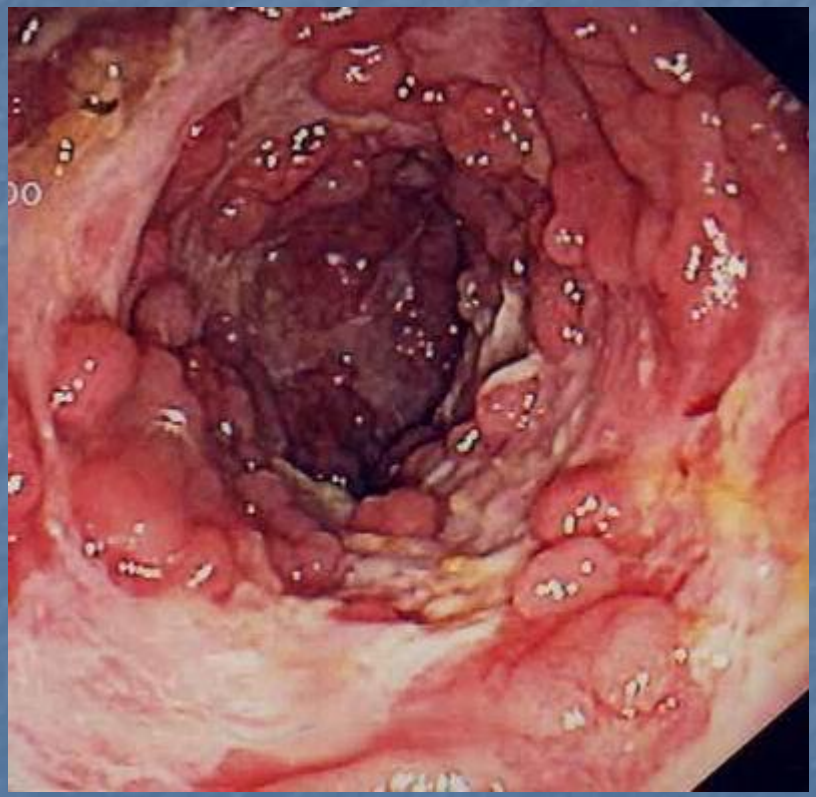


# Endoscopy in IBD – why, when and how

Lars Aabakken
Chief of GI Endoscopy
Dept of Medicine
Rikshospitalet, Oslo, Norway

# Meaning what?

**Aspects**

- Detecting disease
- Diagnosing disease
- Sampling
- Assessing severity and monitoring drug effects
- Endoscopic therapy
- Surveillance

**Modalities**

- **Colonoscopy**
- Upper endoscopy
- Enteroscopy
- Capsule endoscopy

# Time trends of endoscopy

# Detection and diagnosis

# Detection of IBD

- Patient history
- Blood sampling
- Faecal sampling
- Colonoscopy
- Other endoscopy
- Other diagnostic imaging

# Colonoscopy

- Most cases are straight-forward
  - Typical history – and findings
  - Moderate severity
  - Classical features of Crohns or UC
- Sometimes they are not
  - Indeterminate colitis (10%)
  - Atypical phenotype
  - Or – something completely different?

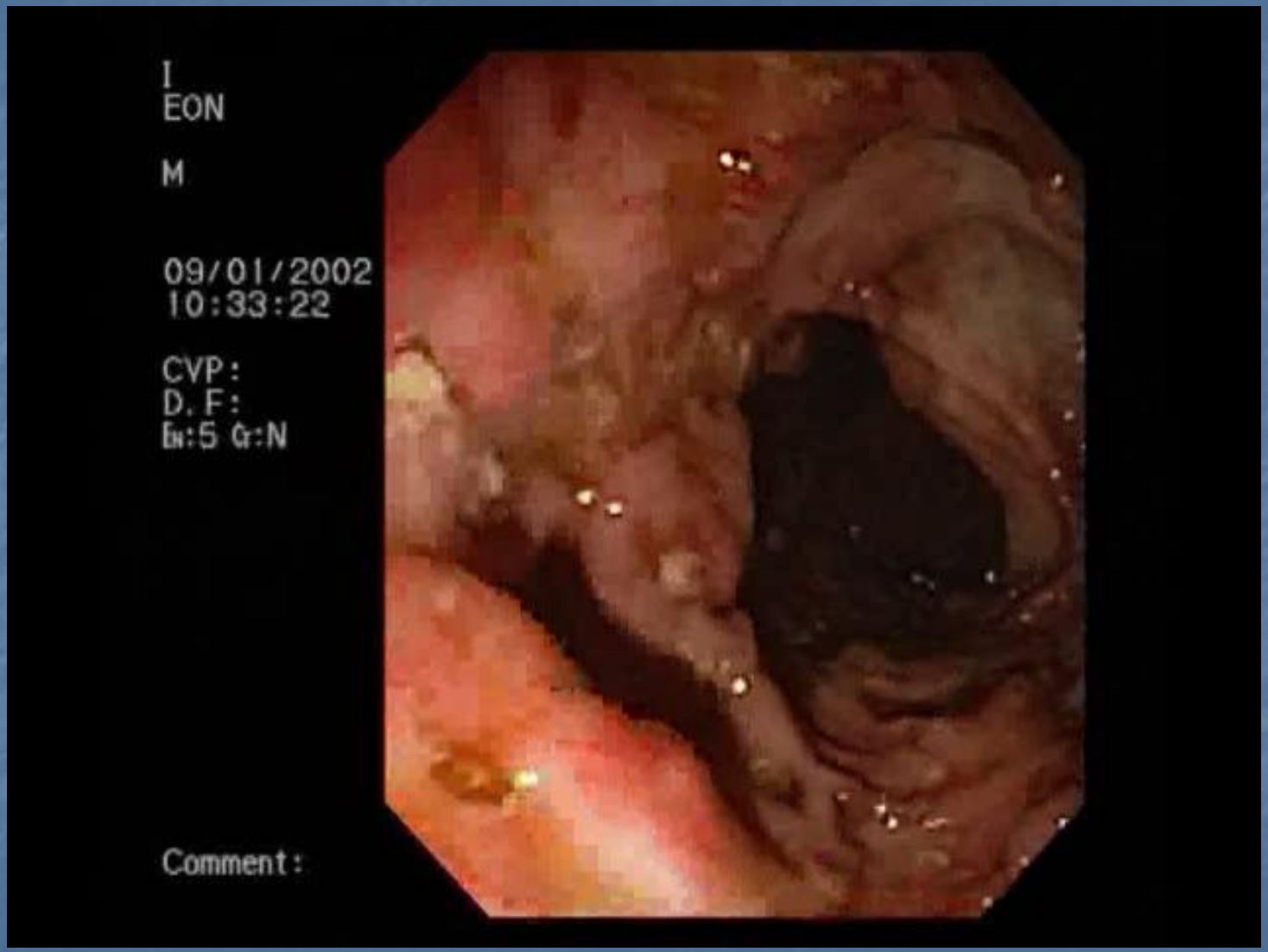
# CD or UC?

**Crohns disease**

- Discontinous involvement
- Cobblestoning
- Aphtous ulcers
- Serpiginous ulcers
- Rectal sparing
- Anal lesions
- Ileocecal valve stenotic/ulcerated

**Ulcerative colitis**

- Continuous involvement
- Erosions/microulcerations
- Loss of vascular pattern
- Rectal involvement
- Ileocecal valve patulous and free of ulceration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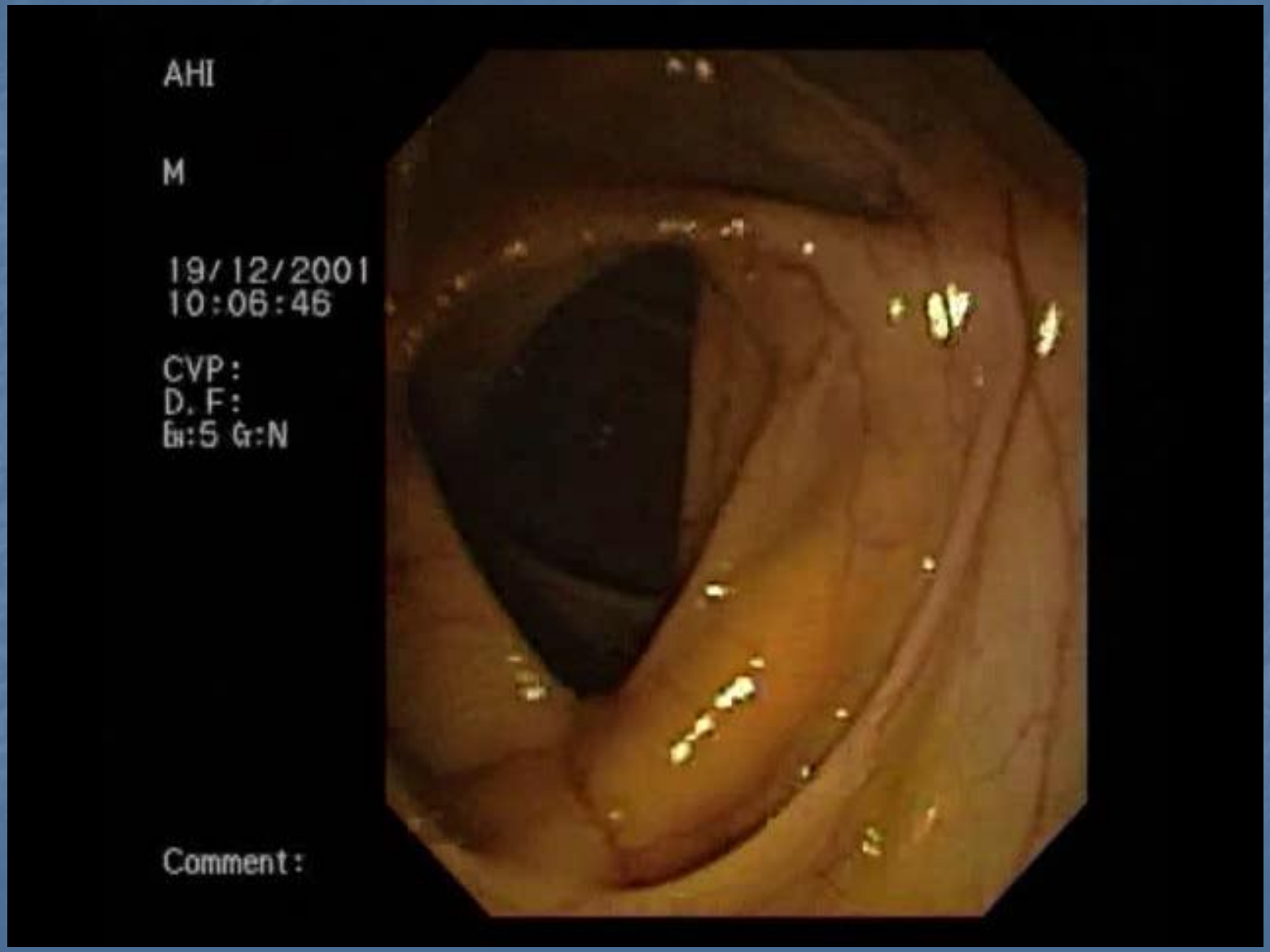
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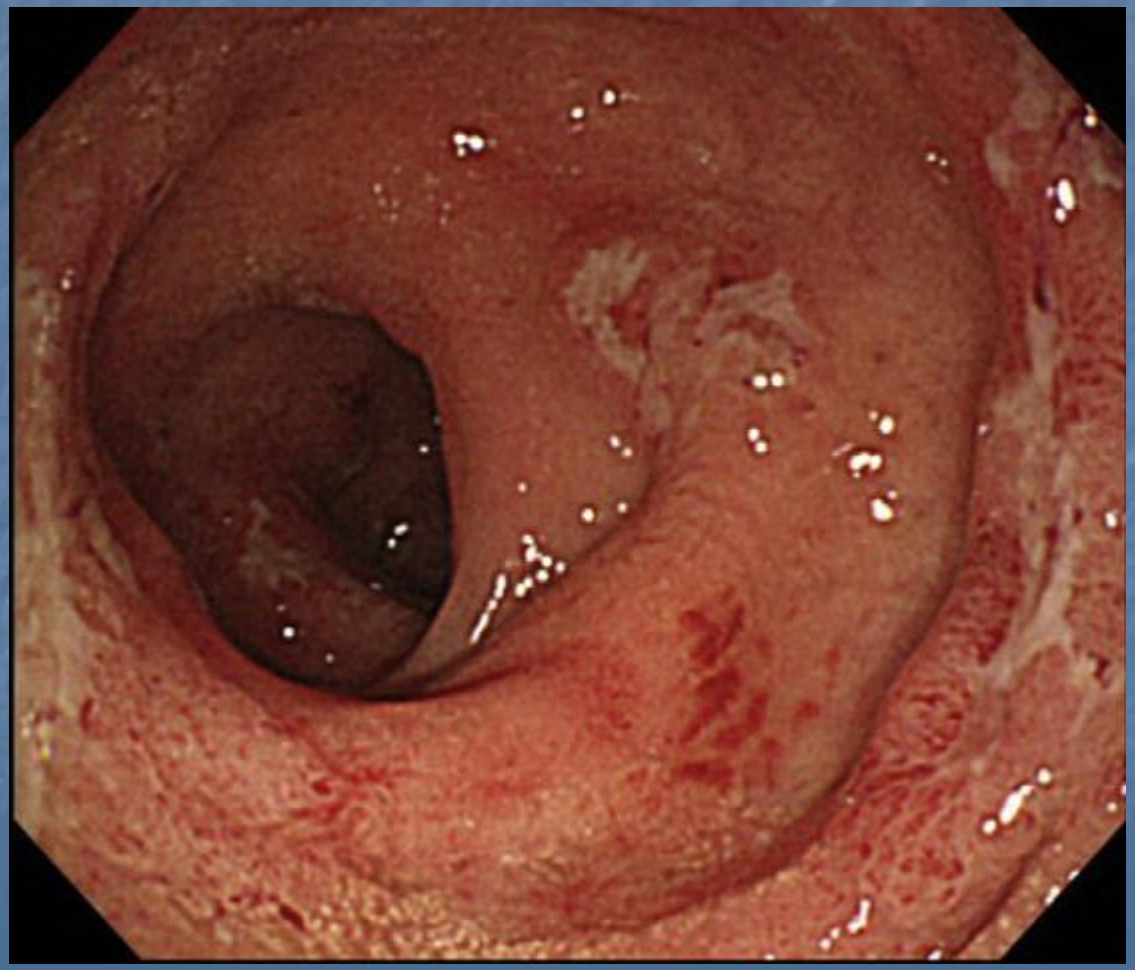
# When to consider differentials

- Atypical presentation
  - Endoscopic pathology
  - Distribution
- History suggesting infectious diarrhoea
- Immunosuppression
- Concomitant disease
- Suspicious drug history

# The relevant differentials

- Ischemic colitis
- Pseudomembranous colitis
- Viral colitis
- Tubercolosis
- Other enteropathogenic microbes

# Amoebic colitis



# Capsule endoscopy

- Introduced 2002 for complete endoluminal visualization of small bowel
- High sensitivity (?)
- Moderate specificity (for Crohns)
- High yield in suspected Crohns
- (Almost) contraindicated in established Crohns

# CE findings

- Erythema
- Erosive lesions
- Ulcerations
- Strictures
- Bleeding

# Differentials of CE Crohns

- Artifacts
- Normal findings
- NSAID lesions
- Other drug effects?
- Tuberculosis

# CE mortality?

# CE - Current role

- Small bowel imaging when Crohns is suspected but not visualized by upper, lower or sectional imaging (or ultrasound)
- Assessment of small bowel activity when colonoscopy is discrepant from clinics/calprotectin
- Prior to balloon enteroscopy

