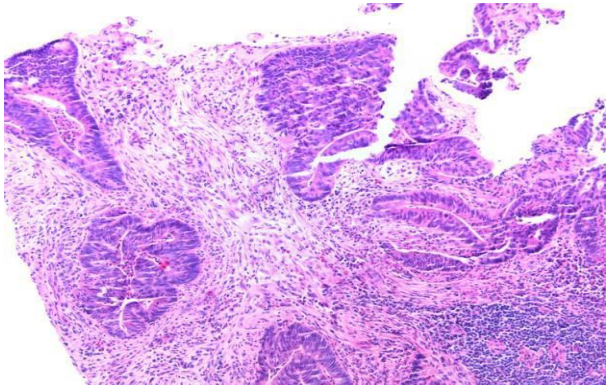
“It’s your job to control surgeons”

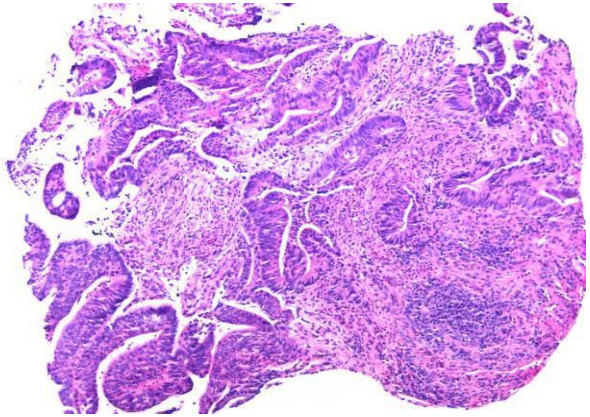
The diagnosis of colorectal cancer on biopsy

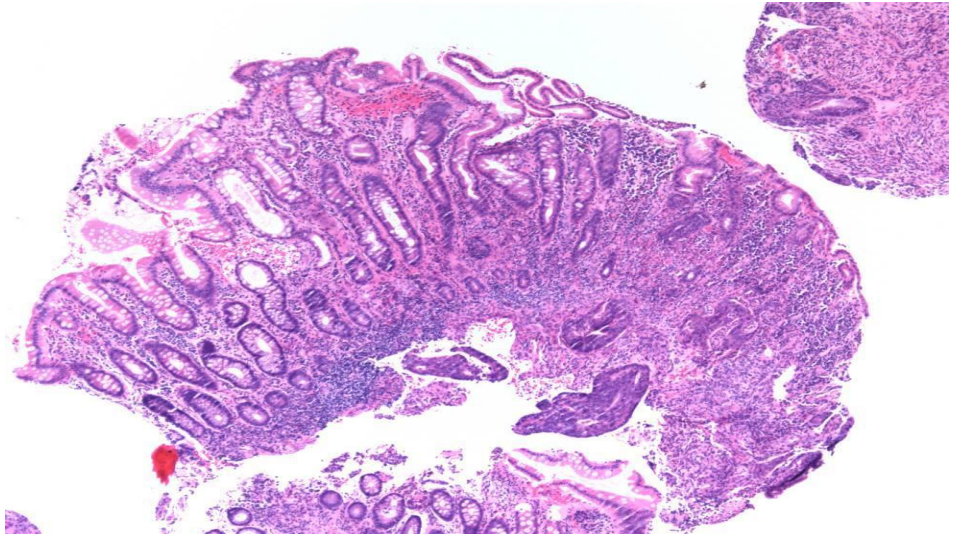
- intramucosal carcinoma not allowed as a diagnosis in the UK
- those cases are called ‘high grade dysplasia’
- lymphatics in mucosa not capable of delivering metastatic disease
- you don’t want a large specimen by return of post…….

- biopsies may not show definite submucosal tissue
- provides considerable difficulties (certainly for UK pathologists)

The diagnosis of colorectal cancer on biopsy

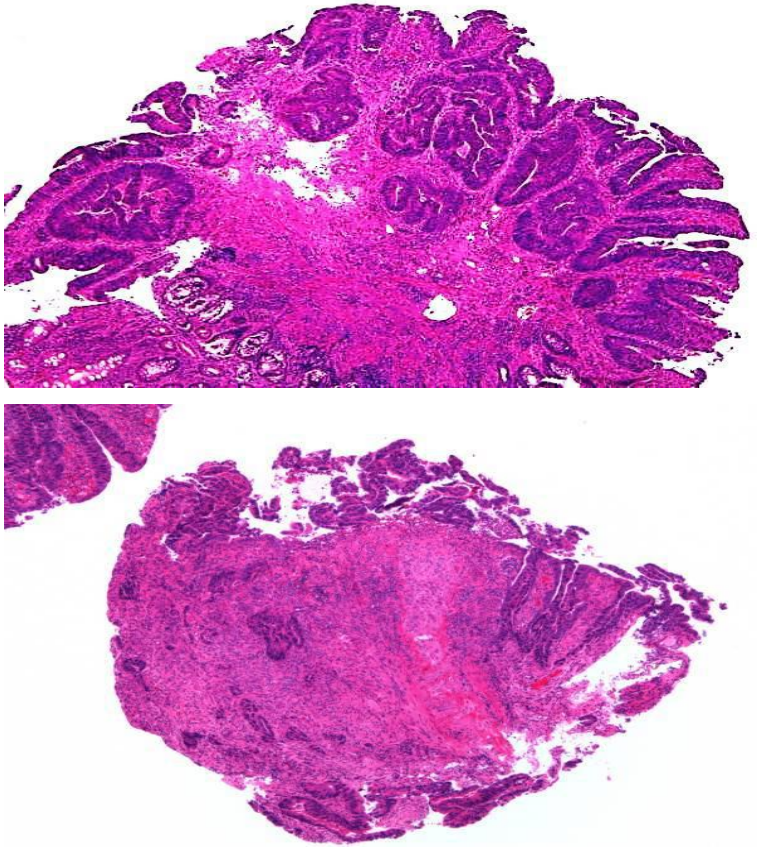






The diagnosis of colorectal cancer on biopsy

- how to demonstrate submucosal involvement?
- juxtaposition to neural structures, fat and large arterioles and venules
- S100 immunohistochemistry?



Although not yet proven in definitive studies, we believe that juxtaposition of neoplastic glands to structures known to be in the submucosa, such as neural structures, fat and larger blood vessels, particularly arterioles and venules, are of considerable help in making a diagnosis of invasive adenocarcinoma. Indeed, some colleagues, in the UK at least, have advocated S100 immunohistochemistry to demonstrate juxtaposition of neoplastic glands to submucosal ganglia and nerve structures. This may be of some utility but requires rigorous observational studies to support this practice.

Loughrey MB, Quirke P, Shepherd NA.
Royal College of Pathologists Dataset for colorectal cancer histopathology reports
December 2017

The need for repeat biopsies?

- 64M
- 52mms mass lesion in the caecum
- biopsies show TVA with low grade dysplasia only

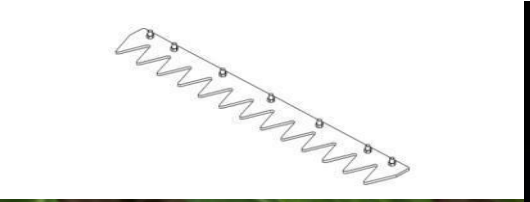
COMMENT: These biopsies do provide evidence of primary colorectal glandular neoplasia. Given the size of the lesion at colonoscopy, it is likely that endoscopic resection cannot be undertaken. In this situation, despite the lack of definitive evidence of invasive malignancy in these biopsies, there would appear to be a clear indication for right hemicolectomy. These facts should direct discussion in the Colorectal MDTM.

….. However, in about half of these (and mainly in the colon), the MDTM decided that further biopsies were not required because the original biopsies had confirmed primary glandular neoplasia and the clinical, endoscopic and imaging features demanded resection. It should be emphasised that these cases were mainly colonic and that rectal cancers, accounting for about 5% of the total number of cases in this audit, did more commonly require further biopsies. This was particularly important when an abdominoperineal resection would have been the proposed management strategy. ***So, particularly in the colon, there may not be a definitive argument for repeat biopsies, if clinical, endoscopic and imaging features demand resection, as long as the biopsies have confirmed primary colorectal glandular neoplasia.***

Loughrey MB, Quirke P, Shepherd NA.
Royal College of Pathologists Dataset for colorectal cancer;
December 2017

Four big issues in bowel cancer screening pathology (and all very relevant to routine colorectal pathology practice….)

- the diagnosis of colorectal cancer on biopsy
- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties
- polyp cancers (pT1 disease) & what we do about it – expected but not the management difficulties
- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties

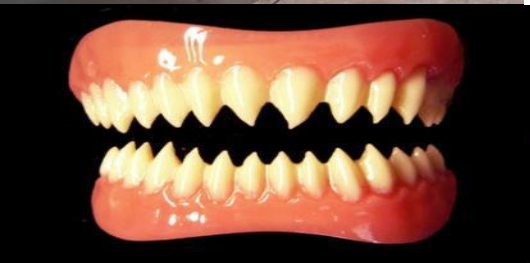


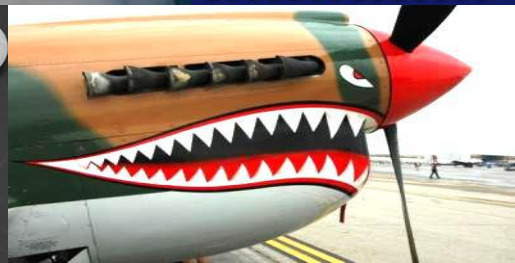






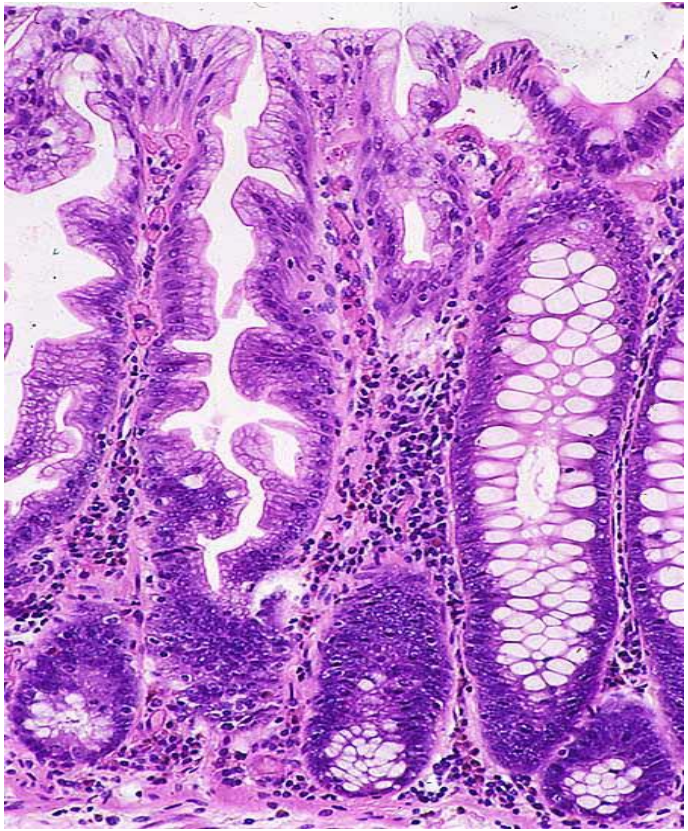
Jagger
65


VBENE


What is serrated pathology?

- a distinctive morphological appearance in the large intestinal mucosa
- with specific molecular fingerprints
- but varied endoscopic and macroscopic features
- and a variable but highly significant neoplastic potential
- representing the most important advance in our understanding of colorectal cancer development in the last decade



25% of CRC develop arise via the serrated pathway

Gastroenterology 2016;150:895–902

Increased Risk of Colorectal Cancer Development Among Patients With Serrated Polyps

Rune Erichsen,[1] John A. Baron,[1,2] Stephen J. Hamilton-Dutoit,[3] Dale C. Snover,[4] Emina Emilia Torlakovic,[5] Lars Pedersen,[1] Trine Frøslev,[1] Mogens Vyberg,[6] Stanley R. Hamilton,[7] and Henrik Toft Sørensen[1,2]

Table 4. Estimated 10-Year Risk of Colorectal Cancer for Each Polyp Type

	Cases/controls	Adjusted OR (95% CI)	Estimated 10-year risk[a]
SSA/P with synchronous conventional adenomas	30/61	2.66 (1.70–4.16)	2.47%
SSA/P without synchronous conventional adenomas	49/81	3.40 (2.35–4.91)	3.16%
SSA/P with cytologic dysplasia	20/25	4.76 (2.59–8.73)	4.43%
SSA/P without cytologic dysplasia	59/117	2.75 (1.99–3.80)	2.56%
Conventional adenomas without SSA/P	727/1631	2.50 (2.24–2.80)	2.33%
Traditional serrated adenomas overall	14/17	4.84 (2.36–9.93)	4.50%
Hyperplastic polyps only	55/235	1.30 (0.96–1.77)	1.21%

[a]The number of colorectal cancers among individuals without polyps (1155) divided by the total number of patients without polyps (209,744) and divided by the mean follow-up period (5.90 y) estimates the annual colorectal cancer risk (r). The 10-year risk for patients without polyps is estimated as 1- (1 - r)^{10} and equals 0.93%. The 10-year risk of colorectal cancer for each polyp type then is estimated as the 10-year risk for patients without polyps times the OR for the relevant polyp type.

Terminology of sessile serrated pathology

- sessile serrated adenoma

  Torlakovic and Snover, 1996

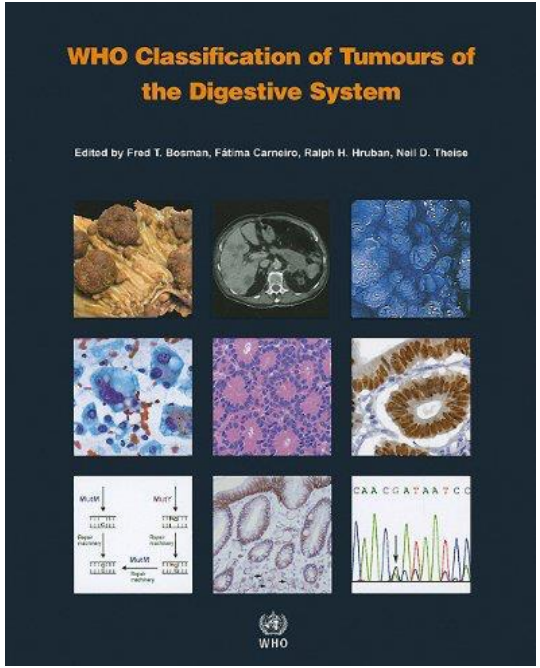
- sessile serrated polyp/adenoma

  WHO, 2010

- sessile serrated polyp

- sessile serrated lesion

  UK & European colorectal screening guidelines



Quality assurance in pathology in colorectal cancer screening and diagnosis—European recommendations

Phil Quirke • Mauro Risio • René Lambert • Lawrence von Karsa • Michael Vieth

UK guidance for the pathological reporting of serrated lesions of the colorectum

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Revised 7 April 2015
Accepted 13 April 2015

ABSTRACT
Bowel cancer screening programmes have highlighted to endoscopists and clinicians the spectrum of serrated colorectal lesions. One of the most significant developments has been the recognition that sessile serrated lesions (SSLs), while bearing histological resemblance to hyperplastic polyps (HPs), may be associated with the enhanced development of epithelial dysplasia and colorectal adenocarcinoma. Different minimum criteria exist for the diagnosis of SSLs and their differentiation from HPs. Furthermore, the spectrum of terminology used to describe the entire range of serrated lesions is wide. This variability has impaired interobserver agreement during their histopathological assessment. Here, we provide guidance for the histopathological reporting of serrated lesions, including a simplified nomenclature system. Essentially, we recommend use of the following terms: HP, SSL, SSL with dysplasia, traditional serrated adenoma (TSA) and mixed polyp. It is hoped that this standardisation of nomenclature will facilitate studies of the biological significance of serrated lesions in terms of the relative risk of disease progression.

these lesions and the risk of disease progression associated with various histopathological factors.

