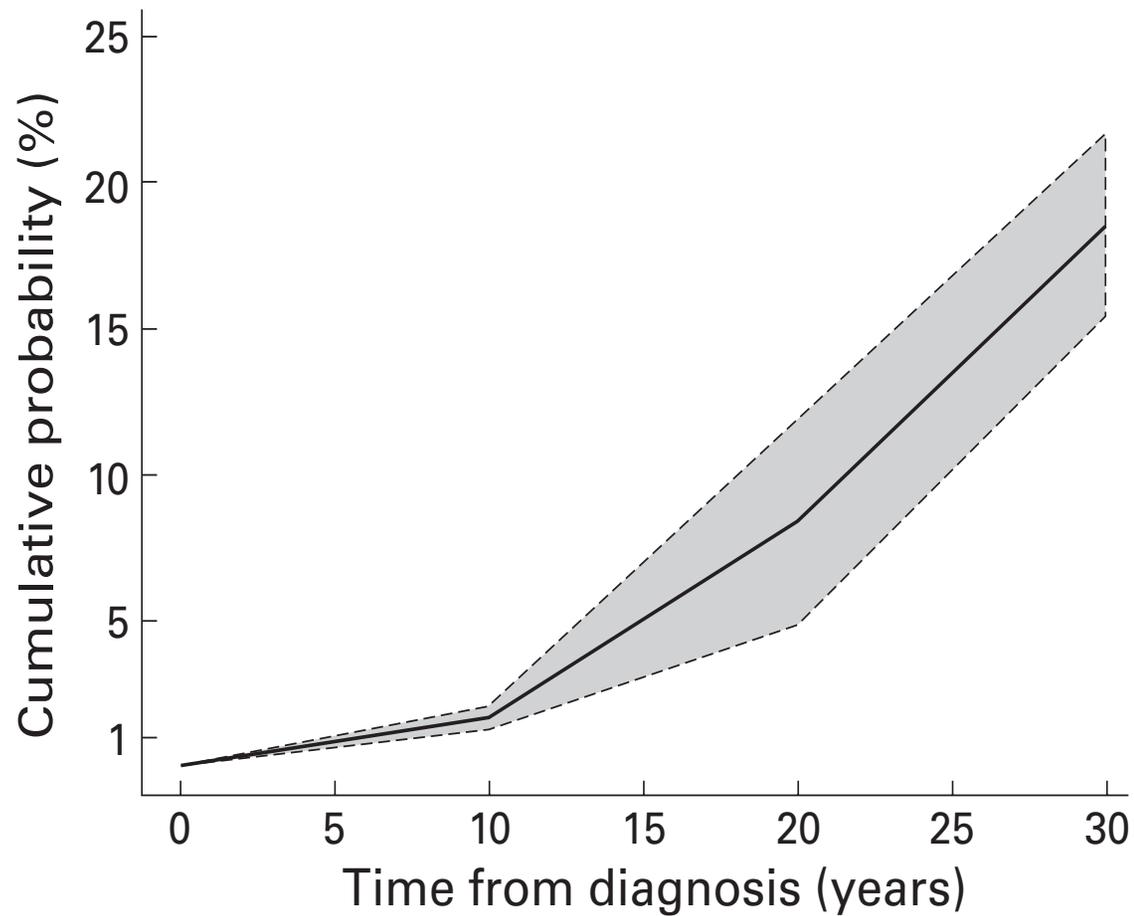




Colon Cancer in IBD: Focus on Surveillance

Marietta Iacucci, MD, PhD
Clinical Associate Professor
IBD Clinic, GI Division
University of Calgary, ALBERTA

Cancer in IBD - meta-analysis 2001



Eaden J et al Gut 2001;48:526

Cancer risk in IBD

Jess et al. Gastroenterology 2012; 143: 375-381

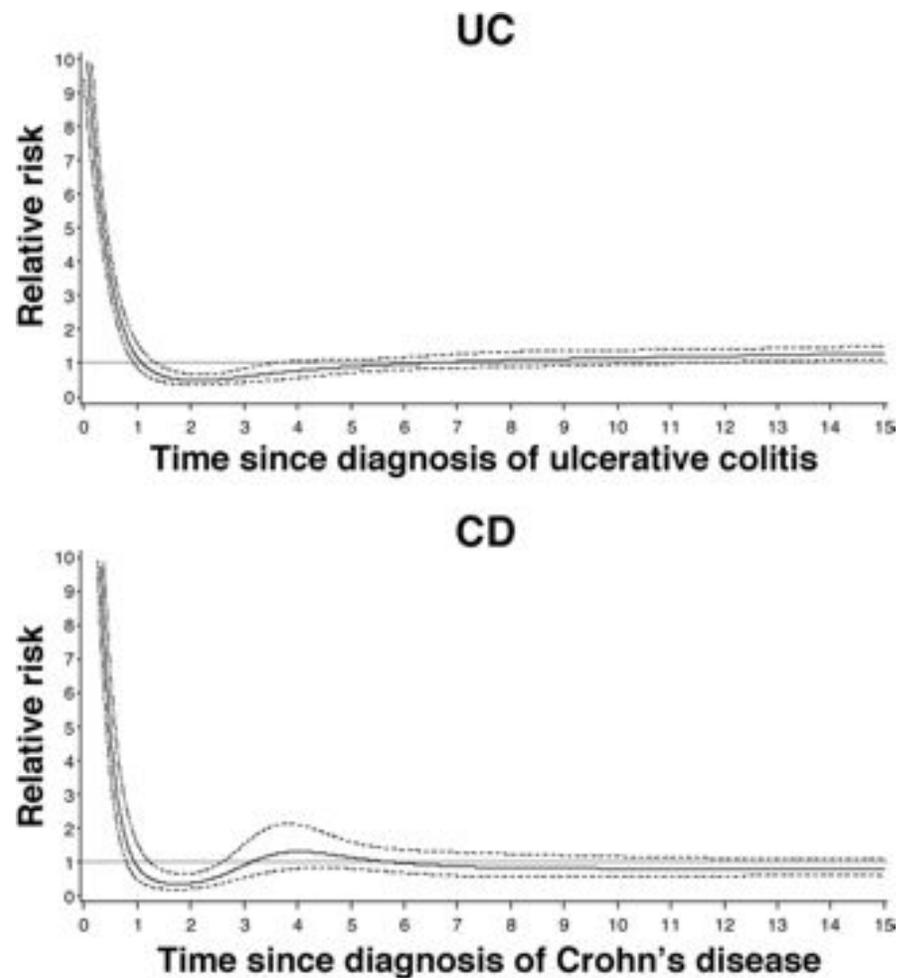
- **National cohort study, Denmark**
 - 47.374 patients with IBD – follow up 30 years
 - 286 patients with ulcerative colitis and 70 patients with Crohn's disease developed colon cancer
- **Cancer risk compared to normal population**
- **Ulcerative colitis** **RR 1,07**
- Cancer risk 1979-1988 RR 1,34
- Cancer risk 1999-2008 RR 0,57
- **Crohn's disease** **RR 0,85**

Conclusions: Crohn's disease is not associated with an elevated cancer risk. Cancer risk in ulcerative colitis is declining. But it is still high under certain conditions.

Risk Factors

- ❖ Extensive Colitis
- ❖ Colonic Stricture
- ❖ Primary Sclerosing Cholangitis
- ❖ Family history Colorectal Cancer ,especially aged <50
- ❖ Personal History of Dysplasia
- ❖ Long standing Inflammation

Relative risk of CRC in IBD by time



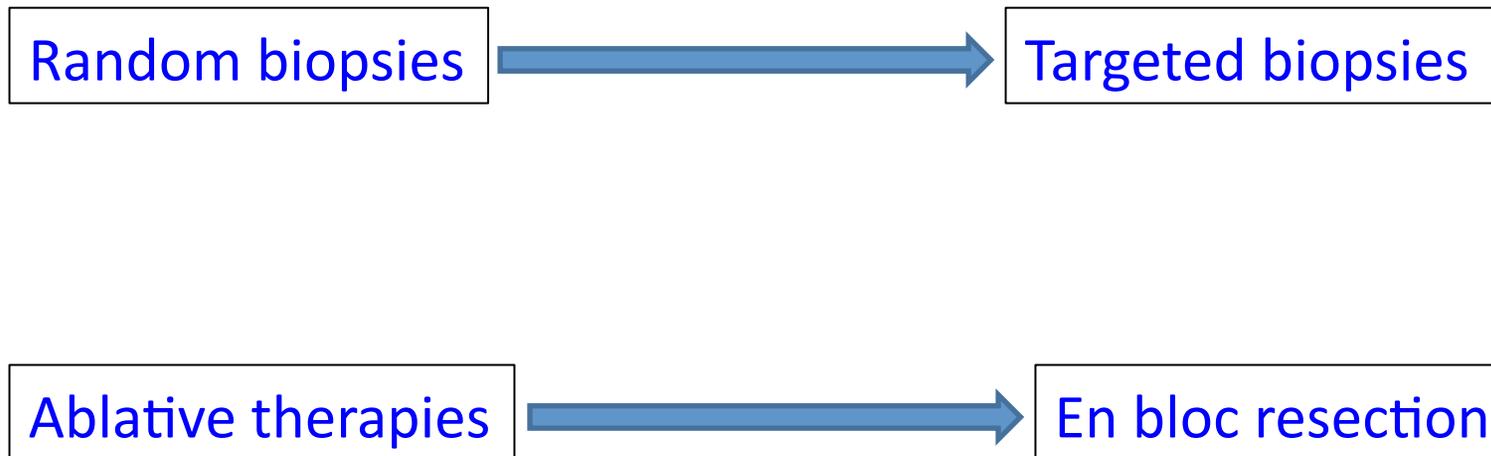
Cancer risk in IBD

Herrinton et al. Gastroenterology 2012 143: 382-389

- **Colon cancer incidence in Northern California (1998-2010)**
- Ulcerative colitis versus Crohn's disease versus normal population
- **Cancer incidence (100.000)**
- **Ulcerative colitis 76,0**
- **Crohn's disease 75,0**
- **Normal population 47,1**
- No difference between 1998-2001 and 2007-2010 for IBD patients. However, colon cancer incidence declined in normal population.

Conclusions for Northern California: Colon cancer incidence is still 60% higher in IBD patients with no decreased incidence over time.

Changing endoscopy trend in dysplasia



Where are we going?

White Light Standard Surveillance

The standard recommendation for surveillance colonoscopy is to perform colonoscopy yearly starting 8-10 years after diagnosis of UC and to take random biopsies from each quadrant every 10 cm. -33-50 jumbo forceps biopsies are needed to detect the highest degree of dysplasia or CRC with 90% confidence.

Jess et al Gastroenterology 2006 ;130:1941-49

Random biopsies surveillance Limitations

- ❖ Random biopsies visualize less than 1% of the total colonic mucosa surface
- ❖ Can often miss flat multifocal lesions
- ❖ Expensive US **\$ 27,150**
- ❖ Time consuming
- ❖ It is often not followed in the clinical practice

Moving Beyond random biopsies

ECCO 2010 - recommendation

Methylene blue or indigo carmine chromoendoscopy is an alternative to random biopsies for appropriately trained endoscopists and is superior to random biopsies in the detection rate of neoplastic lesions [EL1b, RG B]

The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Special situations.

Van Assche G, Dignass A, Reinisch W, van der Woude CJ, Sturm A, De Vos M, Guslandi M, Oldenburg B, Dotan I, Marteau P, Ardizzone A, Baumgart DC, D'Haens G, Gionchetti P, Portela F, Vucelic B, Söderholm J, Escher J, Koletzko S, Kolho KL, Lukas M, Mottet C, Tilg H, Vermeire S, Carbonnel F, Cole A, Novacek G, Reinshagen M, Tsianos E, Herrlinger K, Oldenburg B, Bouhnik Y, Kiesslich R, Stange E, Travis S, Lindsay J; European Crohn's and Colitis Organisation (ECCO).

J Crohns Colitis. 2010 Feb;4(1):63-101. Epub 2009 Dec 21. No abstract available.

ECCO Consensus 2013

- *Upcoming recommendation:*

Chromoendoscopy is recommended for surveillance as the better alternative compared to random biopsies [EL1a, RG B]

IBD surveillance recommendations in North America and in Europe

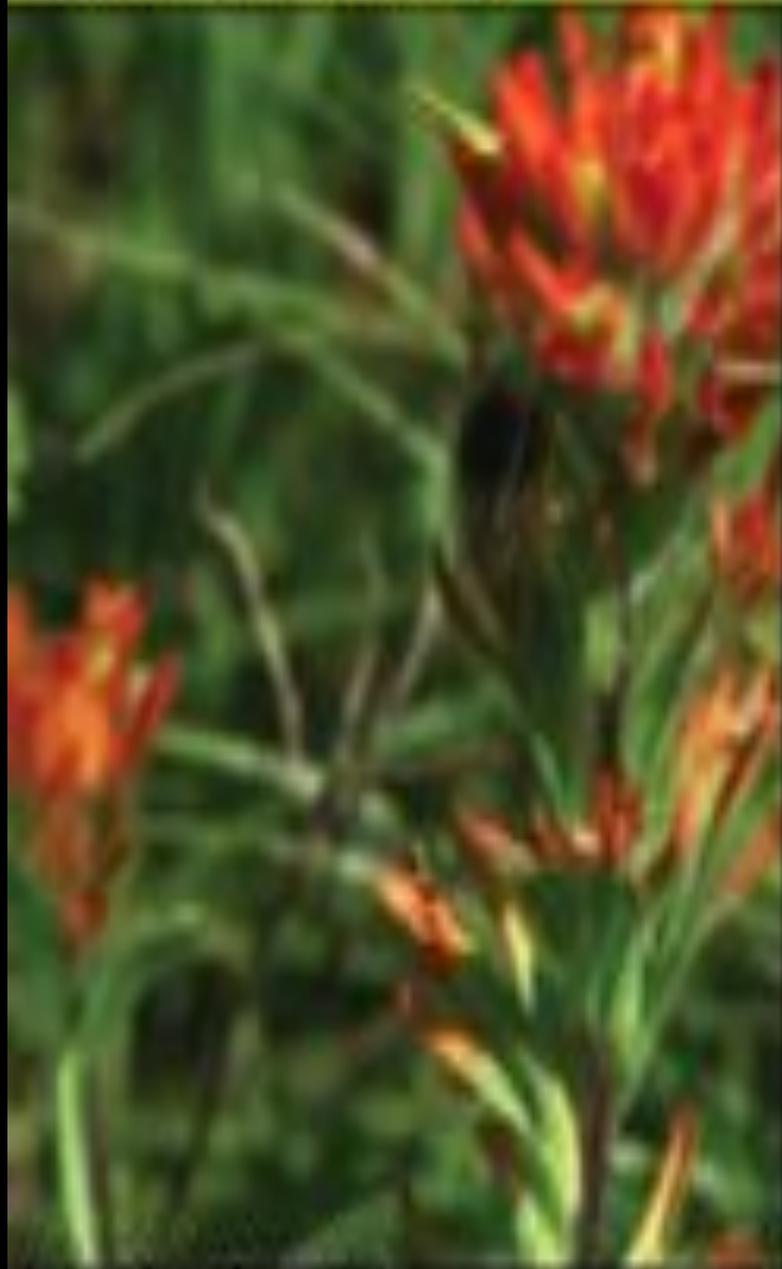
I. Comparison of Screening Recommendation from International Guidelines for Patients with Colitis

	ECCO 2008	BSG 2010 (and NICE)	AGA 2010	ACG 2010
1st screening	8-10 yr	10 yr	Max 8 yr	8-10 yr
Surveillance interval	Extensive: 2 yearly to 20 yr then annually Left sided: 2 yearly starting at 15 yr PSC: 1 yearly	By risk: low 5 yr Intermediate 3 yr High 1 yr	1-3 yr More often at high risk e.g., PSC	1-2 yr
Chromoendoscopy	Superior to white light endoscopy	Recommended	Special cases	Not yet
Biopsies	33+ if no chromo	33+ if no chromo	33+	33+

How can we see more at endoscopy ?