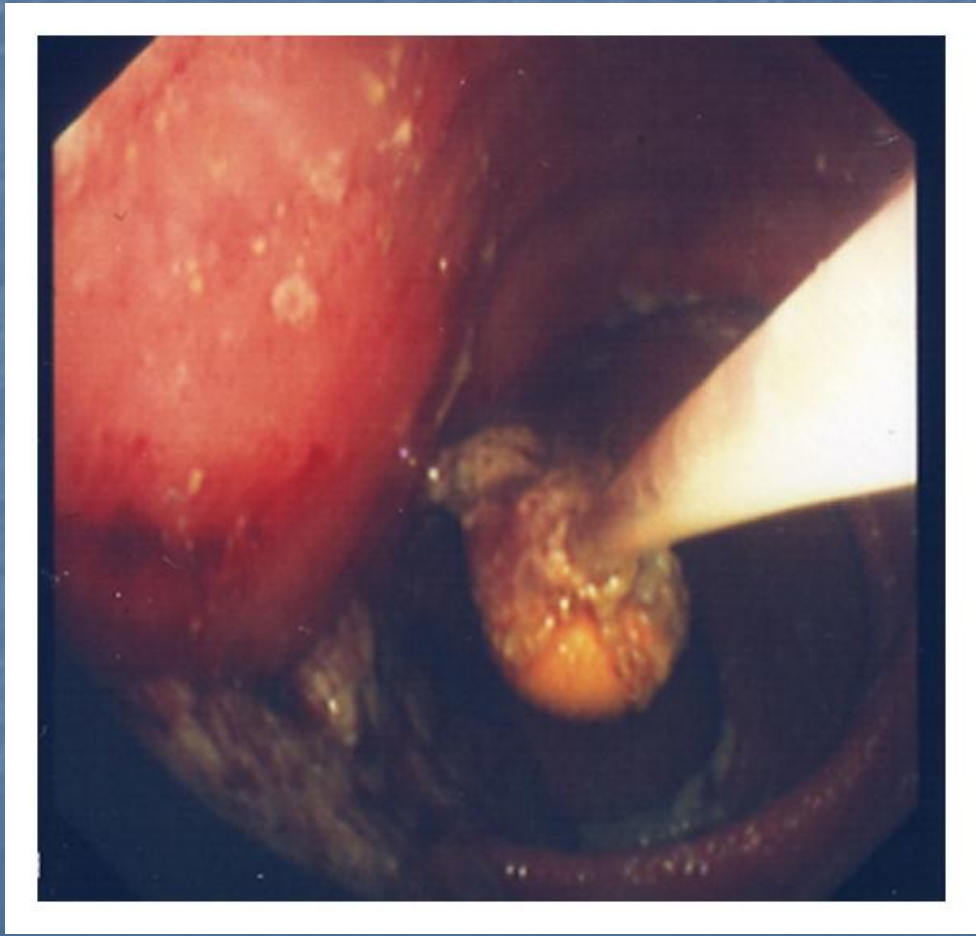
# Balloon enteroscopy

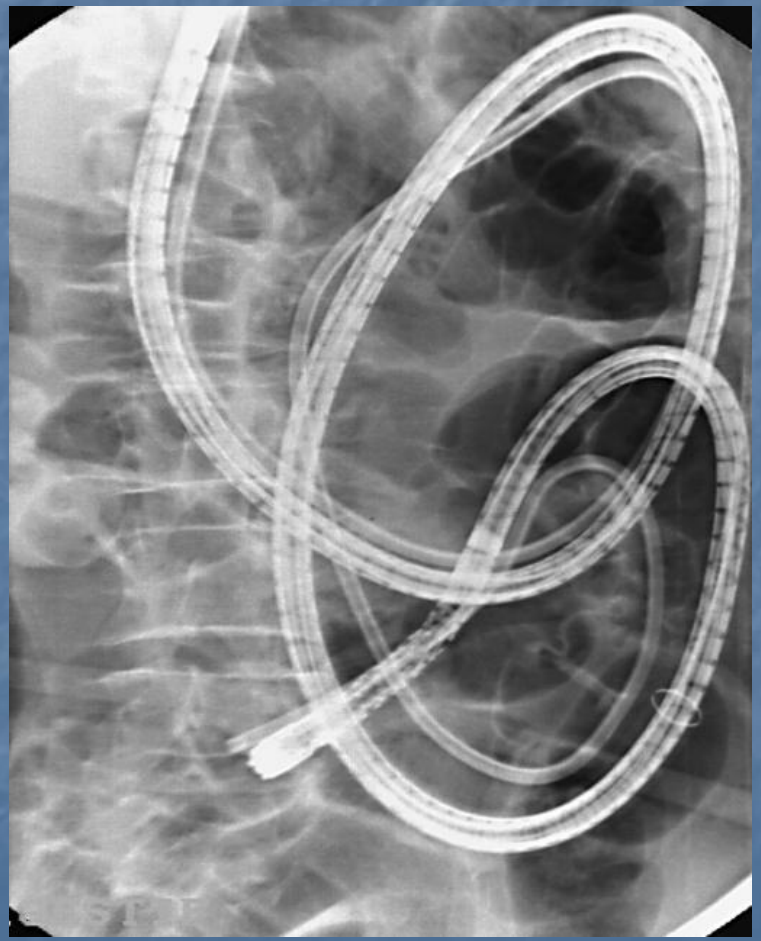
- Deep enteral intubation with overtube/balloon system to pleat mesenteric bowel.
- Allows access to most bowel and most therapy

# DAE in Crohns diagnostics

- Rarely necessary
- Bioptic sampling of nondiagnostic lesions seen with other modalities

# DAE for diagnostic rescue





# Upper endoscopy

- Upper GI Crohns only with distal affection
- Findings in 17-75%, often asymptomatic
- Oral > gastroduodenal > esophageal
- Aphtous ulcers, erosions, strictures
- Include upper GI endoscopy when
  - Inconclusive diagnostics of IBD
  - Upper GI symptoms
- Include duodenal biopsies

# Assessment of severity

# Crohns severity assessment SES-CD

| SEVERITY | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Ulcers | None | Aphtous <0,5cm | Aphtous >0,5cm | >2cm |
| Ulcerated surface | 0% | <10% | 10-30% | >30% |
| Affected surface | 0% | 0-50% | 50-75% | >75% |
| Strictures | None | Single, can be passed | Multiple, can be passed | Cannot be passed |

Score for each of 5 colonic segments is added
n= no of segments affected
SES-CD= raw score sum – 1.4xn

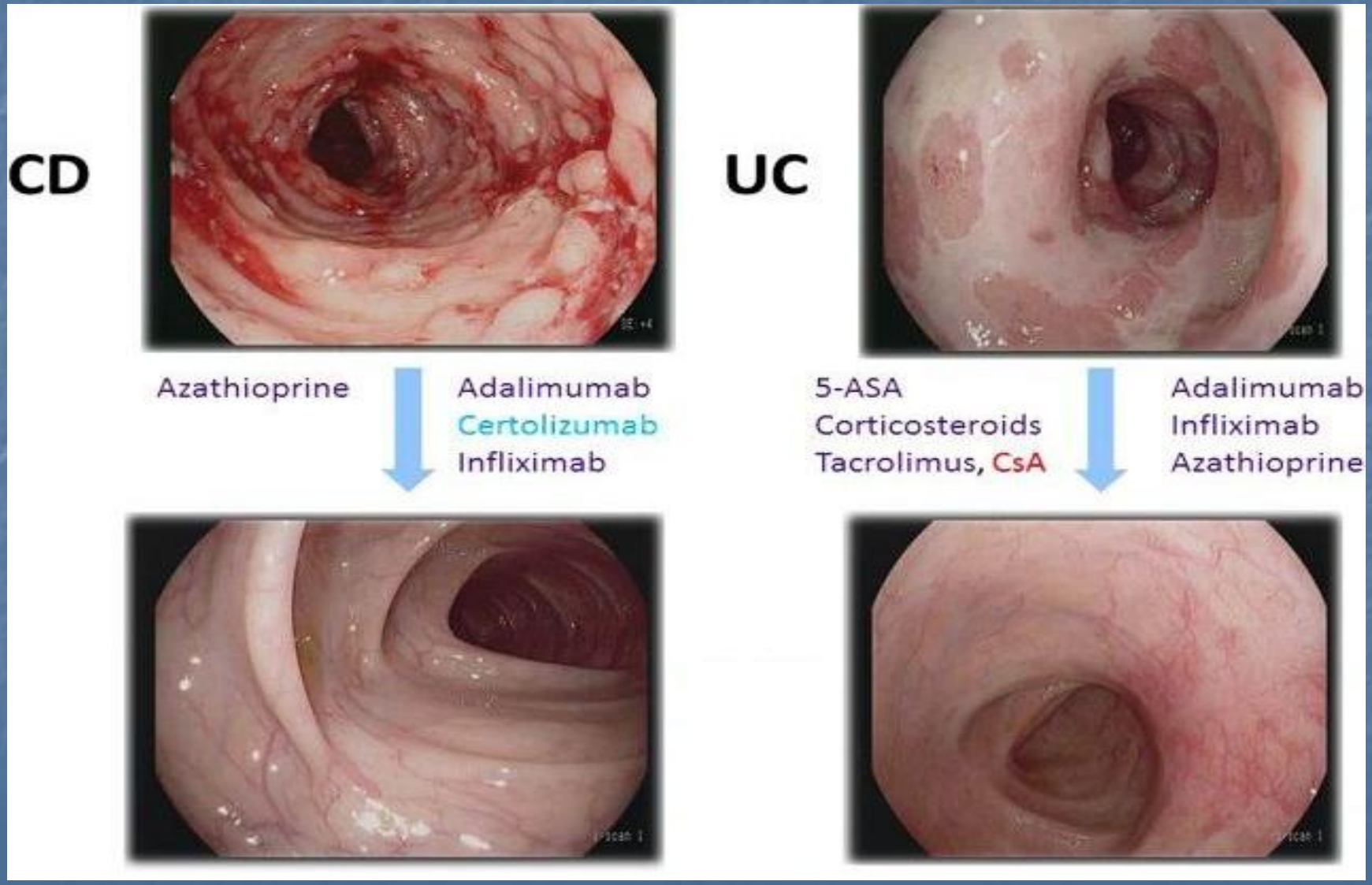
# UC severity assessment
# Mayo score

- 0 = Normal or inactive disease
- 1 = Mild disease (erythema, decreased vascular pattern, mild friability)
- 2 = Moderate disease (marked erythema, lack of vascular pattern, friability, erosions)
- 3 = Severe disease (spontaneous bleeding, ulceration)

# Mucosal healing

- Endoscopic definition
- More difficult to define in UC
- Predicts clinical remission and a better prognosis
- Has become a therapeutic aim beyond clinical objectives
- More relevant with more advanced (and expensive) medical therapy

# Mucosal healing



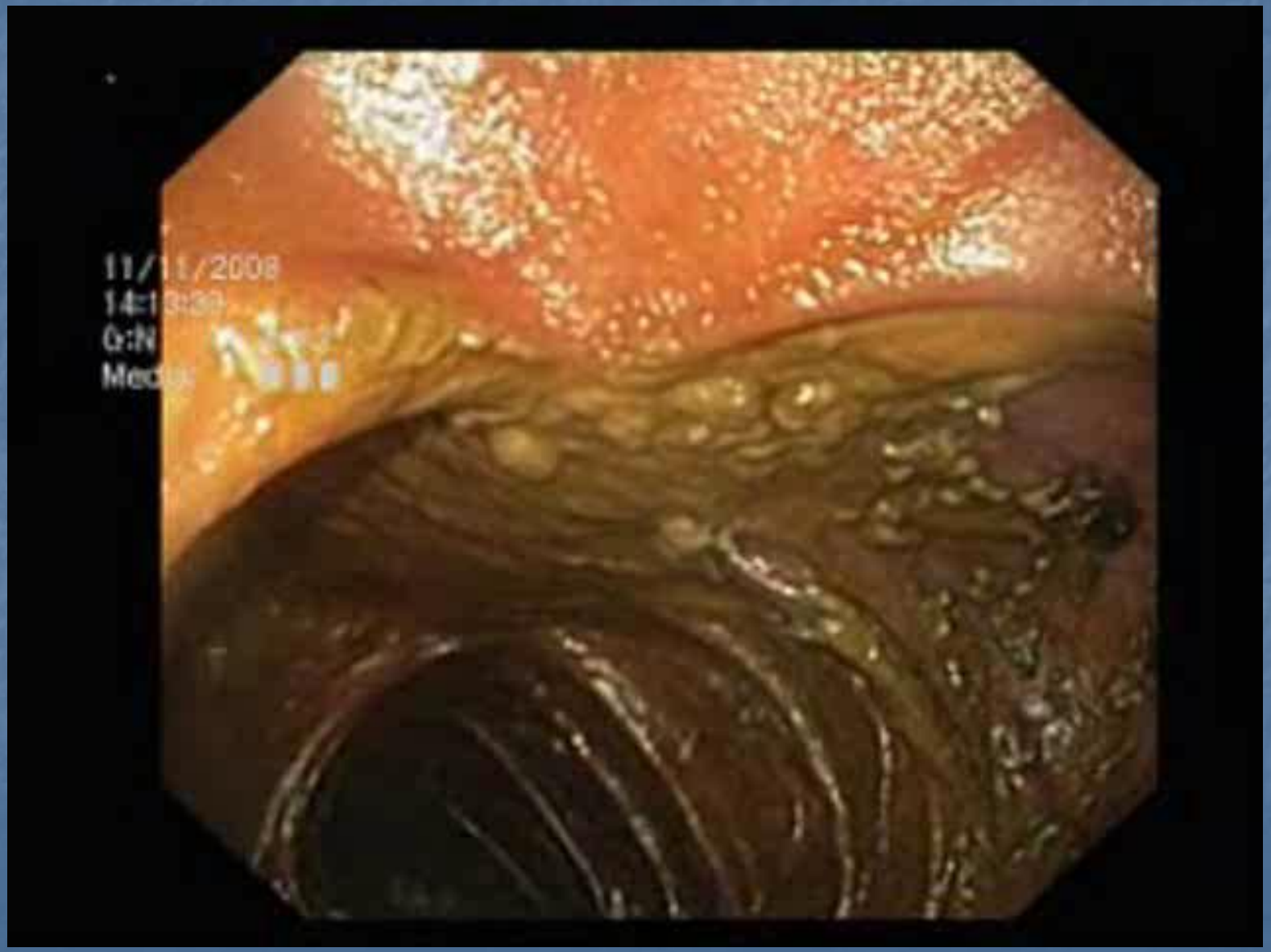
# Therapy

# IBD endoscopic therapy

- Balloon dilation
  - Upper gi (pyloric/duodenal strictures)
  - Small bowel strictures
  - Colonic/anastomotic strictures
- Steroid injection
- Removable (or biodegradable) stents
- Fistular tract closure

# Anastomotic dilation

# Small bowel strictures



# Balloon dilation

- 46 dilations in 27 strictures, native and anastomotic
- 15, then 18mmm (90 sec each)
- 100% technical success, no complications, 92% unsurgery  (mean 41 months9
- 1-4 dilations per stricture;  81% success with 1 dilation.