This review provides guidance relating to a simplified nomenclature and classification system for serrated colorectal lesions.

NOMENCLATURE

The nomenclature of serrated lesions is complex, and there are differences of opinion between UK, European and US pathologists regarding the optimal terminology. We propose that serrated lesions should be given one of the following names according to their morphological features: HP, SSL, SSL with dysplasia, traditional serrated adenoma (TSA) and mixed polyp (box 1). The definitions of these lesions are given below.

Hyperplastic polyp

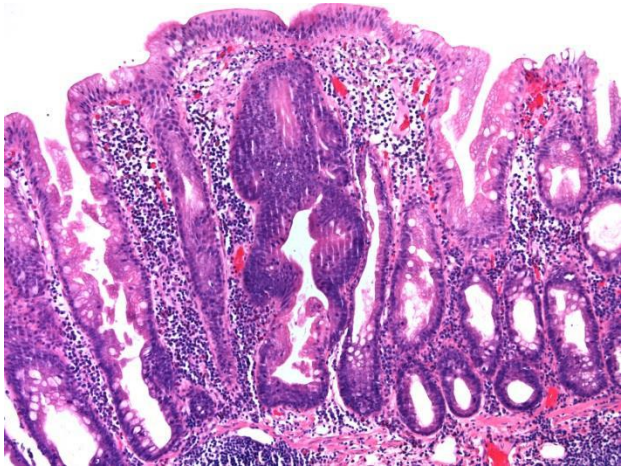
These are small serrated lesions showing no features that would allow categorisation as an SSL and no evidence of dysplasia. *We use the term 'dysplasia' in this context to refer to the morphological appearances of epithelial neoplasia within the mucosa of the colon and rectum, for example, the epithelial*

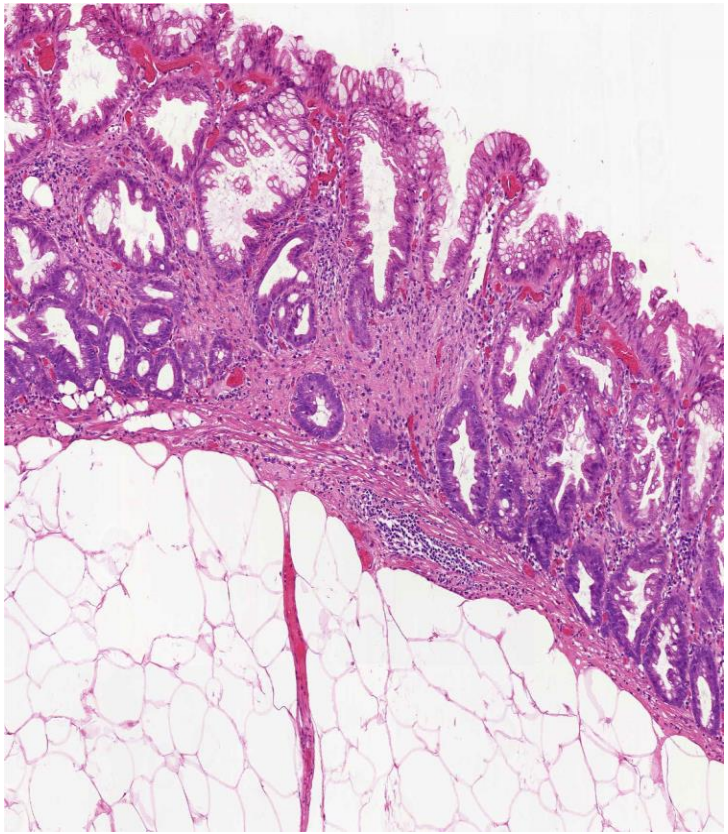
Bateman AC, Shepherd NA. J Clin Pathol 2015: 68: 585-91.

Box 1 Recommended terminology for (non-invasive) serrated lesions of the colon and rectum

- Hyperplastic polyp (HP)
- Sessile serrated lesion (SSL)
- SSL with dysplasia
- Traditional serrated adenoma (TSA)
- Mixed polyp

Approved by BSG Pathology Section, BCSP National Pathology Committee, RCPath, European CRC Screening Pathology Group & BSG Serrated Pathology Working Party





Histologic and Molecular Analyses of Colonic Perineurial-like Proliferations in Serrated Polyps: Perineurial-like Stromal Proliferations Are Seen in Sessile Serrated Adenomas

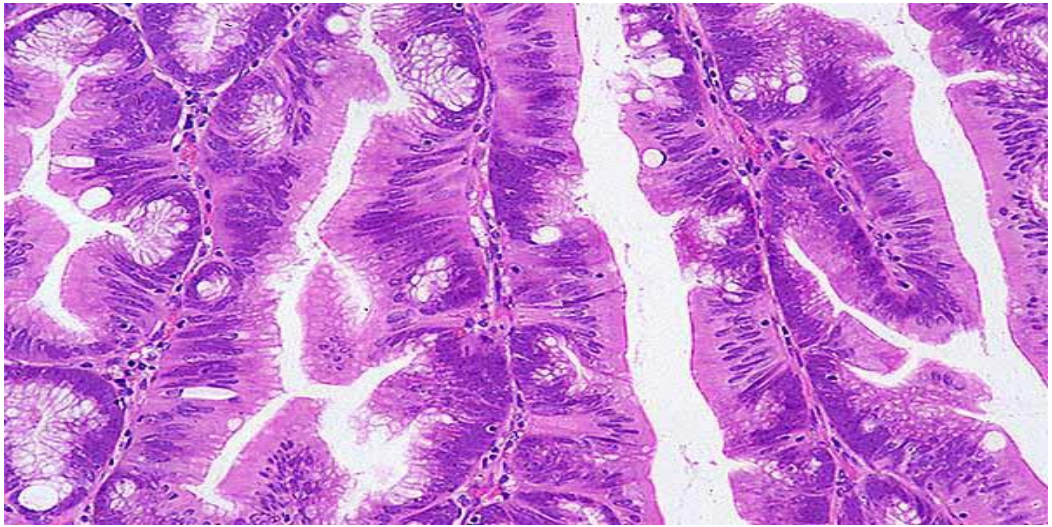
Reetesh K. Pai, MD, Amirkaveh Mojtahed, MD,* Robert V. Rouse, MD,* Roy M. Soetikno, MD, MS,† Tonya Kaltenbach, MD, MS,† Lisa Ma, MS,* Daniel A. Arber, MD,* Thomas P. Plesec, MD,‡ John R. Goldblum, MD,‡ and Rish K. Pai, MD, PhD‡*

Benign Serrated Colorectal Fibroblastic Polyps/Intramucosal Perineuriomas Are True Mixed Epithelial-stromal Polyps (Hybrid Hyperplastic Polyp/Mucosal Perineurioma) With Frequent BRAF Mutations

Abbas Agaimy, MD, Robert Stoehr, PhD,* Michael Vieth, MD,† and Arndt Hartmann, MD**

Traditional serrated adenoma

- usually distal colon/rectum
- up to 2% of all colorectal polyps
- villiform or filiform (tennis racket)
- unequivocal dysplasia
- eosinophilic cytoplasm
- pencillate nuclei
- ectopic crypt formation
- BRAF or KRAS mutation



Ectopic crypt formation in traditional serrated adenoma

- disruption of signalling pathways of stem cell control
- expansion of progenitor cell population in ectopic crypt foci/lateral buds
- these lateral bud cells proliferate and gain somatic mutations
- leading to dysplasia arising outside the stem cell niche
- and more rapid malignant transformation

Aberrant epithelial *GREM1* expression initiates colonic tumorigenesis from cells outside the stem cell niche

Hayley Davis[1,13], Shazia Irshad[1,13], Mukesh Bansal[2], Hannah Rafferty[1], Tatjana Boitsova[1,3], Chiara Bardella[4], Emma Jaeger[4], Annabelle Lewis[4], Luke Freeman-Mills[4], Francesc C Giner[4], Pedro Rodenas-Cuadrado[1], Sreelakshmi Mallappa[5], Susan Clark[5], Huw Thomas[5], Rosemary Jeffery[3], Richard Poulsom[3], Manuel Rodriguez-Justo[6], Marco Novelli[6], Runjan Chetty[7], Andrew Silver[3], Owen J Sansom[8], Florian R Greten[9], Lai Mun Wang[10], James E East[11], Ian Tomlinson[4,12] & Simon J Leedham[1,11]

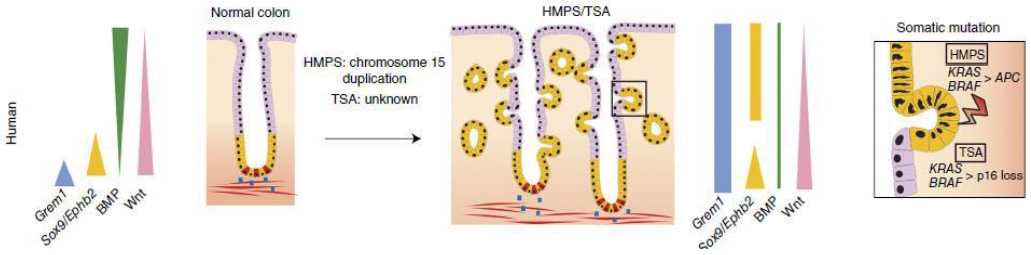
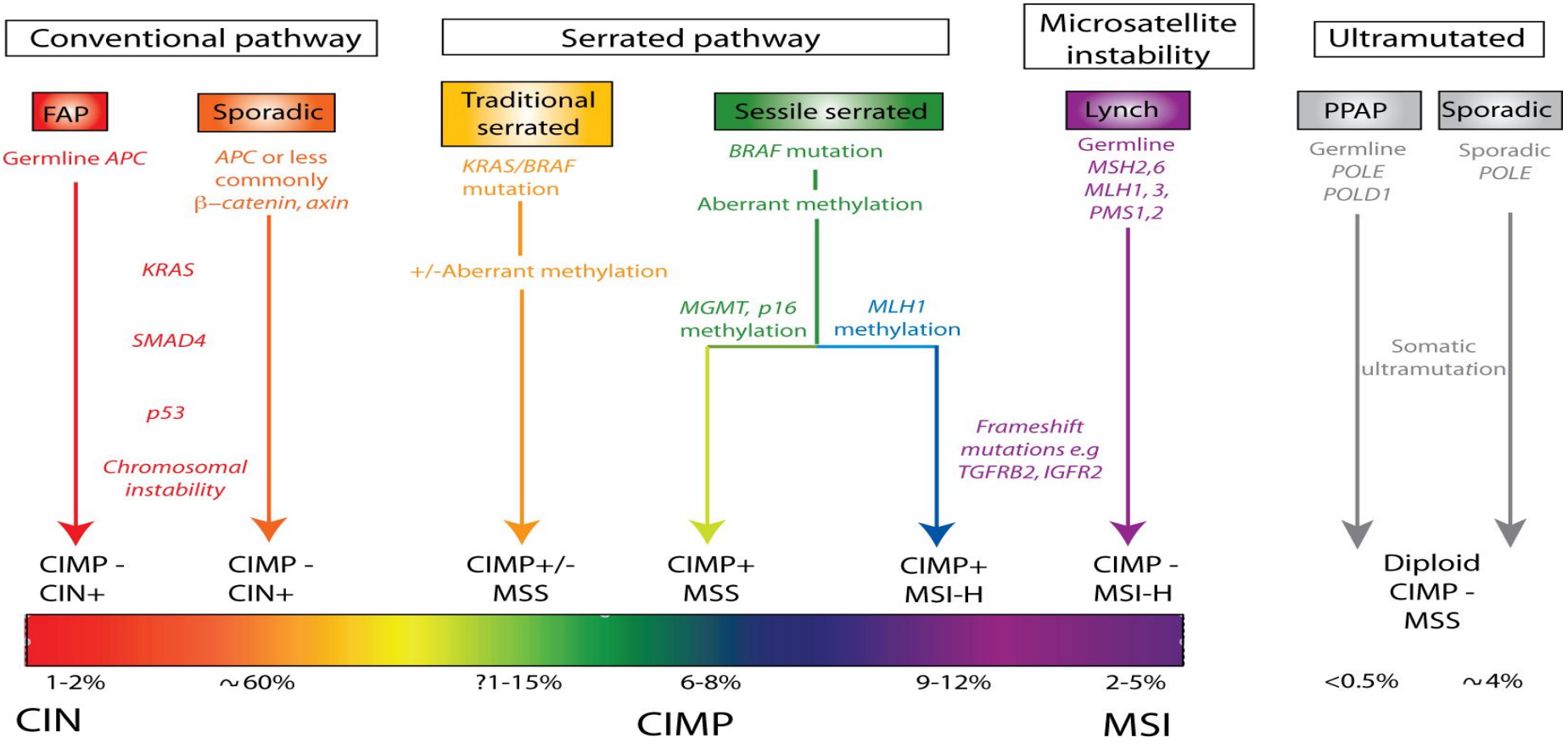


Figure 6 Model summarizing the proposed mechanistic consequences of disrupted *GREM1* morphogen gradients. Aberrant ectopic epithelial expression of *GREM1* disrupts the coupling of cell fate determination to position along the crypt-villus axis and allows persistence and expansion of an *Lgr5*-negative progenitor cell pool (characterized by aberrant SOX9 and EPHB2 expression) that forms orthogonal ectopic crypt foci. Aberrant cell proliferation in this progenitor cell population within these ECFs predisposes toward somatic (epi)mutation events and gives rise to neoplastic transformation (inset boxes). *In vitro*, the persistence of somatically mutated progenitor cells in dissected villi gives rise to clonogenic tumor spheroid growth from cells that have exited the crypt basal stem cell niche. Colored bars represent morphogen and gene expression gradients in the normal and pathological states. Blue squares represent physiological *Grem1* expression from pericryptal myofibroblasts. CBC stem cells are colored red.

Nature Medicine 2015; 21: 62-70.