- Standard white light endoscopy
- **Zoom endoscopy**
- **Dye spraying endoscopy**
- **High definition endoscopy (like HD TV)**
- **Electronic virtual chromoendoscopy**
- **Confocal laser endomicroscopy**

● Spatial-Temporal De-Interlacing



Without NVDA PureVideo



With NVDA PureVideo

NBI Olympus, **I-Scan** Pentax, **FICE** Fuji Electronic (Virtual) Chromoendoscopy

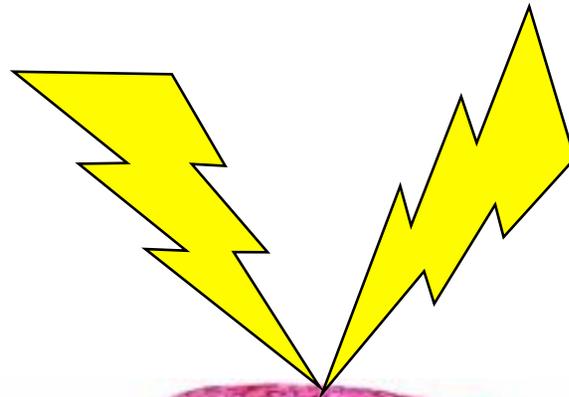
Narrowing of light spectrum

NBI



Effect:

Vessel analysis



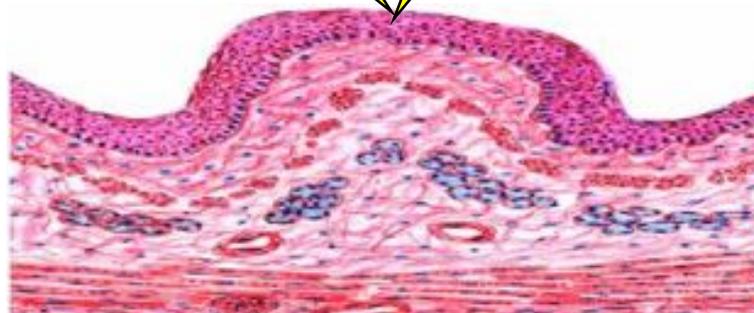
Post Processing of emitted light

I-Scan - FICE



Effects:

Surface analysis Tissue analysis Vessel analysis



PENTAX i-scan™ TECHNOLOGY

PENTAX i-scan is a post-processing image enhancement technology that analyzes the endoscopic image in real-time. It is comprised of three image enhancement algorithms that augment the brightness, contrast and colour settings of the image.

Surface Enhancement (SE)
Contrast Enhancement (CE)
Tone Enhancement (TE)

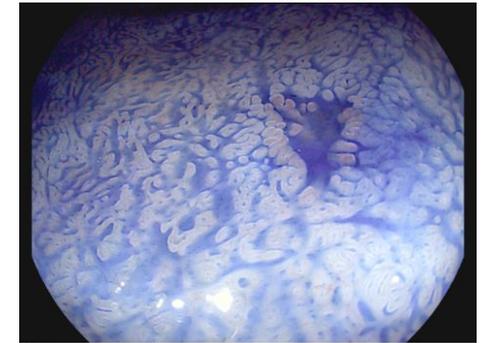


Endoscopic Modalities

- **Present- three available alternatives**
- **Colonoscopy with targeted and random biopsies**
(4 bx every 10 cm)
- Colonoscopy in conjunction with **chromoendoscopy** – targeted biopsies only
- Colonoscopy in conjunction with **chromoendoscopy** and **endomicroscopy** – targeted biopsies on suspicious areas only

Future Endoscopic Modalities

- **Virtual chromoendoscopy or autofluorescence**
- **300° colonoscopy with/without chromoendoscopy**
- **Drug induced chromoendoscopy**
- **Functional and Molecular imaging**



Chromoendoscopy

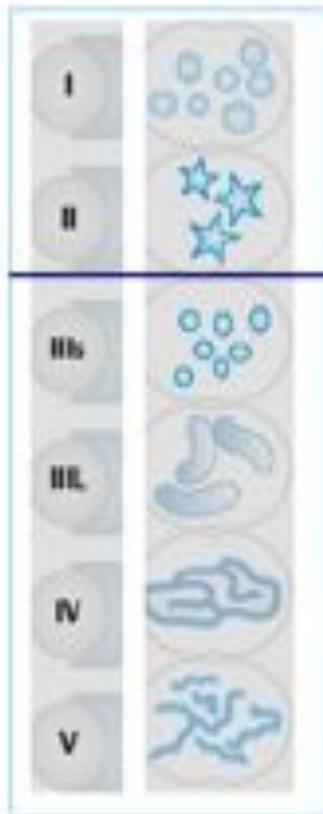
accepted and convincing evidence

White light imaging versus Pan-Chromoendoscopy in UC

Author	N	Method	Increase of diagnostic yield
Kiesslich et al (2003) ²	165	Methylene blue staining	3-fold (per lesions)
Hurlstone et al (2004) ³	162	Indigo carmine staining	4-fold (per lesions)
Rutter et al (2004) ⁴	100	Indigo carmine staining	4.5-fold (per lesions)
Hurlstone et al (2005) ⁵	700	Indigo carmine	3-fold (per lesions)
Kiesslich et al (2007) ⁶	161	Methylene blue staining & Endomicroscopy	4.75-fold (per lesions)
Marion et al (2007) ⁷	102	Methylene blue staining	1.5-fold (per patients)

Total number of patients = 1544 !

Pit Pattern Classification

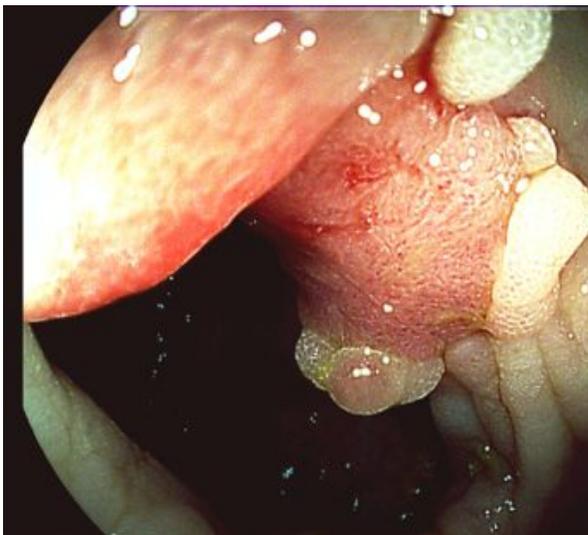


Non-Neoplastic

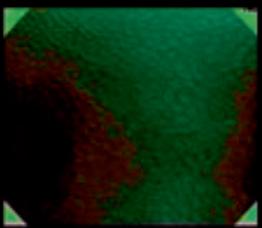
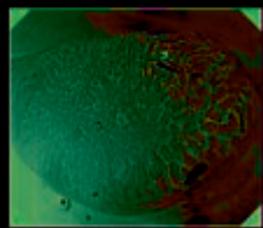
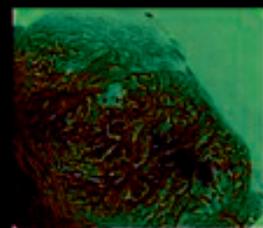
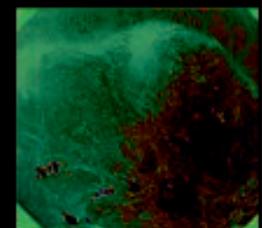
Neoplastic (targeted Bx)

Vessel architecture

i-scan TE - Neoangiogenesis



IMAGING OF EARLY COLORECTAL LESIONS

	I	II	IIIA	IIIB
Endoscopic Findings				
Histopathology	Meshed Capillary Vessels (-) Normal Hyperplastic Polyp	* Meshed Capillary Vessels (+) * Capillary Vessels Surround Mucosal Glands Adenoma M* SM-Superficial**	Meshed Capillary Vessels Characterized by Branching, Curtailed Irregularity & Blind Endings * Lack of Uniformity * High Density of Capillary Vessels	* Nearly Avascular or Loose Microcapillary Vessels SM-Deep***
Treatment Strategy	No Treatment	Endoscopic Treatment (Polypectomy or EMR)	Surgical Treatment	

Uraoka T et al *Digestive Endoscopy* 2011

Optimization of Surveillance in IBD

- ❖ Have optimal bowel preparation- the entire bowel mucosa should be without mucus, pus or stool.
- ❖ Surveillance colonoscopy should be performed in patients with minimal or no inflammation.
- ❖ Withdrawal time and antispasmodic agents have been clearly shown to be associated with improved adenoma detection in non-colitis patients (likely the same in IBD surveillance).

Ghosh S, Iacucci M. Can J Gastroenterol. 2013 Sep;27(9):508.

Iacucci M et. al. Inflamm Bowel Dis. 2013; 19:873-80

Optimization of Surveillance in IBD

- ❖ Use 2 ampules of Indigo Carmine or 1 ampule of Methylene blue in 250 ml of saline throughout the water jet channel using the pump .
- ❖ Upon visualization of the lesion spray Indigo carmine 0.2% or Methylene blue 0.1% to better characterize mucosal pattern and edges of the lesions
- ❖ Resect and snare circumscribed lesion

*Ghosh S, Iacucci M. Can J Gastroenterol. 2013 Sep;27(9):508.
Iacucci M et. al. Inflamm Bowel Dis. 2013; 19:873-8.*

What do you need ?



Zoom Chromoendoscopy



Canon I
-----T

Methylene blue MMX



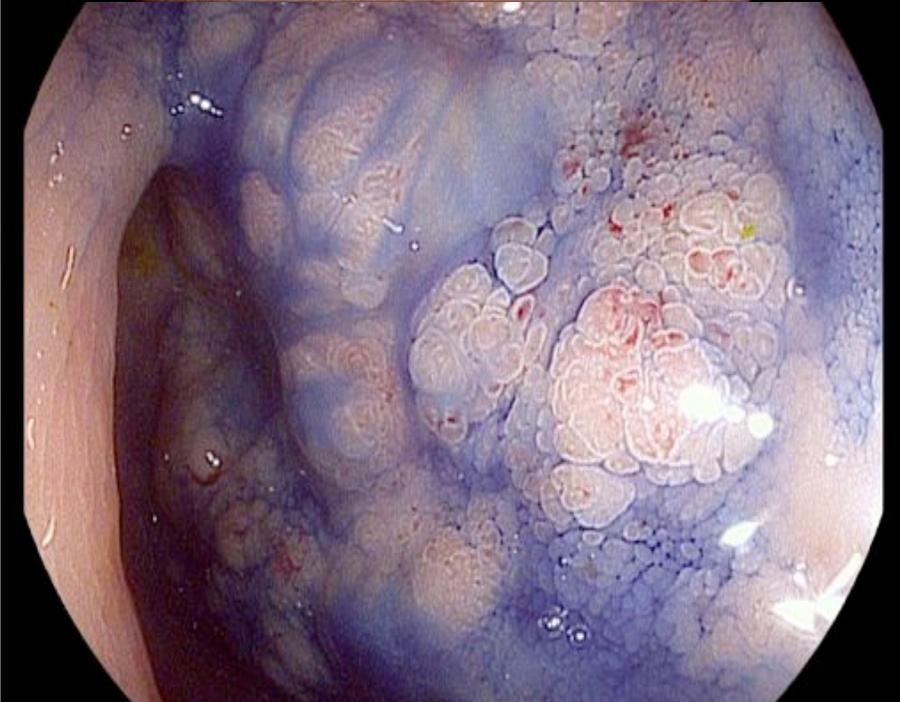
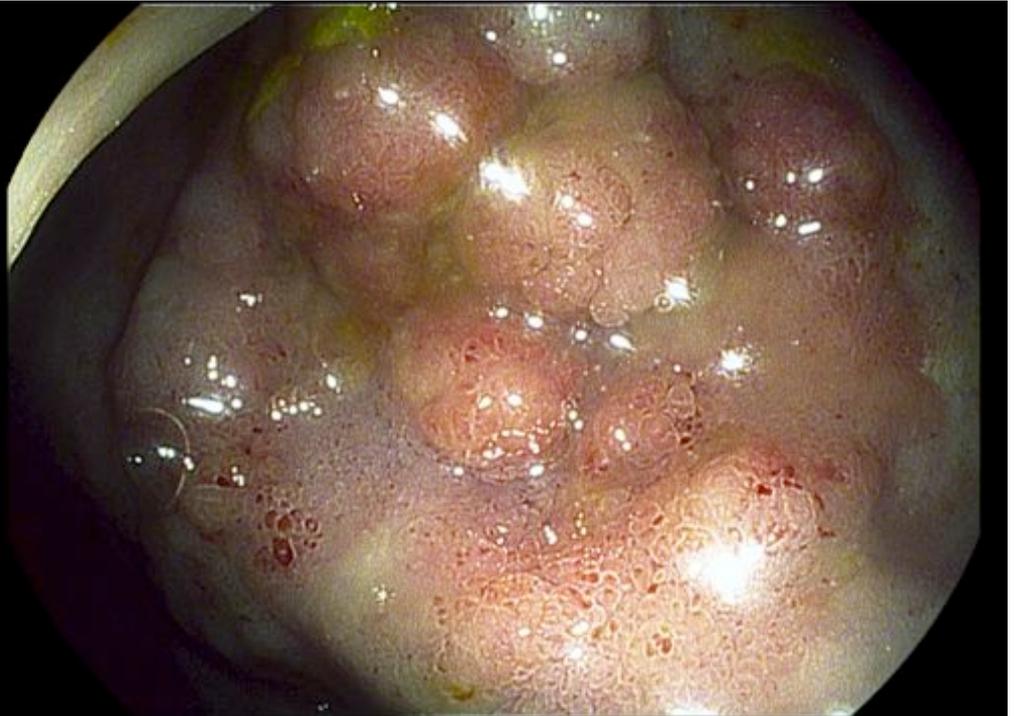
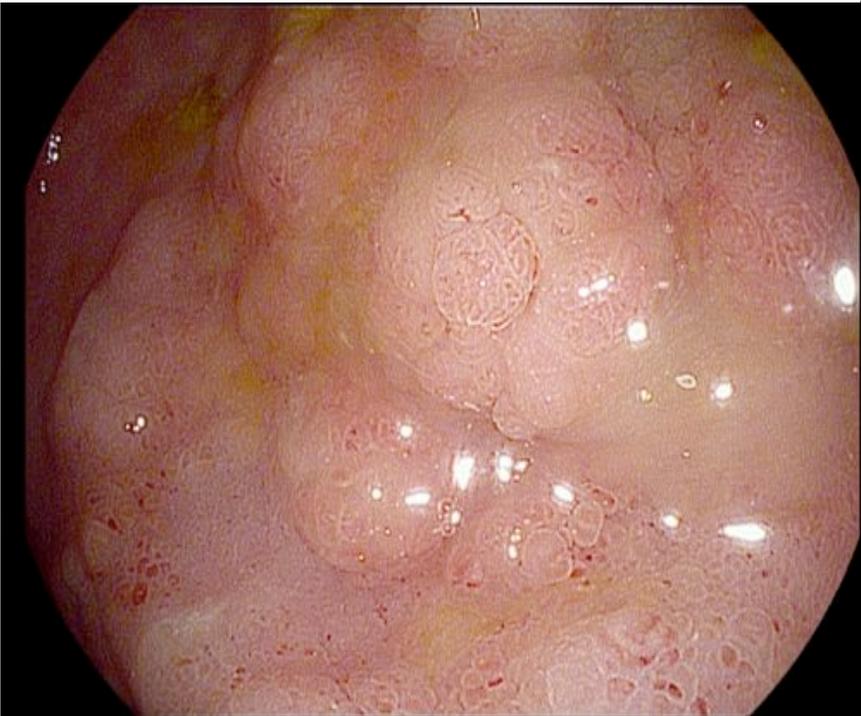
Methylene blue MMX

- **New drug available: Methylene blue capsules with MMX technology (Cosmo, Italy)**
- **Capsules are applied during bowel preparation**
- First study (85 patients) – screening colonoscopy
- Results: Adenoma detection rate 45,6%
- Two huge studies (screening and surveillance) are ongoing.