*dAngelis WJG 2013*

# Needle knife stricturoplasty

# Steroid injection

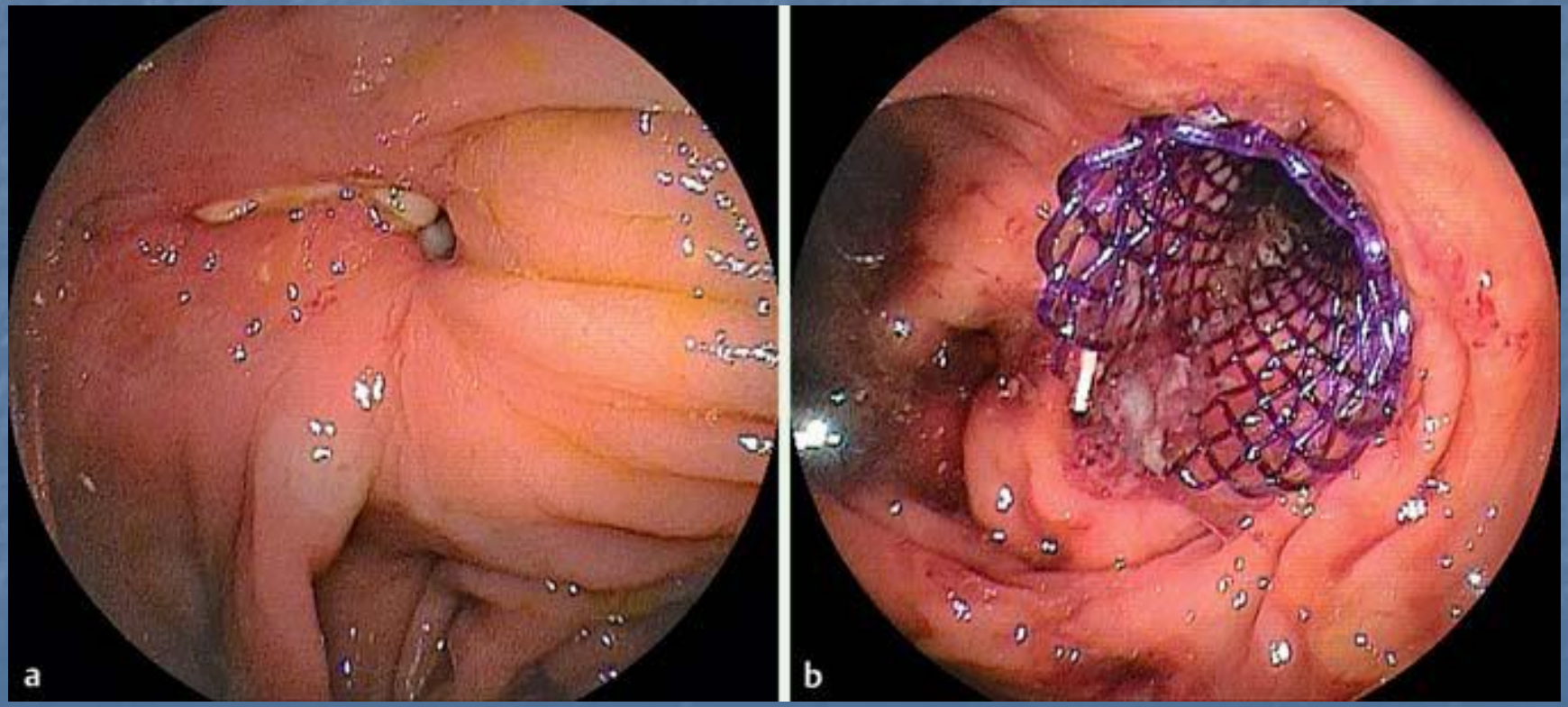
- 40 mg triamcinolone v. Placebo after balloon dilation in 13 patients with anastomostic strictures
- Redilation needed in
  - 5/7 with triamcinolone
  - 1/6 with saline

*East Clin Gastroenterol Hepatol 2007*

# Stent placement

- FC-SEMS
  - Conflicting data
  - Apparently effective but variable risk of stent migration and other complications
- Biodegradable stents
  - Little data
  - Technically more challenging (no TTS)
  - 3/11 early migration

# BD-stent placement



# Surveillance



# SIGMOIDOSCOPIC PICTURE OF CHRONIC ULCERATIVE COLITIS (NON-SPECIFIC).

By Burrill B. Crohn, M.D.,

and

Herman Rosenberg, M.D.,

New York.

(From the Medical Department, Mount Sinai Hospital, New York City.)

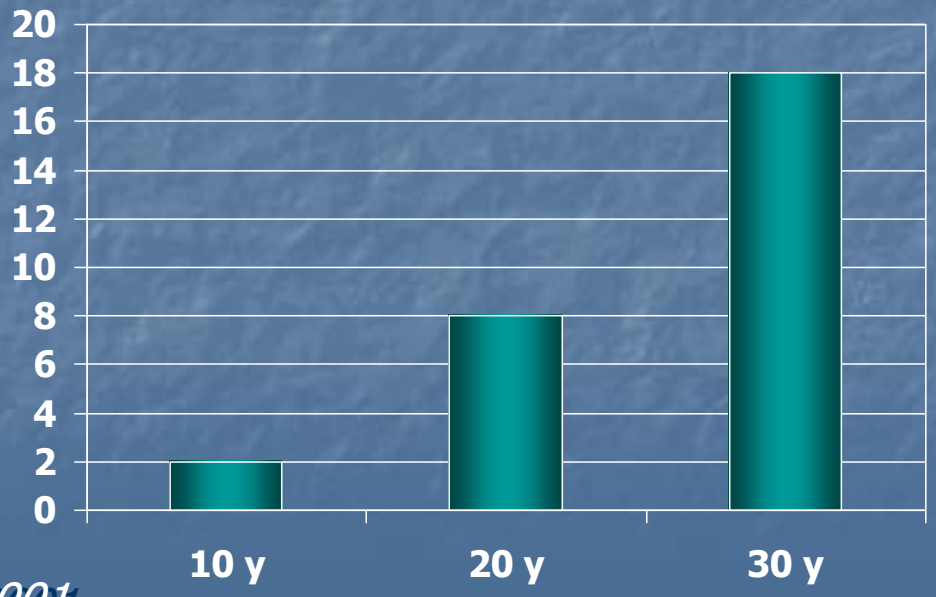
As time passes, we are becoming more and more familiar with the recognition of the course, pathology and the treatment of the malady which is identified under the name of idiopathic ulcerative colitis, simple ulcerative colitis, colitis gravis (Rosenheim), or chronic ulcerative colitis of the nonspecific variety.

.....

Finally, we have observed in 1 case a malignant degeneration of the late stage of a polypoid ulcerative colitis, with the frank occurrence of a carcinoma of the rectal wall. In brief, this was a case of a nonspecific ulcerative lesion of the colon, fourteen years or more in duration. Many years previously a cecostomy had been performed for the relief of symptoms. The relief afforded was disappointing, the symptoms continuing on and off with practically no intermission during the entire period. The polypoid stage of the disease was already in evidence ten years ago.

# UC surveillance

- Ulcerative colitis (and Crohns disease) are significant risk factors of colon cancer
- The risk increases with time.




*Eaden, Gut 2001*

# CRC risk factors in UC

- Duration of disease
- Age at onset
- Distribution and extent of disease
- Degree of inflammation
- Family history of CRC
- Primary sclerosing cholangitis
- Insufficient medical treatment

# CRC risk in PSC/IBD

- Hi risk version of IBD(-like disease)
- Odds ratio 4.0 for developing cancer, compared to non-PSC ulcerative colitis
- May be a marker of long term subclinical disease
- Efficacy of Urso may indicate a role of the altered biliary environment.

# French surveillance guidelines

- Pancolitis: Start at 8 years
- Left-sided colitis: Start at 15 years
- (PSC: Start annually at once)
- 10-20 y: Every 3 years
- >20 y: Every year

*Barthet, Endoscopy 2007*

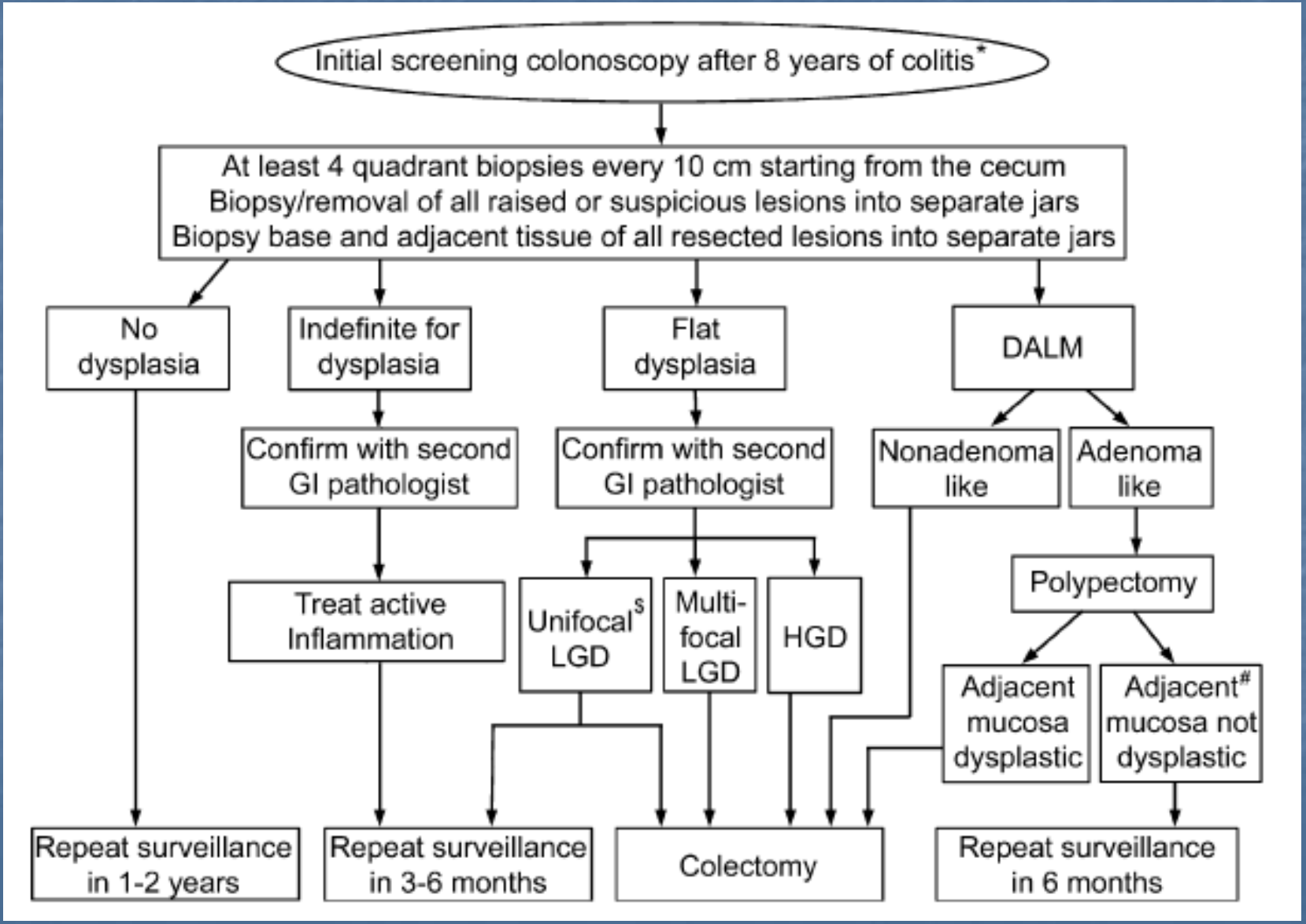
# Biopsy strategy

- (2)-4 quadrant random biopsies every 10 cm throughout the colon
- Additional biopsies at
  - elevated lesions/polyps + adjacent tissue
  - irregular plaques
  - unusual ulcers

# Handling of findings

- Inflammation only: Continue surveillance
- Adenoma in normal tissue: polypectomy
- Unifocal low grade dysplasia: Recheck (?)
- High grade dysplasia: Colectomy
- Multifocal low grade dysplasia: Colectomy
- DALM: Colectomy

# US guidelines



# Does it work?

- St. Marks experience of 30 years:
- 2627 colonoscopies in 600 patients
- 5932 patients years of follow-up
- 74 with neoplasia (12.3%)
- 30 with cancer  (15 interval cancers)
- Still:  No over-all effect on cancer prevention

*Rutter M et al, Gastroenterology 2006*

# The verdict...

- "There is no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive colitis. There is evidence that cancers tend to be detected at an earlier stage in patients who are undergoing surveillance, and these patients have a correspondingly better prognosis, but lead-time bias could contribute substantially to this apparent benefit.
- There is indirect evidence that surveillance is likely to be effective at reducing the risk of death from IBD-associated colorectal cancer and indirect evidence that it may be acceptably cost-effective."

*Collins et al: Cochrane database review 2006*

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# How to improve surveillance?

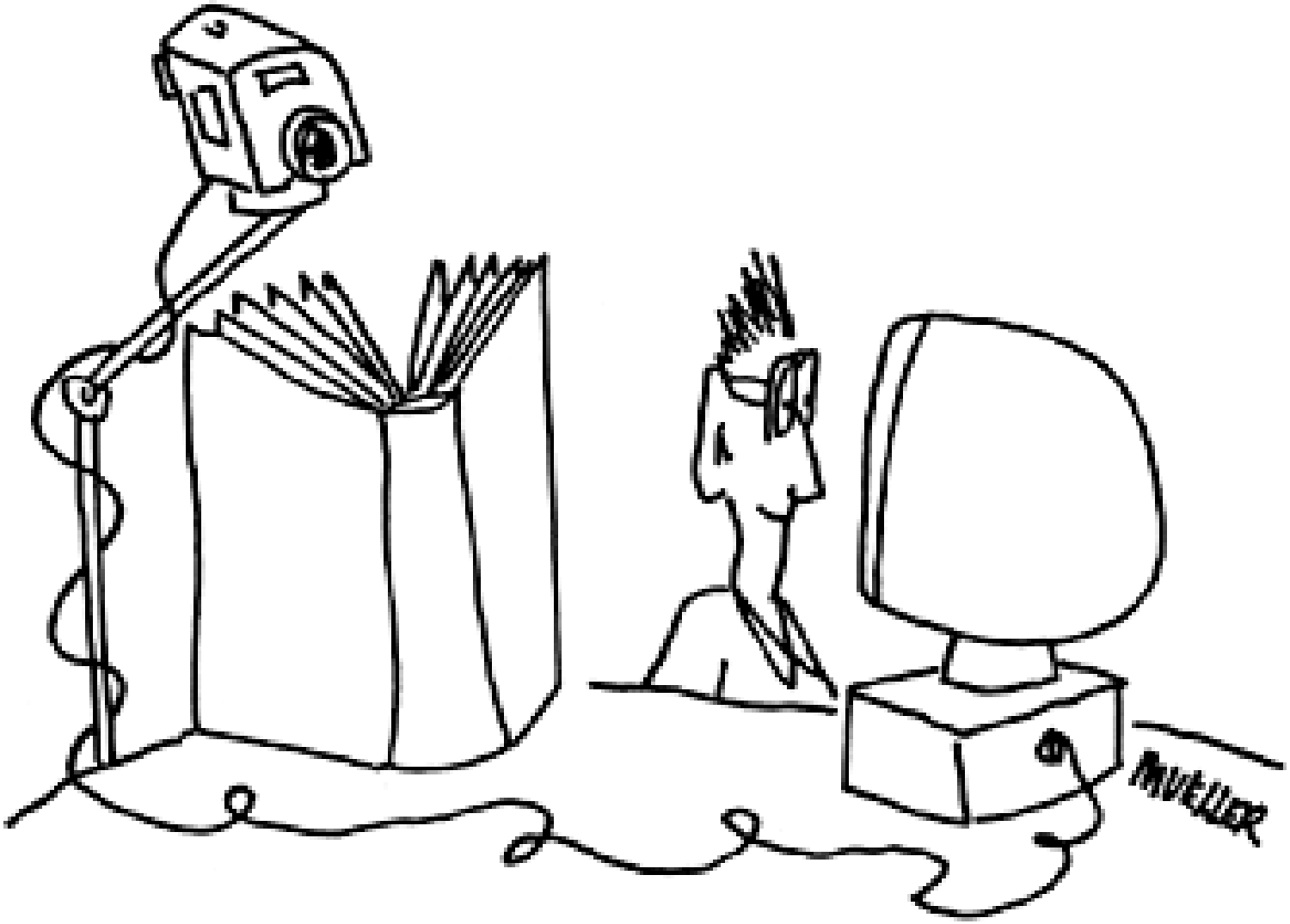
- Improve patient selection
- Improve endoscopy
  - Cleansing
  - Technique
- Improve imaging
  - Improved endoscopic image
  - Manipulated endoscopic image
- Improve sampling
- Improve histology
- Improve protocol adherence

# One note on technology

- All technology requires
  - Proper bowel cleansing
  - Good endoscopic technique
  - Cecal intubation
- HD-imaging:  Only in combinations
- NBI: Does not work
- Autofluorescence: Does not work
- Chromoendoscopy: would work...