Colorectal cancer molecular pathogenesis

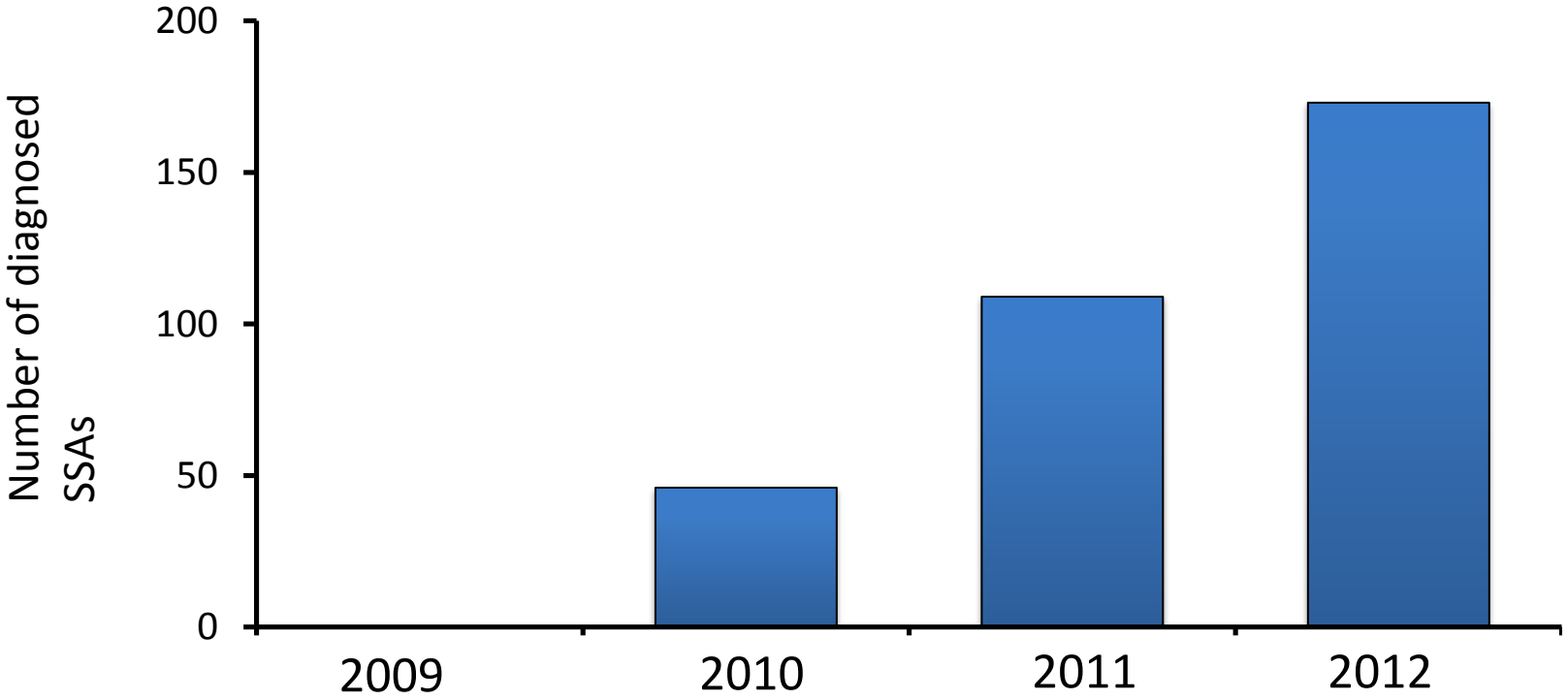


Prevalence of serrated lesions in Western populations

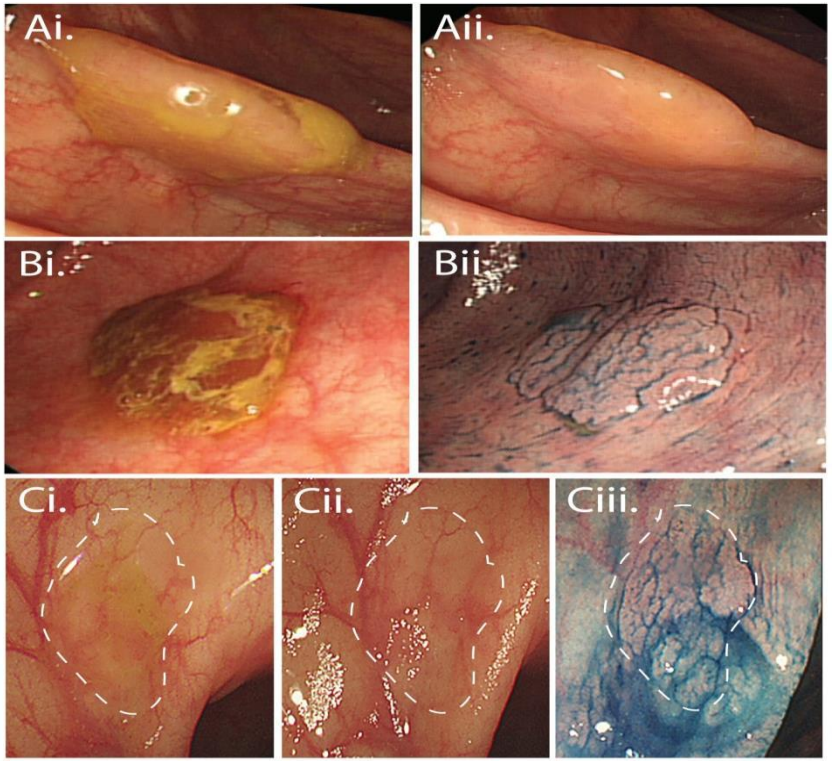
hyperplastic polyp	25 - 30% of all colorectal polyps
sessile serrated lesion	1.7 - 9% of all colorectal polyps
SSL with dysplasia	13% of SSLs
traditional serrated adenoma	0.6 - 1.9% of all colorectal polyps
serrated adenocarcinoma	10 - 25% of all colorectal cancers

Bettington M et al. Histopathology 2013; 62: 367-86.

Oxford audit
Total number SSLs diagnosed



Endoscopic appearances of SSLs



- difficult to spot at endoscopy
- predilection for right side where the prep is usually worse
- flat and often draped over a fold
- adherent mucus often the only clue

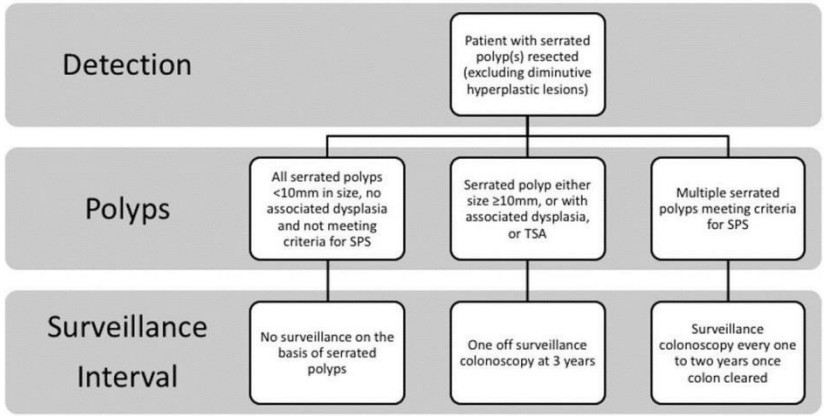
Serrated lesions: pathological lesions

- small, mainly left sided, conventional hyperplastic polyp – common (30% of polyps in BCSP)
- mainly right-sided ‘sessile serrated lesion’ – easily missed but increasingly recognised
- more advanced right-sided sessile serrated lesion with dysplasia – ‘SSL with dysplasia’
- traditional serrated adenoma – left-sided (2% of adenomas)
- larger left-sided (rare) filiform serrated adenoma (less than 0.1% of adenomas)
- serration associated with stromal lesions, perineuriomas, lipomas, etc.
  Primary, secondary or divergent differentiation?!?
- inflammatory bowel disease, especially ulcerative colitis

British Society of Gastroenterology position statement on serrated polyps in the colon and rectum

James E East,[1] Wendy S Atkin,[2] Adrian C Bateman,[3] Susan K Clark,[4] Sunil Dolwani,[5] Shara N Ket,[1] Simon J Leedham,[6] Perminder S Phull,[7] Matt D Rutter,[8,9] Neil A Shepherd,[10] Ian Tomlinson,[11] Colin J Rees[9,12]

Serrated surveillance flowchart



There is no current data to suggest that risk for patients with adenomas and serrated polyps is cumulative and therefore each polyp group should be considered separately for surveillance. The shortest surveillance interval recommended should take precedence.
SPS, Serrated Polyposis Syndrome; TSA, traditional serrated adenoma

Gut 2017; 66: 1181-1196.

Four big issues in bowel cancer screening pathology (and all very relevant to routine colorectal pathology practice….)

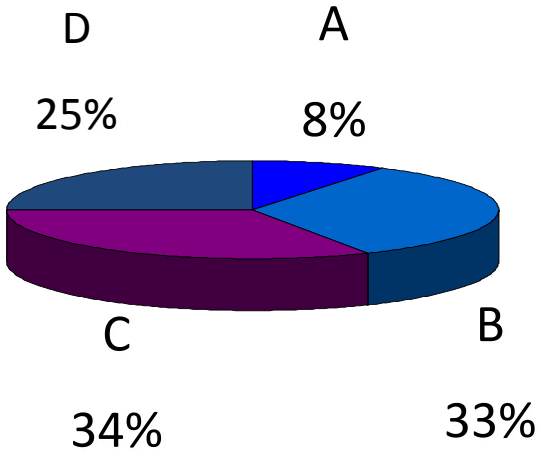
- the diagnosis of colorectal cancer on biopsy
- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties
- polyp cancers (pT1 disease) & what we do about it – expected but not the management difficulties
- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties

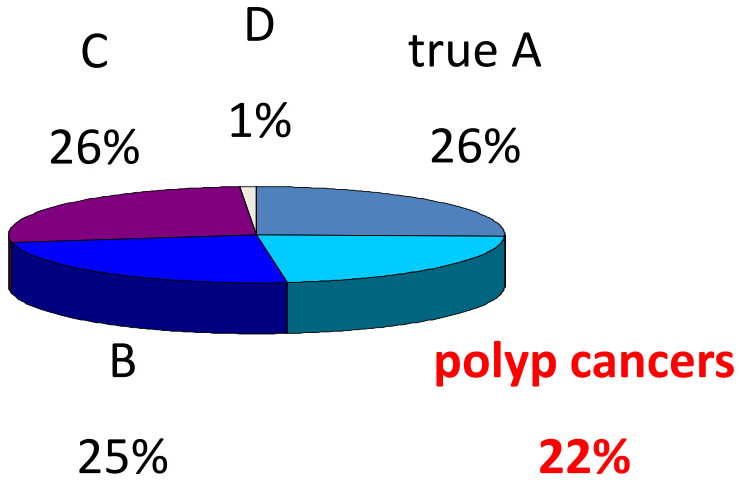
Polyp cancer issues

- is it cancer?
- double reporting recommendation in BCSP since 2012
- the phenomenon of epithelial misplacement/pseudoinvasion in BCS programmes
- other diagnostic issues and mimics
- what do we do about polyp cancer?
  measurement & budding may be king……

What colorectal cancer screening is all about….

- **detecting early stage cancer**

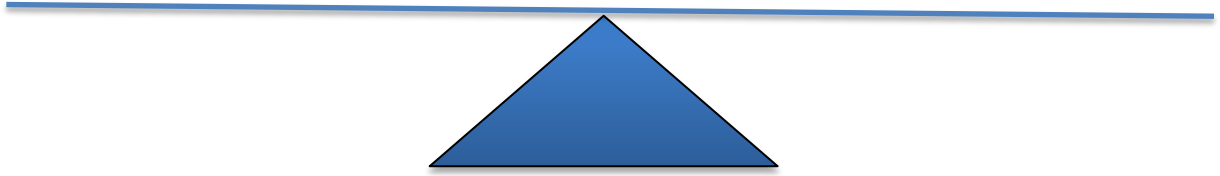




Dukes staging for symptomatic CRC versus screen-detected CRC in the English BCSP

Management of polyp cancers

Resection **No resection**



- reduce recurrence risk
  - risk of positive lymph nodes
  - sub stage pT1
  - site rectum > colon

- complications of surgery
  - mortality: surgical team, age, co-morbidity, country
  - morbidity

- quality of life
  - colostomy, anterior resection syndrome

The adenoma harbouring malignancy: the ‘big three’ criteria

- is it poorly differentiated?
- does it show vascular invasion?
- does it reach the margin? i.e. within 1 mm (or 2mms ?)

Cooper HS et al. Gastroenterology 1995; 108: 1657-65.

What do we do with the adenoma harbouring malignancy? The big three parameters

we can understand vascular invasion & poor differentiation

what about margin involvement?

many papers have attested (25 versus 5) that this is the most predictive parameter for ADVERSE PROGNOSIS, notwithstanding the lack of logic

Cooper et al, 1995;

Geraghty, Williams and Talbot, 1991;

Ueno et al, 2004

Table 2. Literature series of treatment indicators for early invasive colorectal cancers.