Conclusion: Drug based chromoendoscopy could be reality soon and would ease and standardize chromoendoscopy.

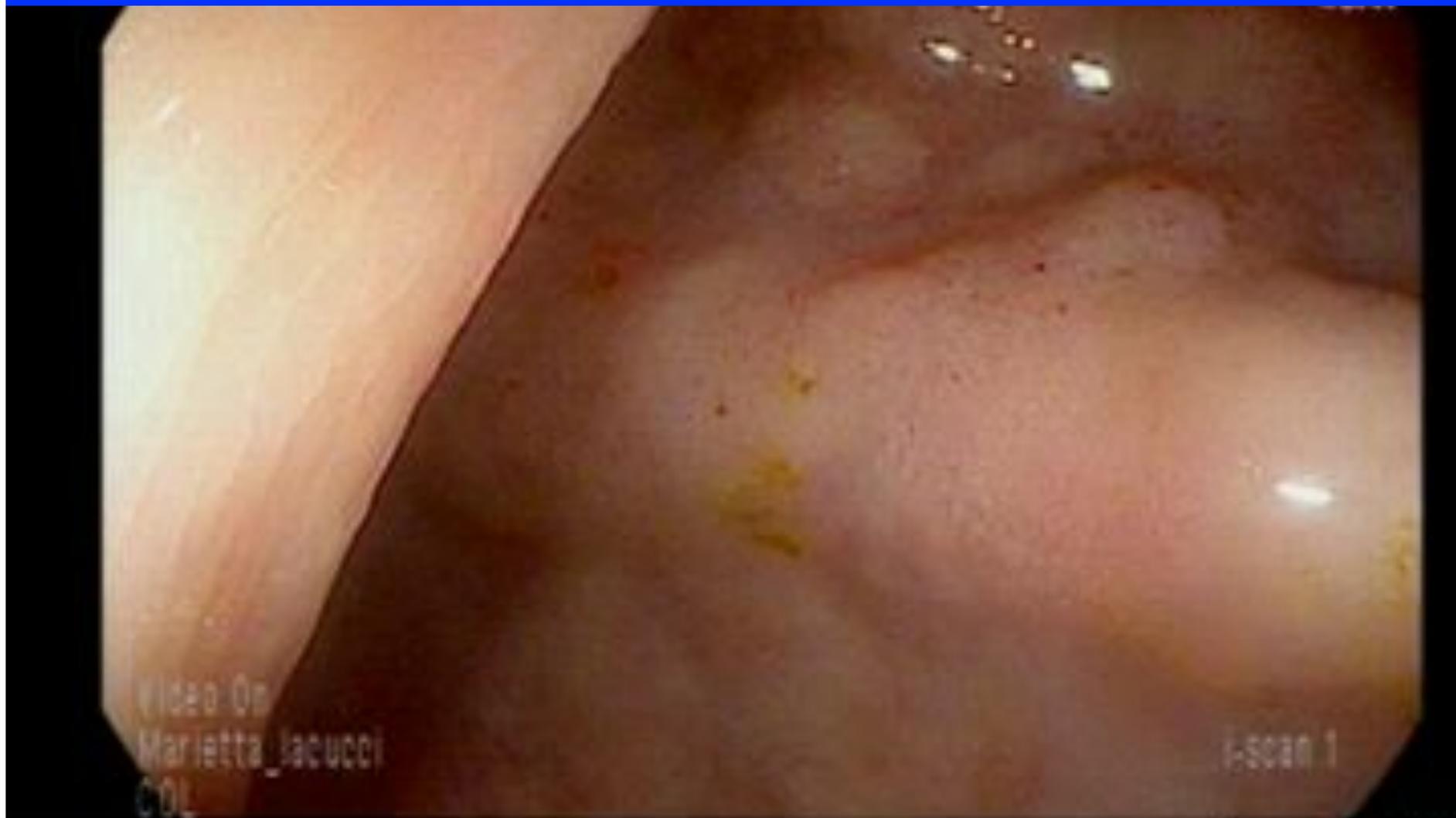
High definition versus Standard definition

- **Retrospective cohort study, UK**
- **SD:**
160 colonoscopies
(101 ulcerative colitis and 59 Crohn's disease)
- **HD:**
209 colonoscopies (147 UC and 62 CD)
- **Results: 32 dysplastic lesions (HD) versus 11 dysplastic lesions (SD)**
- **Conclusions: Prospective studies are warranted**



DALM IN UC +PSC patient

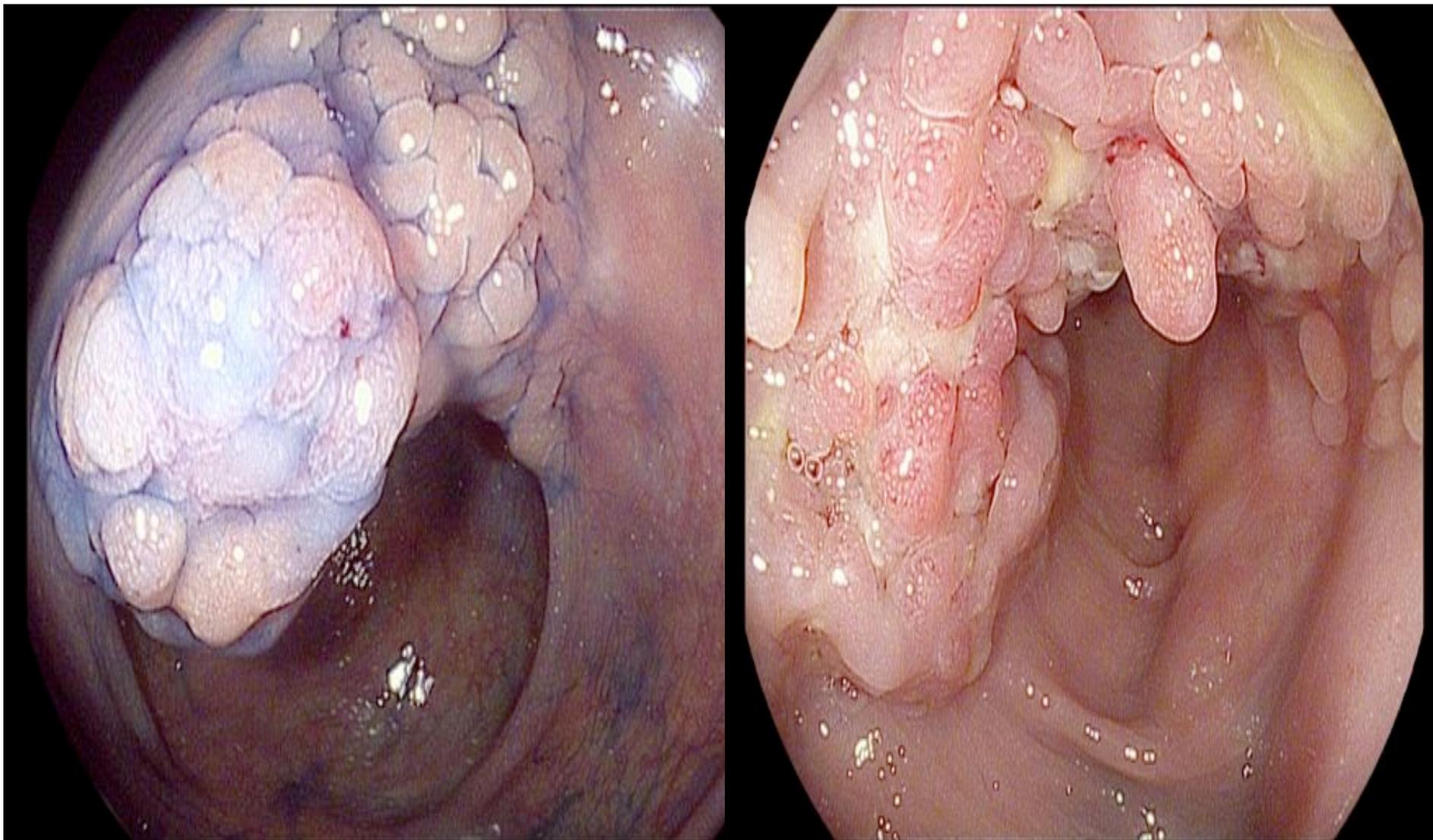
DALM IN IBD

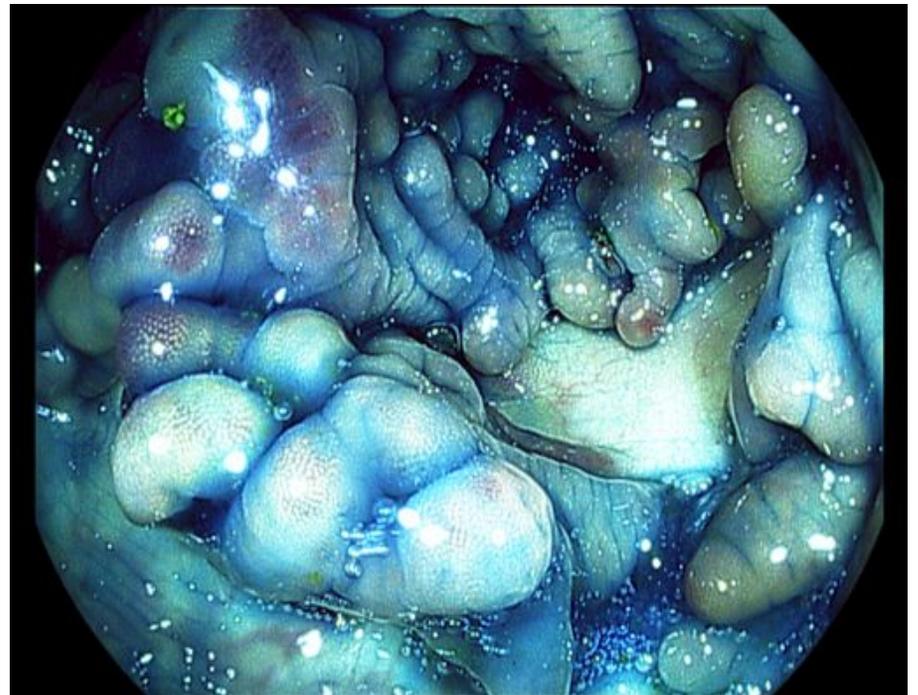
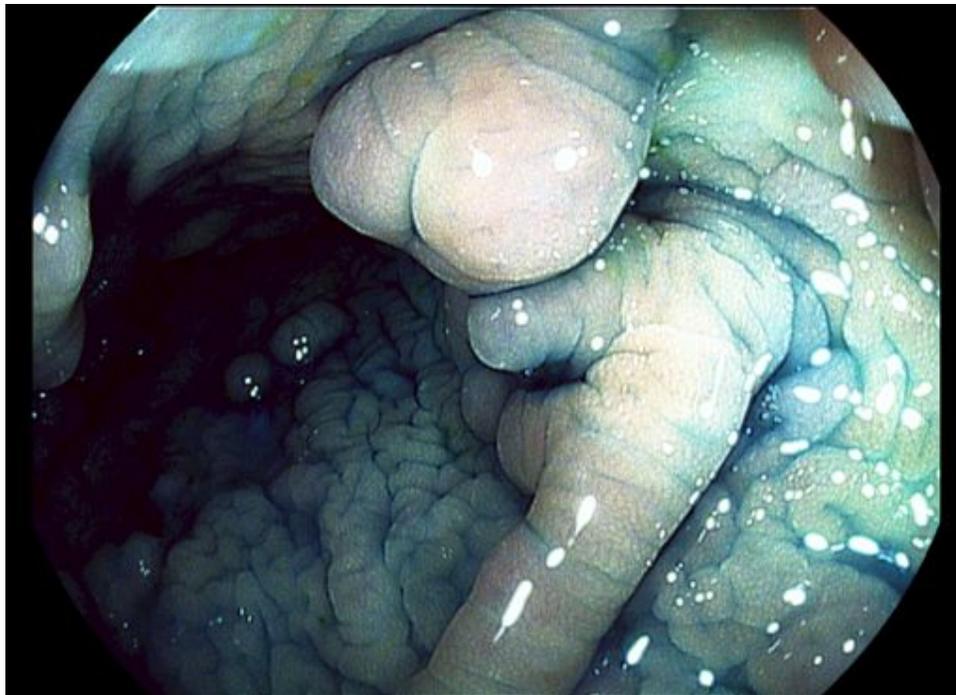
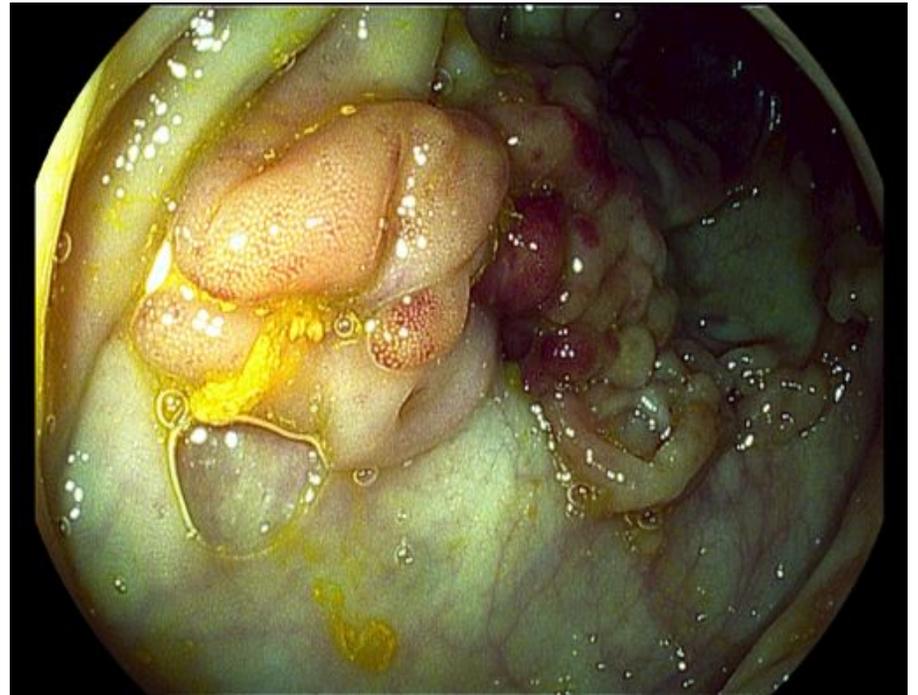
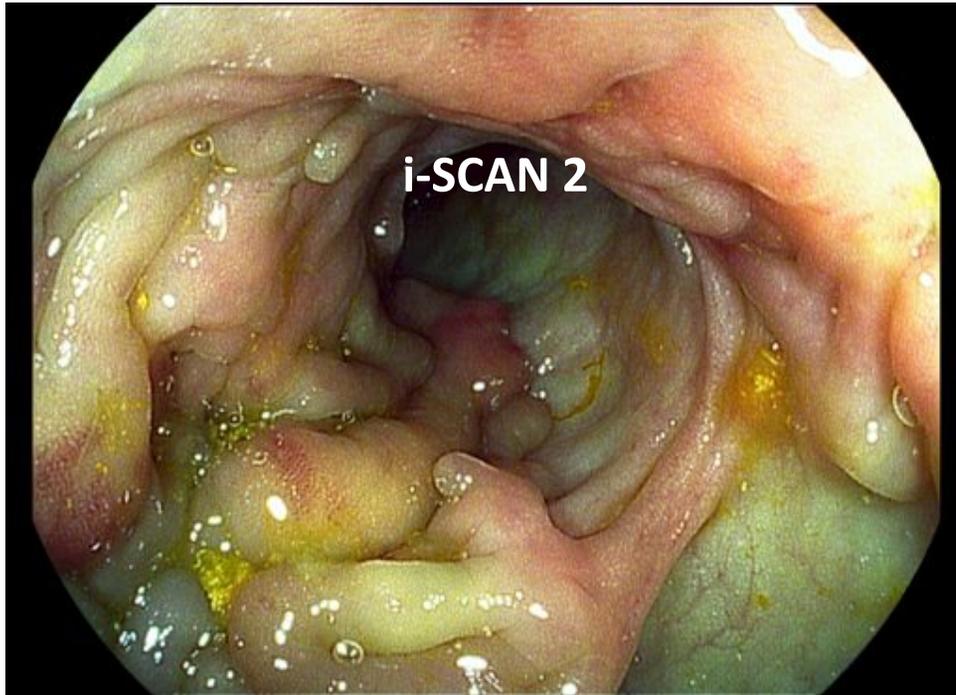