# Conclusions

- Endoscopy has important and diverse roles in IBD care
- Differential diagnostics is crucial
- CE and enteroscopy have become useful additions
- Several new techniques may improve white light surface endoscopy
- None of them replace good endoscopic technique


MUTLUER

# Better technique

- To find a lesion:
  - Optimise general visualization (cleansing, insufflation)
  - Reach the spot (total colonoscopy)
  - Look for the spot (awareness, competence, dedication and time)
  - Reveal the spot (systematic approach, did you check behind every fold?, retroflexion)
- But still....

# Polyp miss rate

- 183 patients, same day back-to-back colonoscopies
- Randomization to same or different colonoscopist
- Overall miss rate **24%**
- Interobserver variation, but significant miss rate in all observers

*Rex et al; Gastroenterology 1997*

# Withdrawal quality

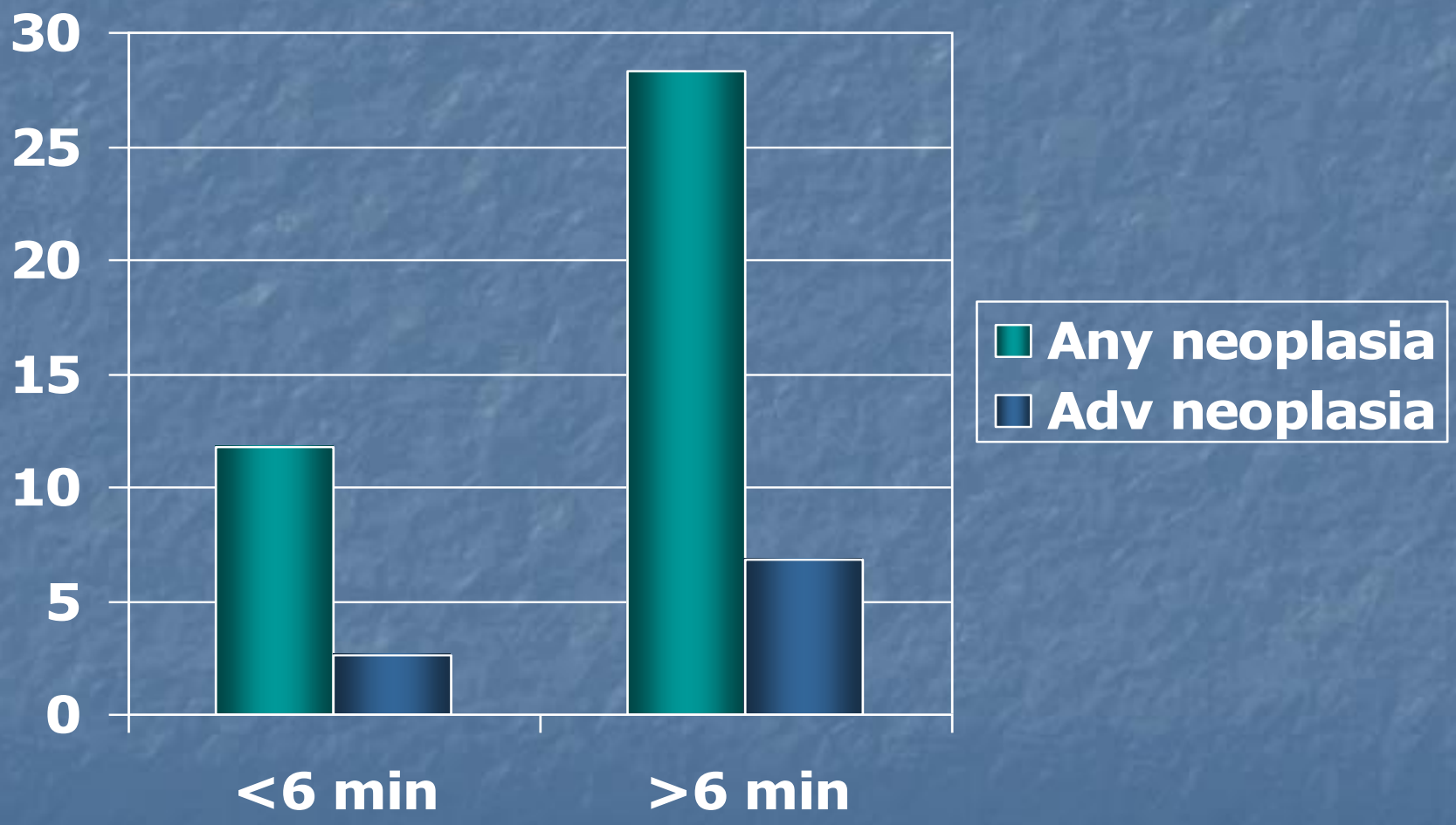
- Visualization of proximal aspect of folds
- Cleansing and suctioning
- Distention
- Time spent on withdrawal (not insertion!)

# Withdrawal time

- 12 colonoscopists, 7882 procedures
- Adenomas in 23% of subjects
- Ranges
  - No of lesions per subject: 0.1-1.05
  - Subjects with adenomas: 9 – 33%
  - Withdrawal time 3.1-16.8 minutes

*Barclay NEJM 2006*

# Withdrawal time




*Barclay NEJM 2006*

# Improved imaging

- Improved resolution
- Optical magnification
- Wide angle optics
- Chromoendoscopy
- Filtered imaging
- Autofluorescence
- And more

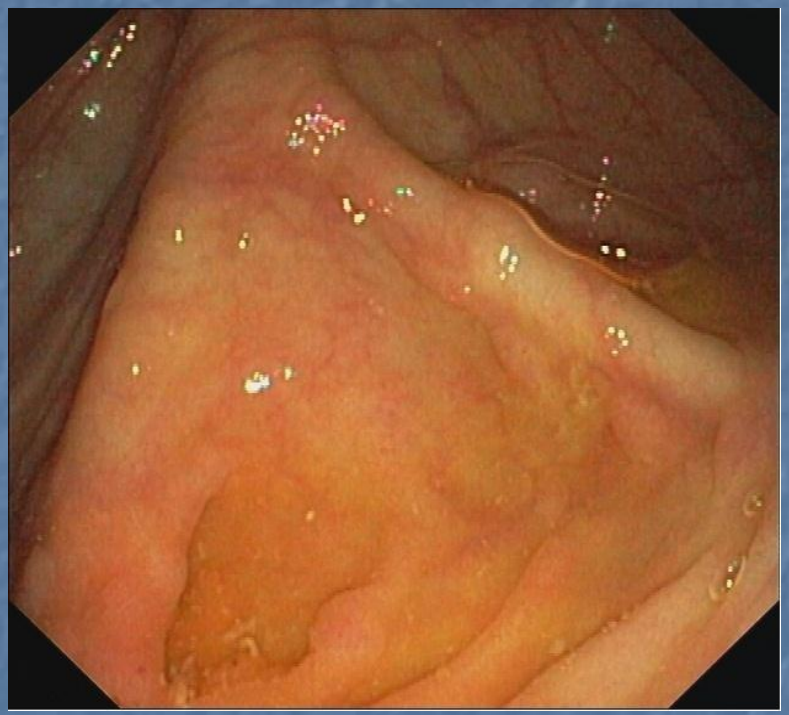
# Wide angle endoscopy

- 170 v. 140 degrees view
- 50 patients, back-to-back colonoscopy:
- Polyp miss rate 20% v. 31%
- 20 patients, same endoscopist, both endoscopes:
- Time reduction 25-30%

*Rex et al; Gastroenterology 2004*

# Chromoendoscopy in the colon

- **Indigocarmine**
  – surface contrast enhancer
- Methylene blue
  – intravital dye, dysplasia detection (?)
- Acetic acid
  – edema and enhanced surface delineation
- Lugol dye
  – squamous epithelium marker



# Flat adenomas in the colon – a Japanese phenomenon?

- 1000 consecutive unselected UK colonoscopies
- Targeted indigo-carmine spraying

| Appearance | Polypoid | Flat | Depressed | Total |
|---|---|---|---|---|
| Mild/moderately dysplastic adenomas | 187 | 102 | 1 | 290 |
| Severely dysplastic adenomas | 15 | 15 | 1 | 31 |
| Dukes' A carcinoma | 2 | 2 | 2 | 6 |
| **Total** | 204 | 119 | 4 | 327 |

Table 2: **Correlation of appearance with histology**

***Rembacken, Fujii et al, Lancet 2000***

# Pancolonic chromoendoscopy or targeting of visualized lesions

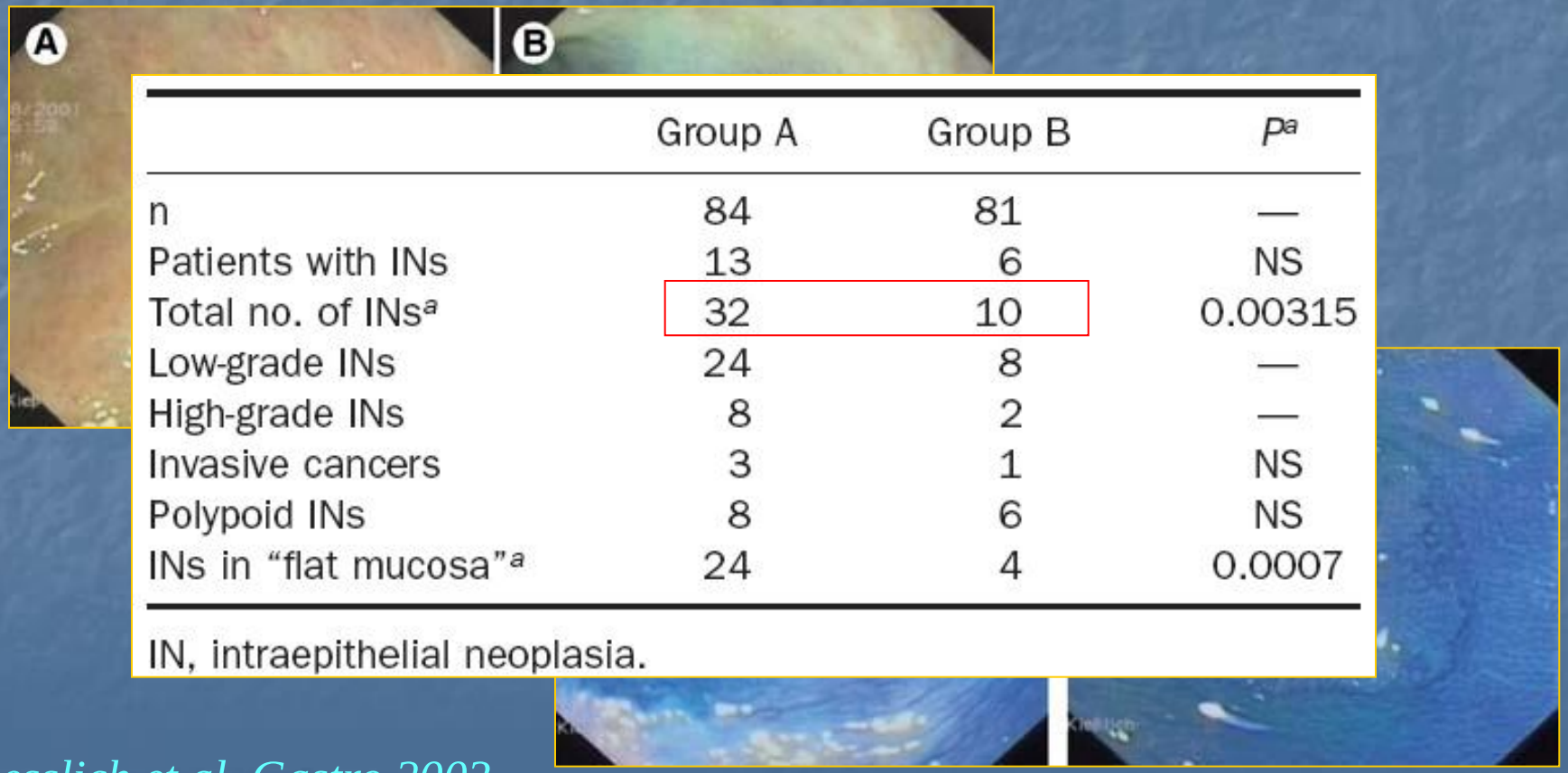
- Randomised study in 259 patients
- Pancolonic indigocarmine vs targeted chromo

| | Targeted | Pancolonic | P-value |
|---|---|---|---|
| **Patients with >1 lesion** | **55** | **83** | **<0.01** |
| **Patients with >1 hyperpl lesion** | **20** | **67** | **0.02** |
| **Patients with ≥ 3 adenomas** | **4** | **13** | **<0.01** |
| **Patients with ≥ HGD adenoma** | **6** | **22** | **0.006** |

***Hurlstone et al, Gut 2004***

# Surveillance of long-standing UC

## Chromoendoscopy (group A) vs standard 4q biopsies (group B)




| | Group A | Group B | P[a] |
|---|---|---|---|
| n | 84 | 81 | — |
| Patients with INs | 13 | 6 | NS |
| Total no. of INs[a] | 32 | 10 | 0.00315 |
| Low-grade INs | 24 | 8 | — |
| High-grade INs | 8 | 2 | — |
| Invasive cancers | 3 | 1 | NS |
| Polypoid INs | 8 | 6 | NS |
| INs in "flat mucosa"[a] | 24 | 4 | 0.0007 |

IN, intraepithelial neoplasia.