First author	Year	Number of tumours	Number of adverse outcomes	Features for adverse outcome
Colacchio	1981	24	6	None
Lipper	1983	51	2	Margin
Haggitt	1985	64	8	Level
Cranley	1986	38	10	Grade, margin, lymphatic invasion
Vanneste	1986	44	3	Grade, margin, vascular invasion, level
Richards	1987	80	10	Grade, margin, stalk invasion, vascular invasion
Coverlizza	1989	31	6	Margin, grade, vascular invasion
Kyzer	1992	44	3	Level
Minamoto	1993	40	6	Grade, level, lymphatic invasion, growth pattern, adenomatous component
Kikuchi	1995	182	21	Level, tumour configuration, location
Hase	1995	79	11	Tumour budding, growth pattern grade, level, lymphatic invasion
Cooper	1995	140	16	Margin, grade, vascular invasion
Volk	1995	47	10	Grade, margin
Whitlow	1997	59	4	Level, margin, grade
Netzer	1998	70	16	Margin, vascular invasion, grade
Ueno	2004	292	50	Margin, vascular invasion, grade, tumour budding, depth/width of submucosal invasion

Geboes K, Ectors N & Geboes KP, 2005

Diseases of the Colon & Rectum

Histologic Risk Factors and Clinical Outcome in Colorectal Malignant Polyp: A Pooled-Data Analysis

Cesare Hassan, M.D.,[1] Angelo Zullo, M.D.,[1] Mauro Risio, M.D.,[2]
Francesco P. Rossini, M.D.,[3] Sergio Morini, M.D.[1]

Dis Colon Rectum 2005; 48: 1588–1596

Table 1.
Relationship Between Histologic Risk Factors and Clinical Outcomes

Risk Factor	Residual Disease	Recurrent Disease	Lymph Node Metastasis	Hematogenous Metastasis	Mortality
Margin of resection					
Positive	55/181 (30.4)[a]	13/77 (16.8)[a]	13/181 (7.2)	30/325 (9.2)[a]	26/325 (8)[a]
Negative	4/142 (2.8)	4/357 (1.12)	13/142 (9.2)	8/655 (1.2)	9/655 (1.4)
Odds ratio	15	17.9	0.8	8.2	6.2
95% CI	(5.3–42.7)	(5.7–56.7)	(0.3–1.7)	(3.7–18.2)	(2.9–13.5)
Poor differentiation					
Positive	10/56 (17.8%)	—	13/56 (23.2)[a]	11/14 (9.6)[a]	14/96 (14.6)[a]
Negative	29/324 (9%)	—	23/324 (7.1)	40/1,520 (2.6)	27/1,487 (1.8)
Odds ratio	2.2		3.9	3.9	9.2
95% CI	(1–4.8)		(1.9–8.4)	(2–7.9)	(4.7–18.3)
Vascular Invasion					
Positive	6/34 (17.6%)	—	12/34 (35.3)[a]	13/250 (5.2)	7/210 (3.3)
Negative	17/111 (15.3%)	—	8/111 (7.2)	38/1,279 (3)	28/1,194 (2.3)
Odds ratio	1.2		7	1.8	1.4
95% CI	(0.4–3.3)		(2.6–19.2)	(0.9–3.4)	(0.6–3.3)

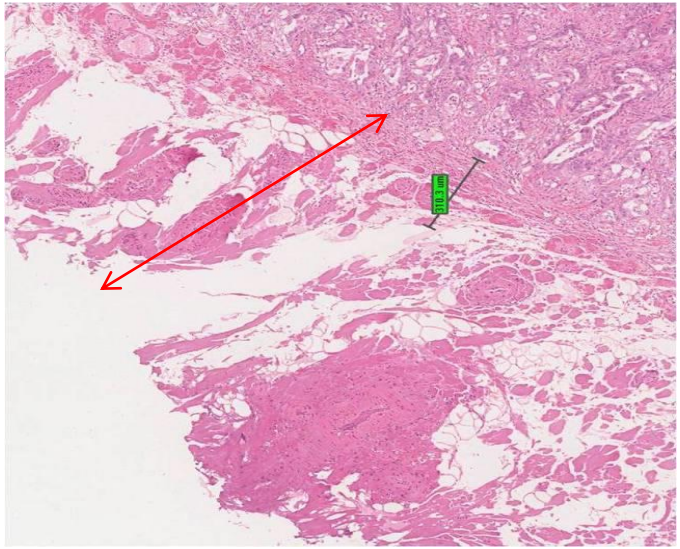
CI = confidence interval.
Data are numbers with percentages in parentheses unless otherwise indicated.
[a]$P < 0.05$.

Selecting patients for resection

- a careful balance between risks of metastatic disease & risks of surgery
- happy about poorly differentiated and vascular invasion: difficulty is margin involvement……
- age and co-morbidity are important
- crucial MDTM/Tumour Board discussion

Margin involvement by cancer in malignant polyps

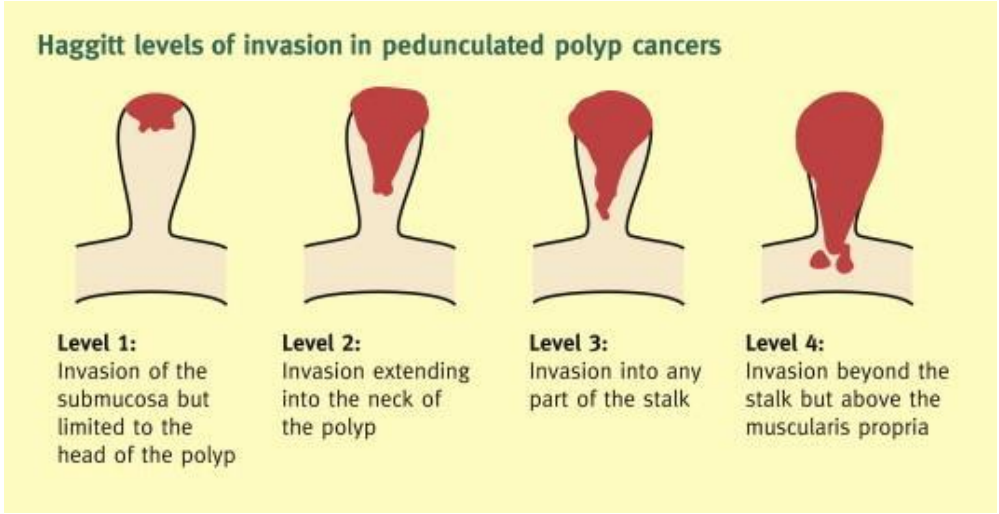
- commonest adverse prognostic parameter
- commonest isolated adverse prognostic parameter
- definition ?!?
- now at margin (we recommend…) and not within 1mm (for polyp cancers)
- margin is external border of diathermy mark
- ignore artefacts and cracks



Loughrey MB, Bateman AC, Shepherd NA, Quirke P.
BCSP polyp reporting guidelines, 2018

Classification of early colorectal cancer in polyps

Haggitt RC et al, 1985



Issues with pathological assessments

margin involvement	lacks logic: is evidence good enough? definitions
poor differentiation & lymphovascular invasion	less problems but still subjective
Kikuchi	needs muscularis mucosae & propria only for sessile lesions?
Haggitt	sessile v polypoid subjective
differences in polyp type and influence on endoscopic resection	pedunculated, sub-pedunculated & sessile
budding	subjective; definitions
measuring: depth, width	inter-observer variation

Measuring depth and width of invasion: Japanese methodology

Assessment of depth of invasion (*if completely excised*)

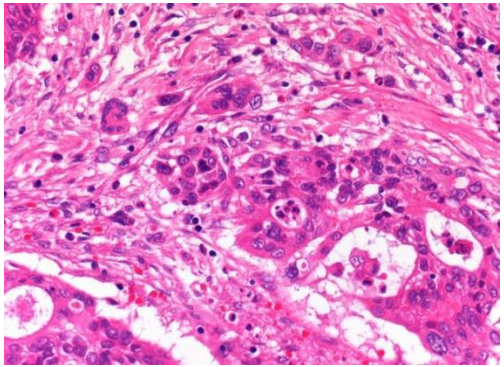
direct measurement from muscularis mucosae

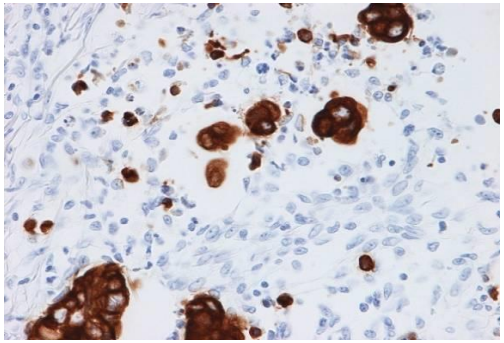
depth > 2mm	20% nodal +ve (vs 5%)
width of invasive front > 4mm	20% nodal +ve (vs 4%)

Ueno et al. Gastroenterology 2004; 127: 385-394.


CHAMPION BEER
of Gloucestershire
2005 & 2006
BUDDING
Stroud Brewery
Pale Ale
4.5%

Where are we with tumour budding?





- independent prognostic significance in polyp cancers

  Ueno et al, 2004

- independent significance in Dukes B/stage II colon cancers

  Wang et al, 2009

- less powerful in Dukes C/stage III

- issues: varying methods of assessment, heterogeneity, reproducibility

- now international standardisation on methodology

  Lugli et al, 2017

- not currently recommended for routine reporting but one for the future?

BCSP polyp cancer inter-observer study
Leeds, February 2013

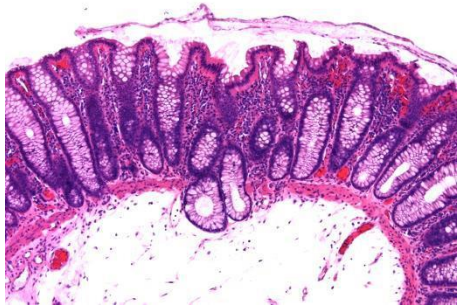
- poor levels of agreement with differentiation, lymphatic spread, vascular spread, margin positivity, even Haggitt…..
- good levels of agreement with margin positivity once definitions of margin had been established.
- best levels of agreement with MEASURING – depth of spread, width of cancer, distance from margin.
- measuring may be the future…..

The most useful tool in BCSP?!?

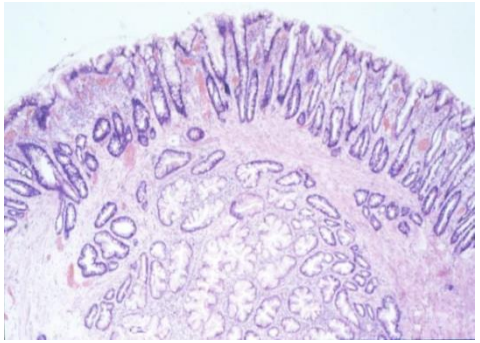
Four big issues in bowel cancer screening pathology (and all very relevant to routine colorectal pathology practice….)

- the diagnosis of colorectal cancer on biopsy
- serrated pathology & what do we do about it – expected but not the amount nor the diagnostic difficulties
- polyp cancers (pT1 disease) & what we do about it – expected but not the management difficulties
- the large adenomatous polyp of the sigmoid colon – expected but not the amount nor the diagnostic difficulties

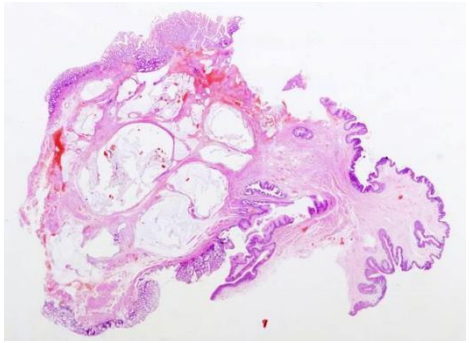
Epithelial misplacement (pseudo-invasion)



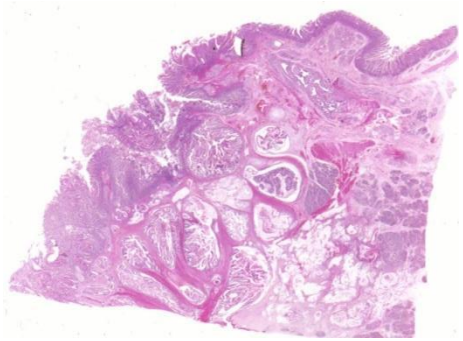
‘Normal’ colonic mucosa



Hyperplastic polyp (& SSL)