Video On
Marietta_lacucci
COL

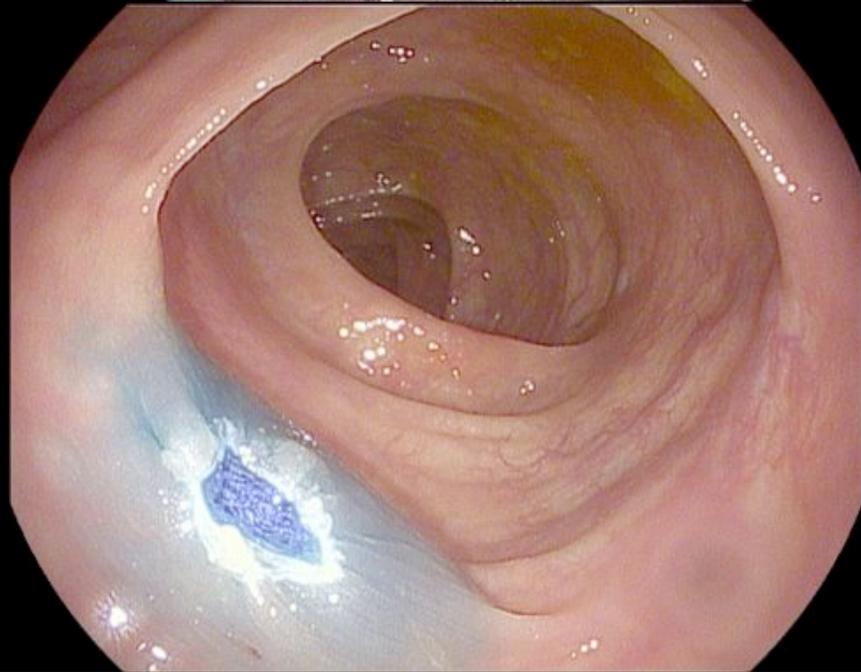
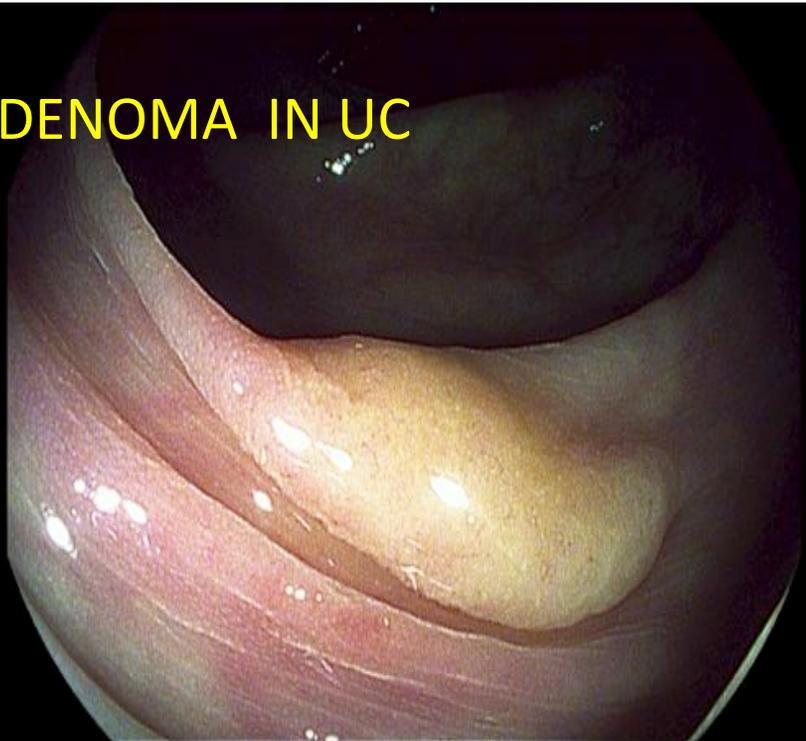
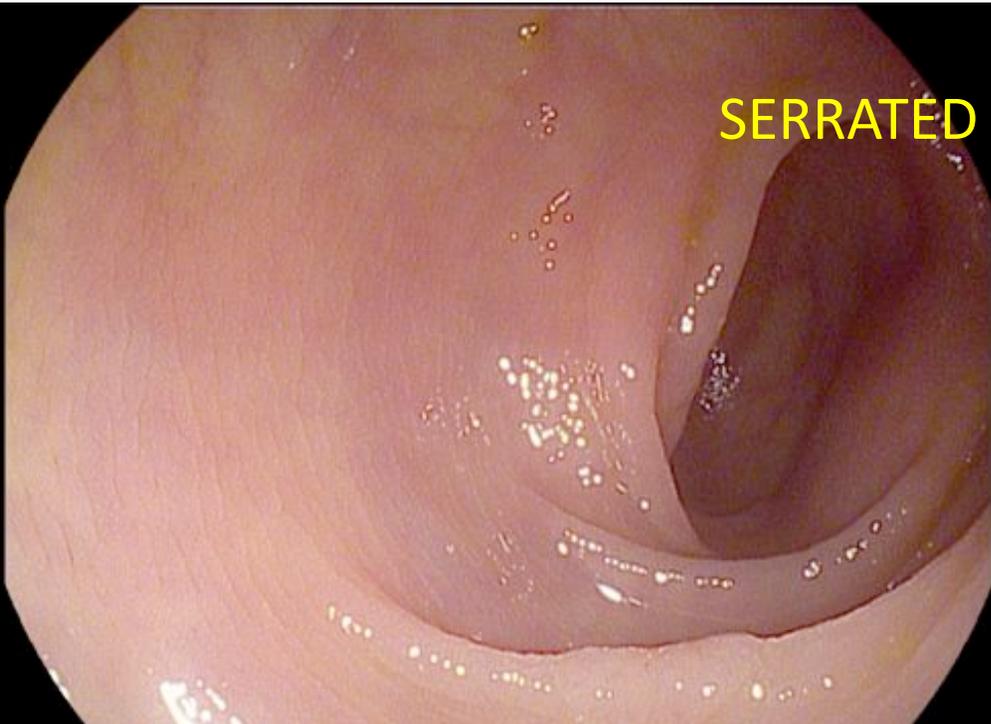
i-scan 1

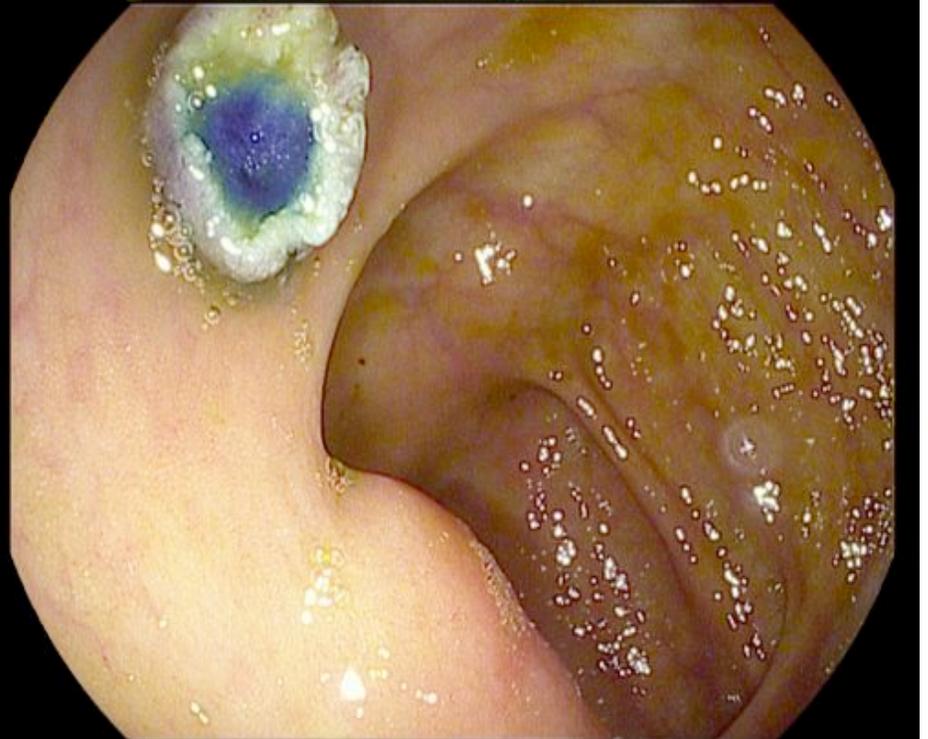
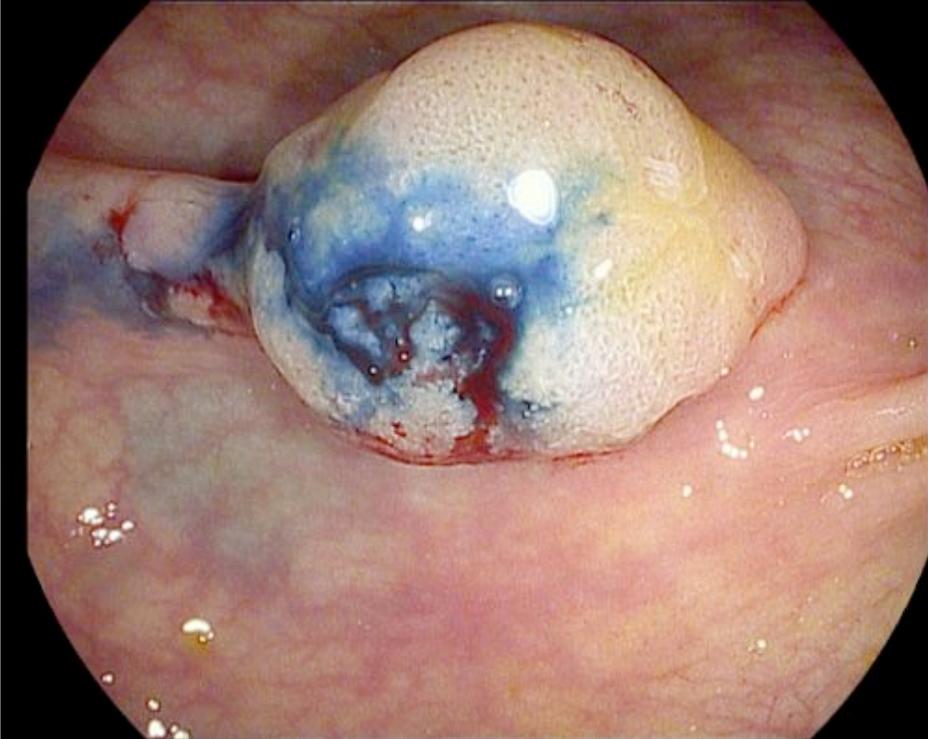
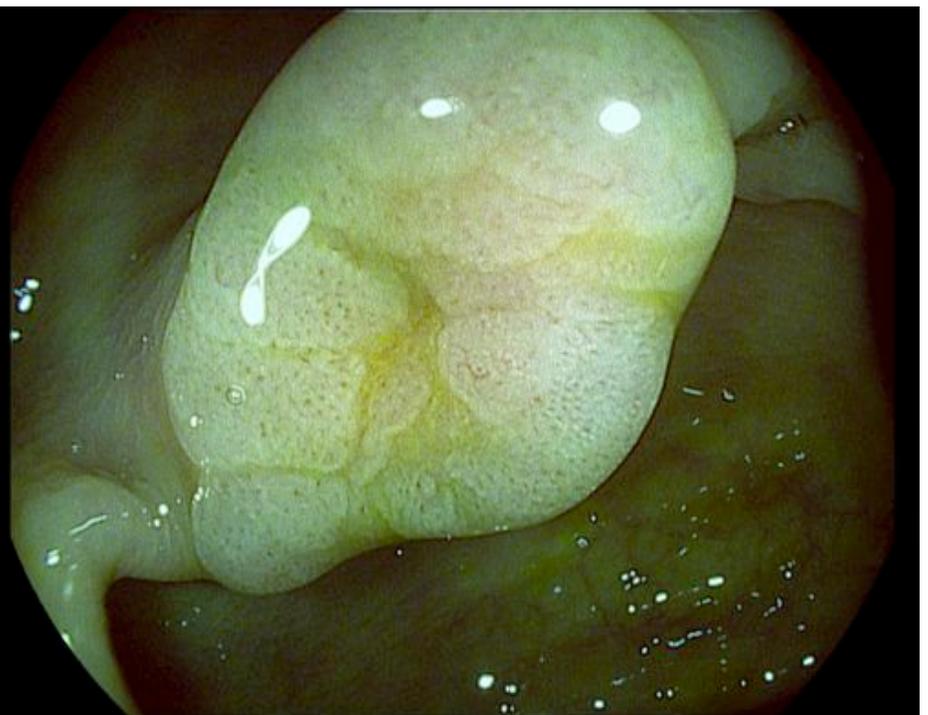
Pseudopolyps mass associated with sporadic adenoma

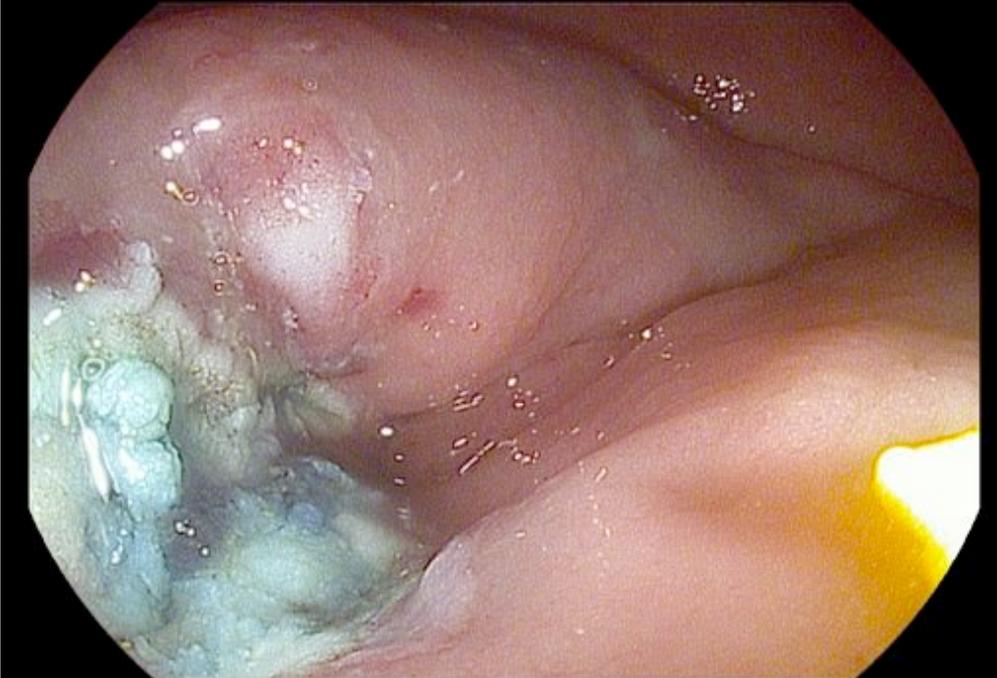
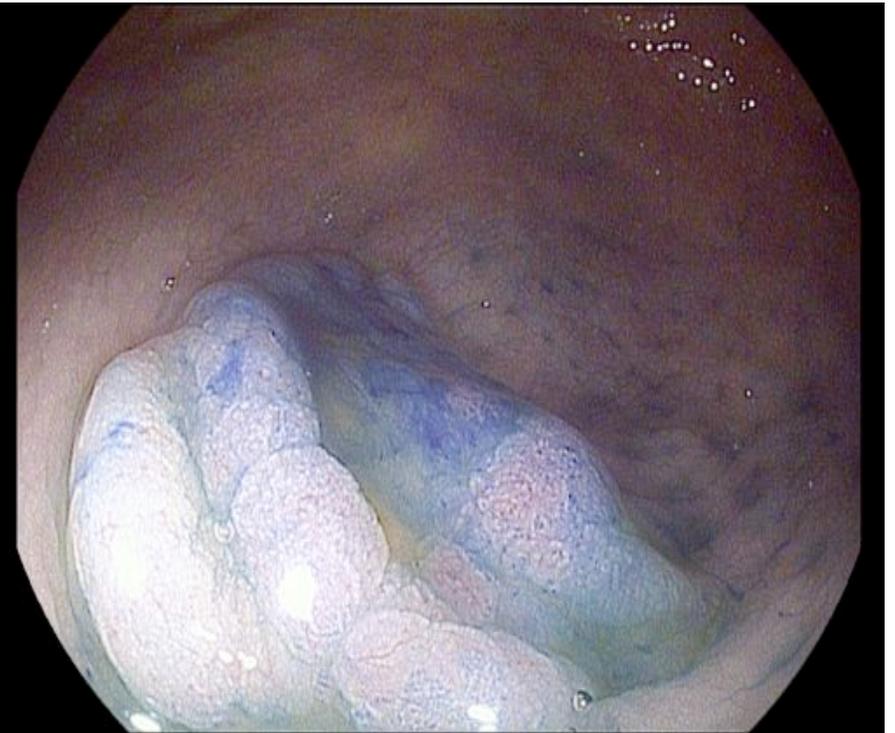




