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SCHOOL OF MEDICINE

Optical Biopsy of Colon Polyps

2016 PNWGS State-of-the-Art in Gastrointestinal Endoscopy Course

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Outline

- What is optical biopsy?
- Available modalities
- Applications to colon polyps
- Ready for practice?

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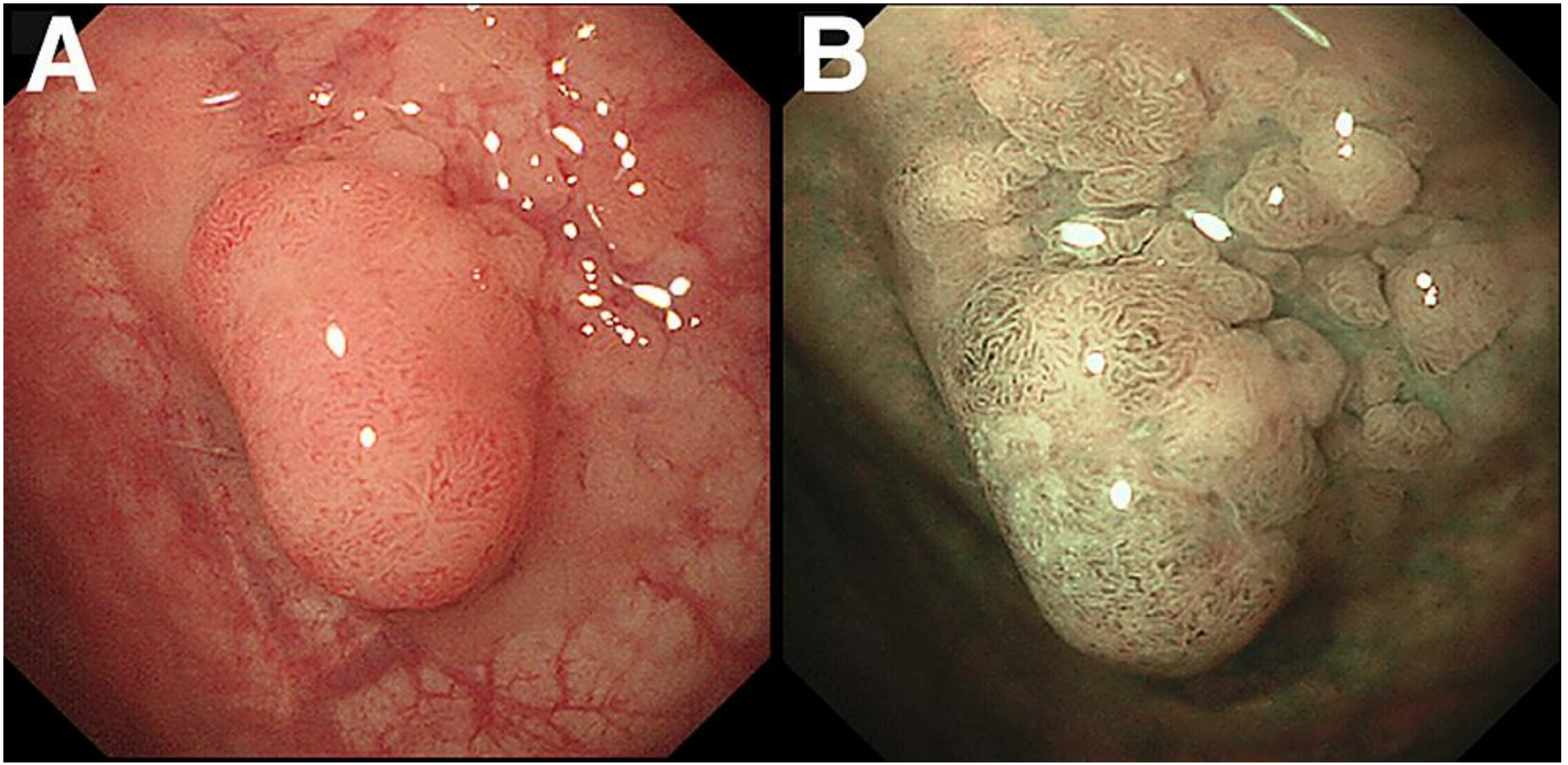
Optical biopsy

- Narrower definition: “histology through the endoscope”
  - Confocal laser endomicroscopy (CLE) approaches this the most
- Broader definition: “endoscopic features that *correlate* with histology”
  - *e.g.* “virtual chromoendoscopy” techniques

Optical biopsy of colon polyps

- What type of polyp is this?
  - Adenoma vs. hyperplasitc
  - Sessile serrated
- “High grade” features?
  - High grade dysplasia?
  - Malignancy?
- Extent of involvement / adequacy of resection