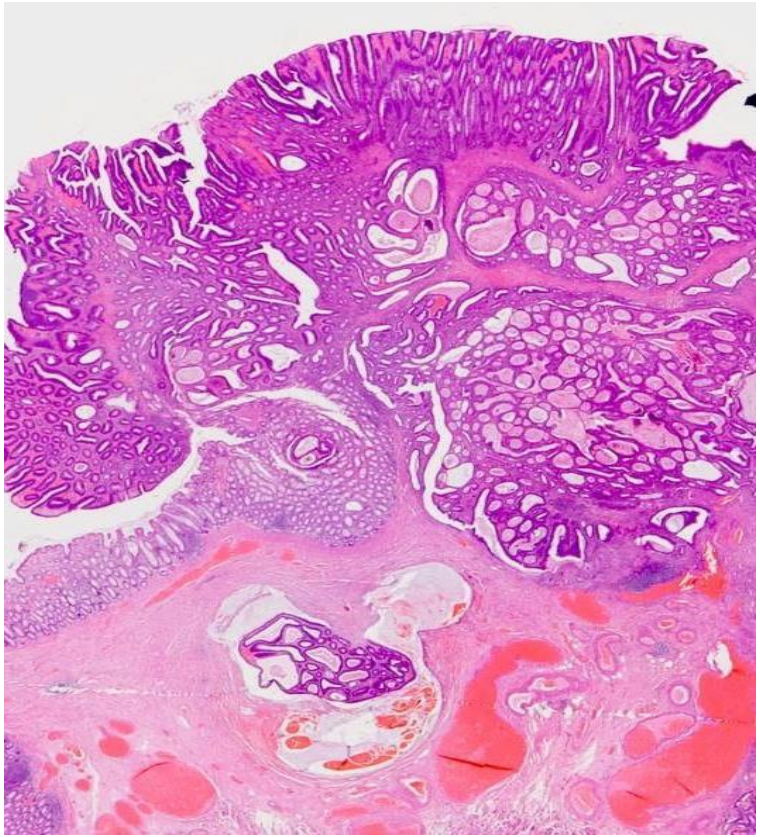
Inflammatory cloacogenic polyp



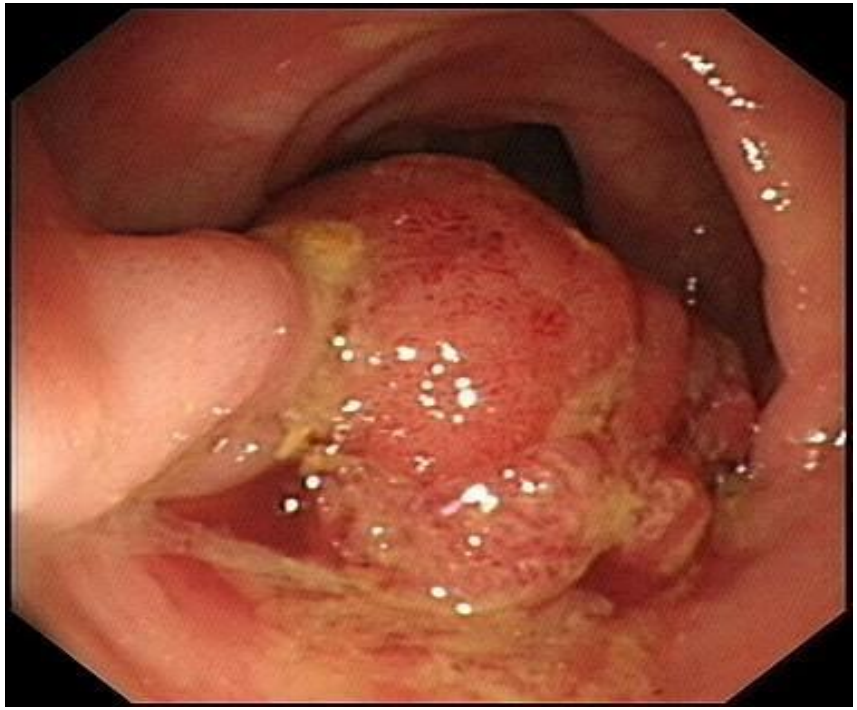
Peutz-Jeghers polyp

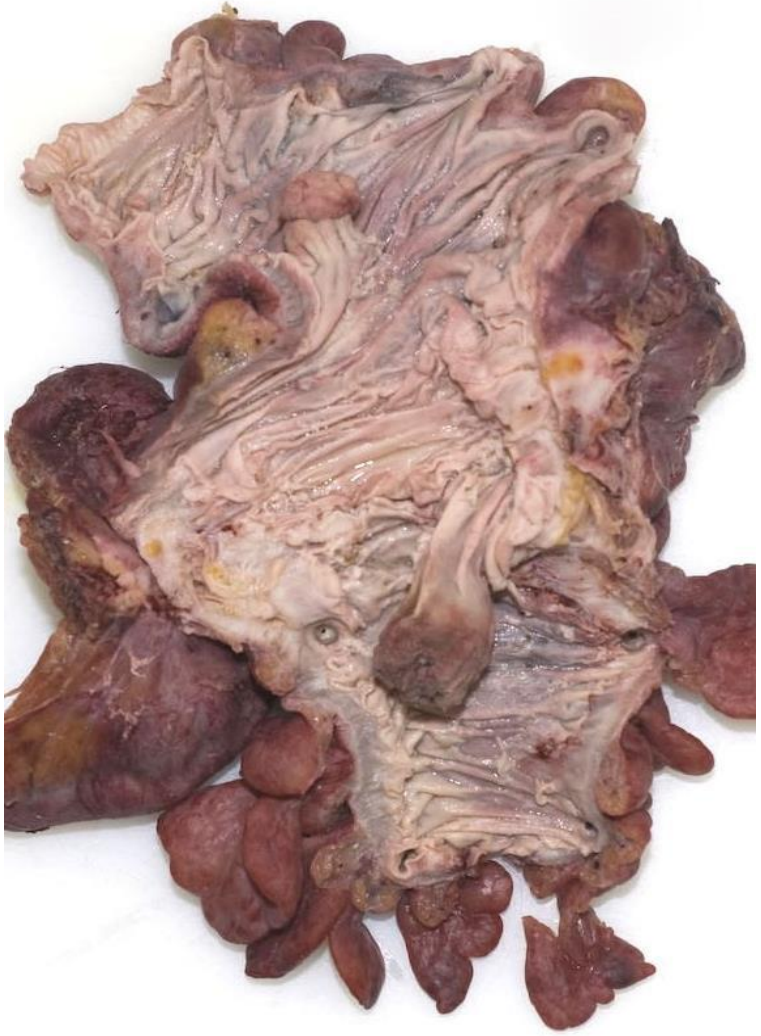
Epithelial misplacement in adenomas

- 85% in sigmoid colon
- unusual in rectum (unless there has been previous intervention)
- same epithelium as surface, accompanied by lamina propria, haemosiderin deposition, continuity (in 3D)
- what about misplaced epithelium at the diathermy margin?
- intense pathological mimicry of invasive cancer

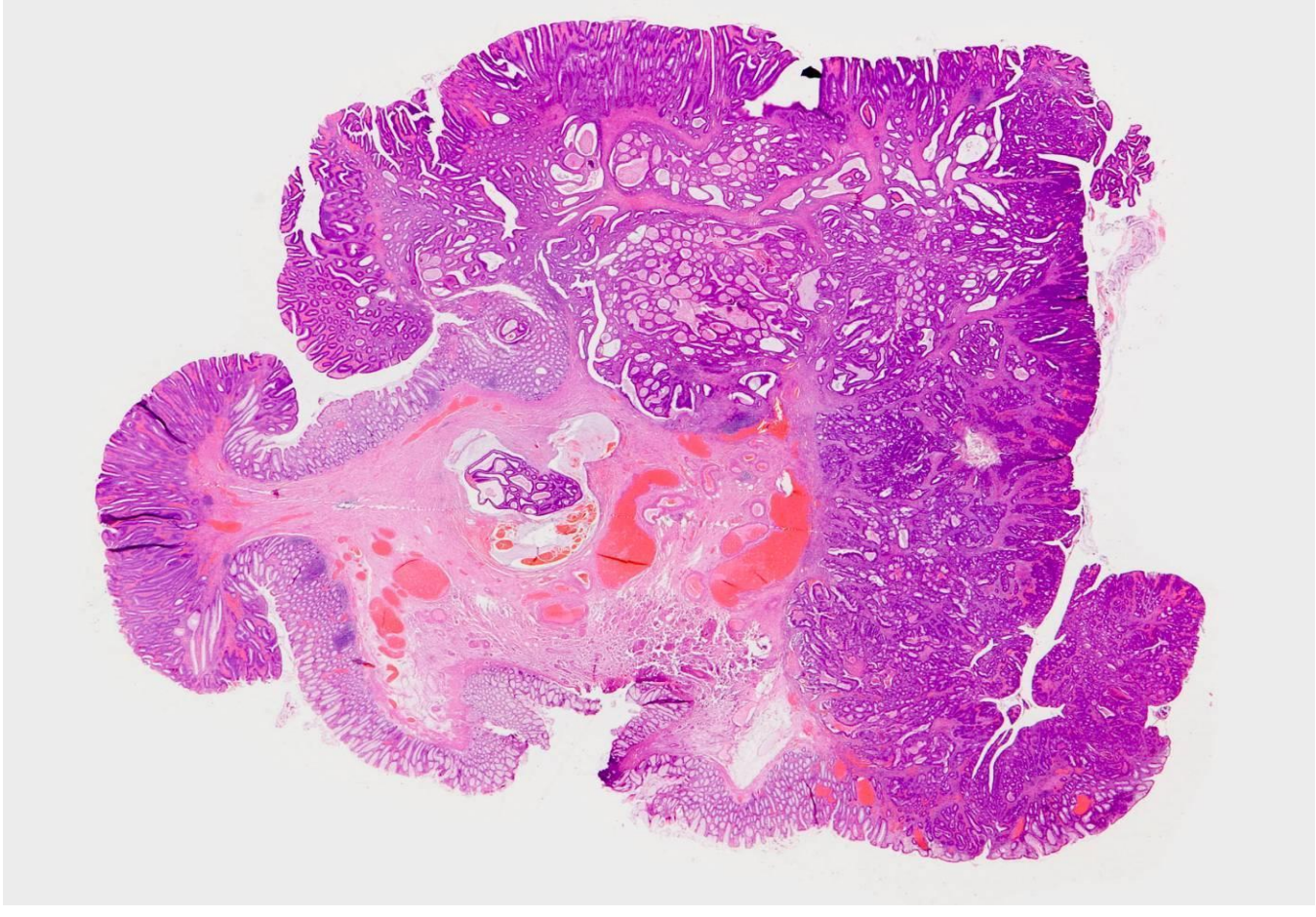


Why the sigmoid colon?



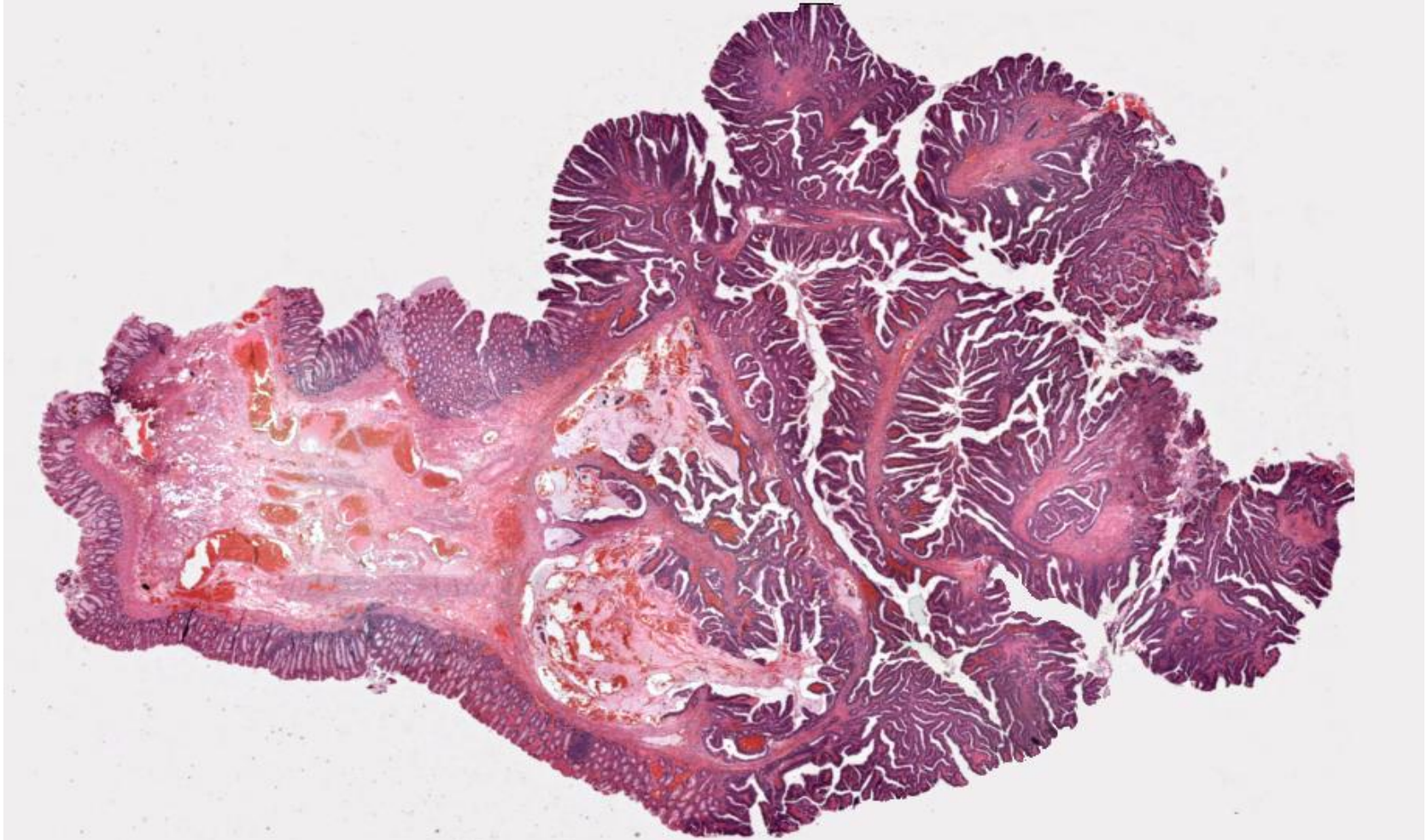


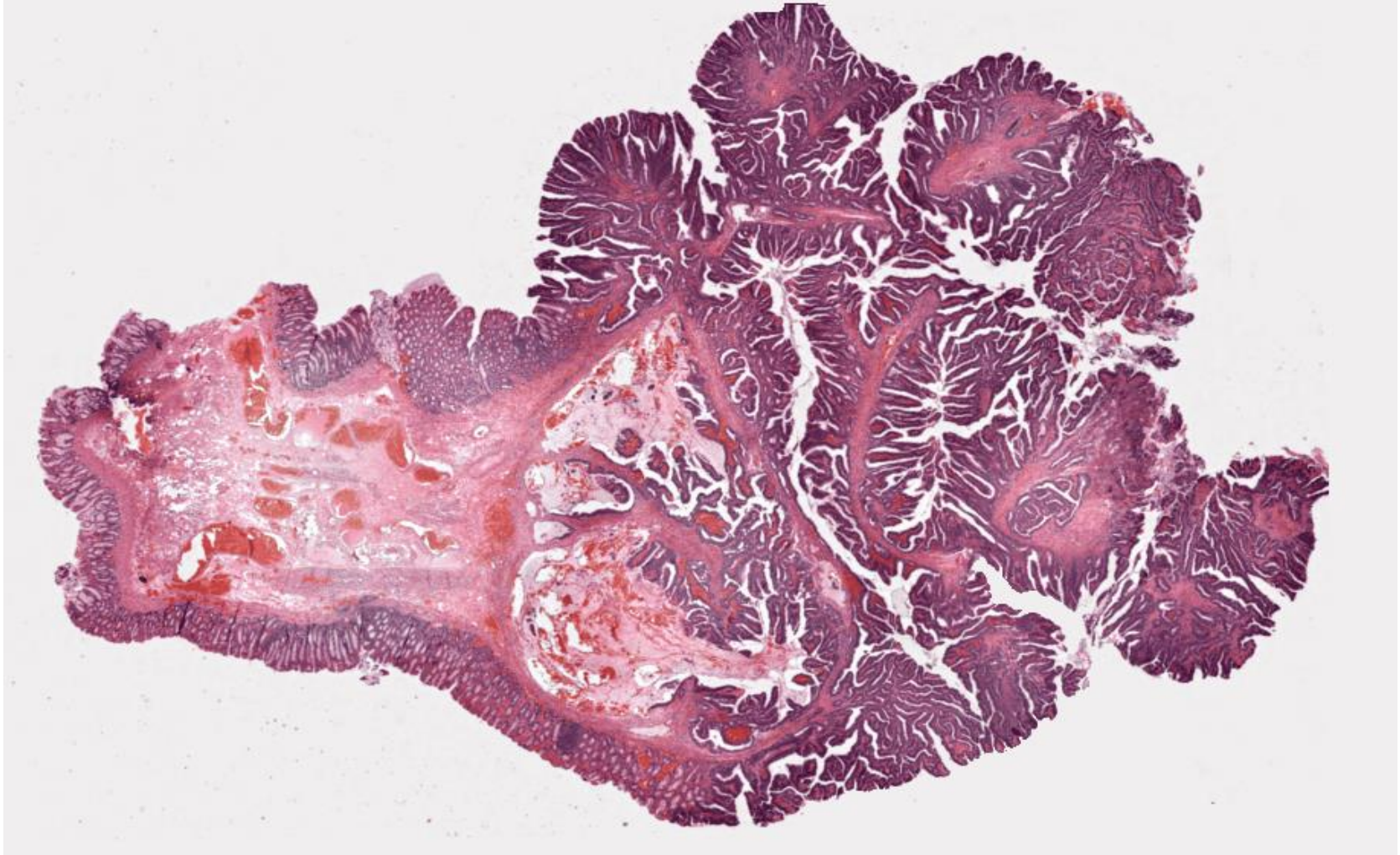
Epithelial misplacement vs invasive carcinoma



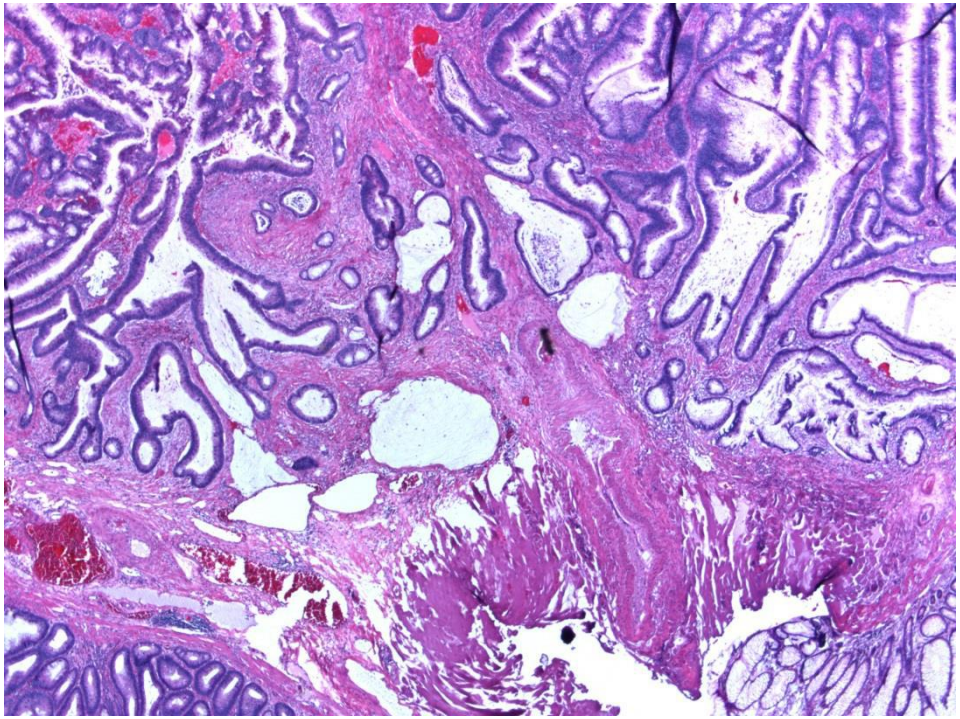
Epithelial misplacement vs carcinoma: what to look for