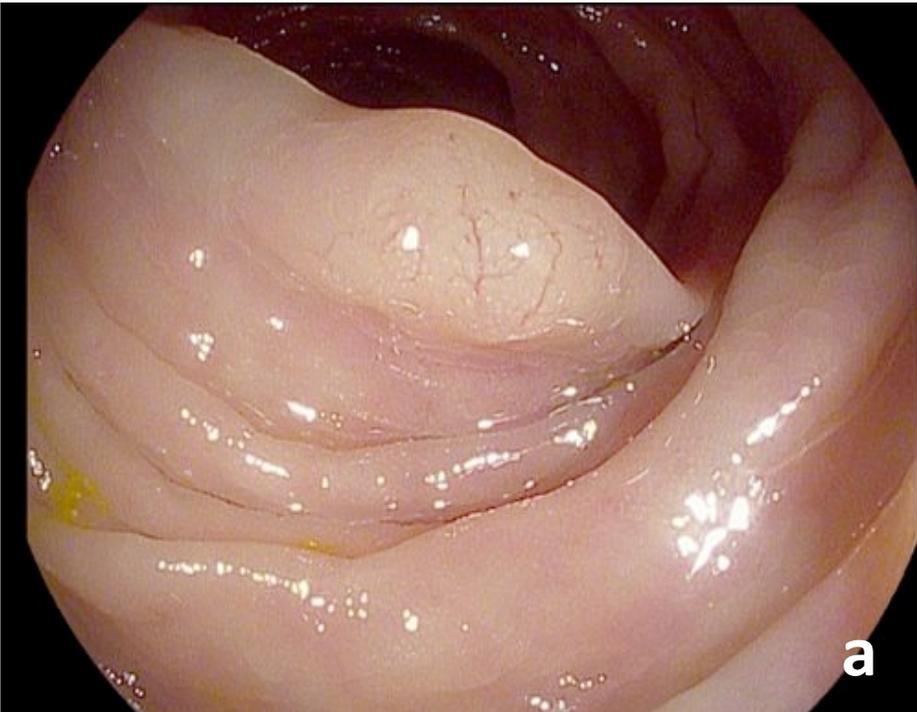
SERRATED ADENOMA IN UC



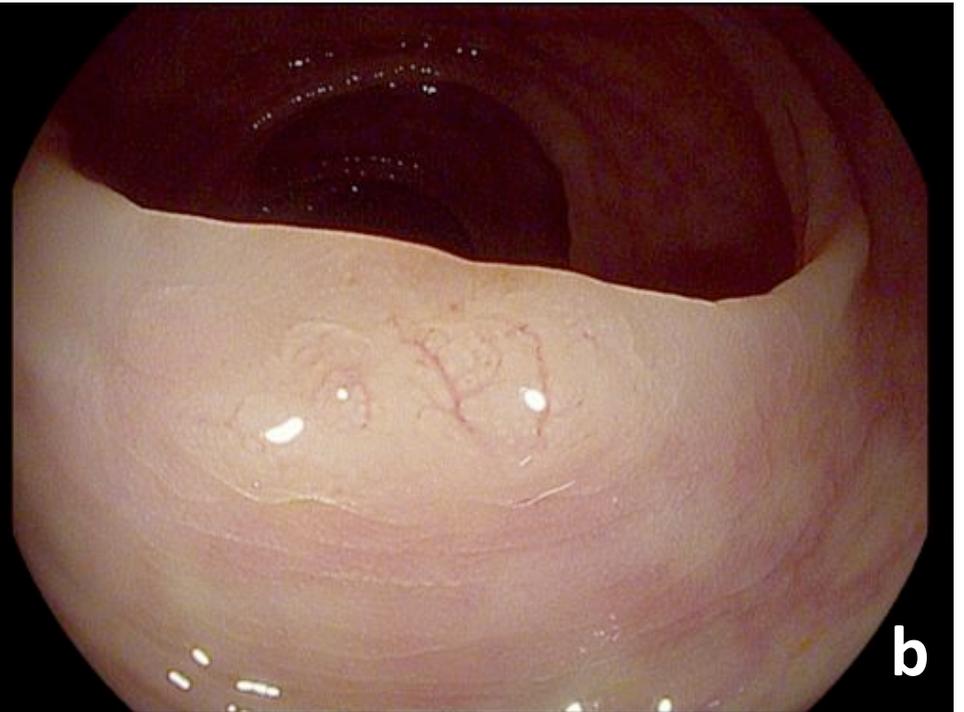




Serrated Adenoma in IBD



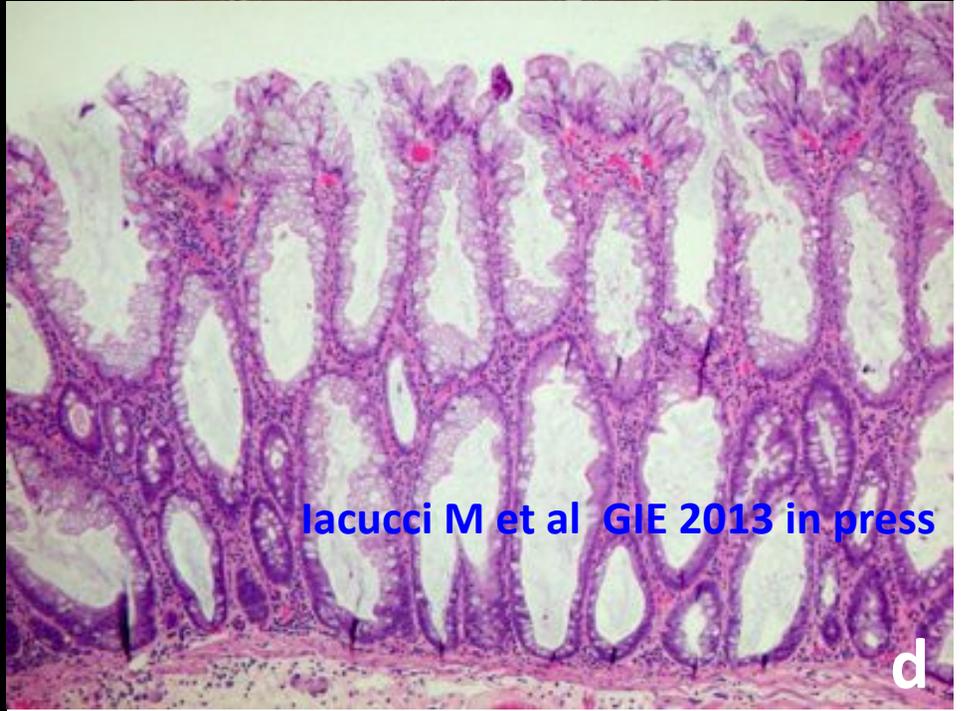
a



b



c



d

Iacucci M et al GIE 2013 in press

Serrated Adenoma in IBD



Endomicroscopy

It's not about predicting histology

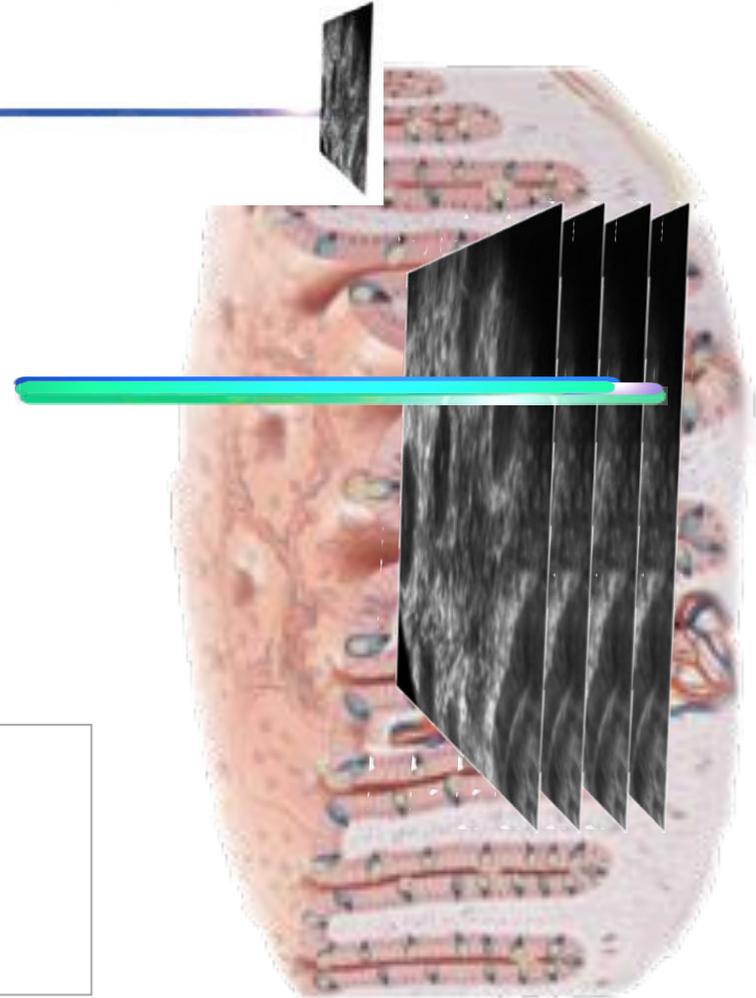
*It is about **seeing** histology*

Endomicroscopy

Mini probe



Standard endoscope



Field of view: $500 \times 500 \mu\text{m}$

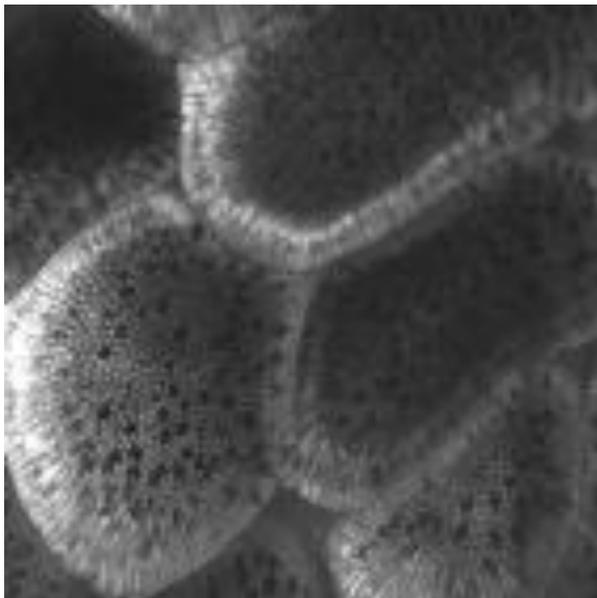
Range: $0\text{-}250 \mu\text{m}$

Lateral resolution: $<1 \mu\text{m}$

Endomicroscopy: Contrast agents

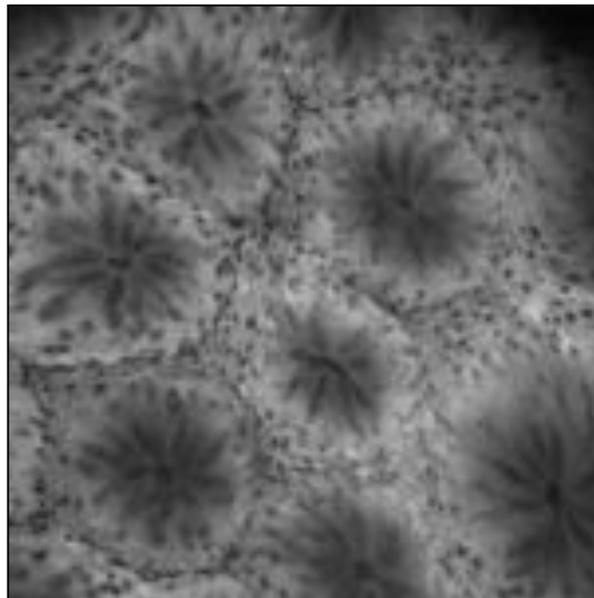
Acridavine

topical



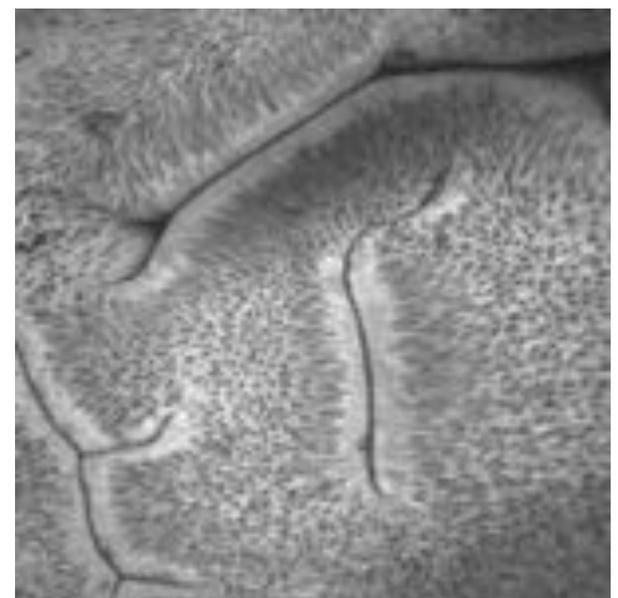