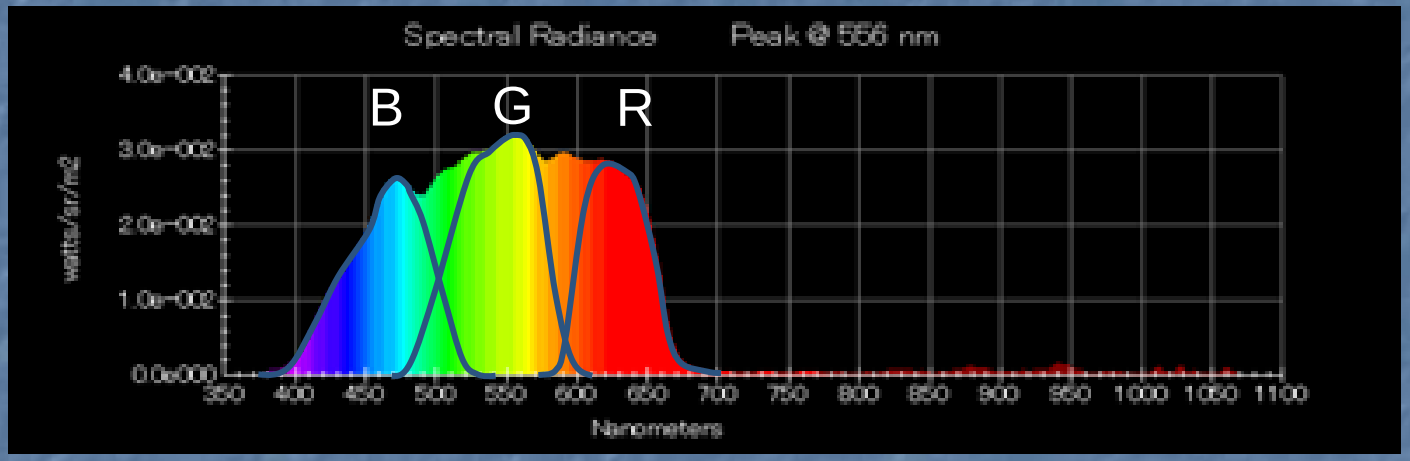
*Kiesslich et al, Gastro 2003*

# Disadvantages of chromoendoscopy:

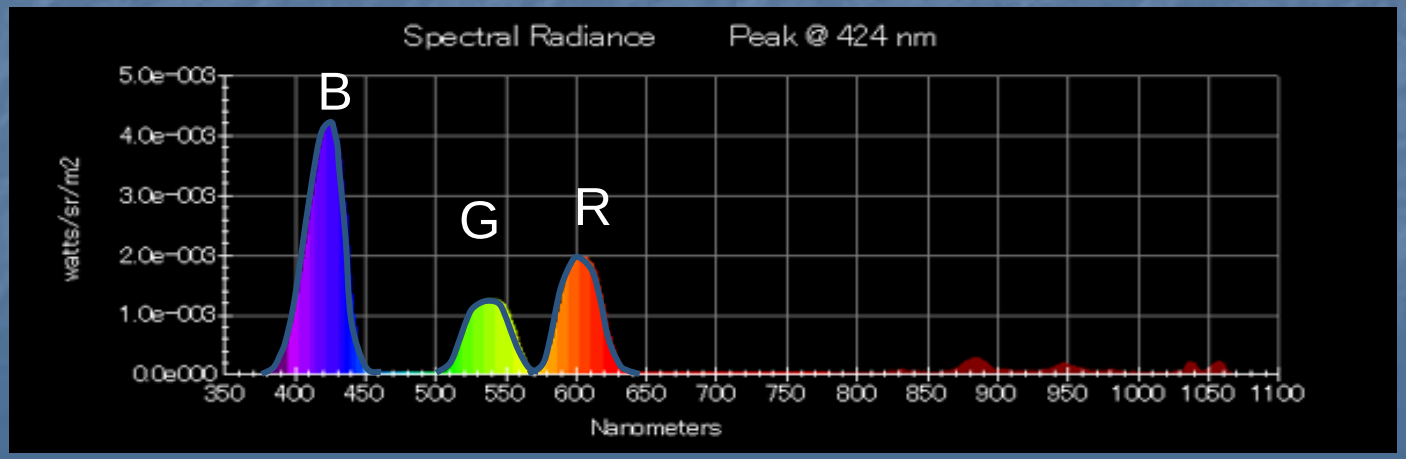
- Labor-intensive and messy
- Learning curve
- Unequal distribution of dye
- No possibility to switch back and forth

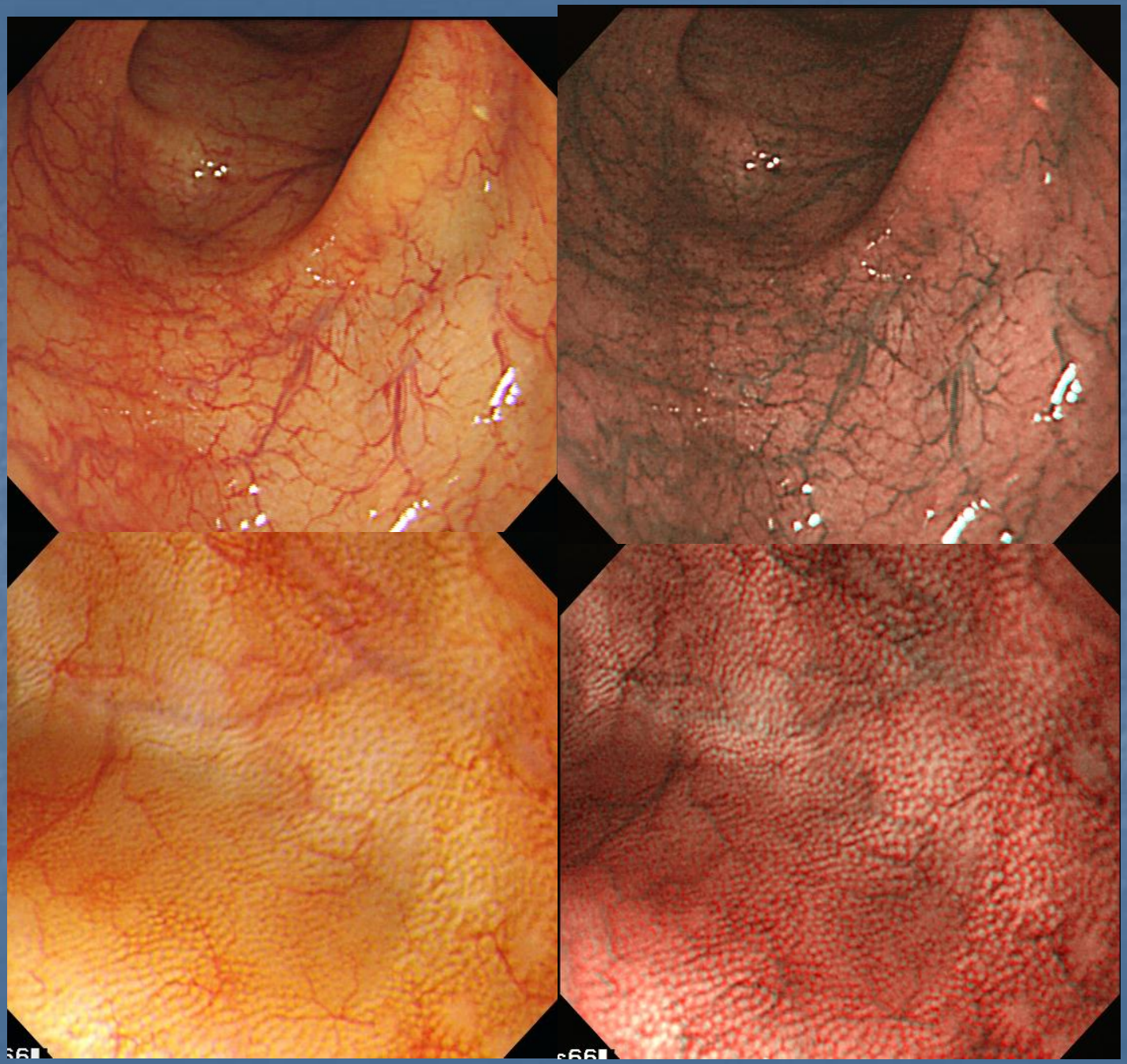
# Filtered imaging

Conventional Filter




NBI Filter





# Narrow Band Imaging – UC surveillance

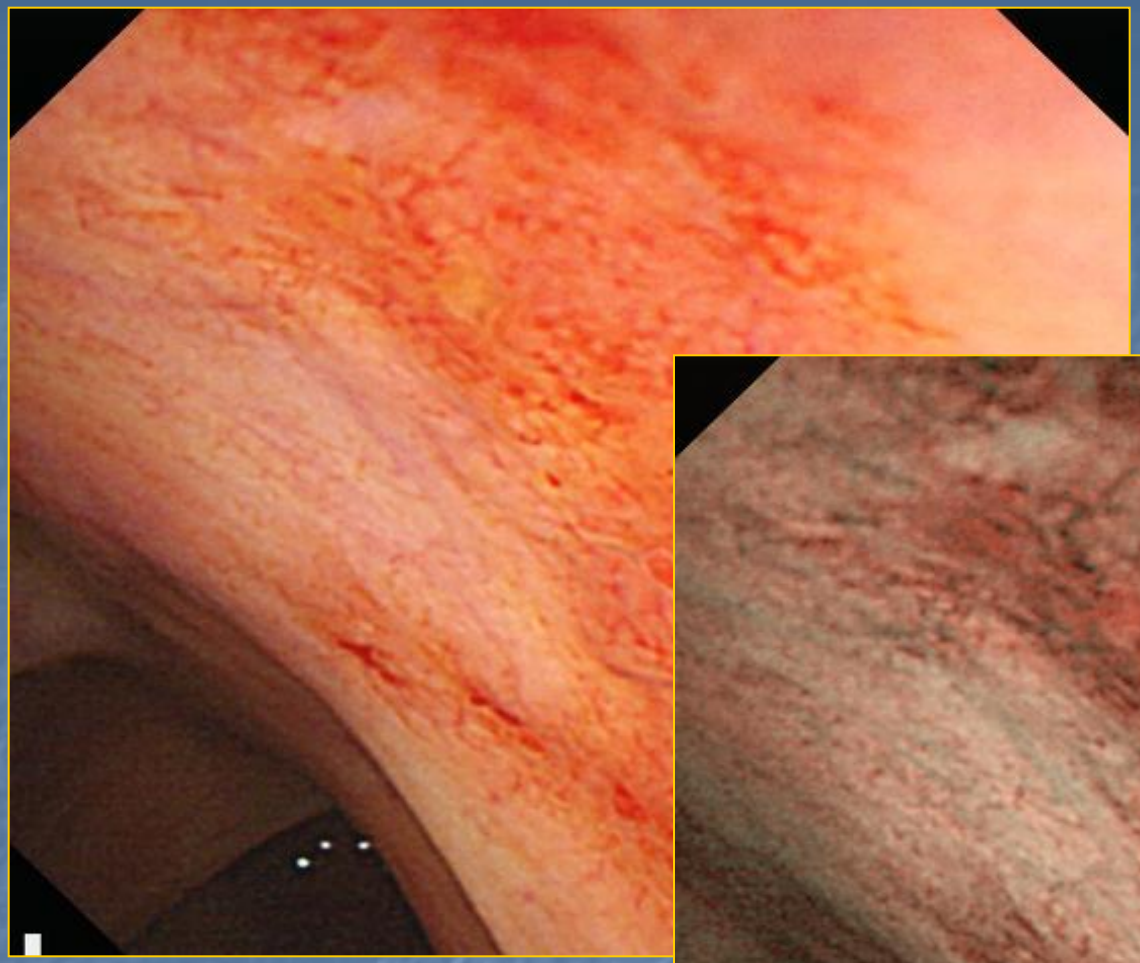
- 42 UC-surveillance patients
- 2 crossover colonoscopies 6-8 wks apart
  - NBI with targeted biopsies or
  - Standard colonoscopy with 4 biopsies / 10cm
  - Different endoscopists

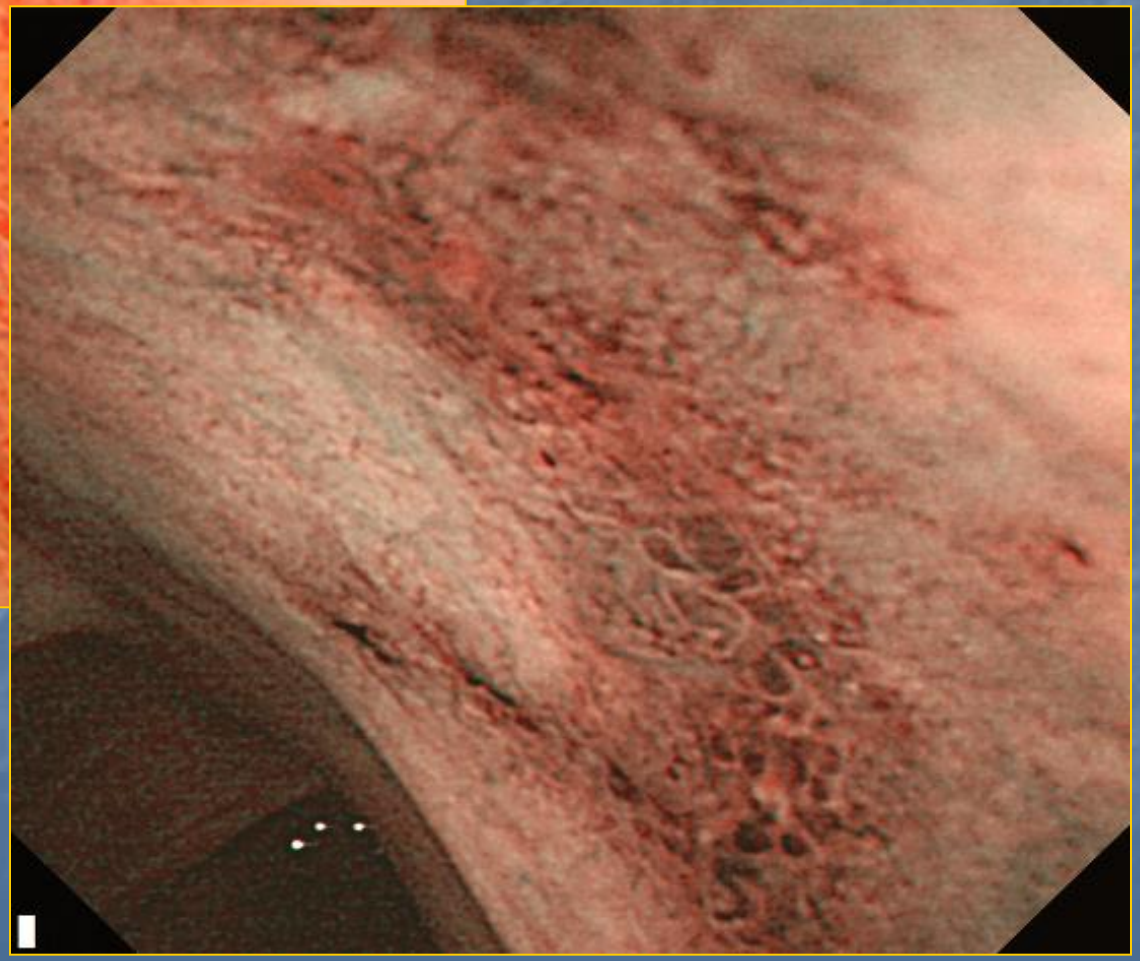
*Dekker et al, Endoscopy 2007*

**NBI**

in UC

chronic inflammation

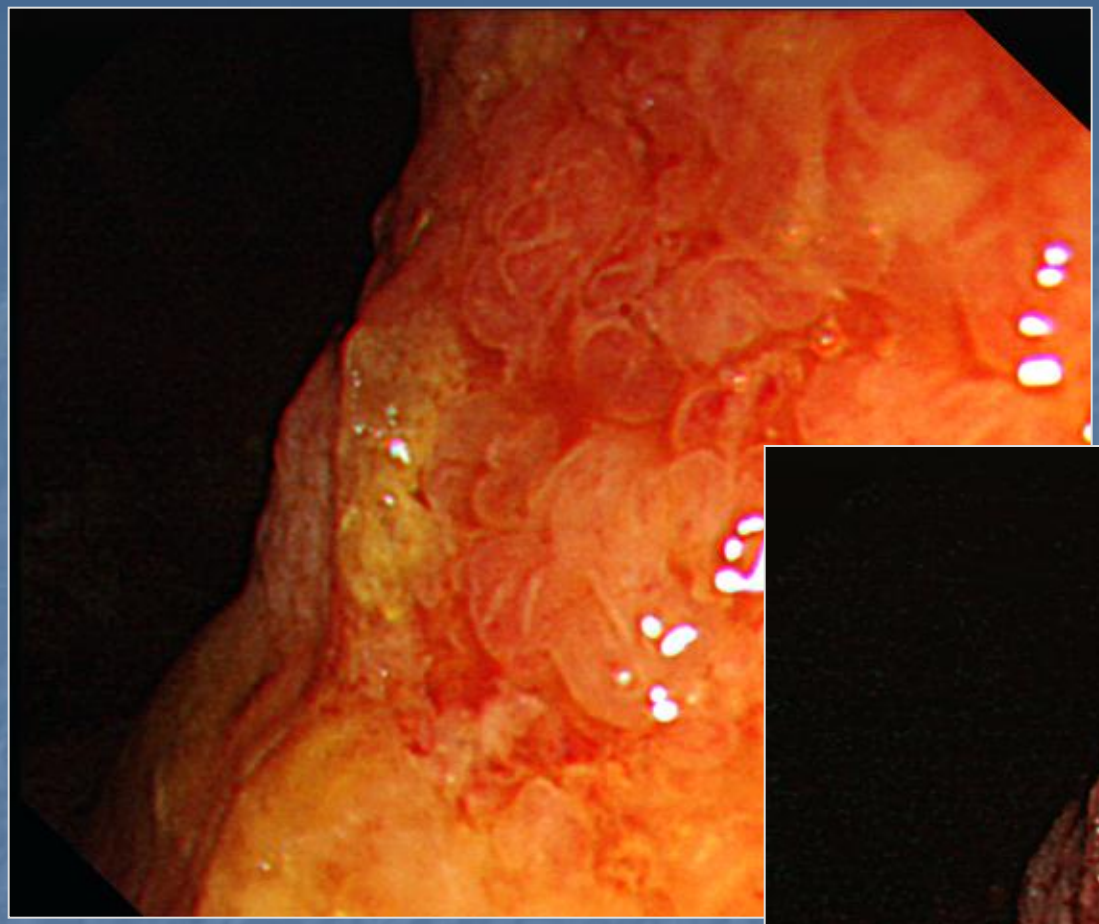




**NBI**

in UC

DALM with HGD



# Narrow Band Imaging – UC surveillance

| | Conventional | NBI |
|---|---|---|
| Procedure time | 47 | 50 |
| Number of lesions/pts | 28/13 | 52/17 |
| True positive lesions | 12 | 9 |
| False positive lesions | 16 | 43 |
| Mean no of random bx | 36 | - |
| No of addt. findings in random bx | 1 (8%) | - |