- lamina propria accompaniment
- lack of desmoplastic reaction
- haemosiderin deposition
- muscular proliferation as in mucosal prolapse
- acute changes of infarction adjacent
- accompaniment by non-neoplastic epithelium (especially after previous intervention)
- continuity of epithelium (in 3D, at least) between superficial and deep components

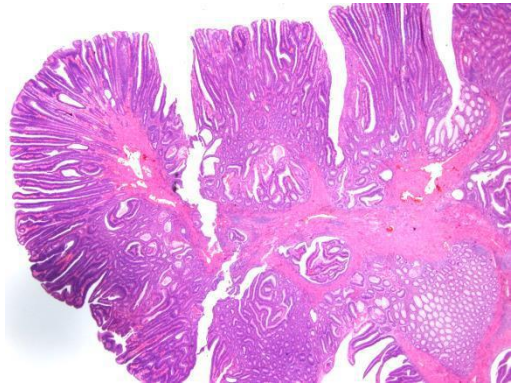


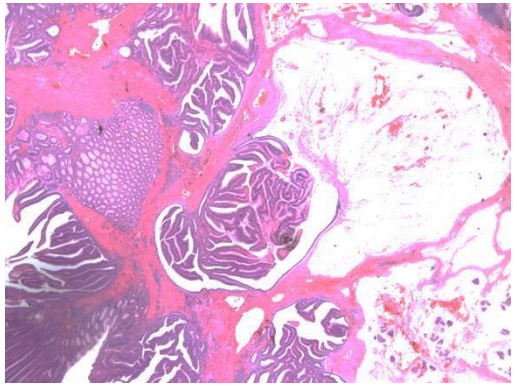


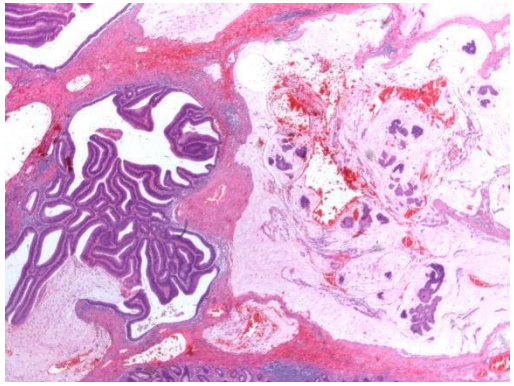
Do you see epithelial continuity in cancer?

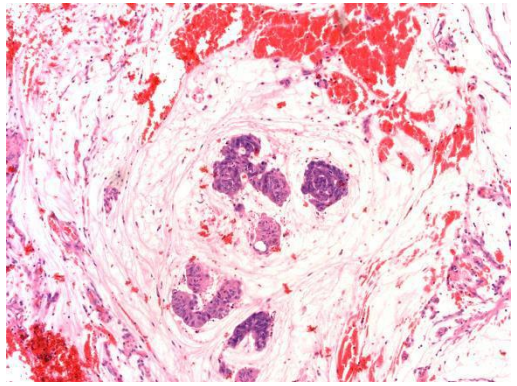


64M. 22mm sigmoid colonic polyp.

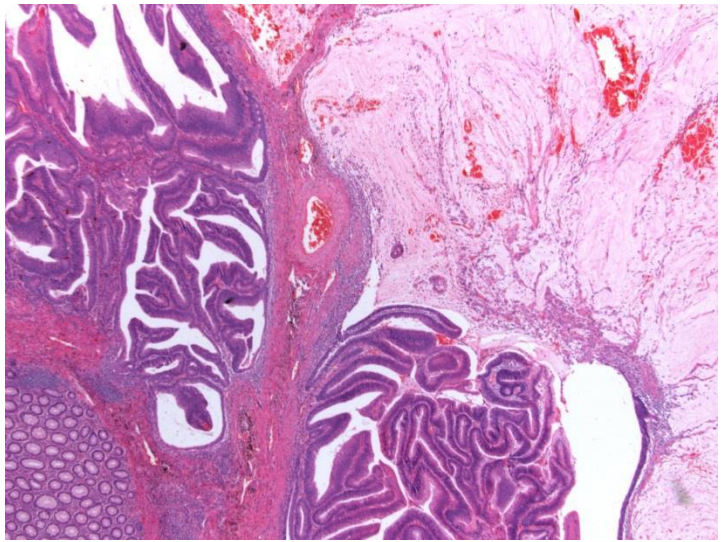


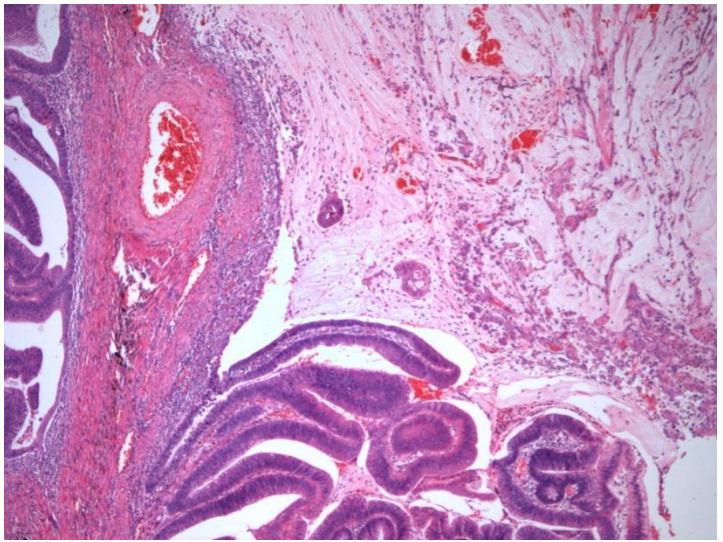




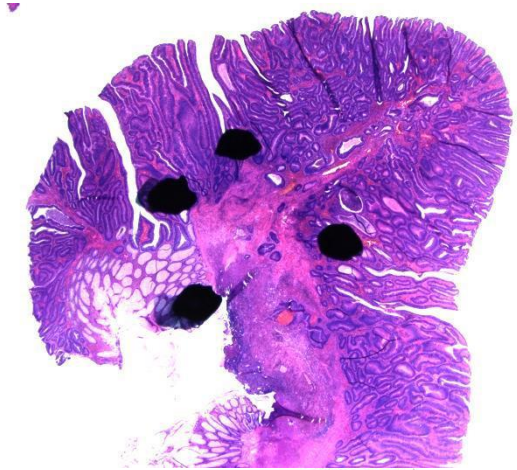


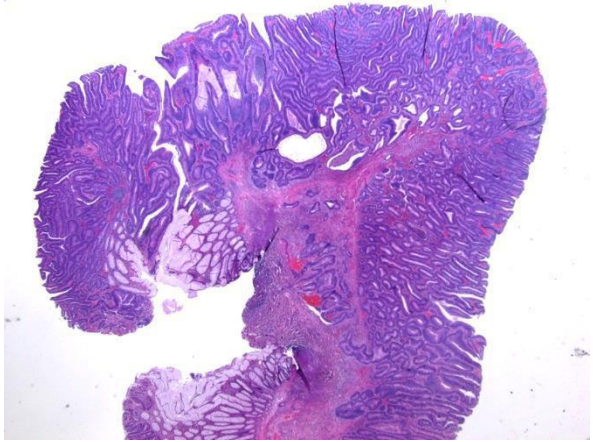
64M. 22mm sigmoid colonic polyp.

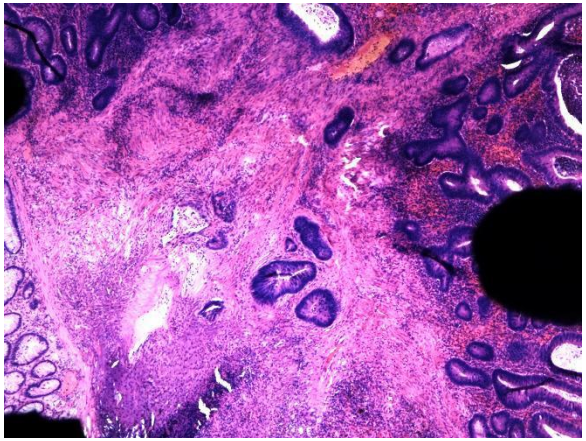


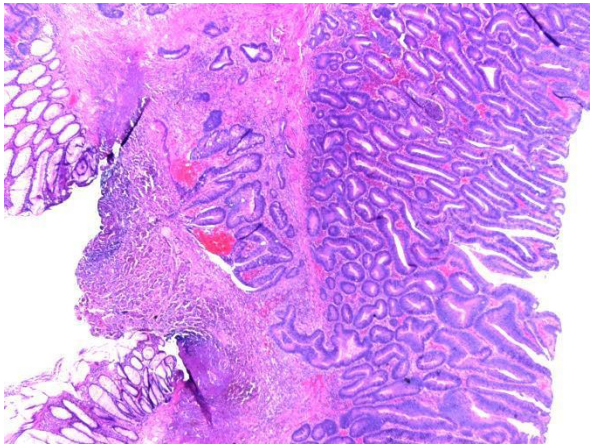


The importance of deeper levels

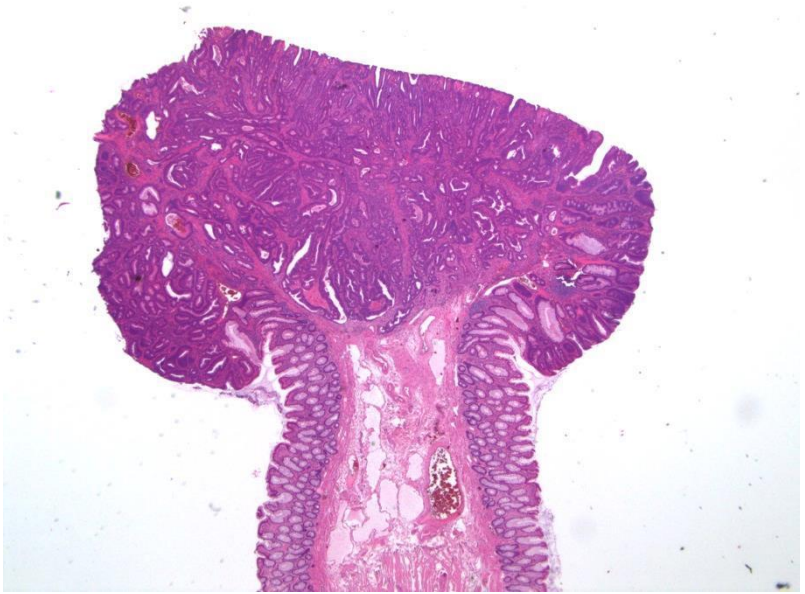


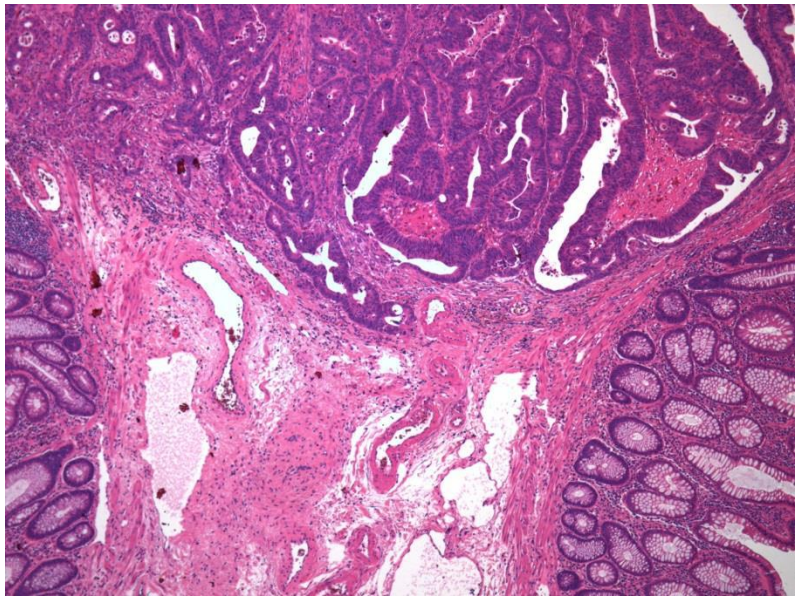




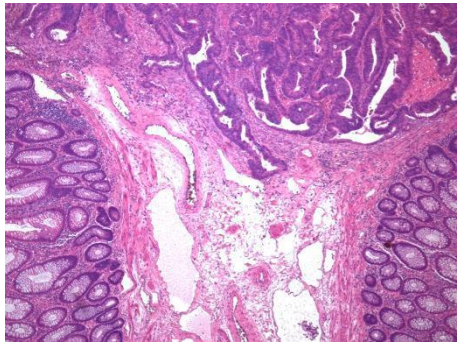


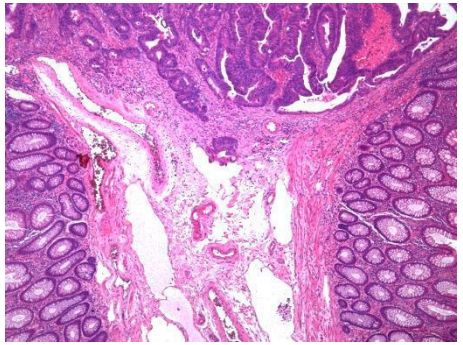
The importance of deeper levels:
67F. Sigmoid colonic polyp.

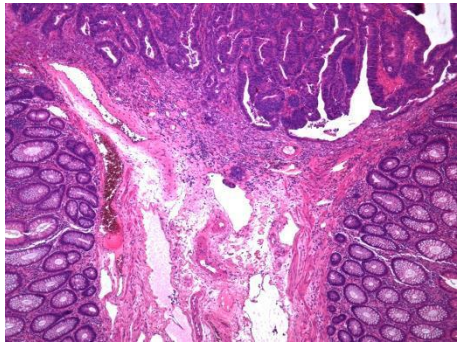


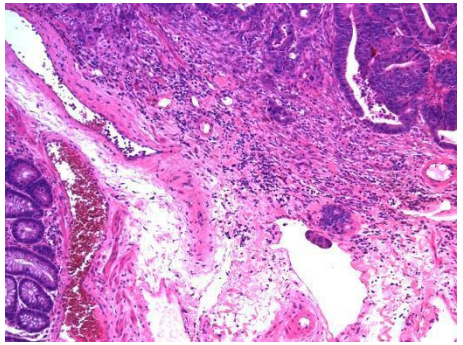


The importance of deeper levels:
67F. Sigmoid colonic polyp.