Fluorescein

systemic



Cresyl violet

topical



Kiesslich et al., Gastroenterology 2004

Wallace et al., APT 2010

Goetz et al. Gastrointest Endosc 2009

Normal colonic surface epithelium

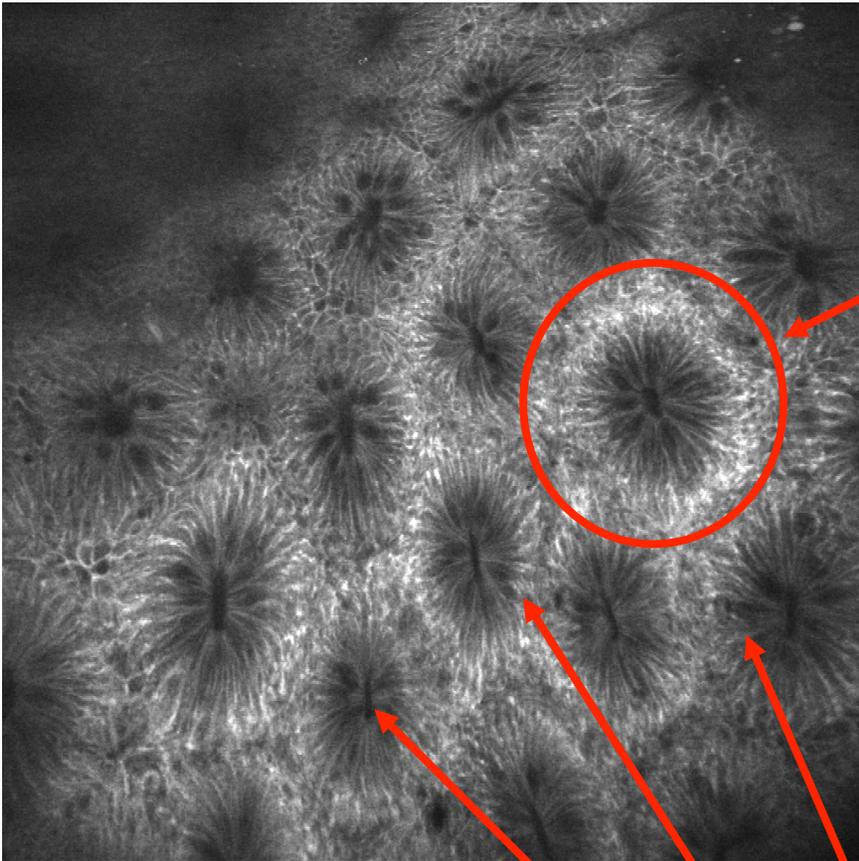
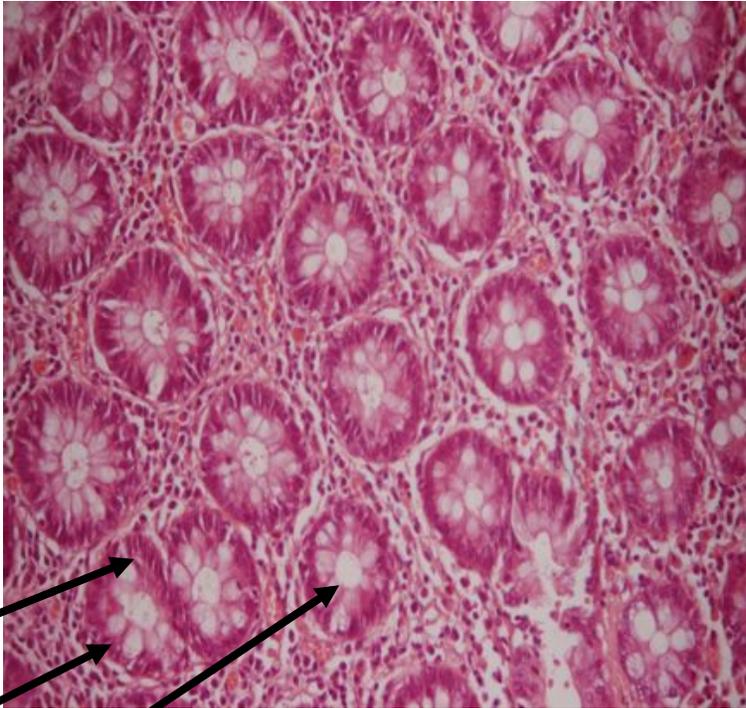


IMAGE CONTENT:
Single crypt on the mucosal surface, with dark luminal opening and mucus in the centre of each crypt.



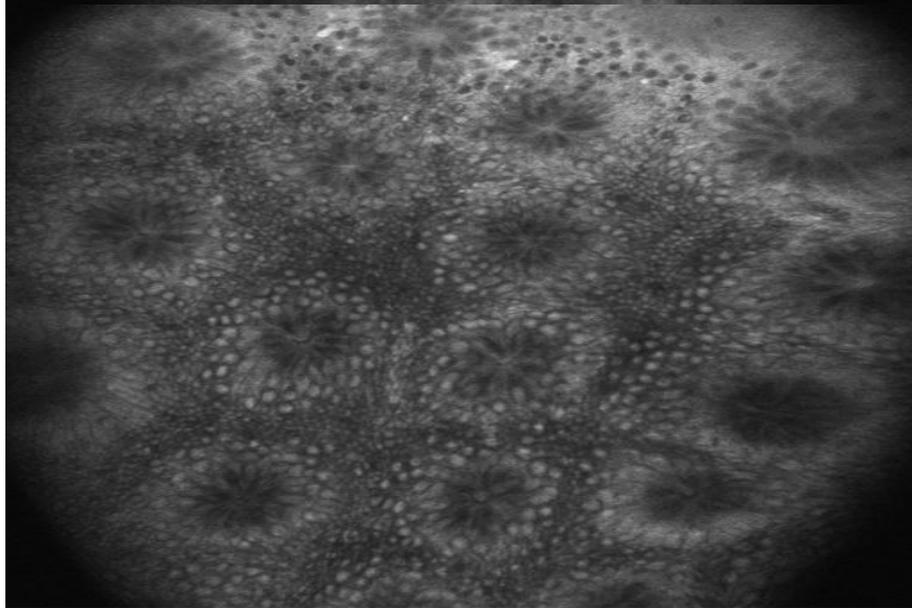
Goblet Cell
Columnar Epithelial Cell
Crypt Lumen

Confocal – colon

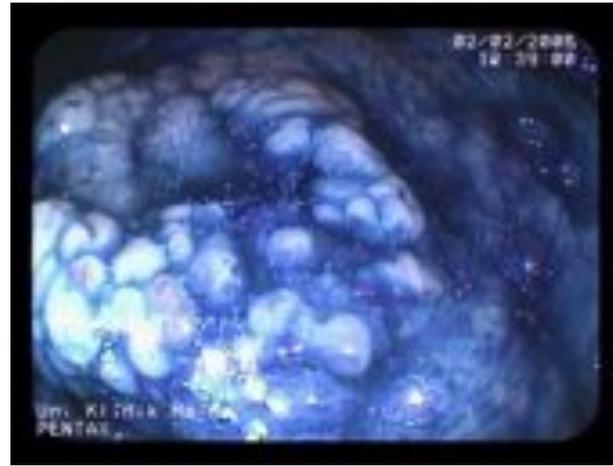
Normal crypt -daisy-



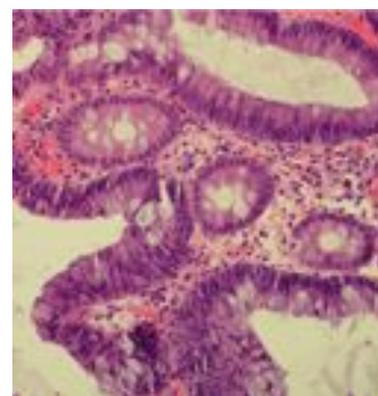
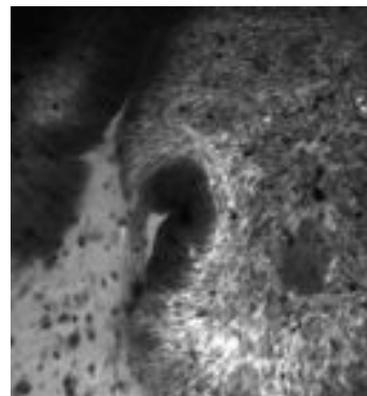
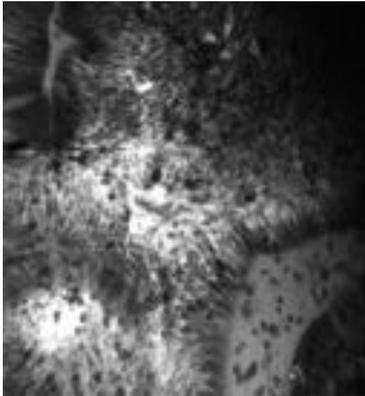
Blood cells in lamina propria vessels