Lateral spread: HD white light vs. NBI



Subramanian and Ragunath, CGH 2014, 12:368

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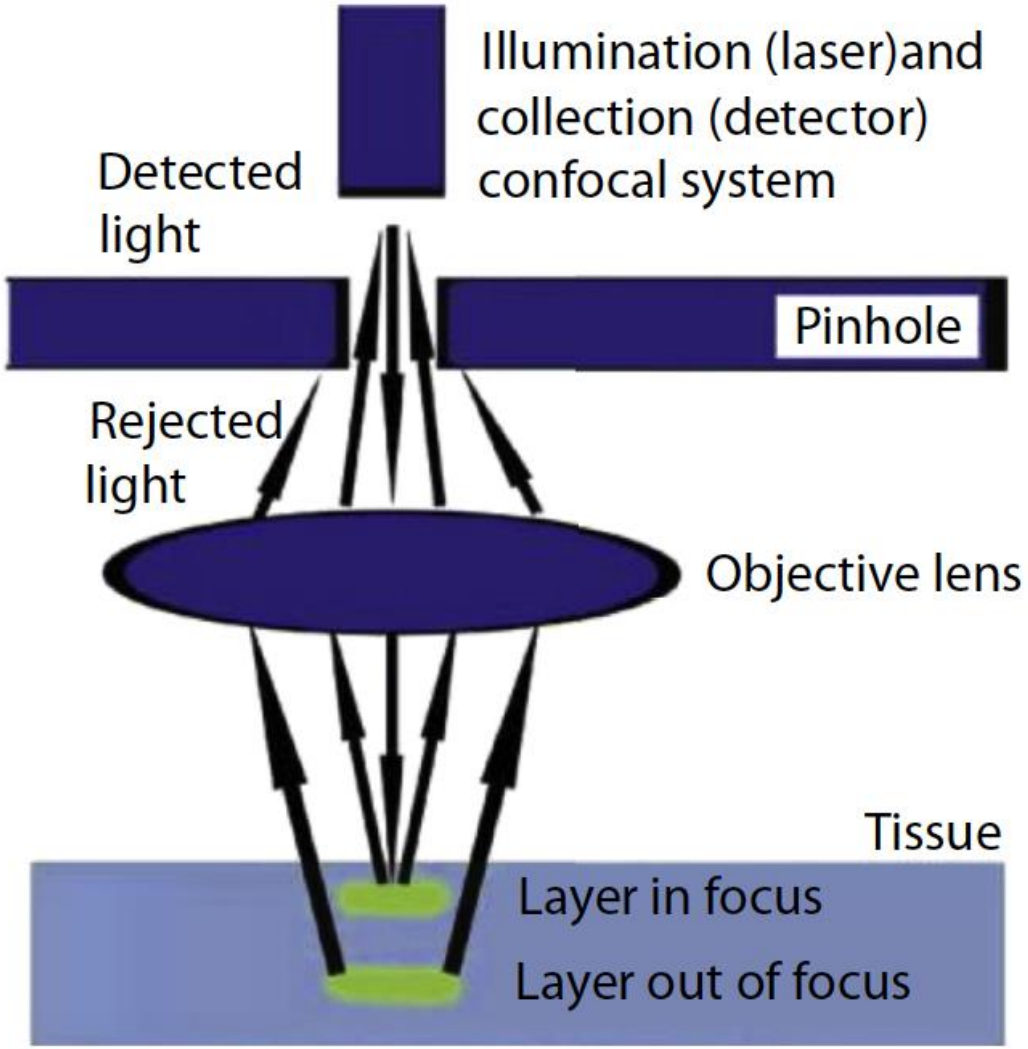
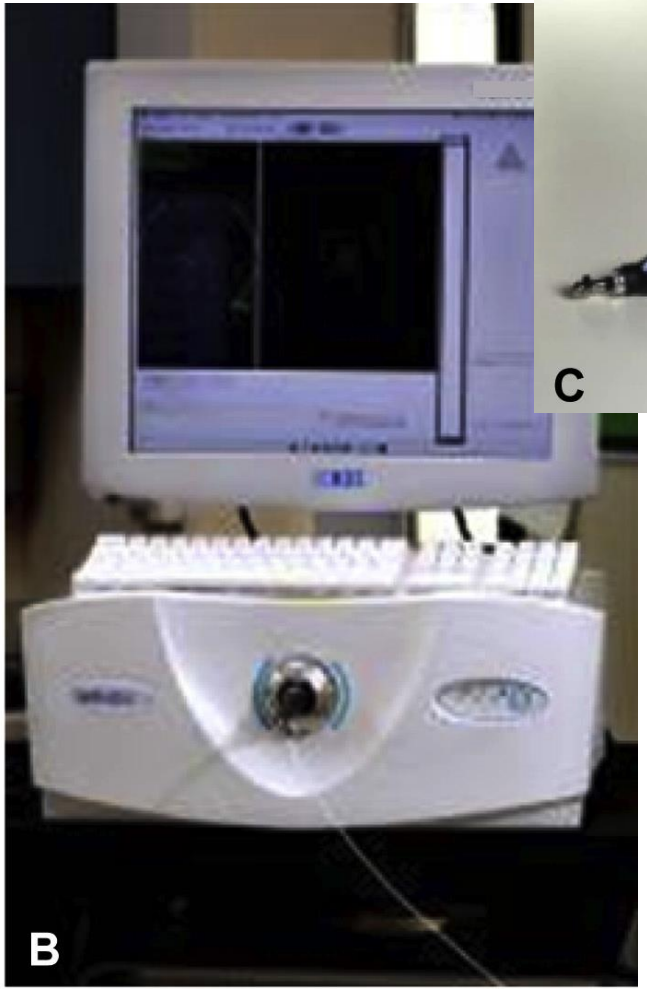
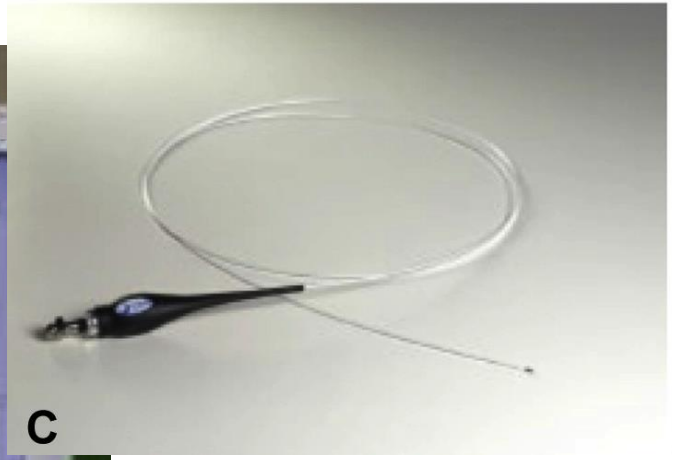
Confocal laser endomicroscopy