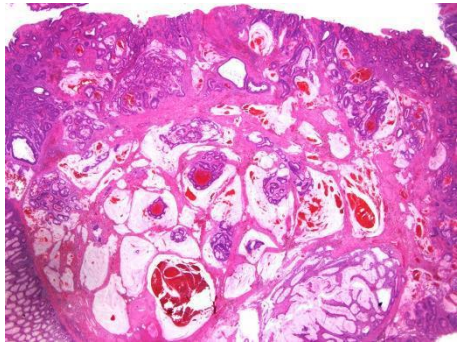


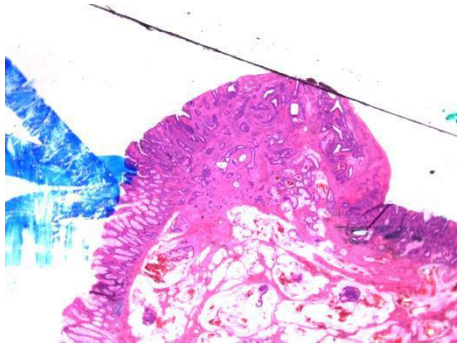


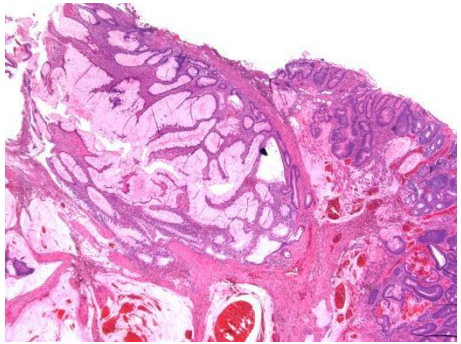


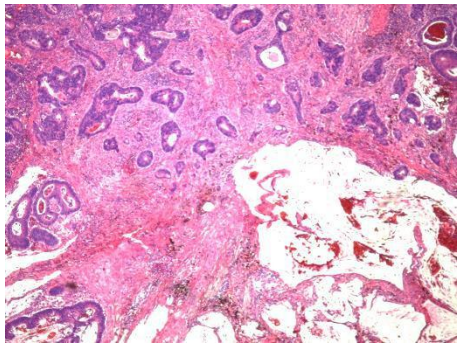


Accompaniment by non-neoplastic mucosa



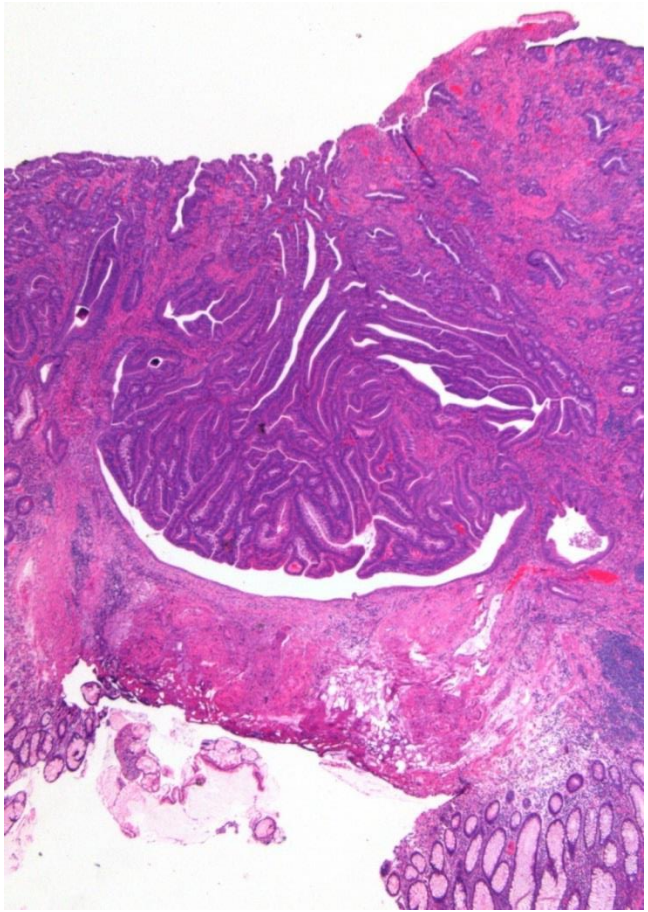


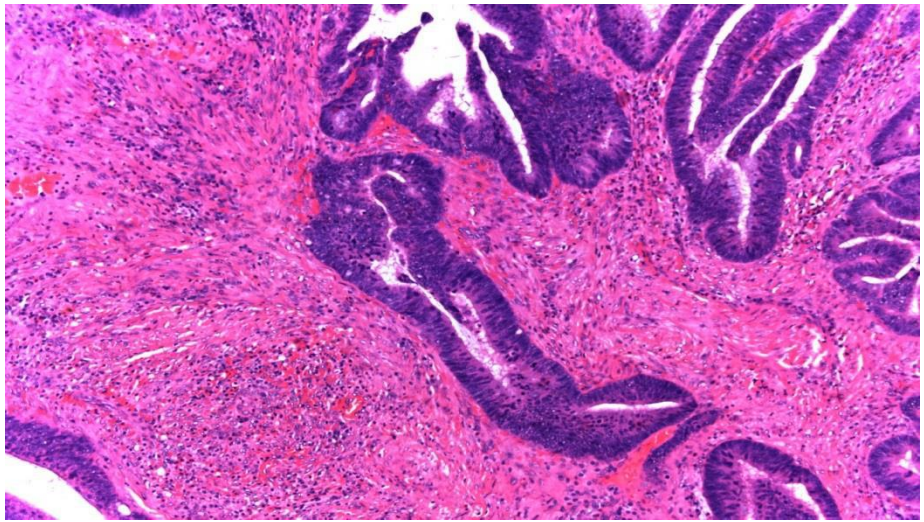




Panarelli NC, Somarathna T, Samowitz WS, Kornacki S, Sanders DSA, Novelli MR, Shepherd NA, Yantiss RY. Am J Surg Pathol 2016; 40: 1075-83.

Adenomatous epithelial inversion & stromal muscularisation





Pathological conundra in BCSP

- epithelial misplacement mimicking cancer
- 85% in sigmoid colon
- selected into BSCP as large prolapsing adenomatous polyps that bleed
- can be very difficult and some almost impossible
- require ‘Expert Board’ and BCSP-funded research
- but some are more straight forward and yet may be miscalled by pathologists….

Table 2. A comparison of the pathological features that may be valuable in differentiating epithelial misplacement from invasive adenocarcinoma

	Epithelial misplacement (EM)	Adenocarcinoma
Epithelial 'differentiation'	Usually similar to that of the surface adenomatous component	Variable and usually different to the surface adenomatous component
Lamina propria accompaniment	Characteristic but may be lacking when there is secondary inflammation and epithelial destruction	Usually absent. Can be present in rare, very well-differentiated carcinoma
Accompaniment by non-adenomatous epithelium	Characteristically seen when EM is due to previous intervention	Absent
Haemosiderin deposition	Characteristic and indicative of previous necrosis and/or haemorrhage	Usually absent
Mucosal prolapse changes	Often present	Usually absent
Mucus cysts	Characteristic. They probably represent epithelial misplacement that has become 'detached' from the more superficial components	Only present, usually, in mucinous tumours
Continuity with surface adenomatous component	Characteristic but often only appreciated in multiple levels and/or 3D reconstruction studies	Usually absent but some cases do show continuity, even in 3D reconstruction studies.
Involvement of muscularis propria (MP)	Usually absent. Can be seen very rarely, especially after previous intervention	Present if at least pT2
Budding	Usually absent but a similar phenomenon can be seen as a result of epithelial destruction and/or inflammation	Often present
Desmoplastic reaction to glands	Usually absent but fibromuscular stromal proliferation can accompany EM	Usually present
Lymphatic and/or vascular invasion	Absent	Diagnostic of cancer

Loughrey & Shepherd, Histopathology ARI, January 2015

Adjunctive tests

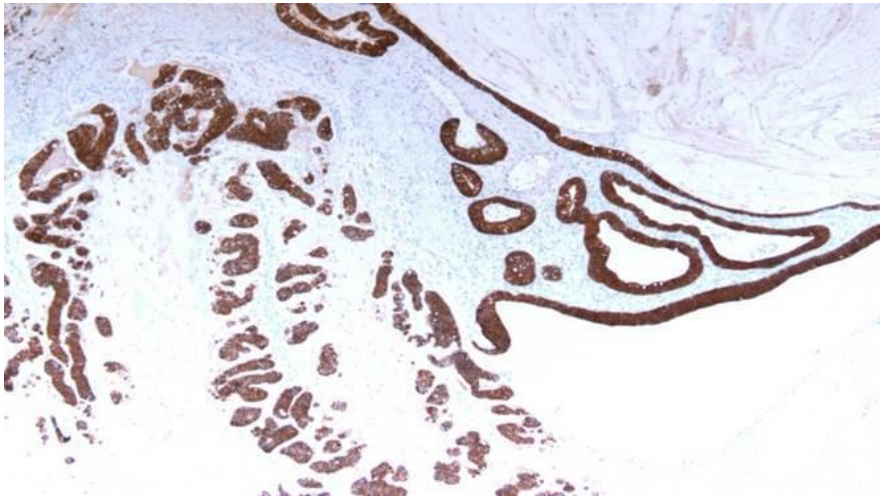
If it’s so difficult for us morphologists, do we have any reliable adjunctive tests?

- immunohistochemistry
- three dimensional reconstruction
- in-situ molecular analysis

Immunohistochemistry

MMP-1
p53
collagen IV
e-cadherin

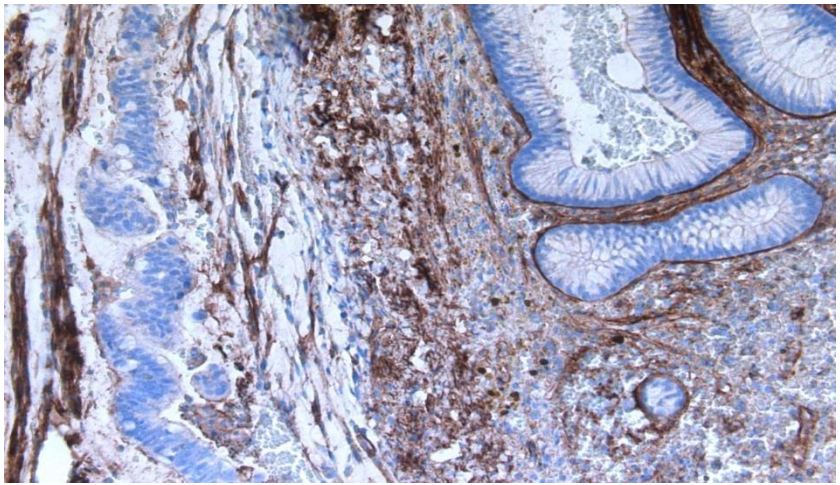
Ki67/MIB1



e-cadherin

Yantiss RK, Bosenberg MW, Antonioli DA, Odze RD. Utility of MMP-1, p53, e-cadherin and collagen IV immunohistochemical stains in the differential diagnosis of adenomas with misplaced epithelium versus adenomas with invasive adenocarcinoma. Am J Surg Pathol 2002; 26: 206-215.

Immunohistochemistry

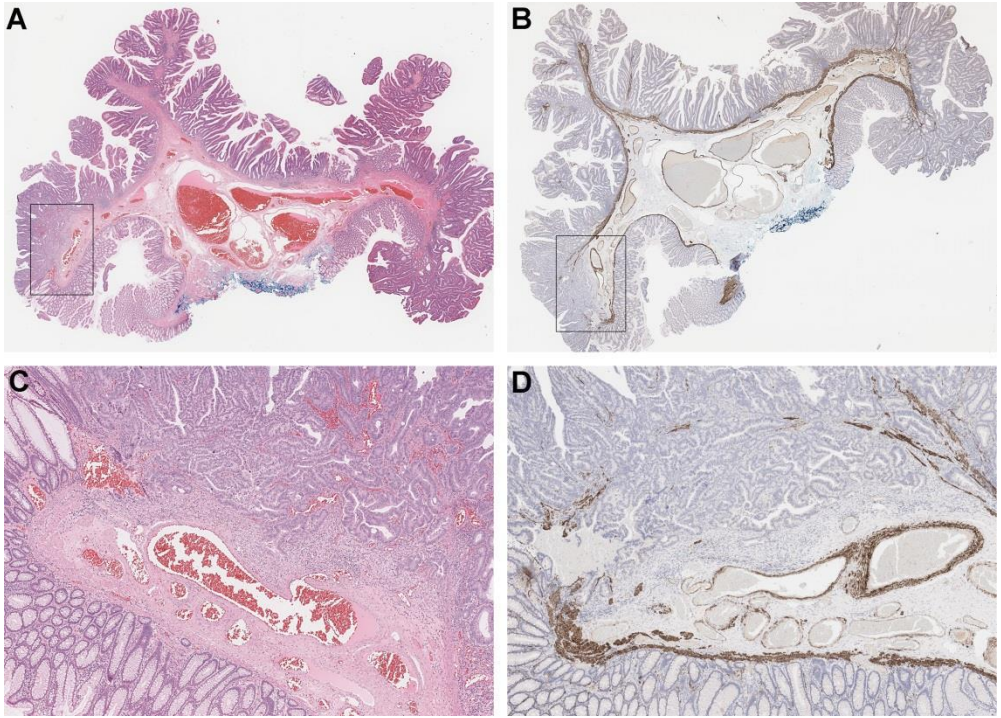


collagen IV

Yantiss RK, Bosenberg MW, Antonioli DA, Odze RD. Am J Surg Pathol 2002; 26: 206-215.