Modern concept in ulcerative colitis

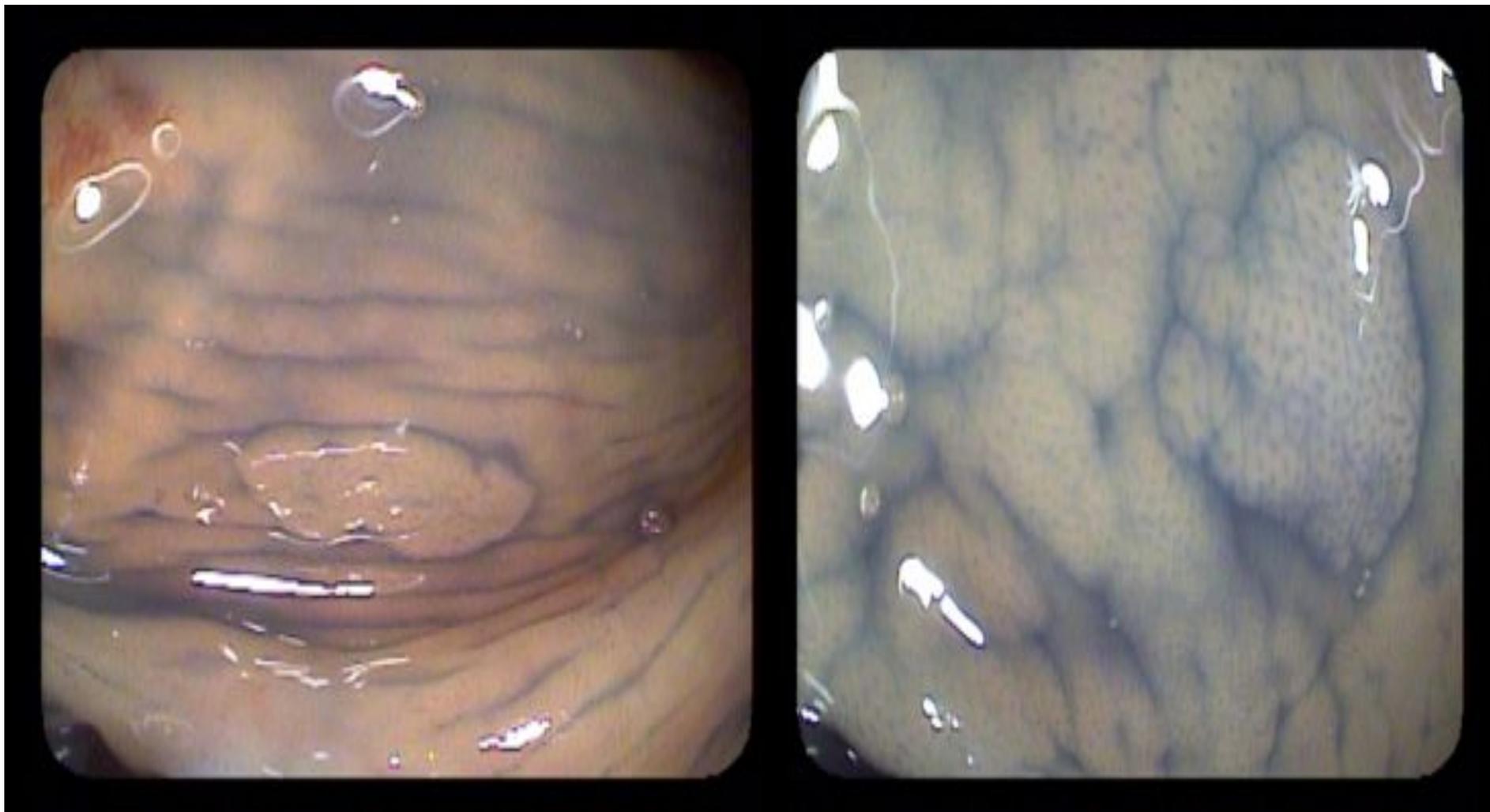


Chromoendoscopy
4-fold increased diagnostic
yield of intraepithelial
neoplasias

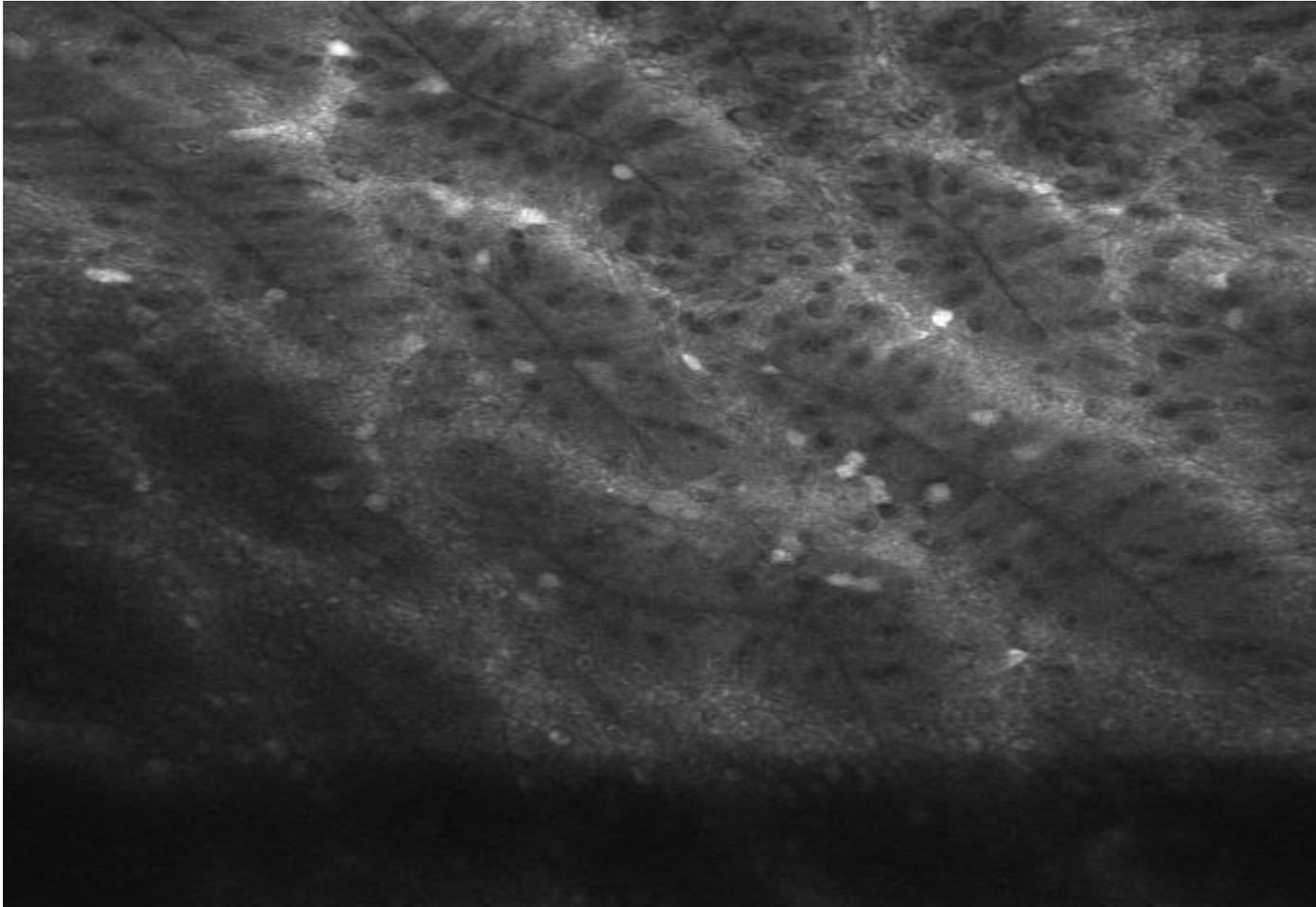


Endomicroscopy
10-times reduction of
biopsies per patient
~ 4 Bx/patient

Surveillance PSC-IBD patients



Adenoma polyp



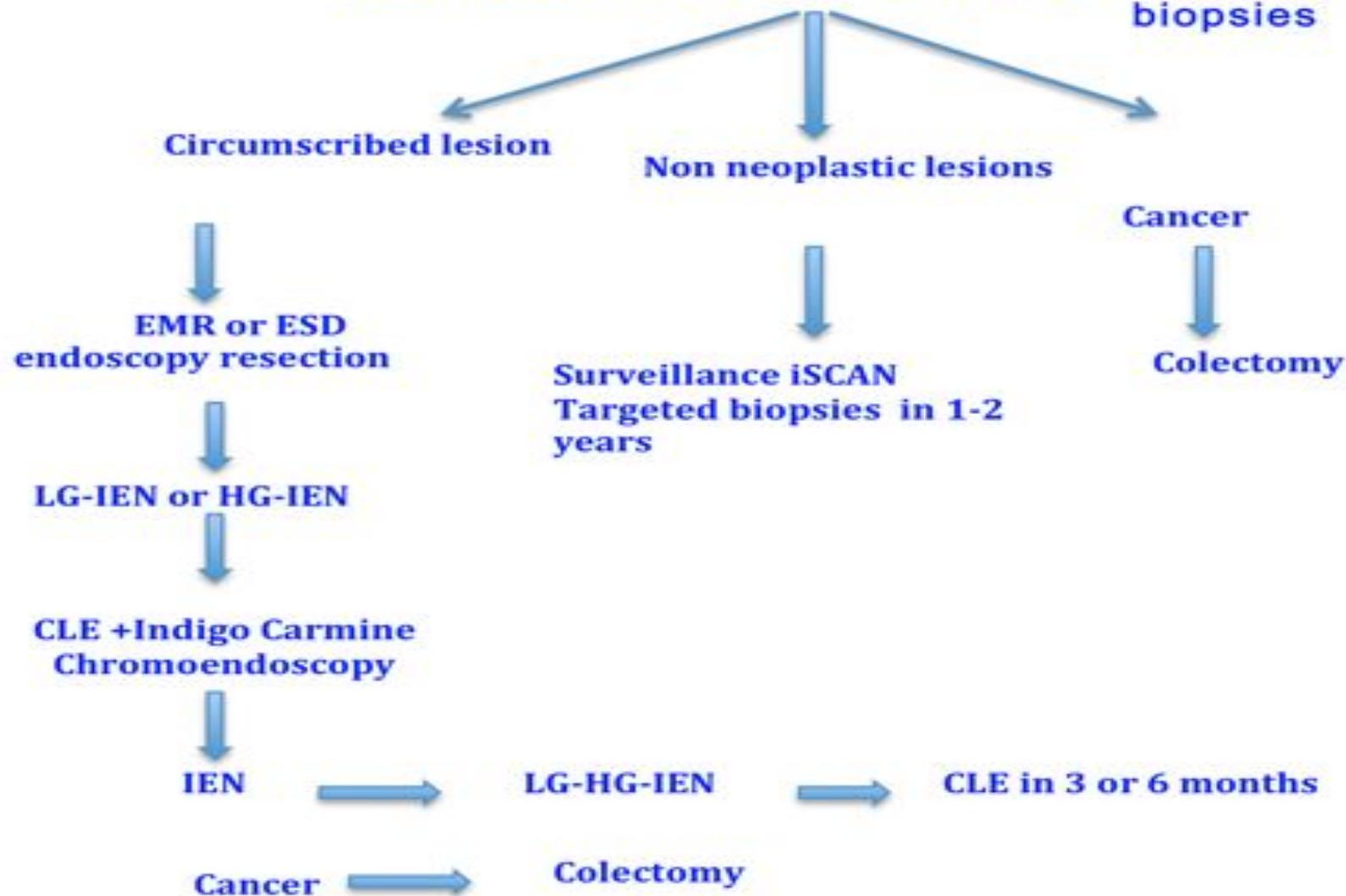
CHROMOENDOSCOPY IN COMBINATION WITH CLE IN IBD

Video On
Marietta_jacucci
COL

FUTURE ENDOSCOPIC APPROACH

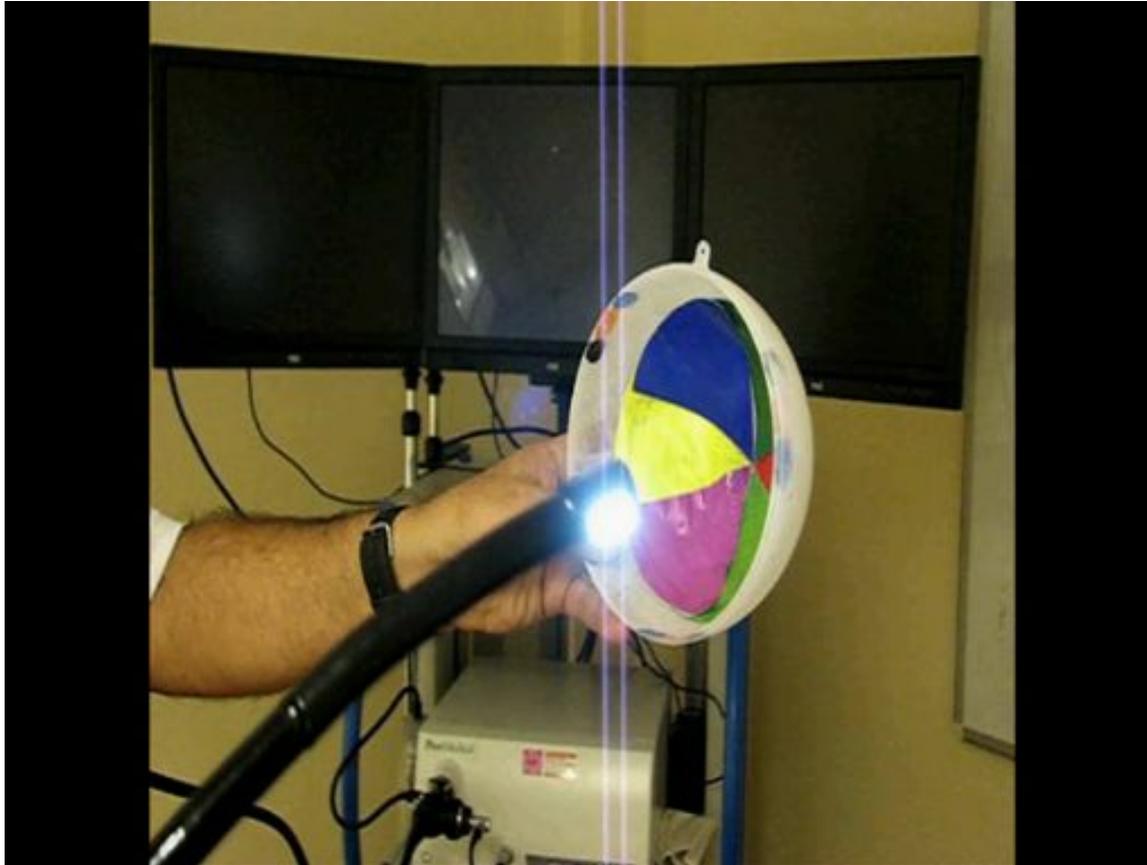
Surveillance in long standing IBD patients

High definition-iSCAN technique colonoscopy alone or in combination with Indigo carmine 0.2 % and targeted biopsies

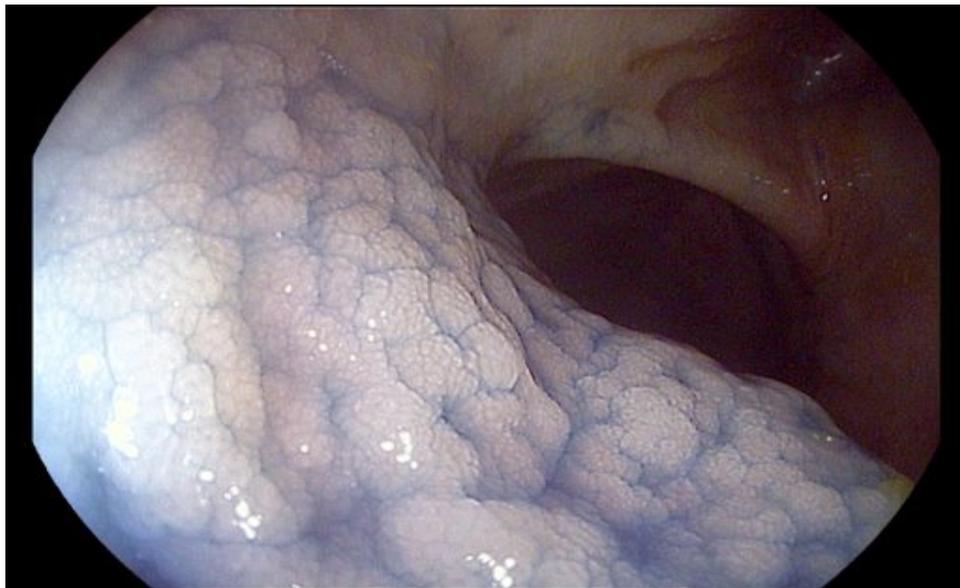
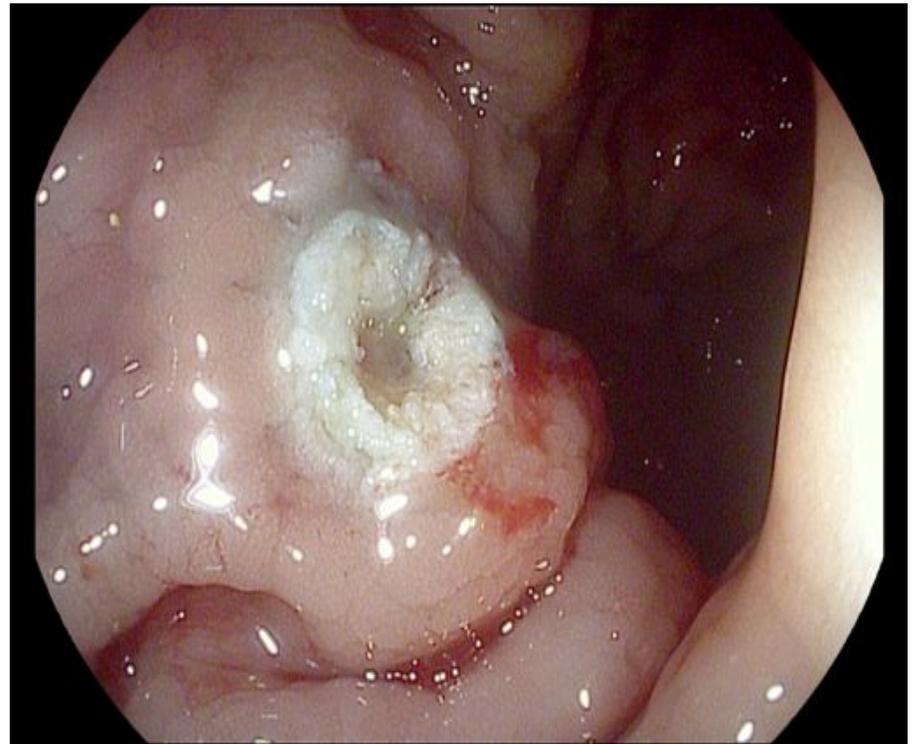
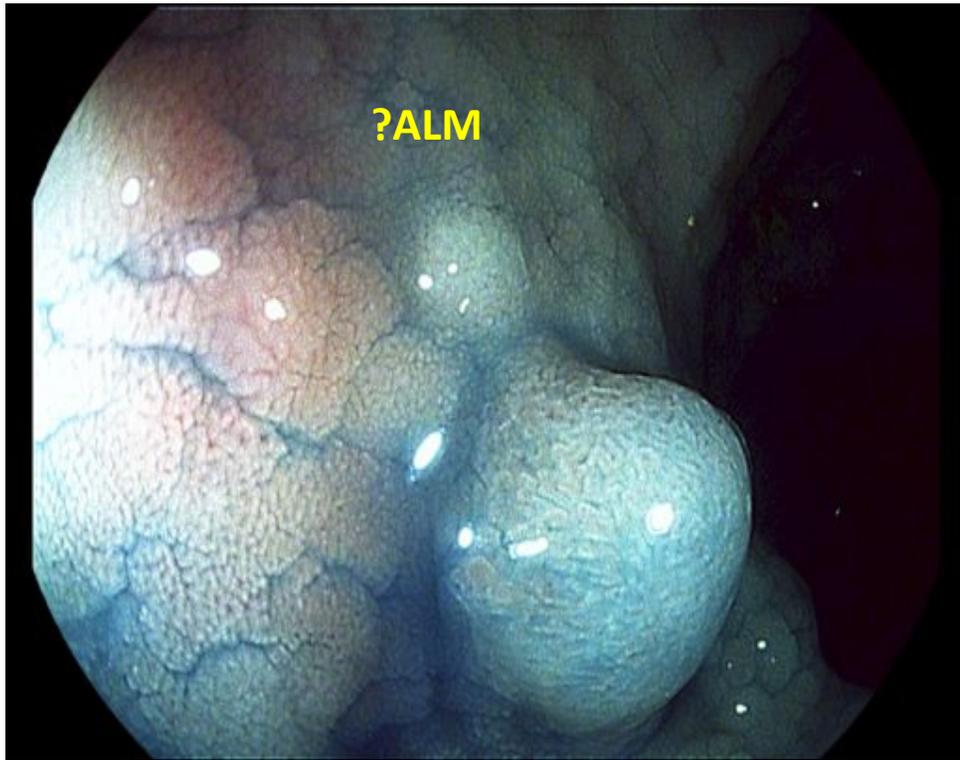