ASGE, GIE 2014, 80(6):928

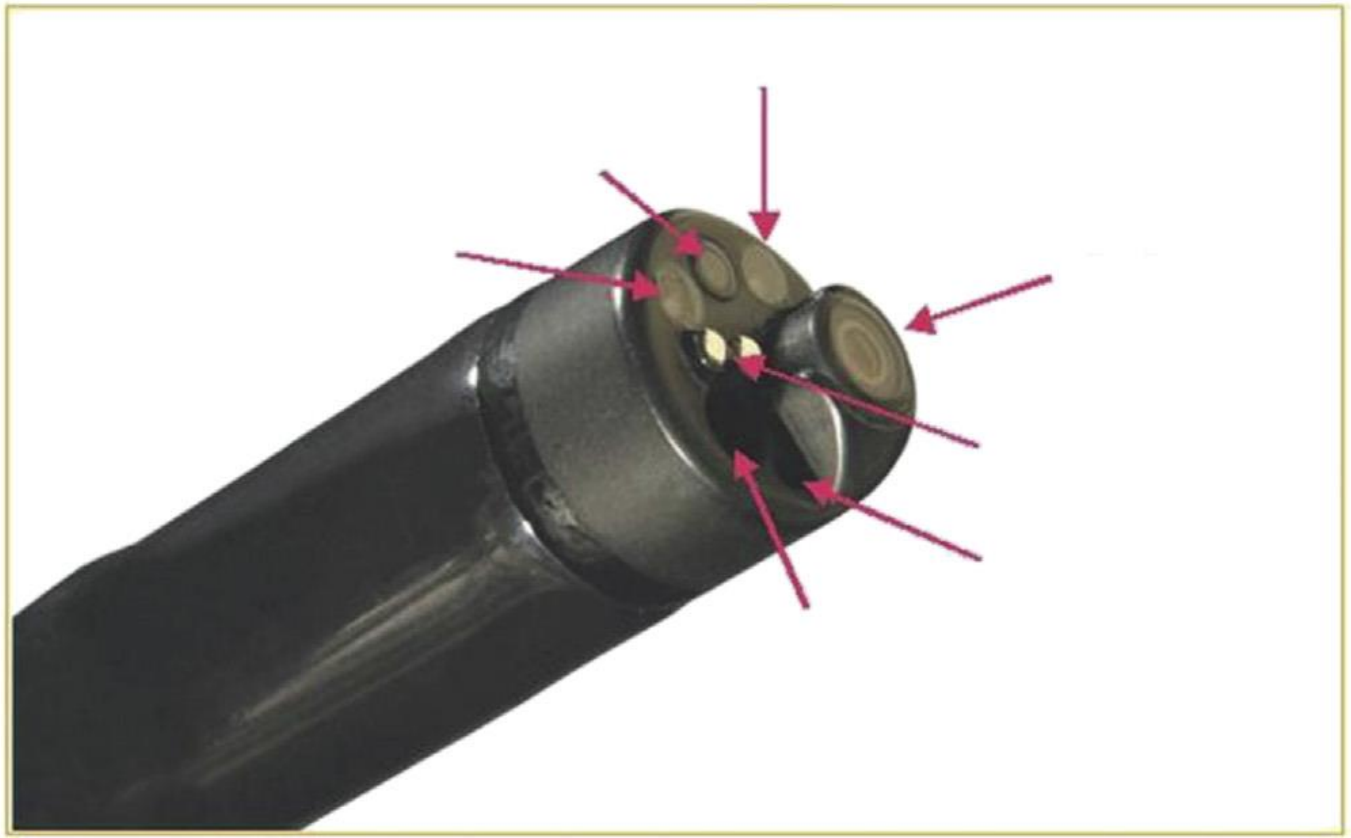
Confocal laser endomicroscopy – probe





ASGE, GIE 2014, 80(6):928

Confocal laser endomicroscopy – scope

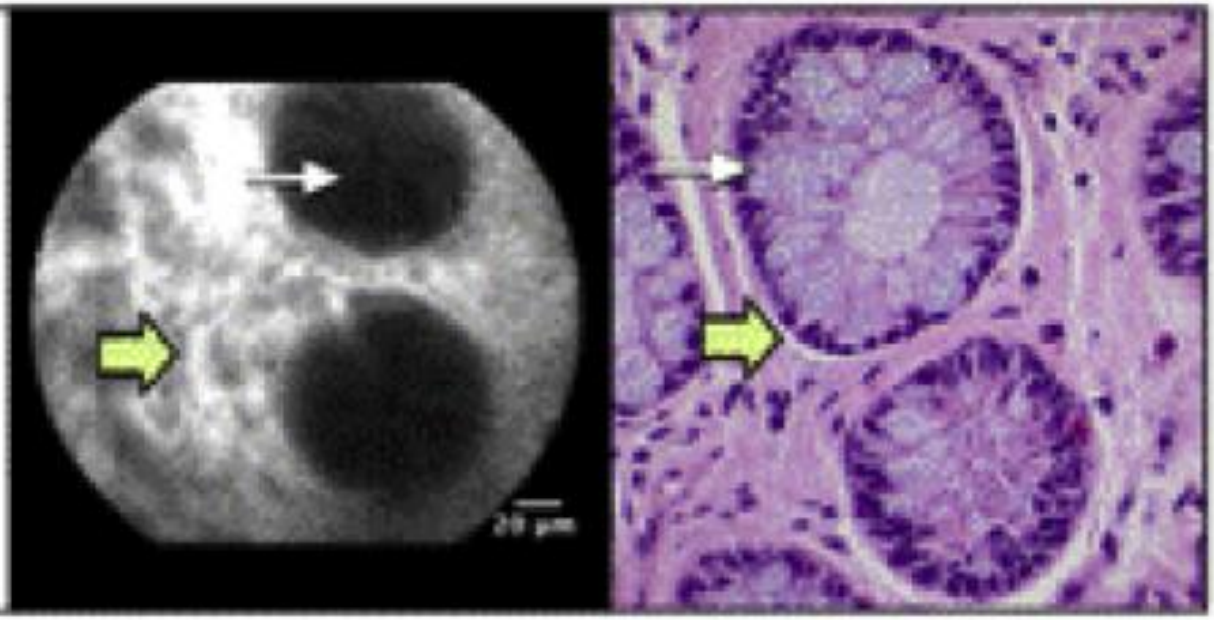


ASGE, GIE 2014, 80(6):928

Confocal laser endomicroscopy

Normal Colon

- Round crypt structures
- Dark goblet cells (arrow)
- Regular, narrow vessels surrounding crypts (block arrow)