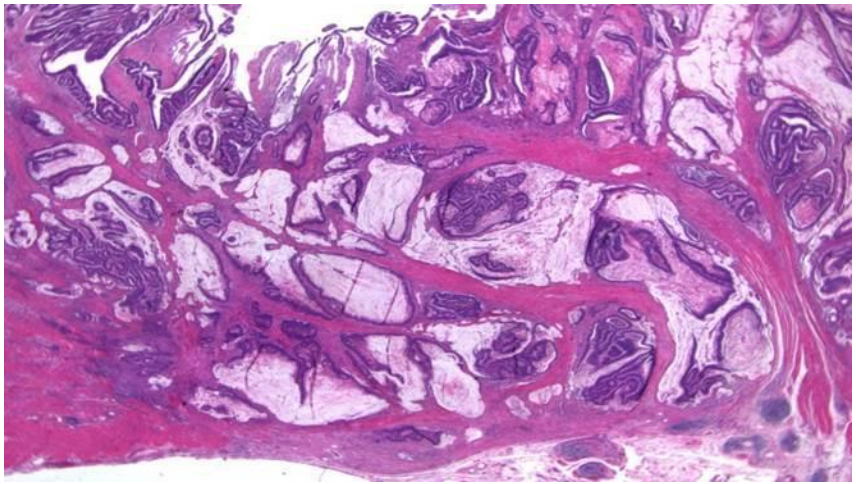
- works well in classic cases of pseudoinvasion and cancer
- not so good in marginal cases

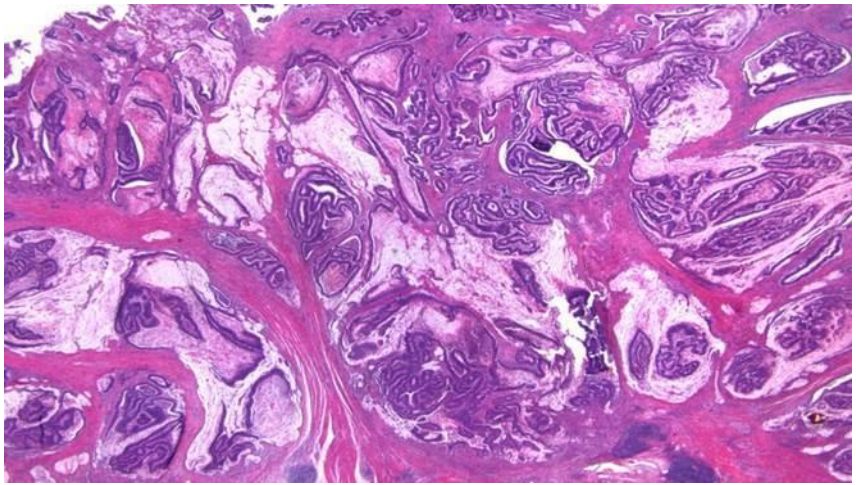
Immunohistochemistry: desmin and other SM markers are useful to demonstrate submucosal involvement



Loughrey MB, Shepherd NA. Problematic colorectal polyps: is it cancer and what do I need to do about it? Surgical Pathology Clinics (ed Yantiss RK) 2017; 10: 947-960.

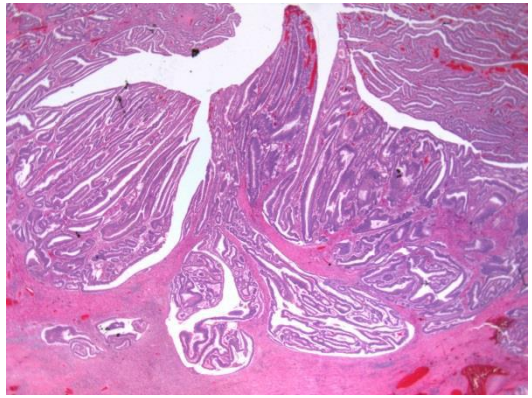
Adenoma-like adenocarcinoma

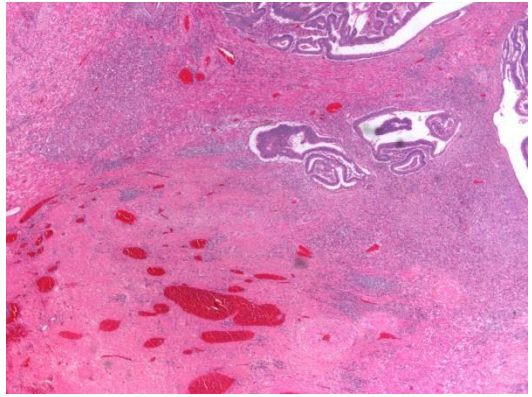


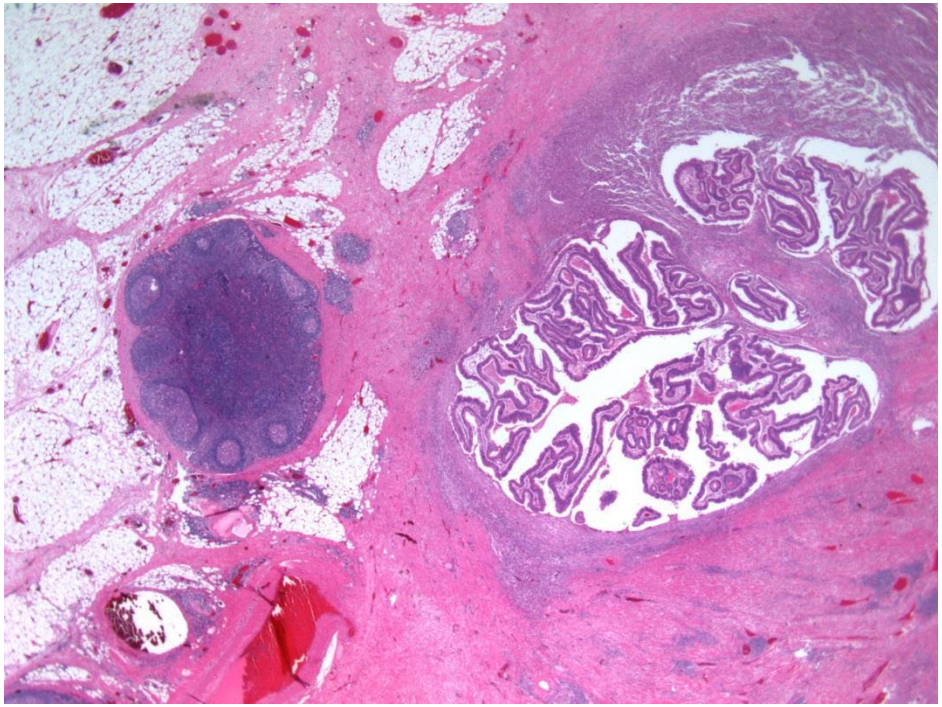


Gonzalez RS, Cates JMM, Washington MK, Beauchamp RD, Coffey RJ, Shi C. Adenoma-like adenocarcinoma: a subtype of colorectal carcinoma with good prognosis, deceptive appearance and frequent KRAS mutation. Histopathology 2016; 68: 183-190.

57M. Caecal polyp.







Epithelial misplacement/cancer and difficult BCSP polyps

- the most extraordinary diagnostic conundrum I have seen (or, perhaps, recognised!) in my professional career
- low levels of inter-observer agreement amongst ‘general’ pathologists
- not perfect inter-observer agreement amongst ‘experts’
- surely matched only by melanocytic lesions of the skin.....

BCSP Expert Board

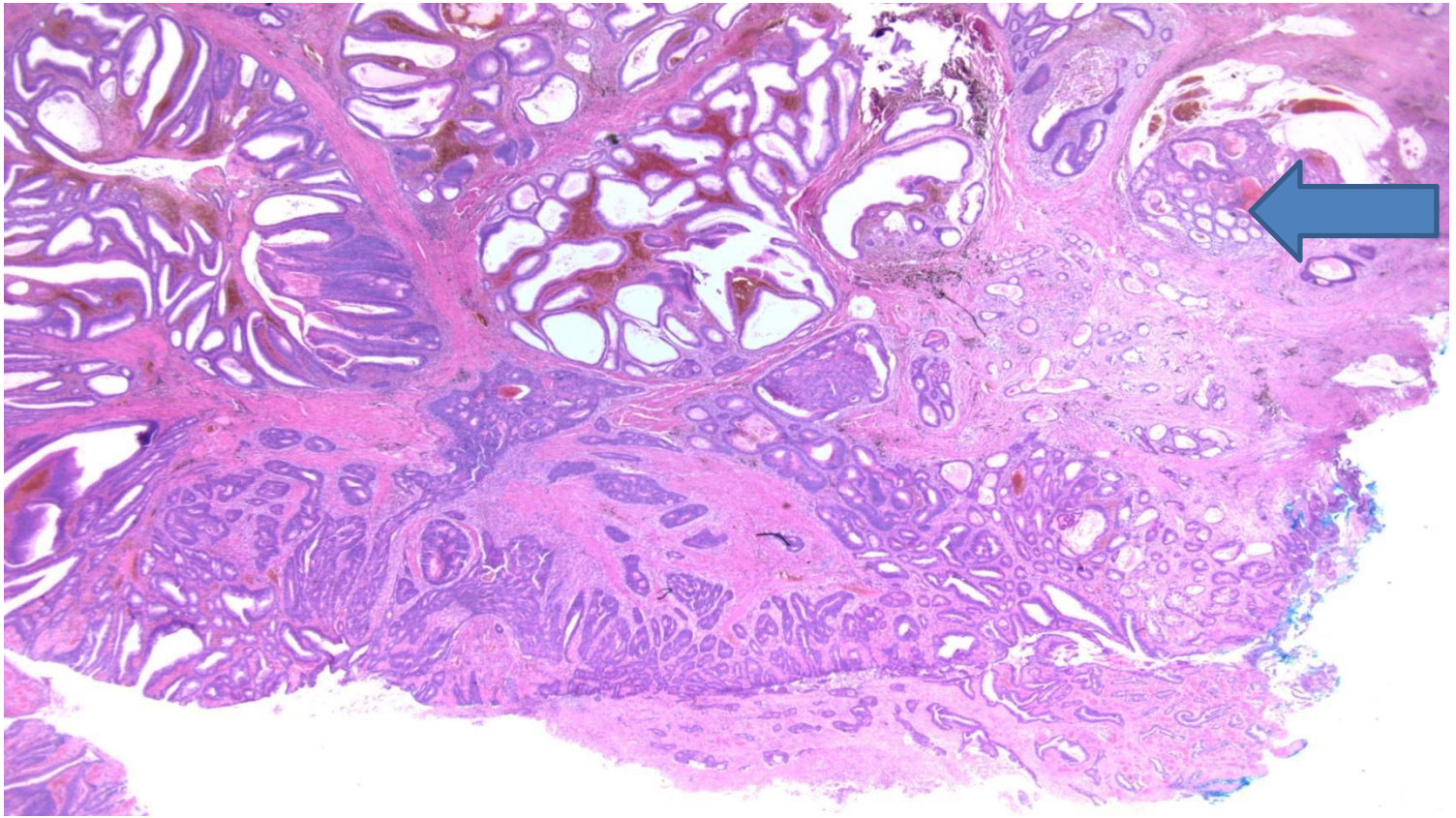
- three pathologists – you need a majority for this highly subjective and difficult assessment
- N A Shepherd, A C Bateman & M R Novelli
- funded (IT, postage, secretarial support) in England by BCSP
- opportunity for education and research into difficult EM v Ca cases

Expert Board assessments

2009-16

- 249 cases: 20 cases in 2009; 72 in 2016
- EB three-way agreement of 80.3%: kappa score of 0.67 (substantial agreement)
- originating pathologist(s) v EB:
  - benign diagnosis 30.6% v 80.2% (originator(s) v EB)
  - diagnosis changed from originating pathologist(s) to EB in 50%
  - mainly malignant to benign
- double diagnosis (ie EM and carcinoma) in 3% of cases

Expert Board:
double diagnosis (ie EM & carcinoma) in 3% of cases



The UK ‘Expert Board’

Griggs RKS, Novelli MR, Sanders DSA, Warren BF,

Williams GT, Quirke P, Shepherd NA.

Challenging diagnostic issues in adenomatous polyps with epithelial misplacement in bowel cancer screening: five years’ experience of the BCSP Expert Board.

Histopathology 2017; 70: 466–472.

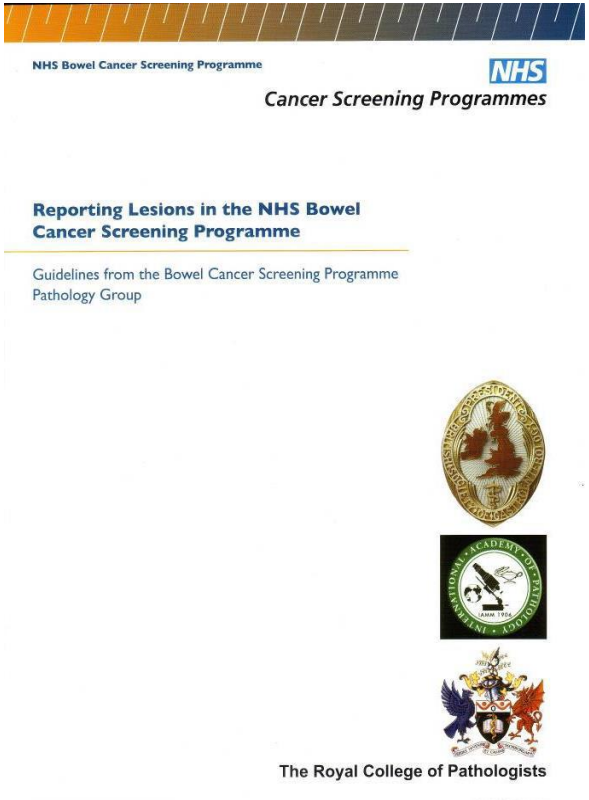
Epithelial misplacement in sigmoid colonic polyps: a major conundrum in BCSP

- epithelial misplacement mimicking cancer: 85% in sigmoid colon
- selected into BSCP as these are large prolapsing adenomatous polyps that bleed – detected by FOB and FIT screening
- can be very difficult and some almost impossible, a phenomenon not really seen before in UK GI pathology

Shepherd NA, Griggs RKS. Epithelial misplacement in sigmoid colonic adenomatous polyps: bowel cancer screening-generated diagnostic conundrum of the century. Modern Pathology 2015; 28: S88-94.

- require 'Expert Board' and BCSP-funded research
- a major source of diagnostic error, especially detected through rigid QA procedures – will it be as prevalent or as problematic in FIT screening?
- has been seen in other screening programmes but seemingly preferentially in population screening programmes: Scotland, Wales, Northern Ireland, Republic of Ireland, Canada, France, Netherlands, Slovenia - some are establishing similar diagnostic boards for this extraordinary problem

Setting bowel cancer screening pathology standards



Quality assurance in pathology in colorectal cancer screening and diagnosis—European recommendations

Phil Quirke • Mauro Risio • René Lambert • Lawrence von Karsa • Michael Vieth

CRC screening as a driver for enhanced overall colorectal pathology service quality

- adenoma pathology: classification and grading of dysplasia; villosity
- serrated pathology : sensible reclassification
- use of performance indicators and quality measures to drive up colorectal cancer reporting quality, especially through BCS QA

Loughrey MB, Quirke P, Shepherd NA.
RCPath guidelines for the reporting of colorectal cancer, 2014 & 2018

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Take home messages

- bowel cancer screening and its QA continues to improve the overall quality of colorectal pathology
- we really must make ourselves more useful for surveillance by ensuring good agreement levels with high grade dysplasia and villosity, in particular
- our knowledge of serrated pathology is increasing exponentially but we still have a lot to learn
- we have real management problems with polyp cancers: measurement +/- budding may be the answer in the future….
- epithelial misplacement v cancer – the diagnostic conundrum of the century (in the UK at least…)
- bowel cancer screening, with its quality induced by comprehensive quality assurance, quite massive numbers and comprehensive datasets, will ultimately give us the answers to many of these vexatious questions……..

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