New colonoscope with 300° optics

Grainek et al. Endoscopy 2012, Abstract 385



Highlight UEGW ²⁰¹² - Amsterdam

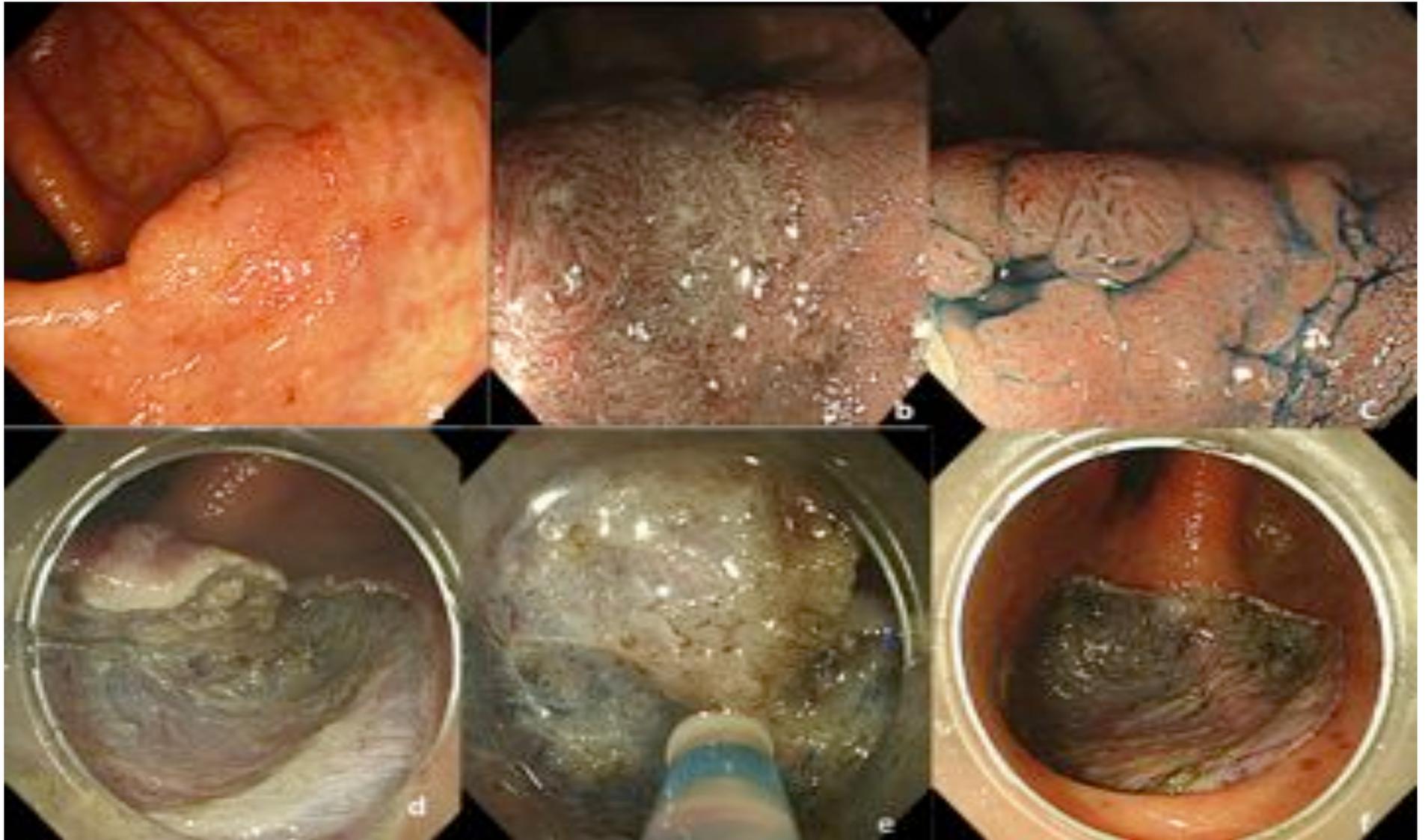


Endoscopic submucosal dissection: ESD TOOLS



Coagrasper

ESD TECHNIQUE



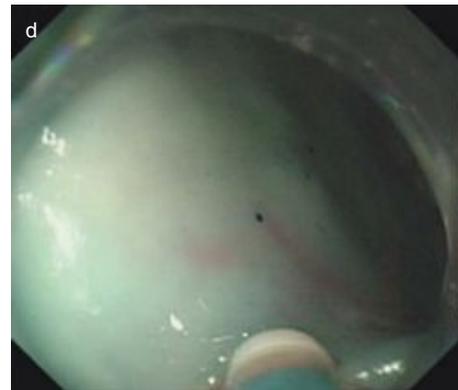
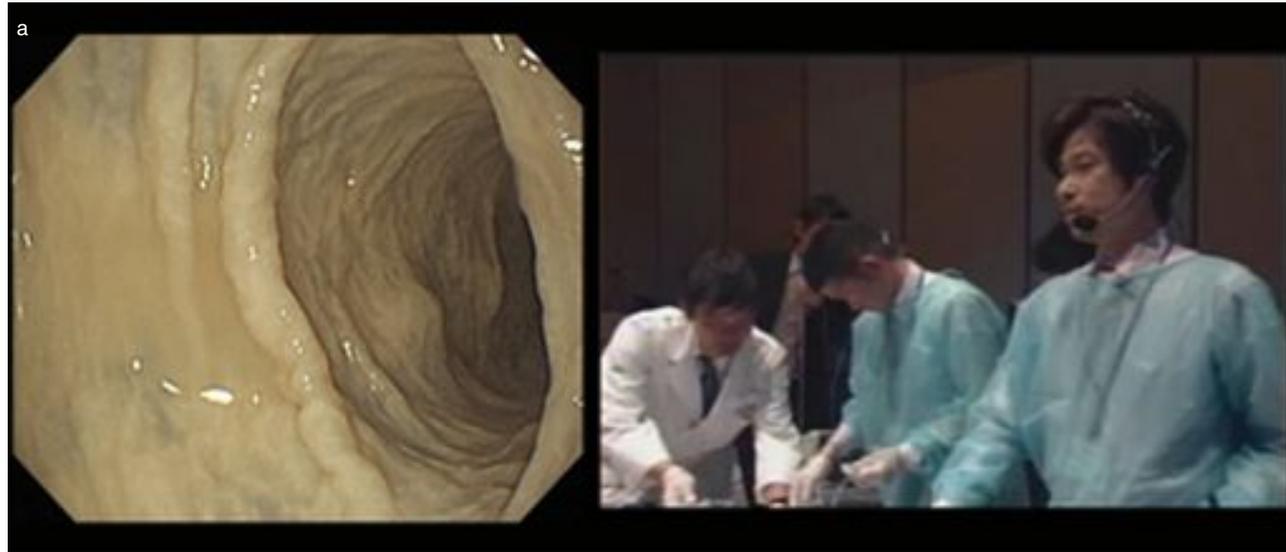
Step-by step

Before attempting CR-ESD

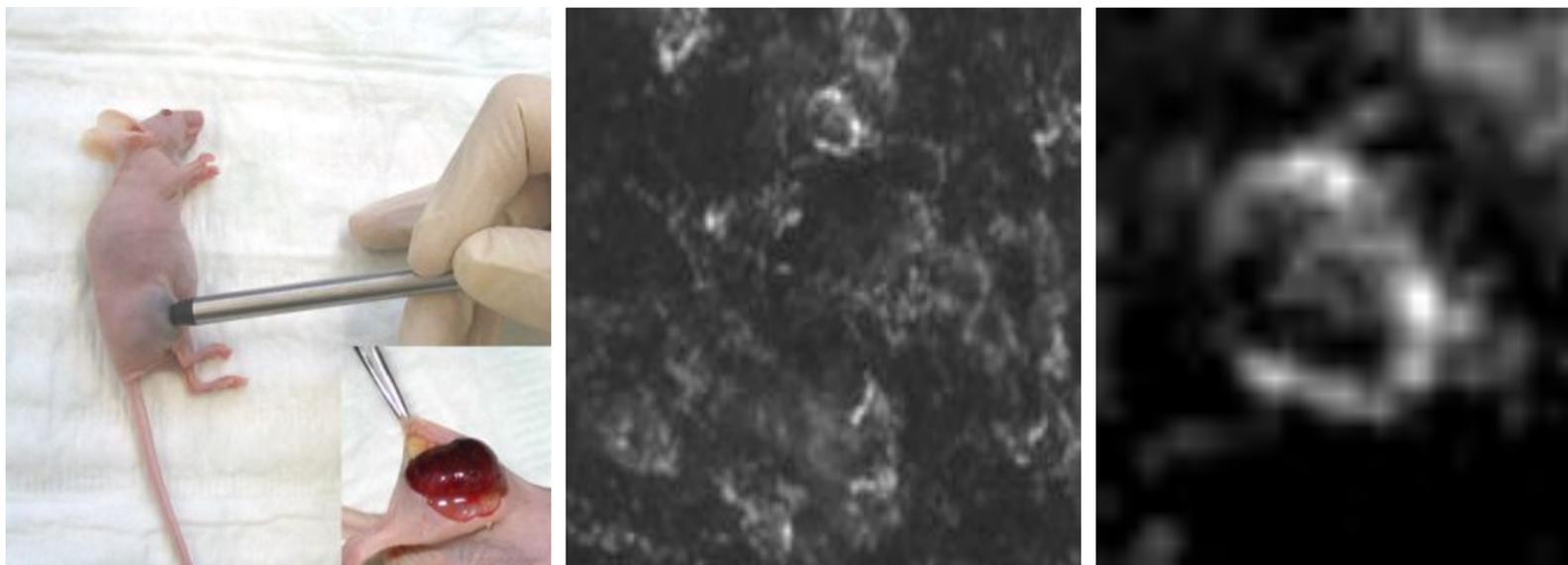
- Observe actual procedures performed by experts
- Training with isolated animal stomach and/or colon models
- ESD training using live pig with supervision by Japanese and western experts

Attempting CR-ESD

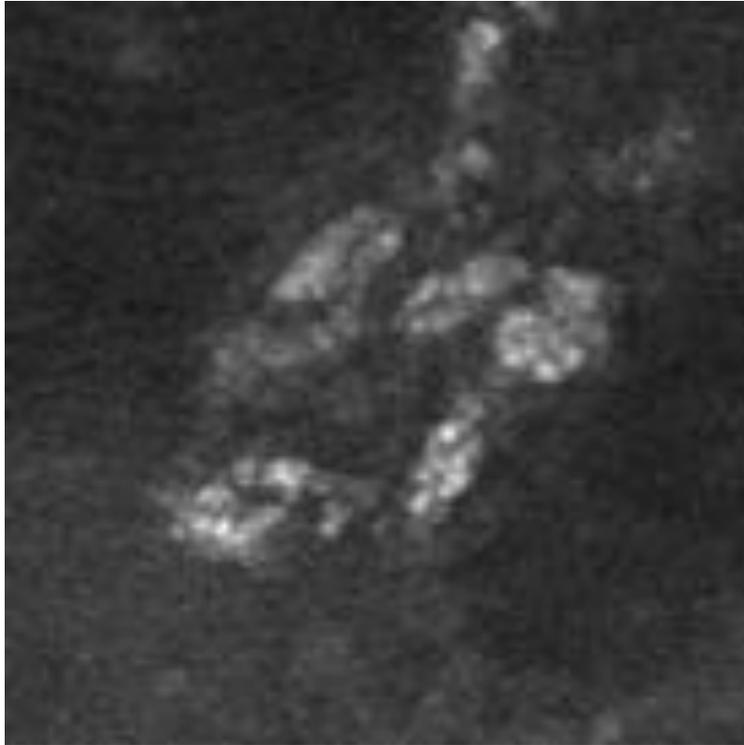
- Registration of all clinical CR-ESD cases
- Review of all CR-ESD procedures performed using video recordings and endoscopic photos
- Step-by-step progress in clinical cases
 1. LST-G 2–3 cm in diameter located in rectum[†]
 2. LST-G \geq 2–3 cm located in ascending, transverse, descending and sigmoid colon and flexures in order[†]



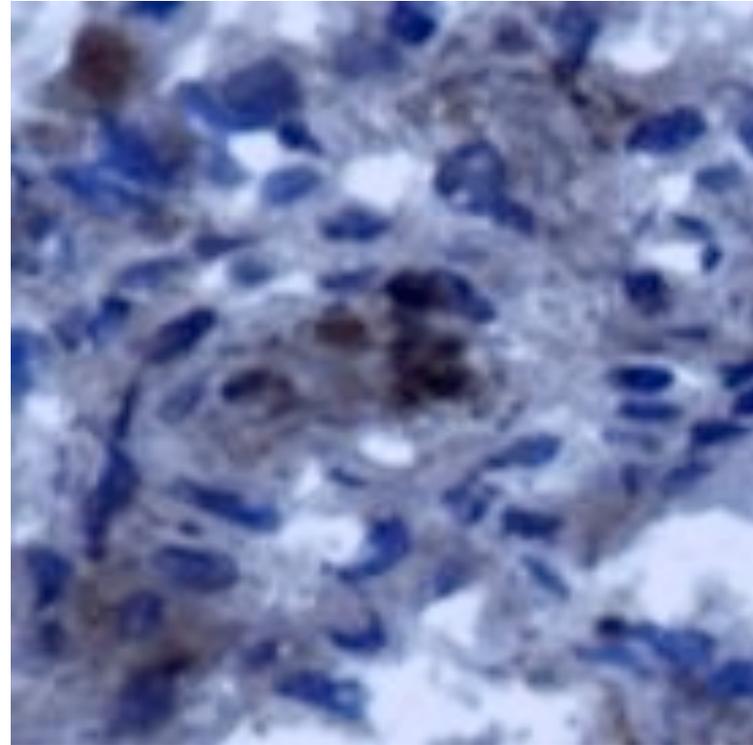
Molecular imaging - EGFR



Molecular imaging - VEGF

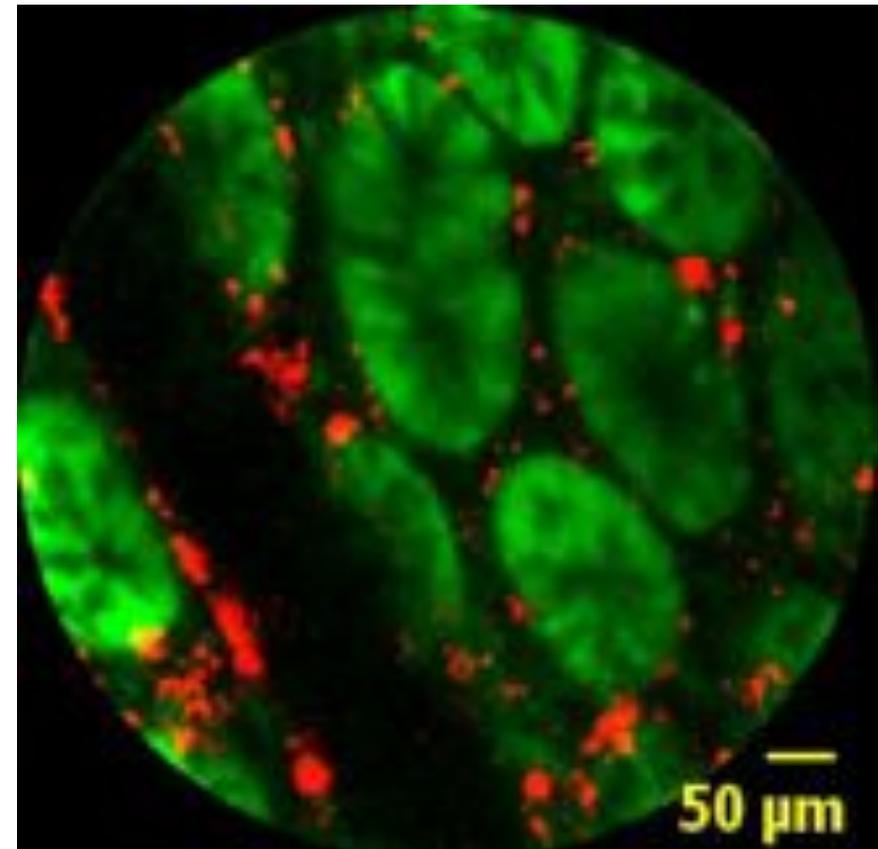
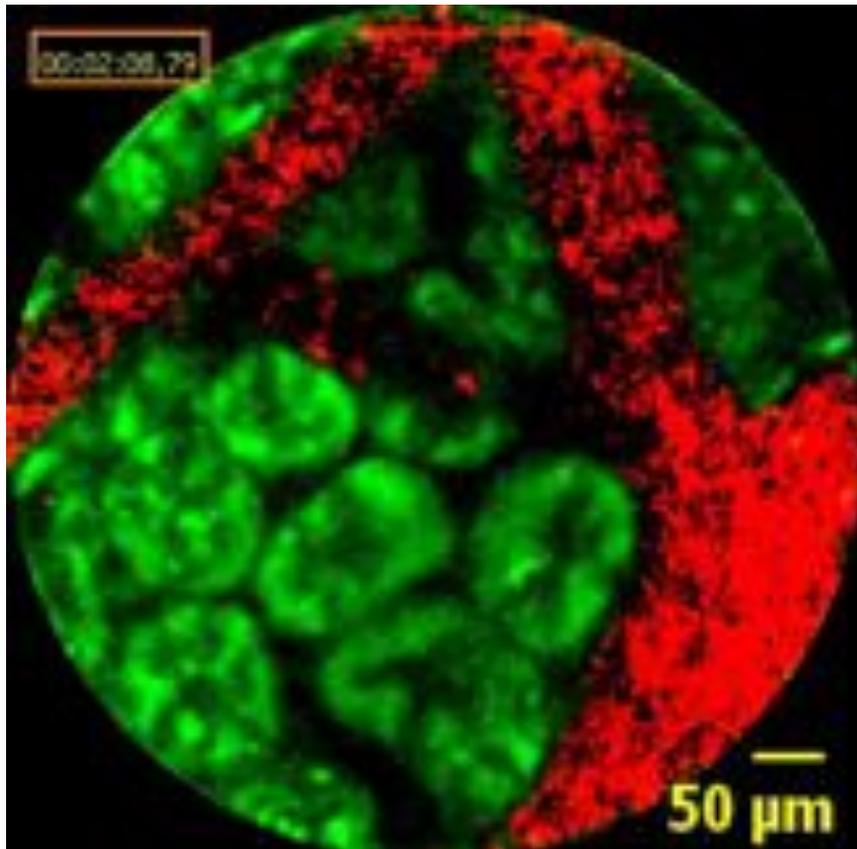


Endomicroscopy:
Anti-VEGF



Immune Histochemistry

Dual Band Endomicroscopy



Mouse Colon



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THANK YOU