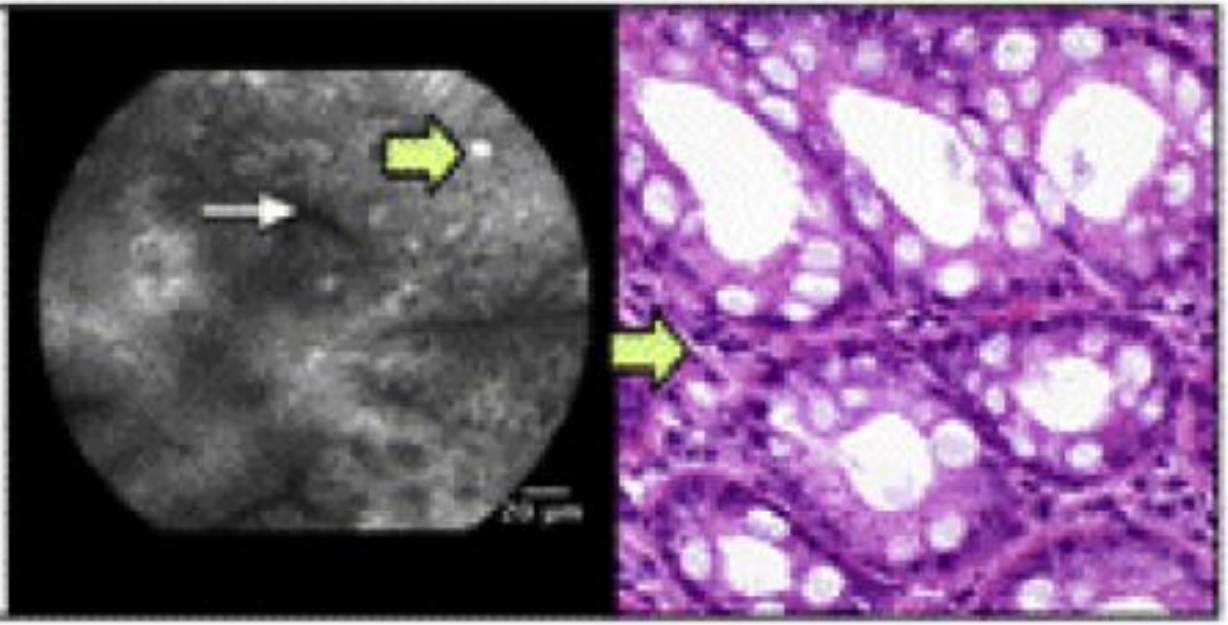


ASGE, GIE 2014, 80(6):928

Confocal laser endomicroscopy

Hyperplastic Polyp

- Crypts with slit or stellate openings (pits)
- Bright non-thickened, uniform epithelium
- Dark "goblet" cells (thin arrow)
- Small vessels (block arrow)

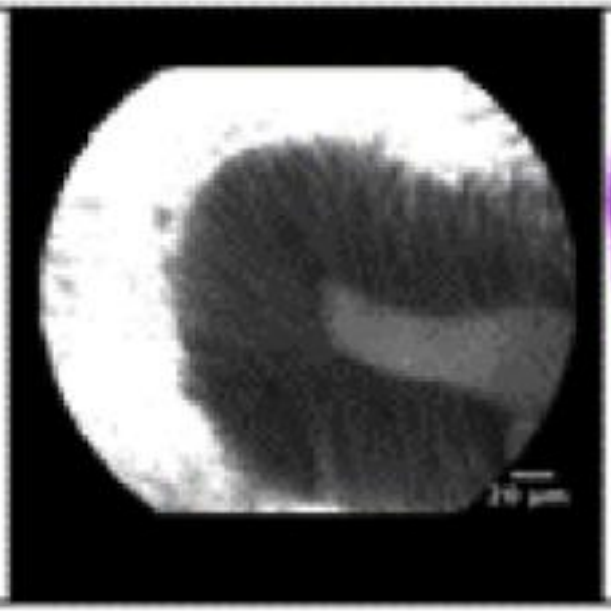


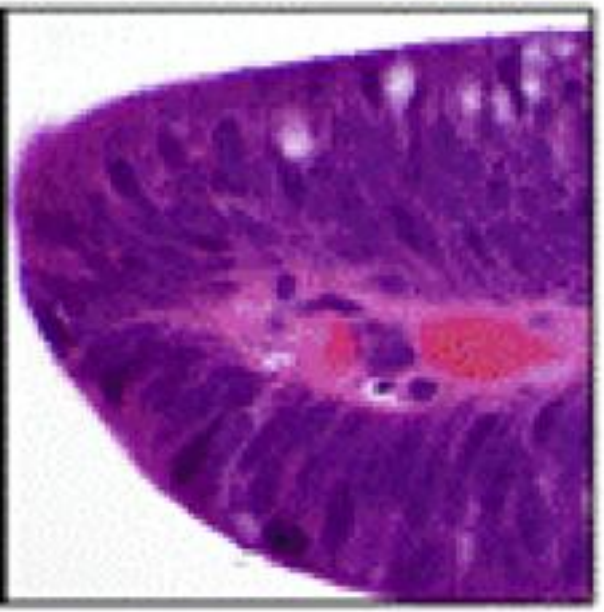
ASGE, GIE 2014, 80(6):928

Confocal laser endomicroscopy

Adenoma

- Irregular or villiform structure (note even "tubular" adenoma may have villiform structure on pCLE)
- Dark, irregularly thickened epithelium
- Decreased goblet cells