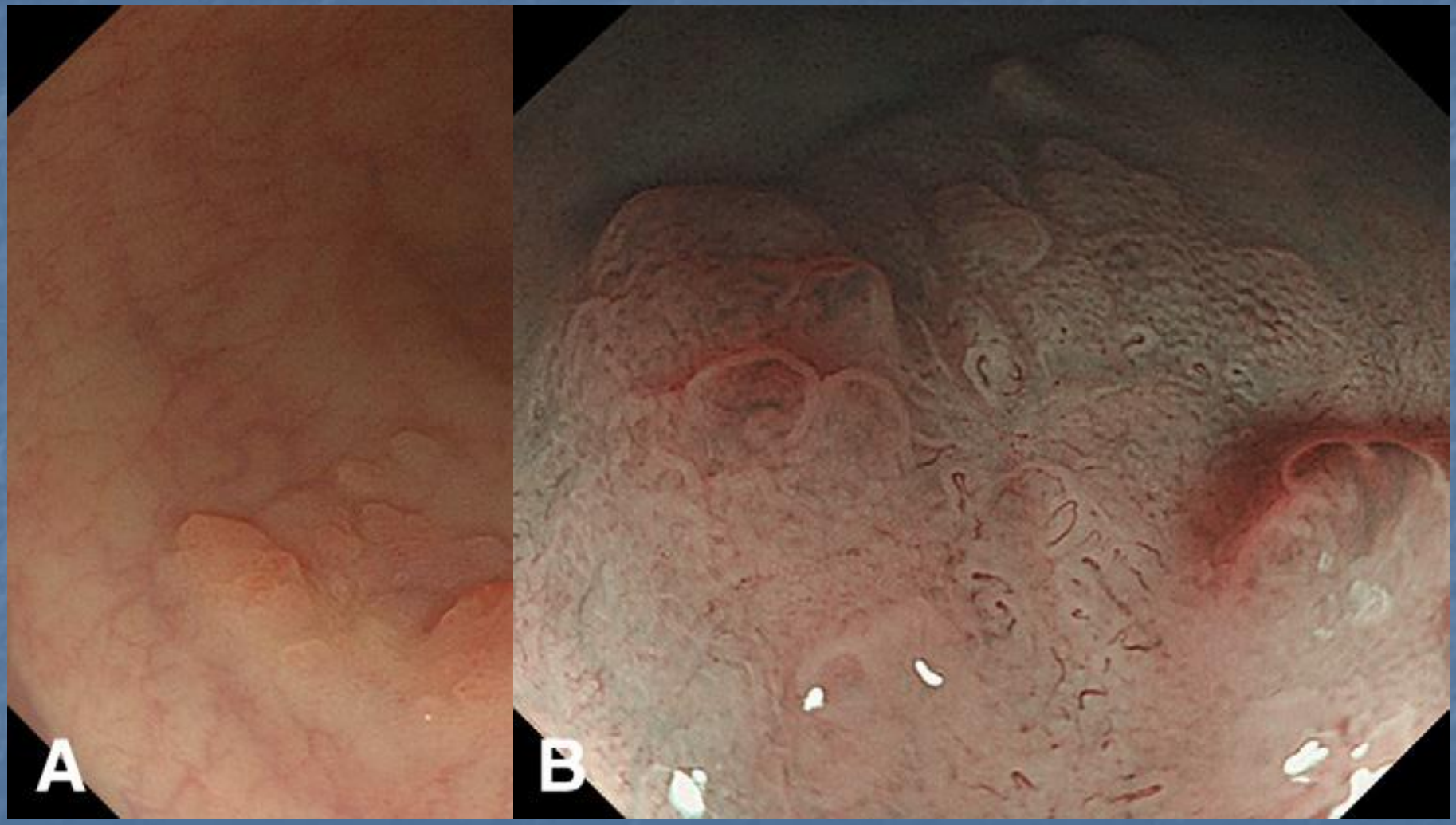
*Dekker et al, Endoscopy 2007*

# NBI surface analysis in UC

- 46 consecutive patients with UC
- Conventional and NBI imaging
- 296 samples, categorized to
  - honeycomblike (161 sites)
  - villous (85 sites)
  - tortous (50 sites)
- Dysplasia rate higher in elevated lesions with tortous vessel pattern

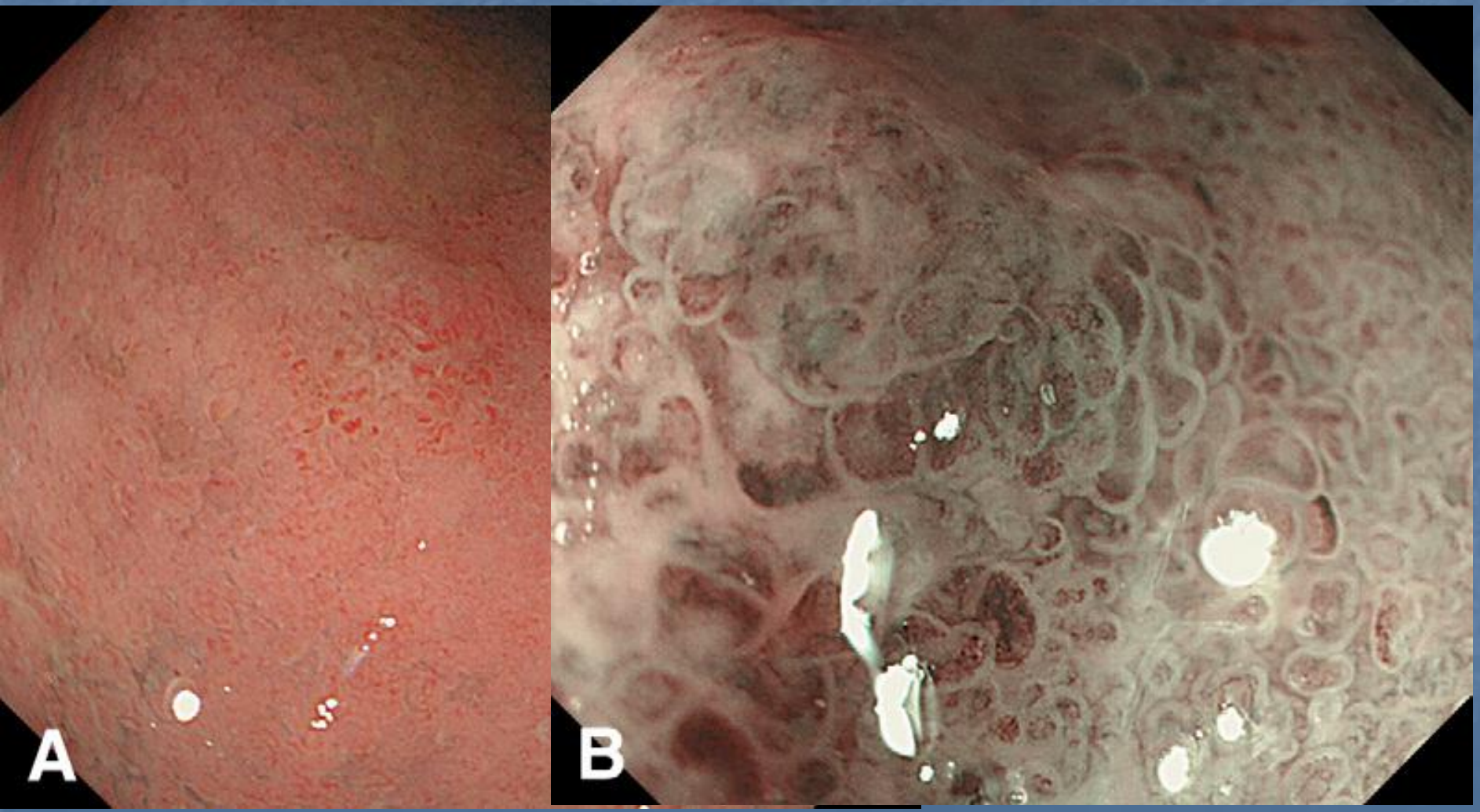
*Matsumoto GI Endoscopy 2007*

# LGD in elevated lesion




*Matsumoto GI Endoscopy 2007*

# HGD in flat mucosa

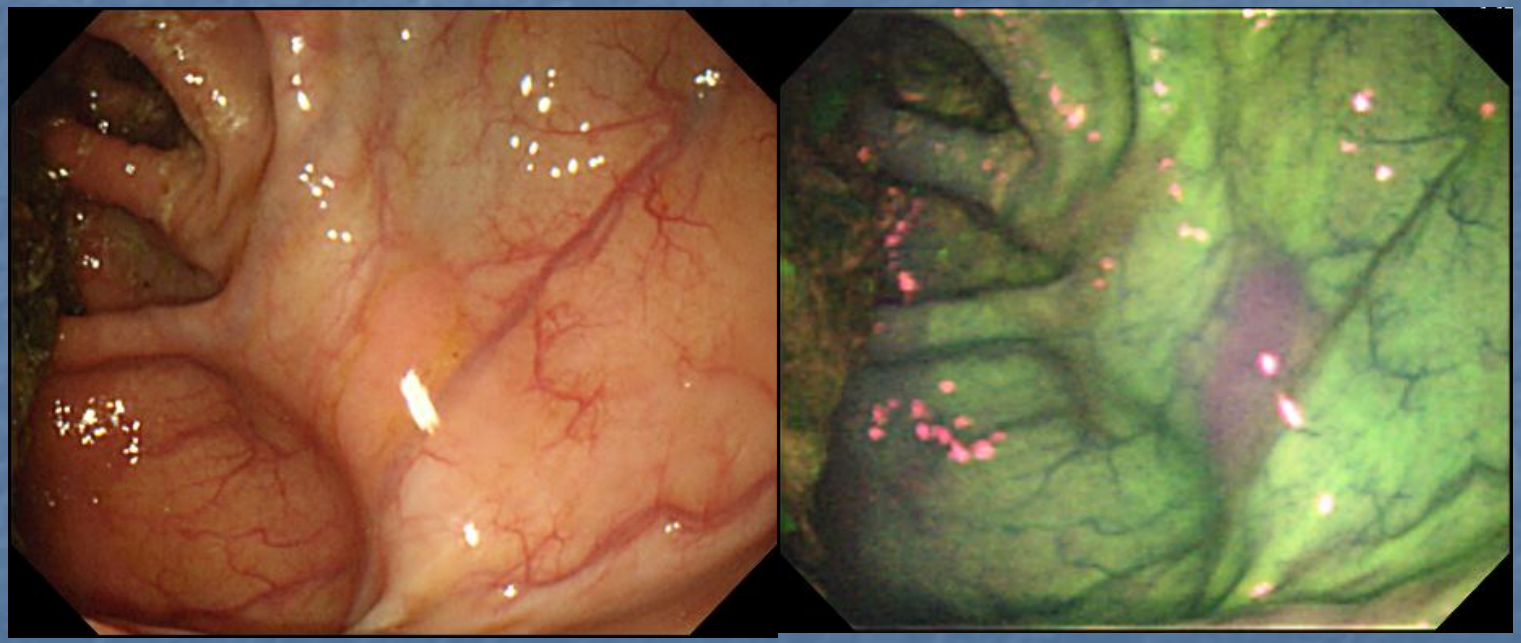



*Matsumoto GI Endoscopy 2007*

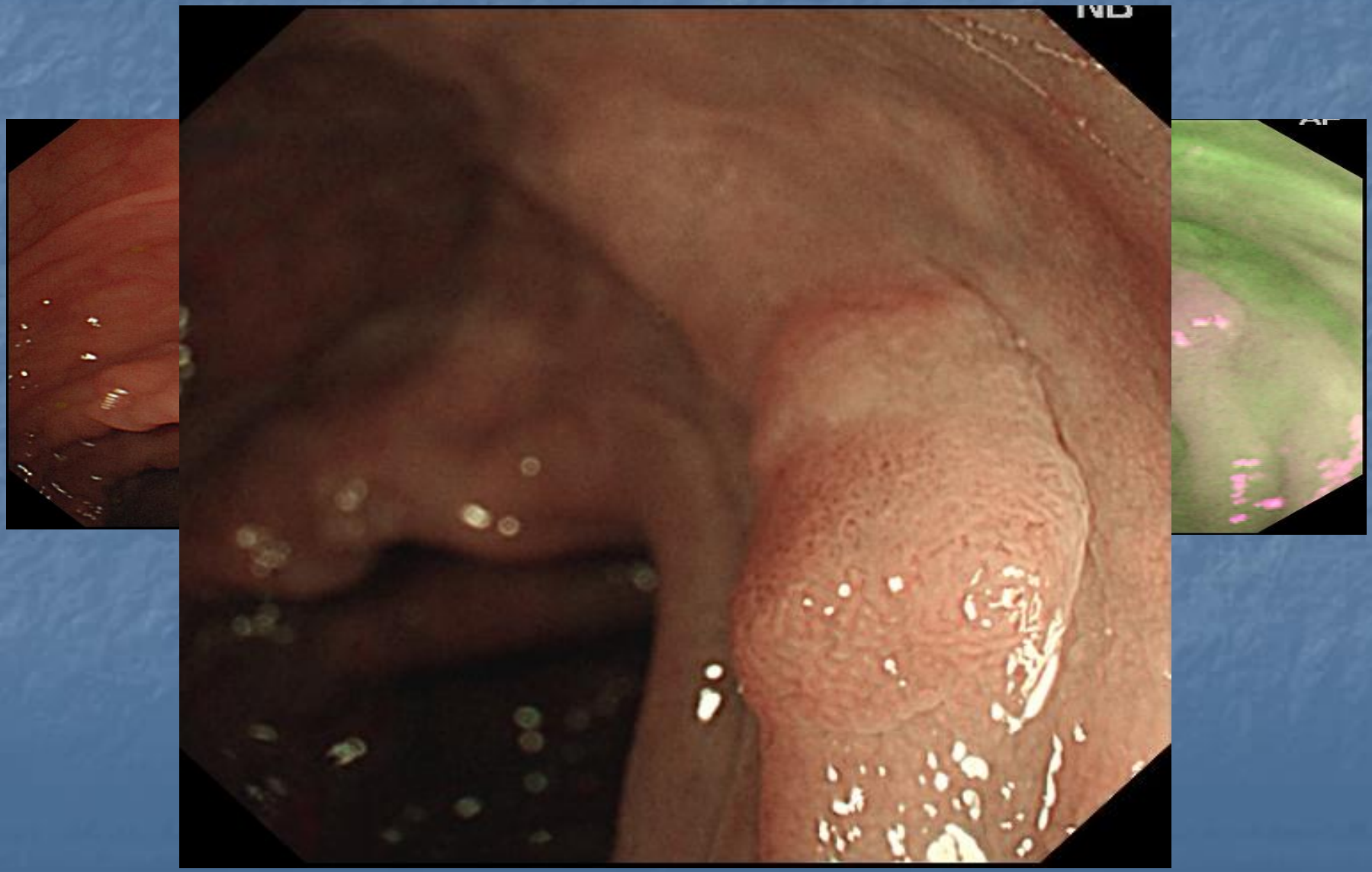
# Fluorescence imaging - red flag technique