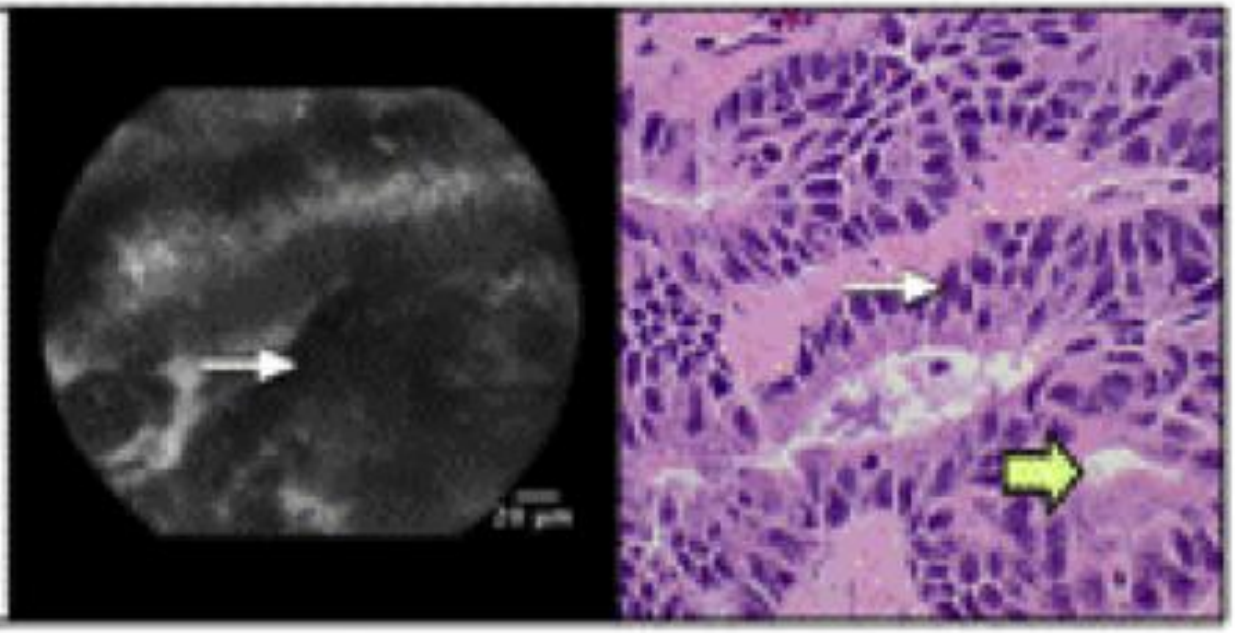


ASGE, GIE 2014, 80(6):928

Confocal laser endomicroscopy

Adenocarcinoma

- Disorganized villiform or lack of structure
- Dark, irregurlarly thickened epithelium (thin arrow)
- Dilated vessels (block arrow on H&E)



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Optical biopsy

- Narrower definition: “histology through the endoscope”
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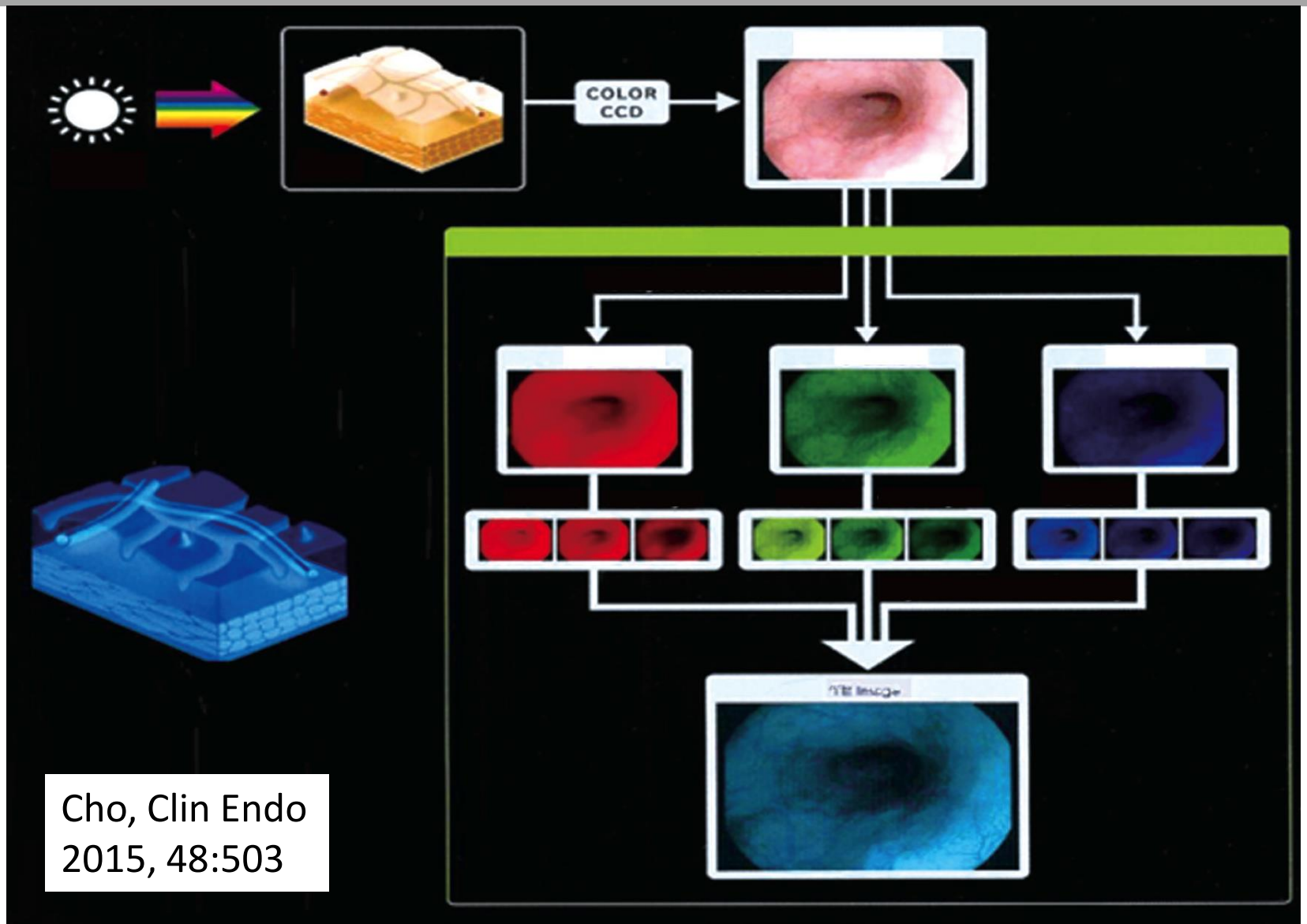
Electronic Chromoendoscopy