- Autofluorescence or contrast induced fluorescence (5-ALA)
- More mitochondria and lysosomes in dysplastic tissue cause stronger autofluorescence
- May be used for targeting in non-magnified imaging

# Detection of flat adenoma with AFI



# Trimodal imaging: flat adenoma



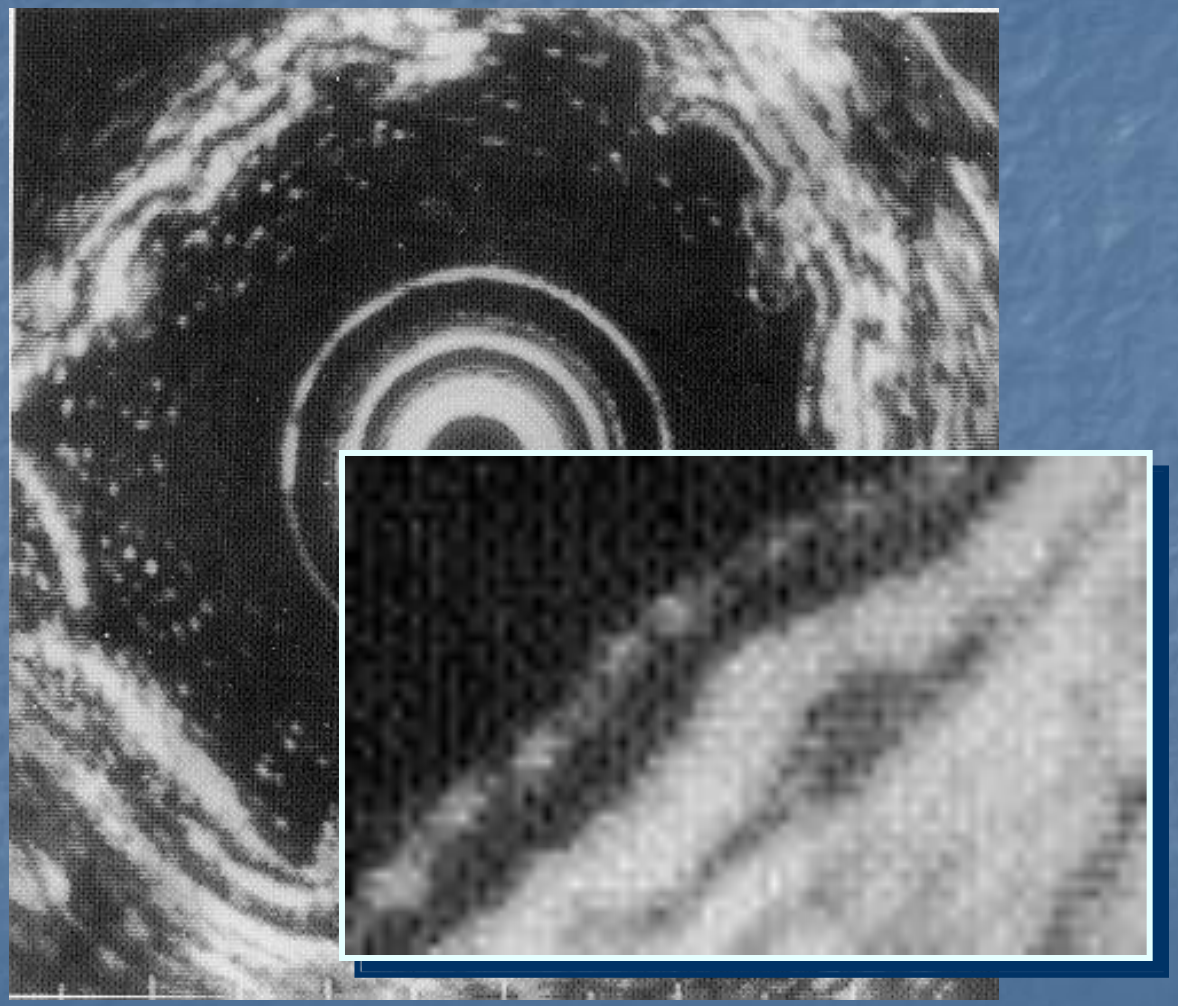
# Pseudoimaging and endomicroscopy

- Optical coherence tomography (OCT)
- Laser confocal microscopy
- Elastic scattering spectroscopy
- Raman spectroscopy
- Immunoscopy, molecular imaging

# Optical coherence tomography (OCT)

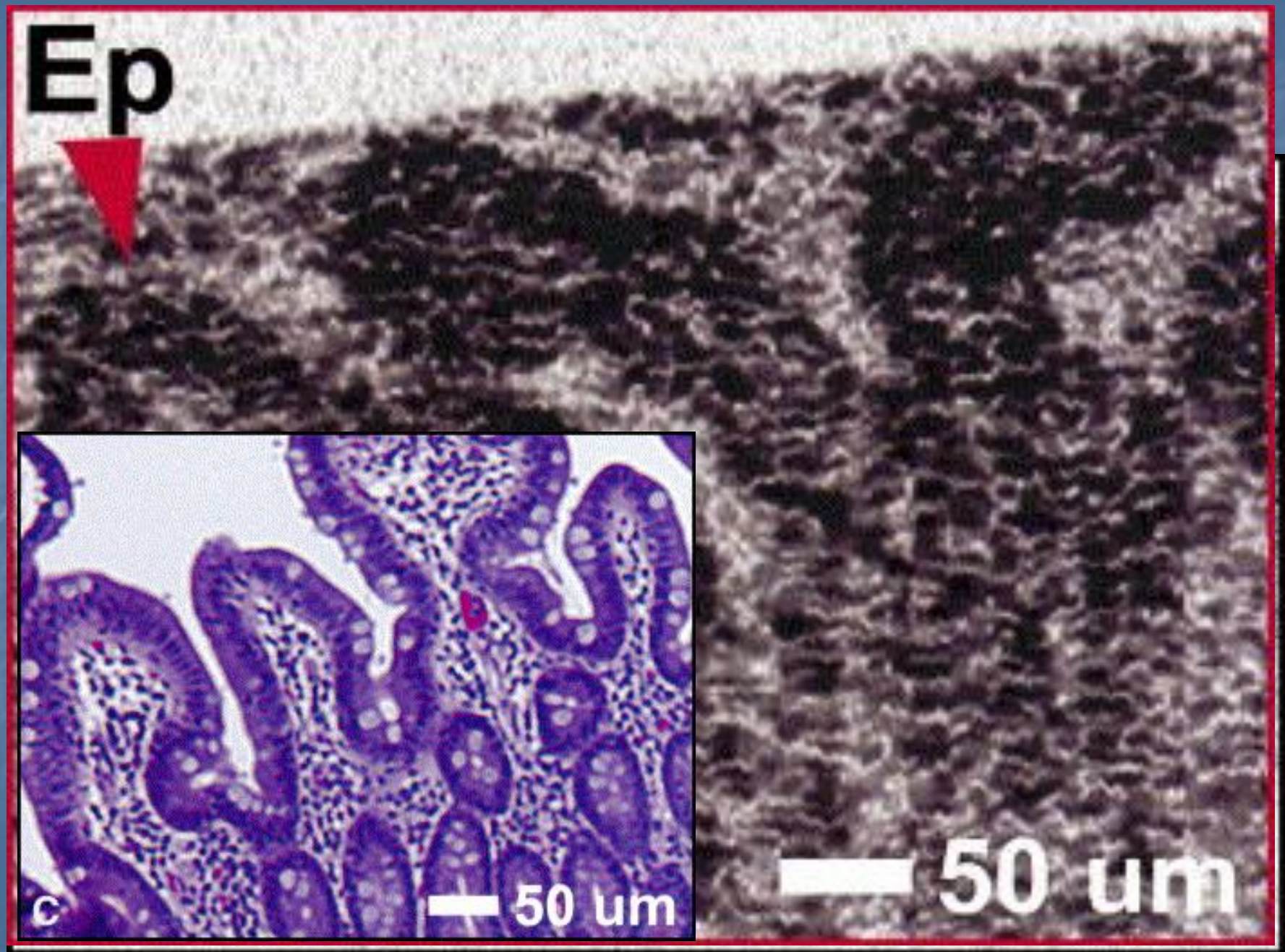
- Optical analogue to ultrasound.
- Hi resolution, short-range imaging based on interference of light waves
- Cross-sectional hi resolution imaging
- Spatial resolution 10μm in depth, 25 μm transversely. 2 mm depth penetration

# OCT v. EUS resolution



EUS

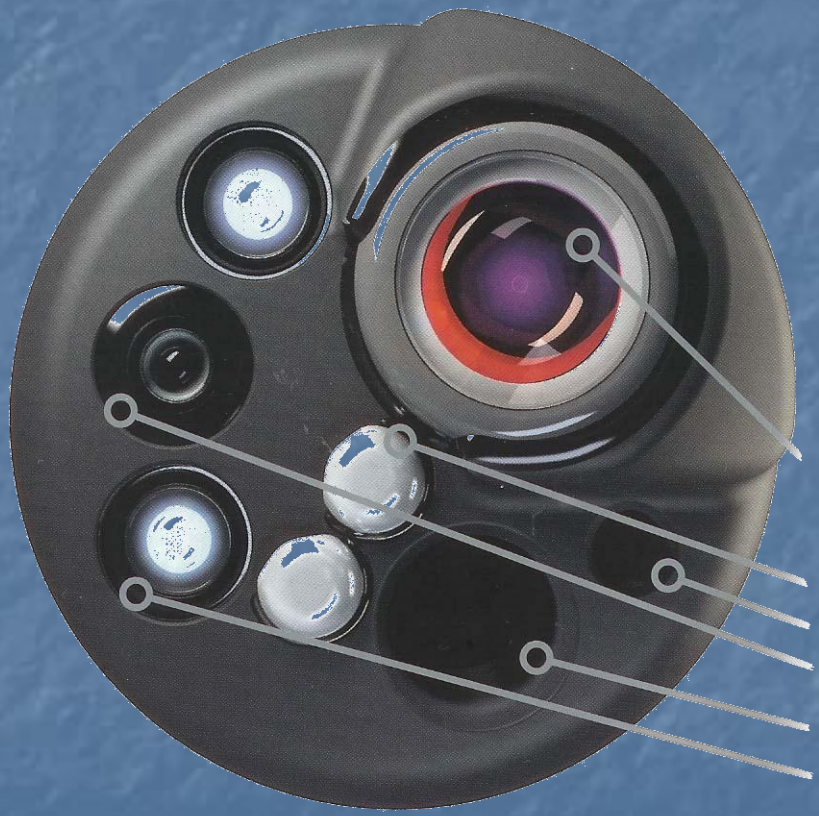
OCT


Ep
50 um
C
50 um

# Confocal laser endomicroscopy

- Injection or surface application of fluorophore (fluorescein or acriflavine)
- Application of single line laser light (488nm excitation wavelength)
- Slize thickness 7 um
- Lateral resolution 0.7um (OCT 25)
- Field of view 500 x 500 um
- Surface and subsurface imaging (0-250um)

# Equipment

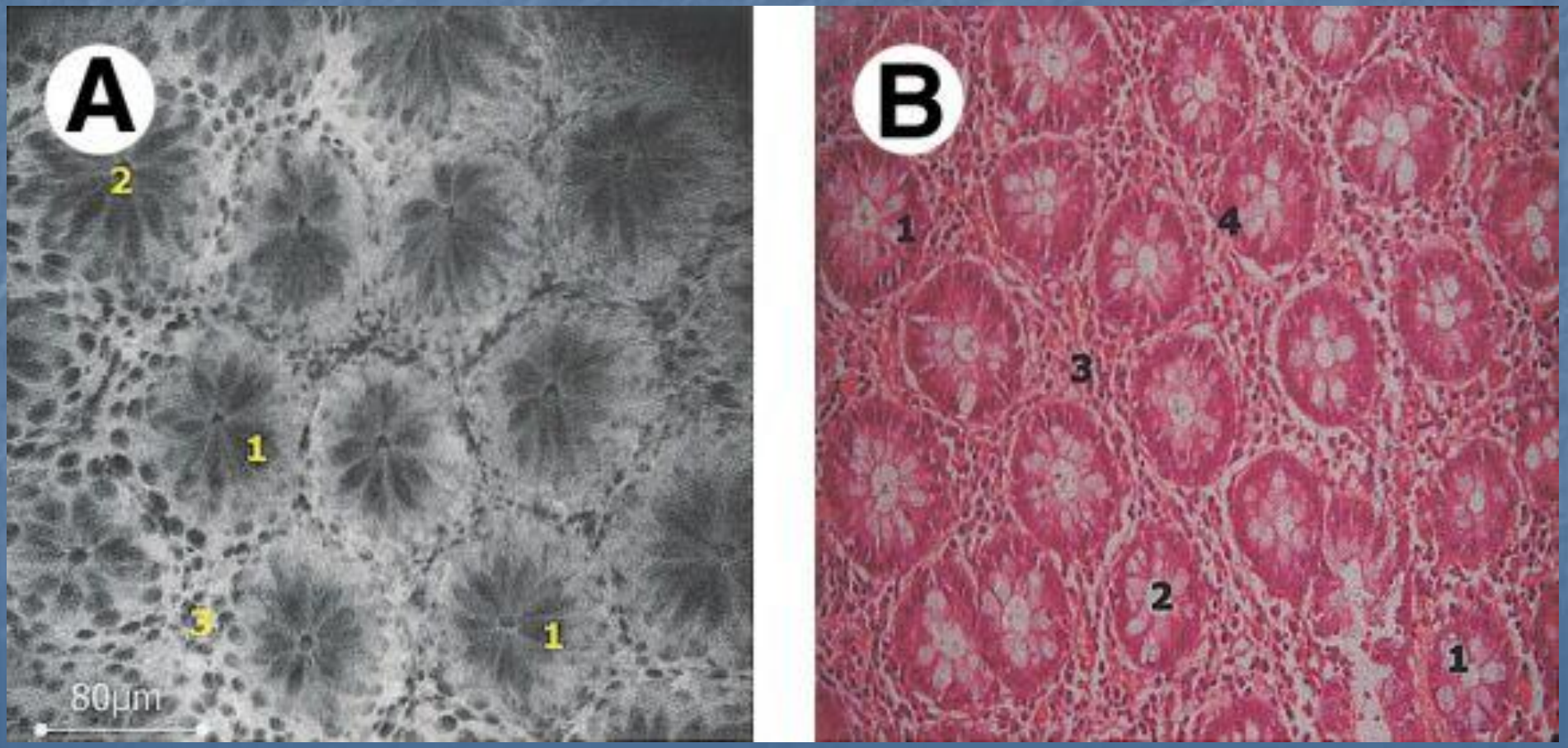


12.8 mm endoscope
2.8 mm working channel

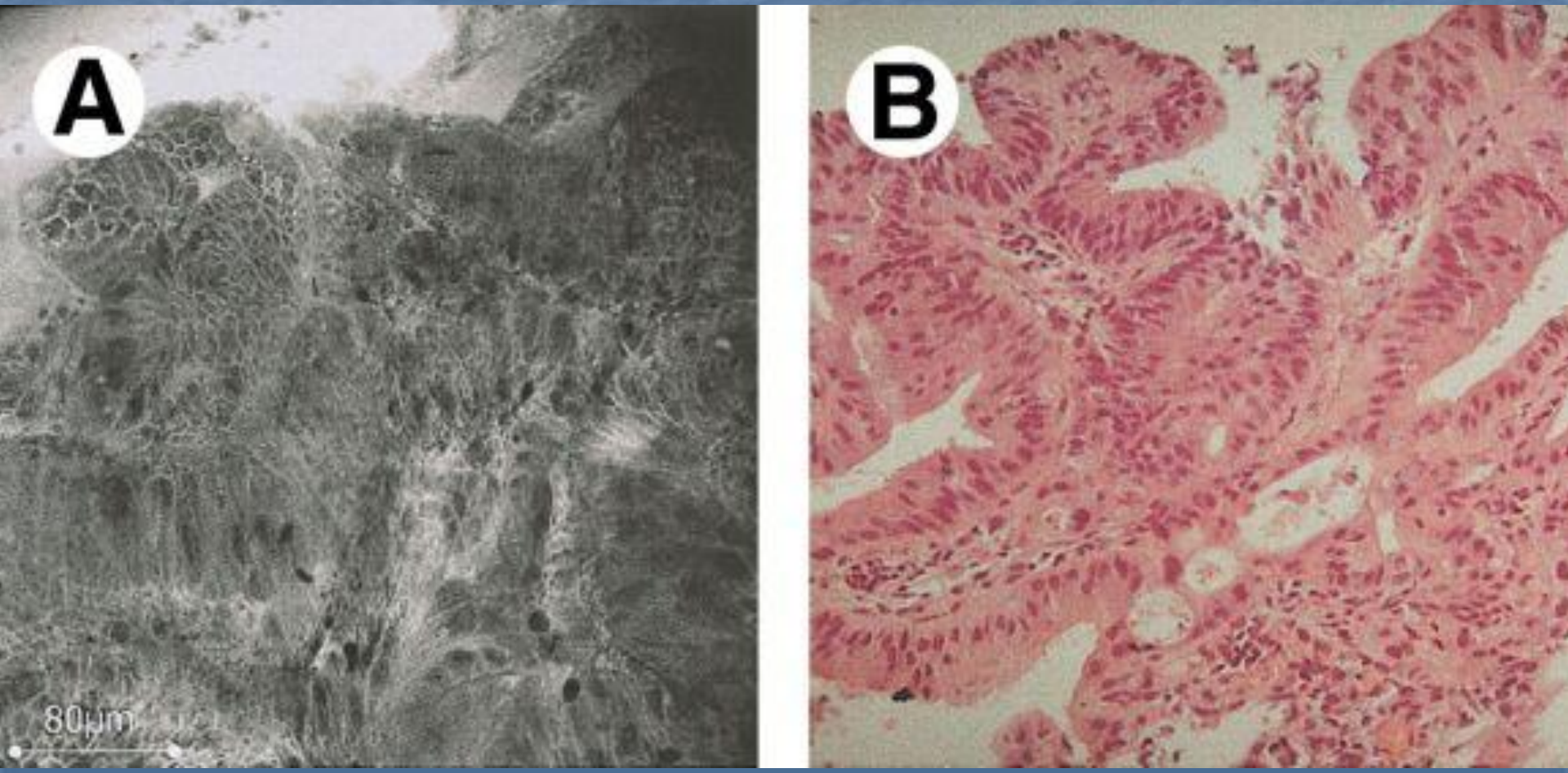
**Confocal microscope**

**Air/water nozzles**
**Water jet**
**Objective lens**
**Instrument channel**
**Light guide**

# Normal rectum



# Colorectal cancer

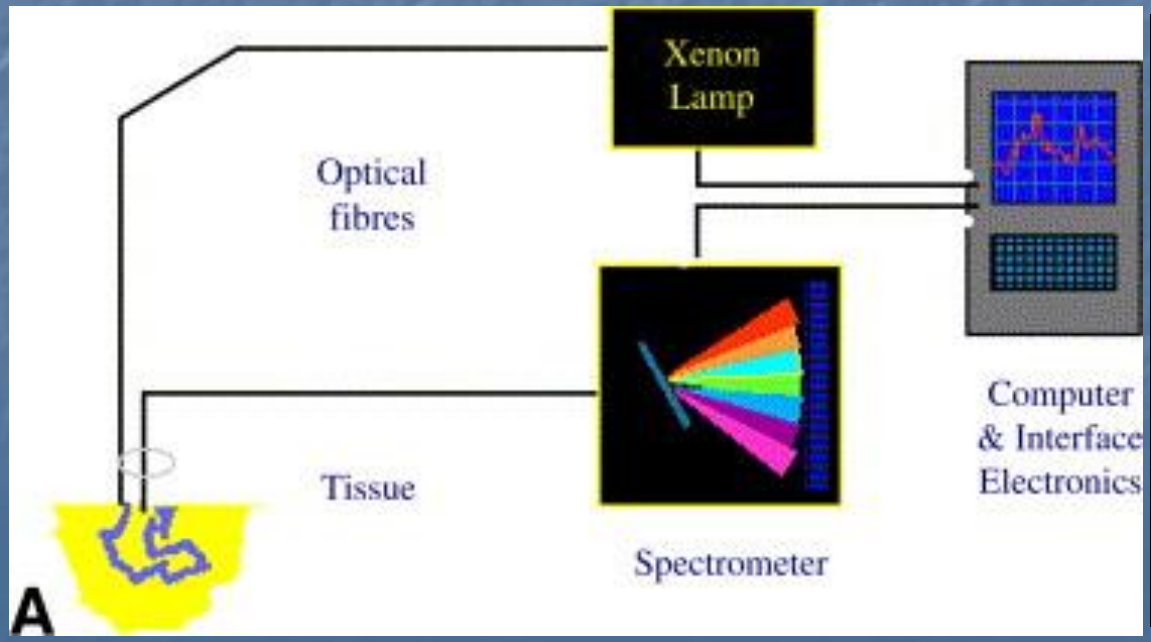


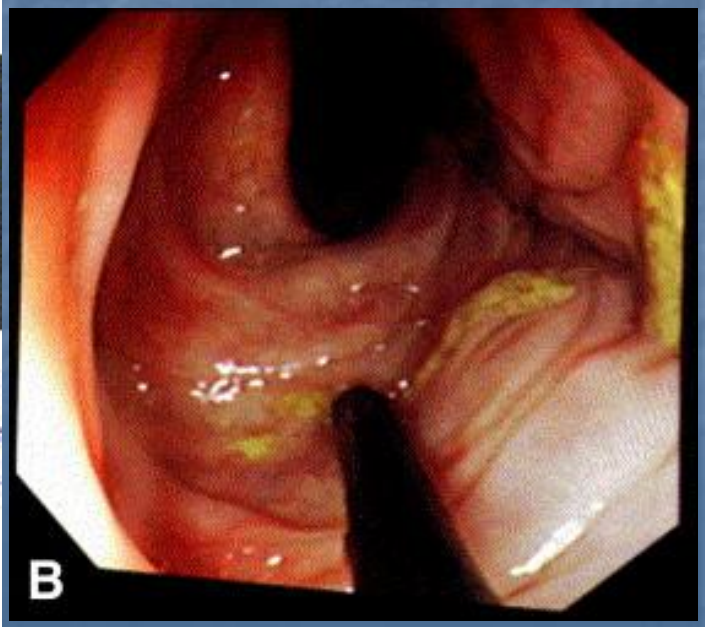
# Study results

- 42 consecutive patients
- To cecum: 9’, withdrawal: 48’
- CEM every 10 cm and from 134 identified lesions
  - 35 intraepithelial neoplasias
  - 3 cancers
  - 79 hyperplastic polyps
  - 12 inflamed areas
  - 5 normal areas

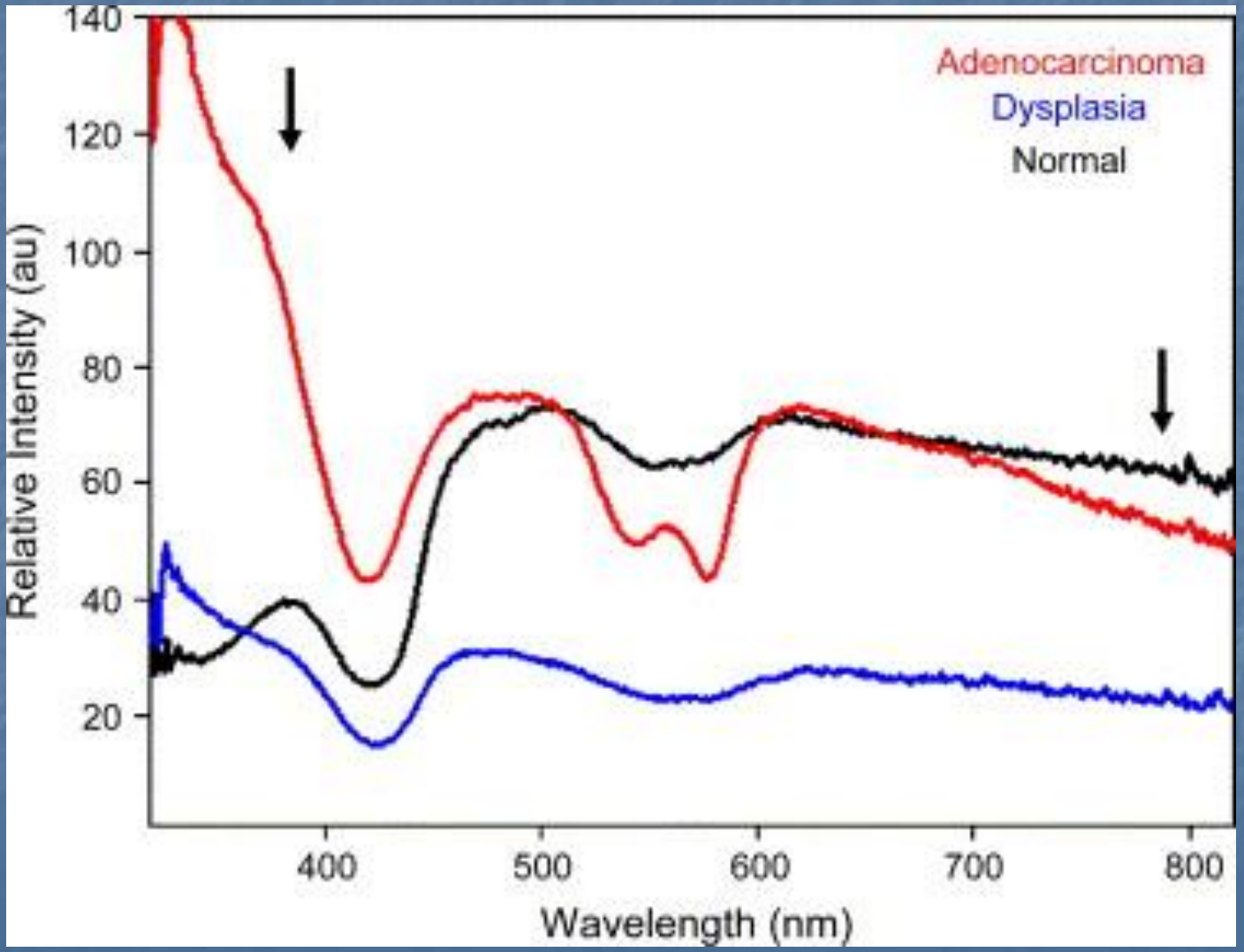
# Elastic scattering spectroscopy

- Probe-based, spectroscopic analysis of xenon pulsed light back-scattering
- Spectral analysis, not imaging



# Tissue spectral patterns

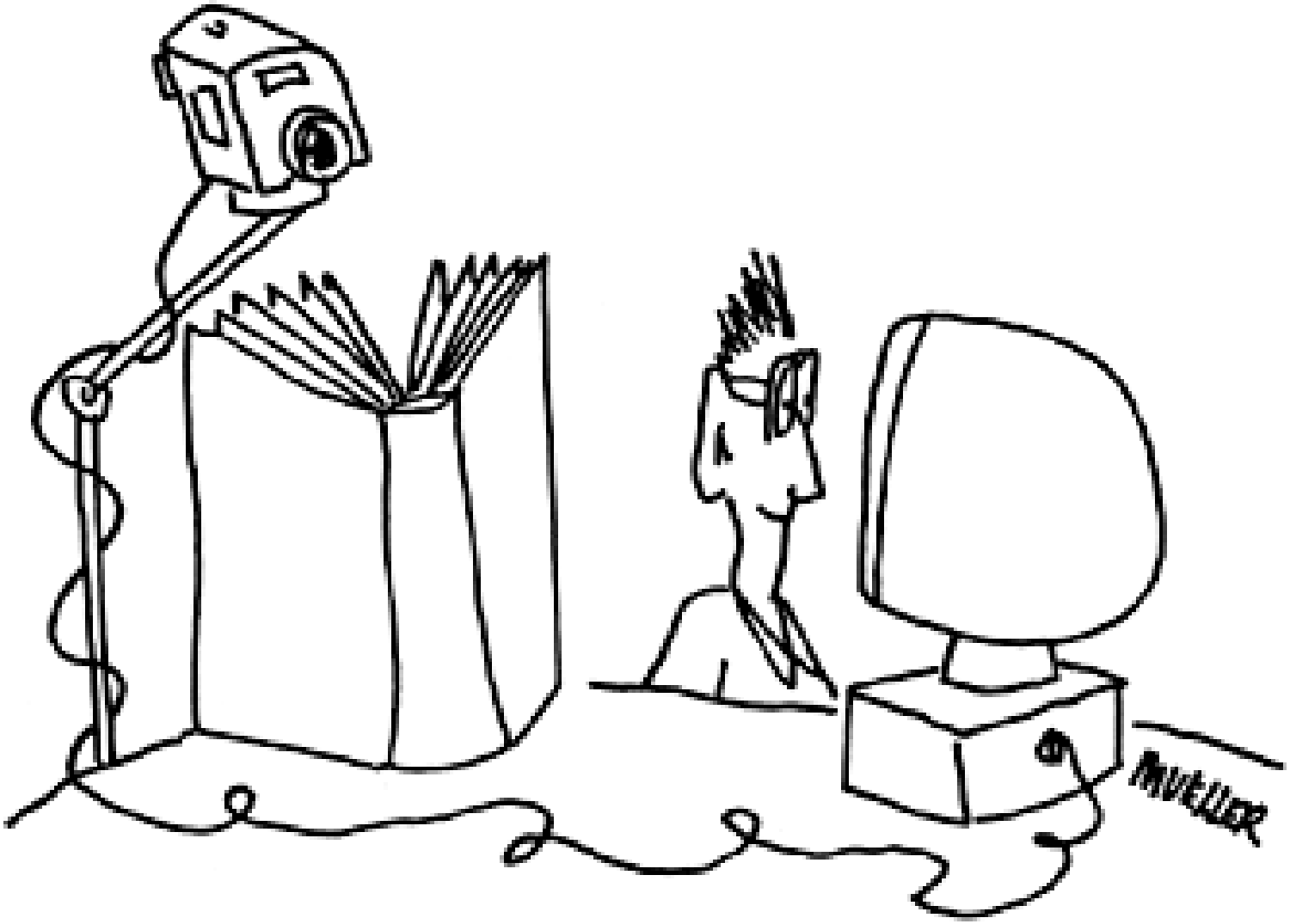


# ESS results

| Category | Sensitivity | Specificity |
|---|---|---|
| All pathology vs. normal | 92 | 82 |
| Cancer vs. normal | 80 | 86 |
| Adenomatous vs. hyperplastic polyp– | 84 | 84 |
| Cancer vs. adenomatous polyp | 80 | 75 |
| Colitis vs. normal | 77 | 82 |
| Dysplasia vs. colitis | 85 | 88 |

# Conclusions

- Endoscopy is still essential in the handling of ulcerative colitis
- Ulcerative colitis surveillance is recommended but at present insufficient
- Chromoendoscopy and NBI may improve surveillance benefits
- Several new techniques may add to white light surface endoscopy
- None of them replace good endoscopic technique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