- Selected wavelength tissue-light interaction
- Software post-image processing
  - i-SCAN (PENTAX Endoscopy)
  - Flexible spectral imaging color enhancement (FICE) (Fujinon)
- Endogenous autofluorescence
  - Aurofluorescence imaging (AFI) (Olympus)
- Optical filtering of white light
  - Narrow-band imaging (NBI) (Olympus)

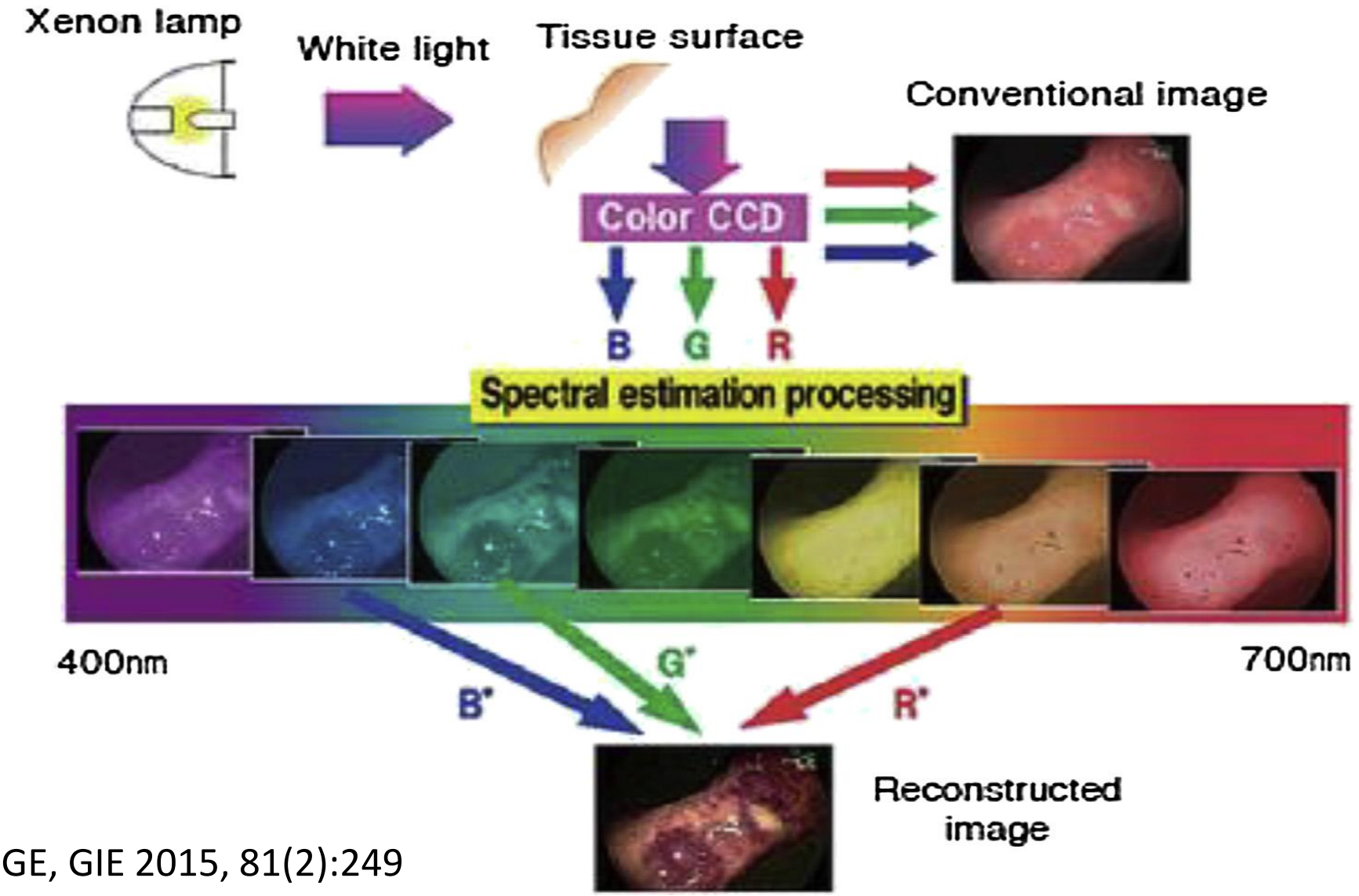
ASGE, GIE 2015, 81(2):249

Tone enhancement (i-Scan)



Cho, Clin Endo 2015, 48:503

FICE



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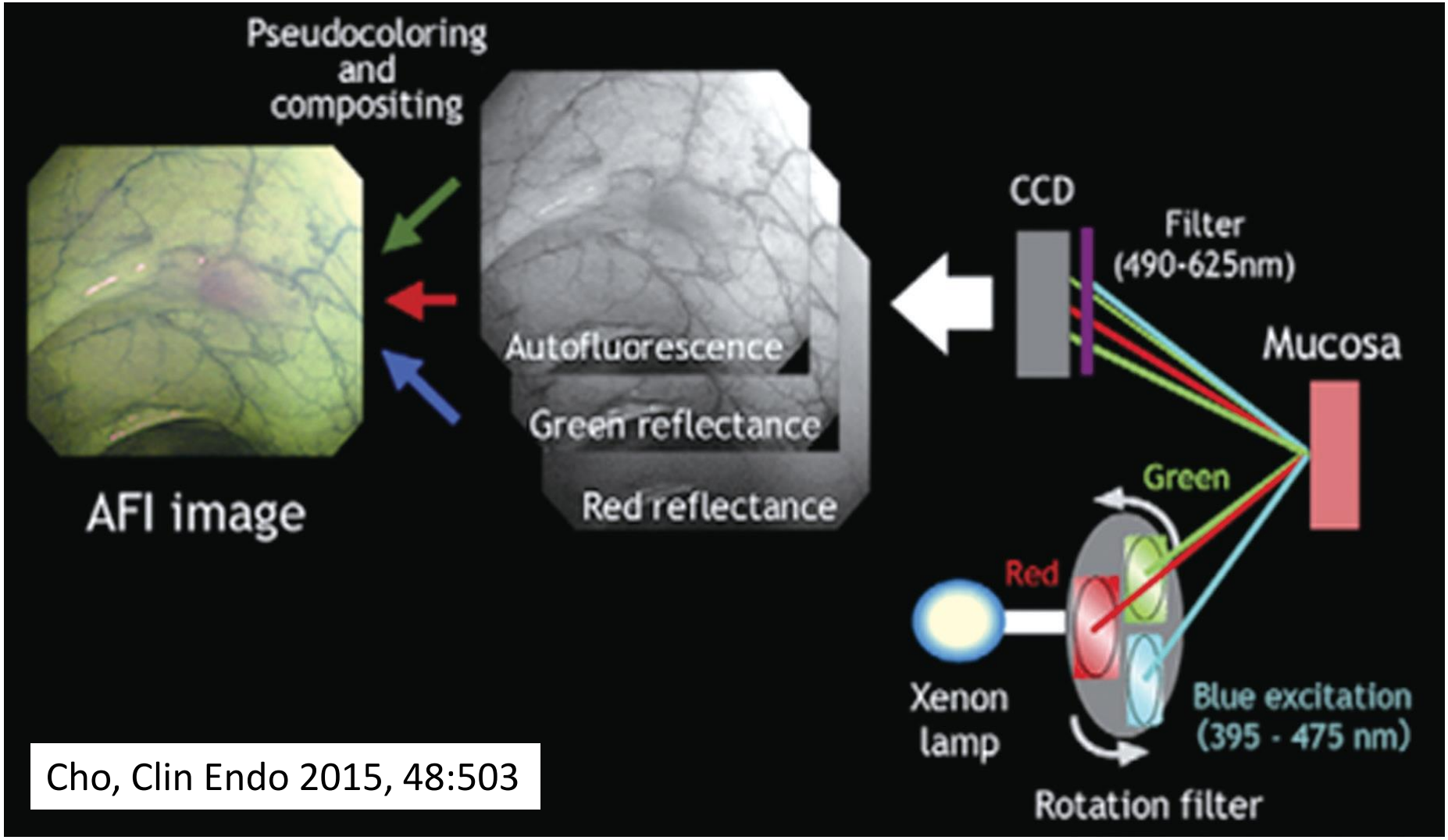
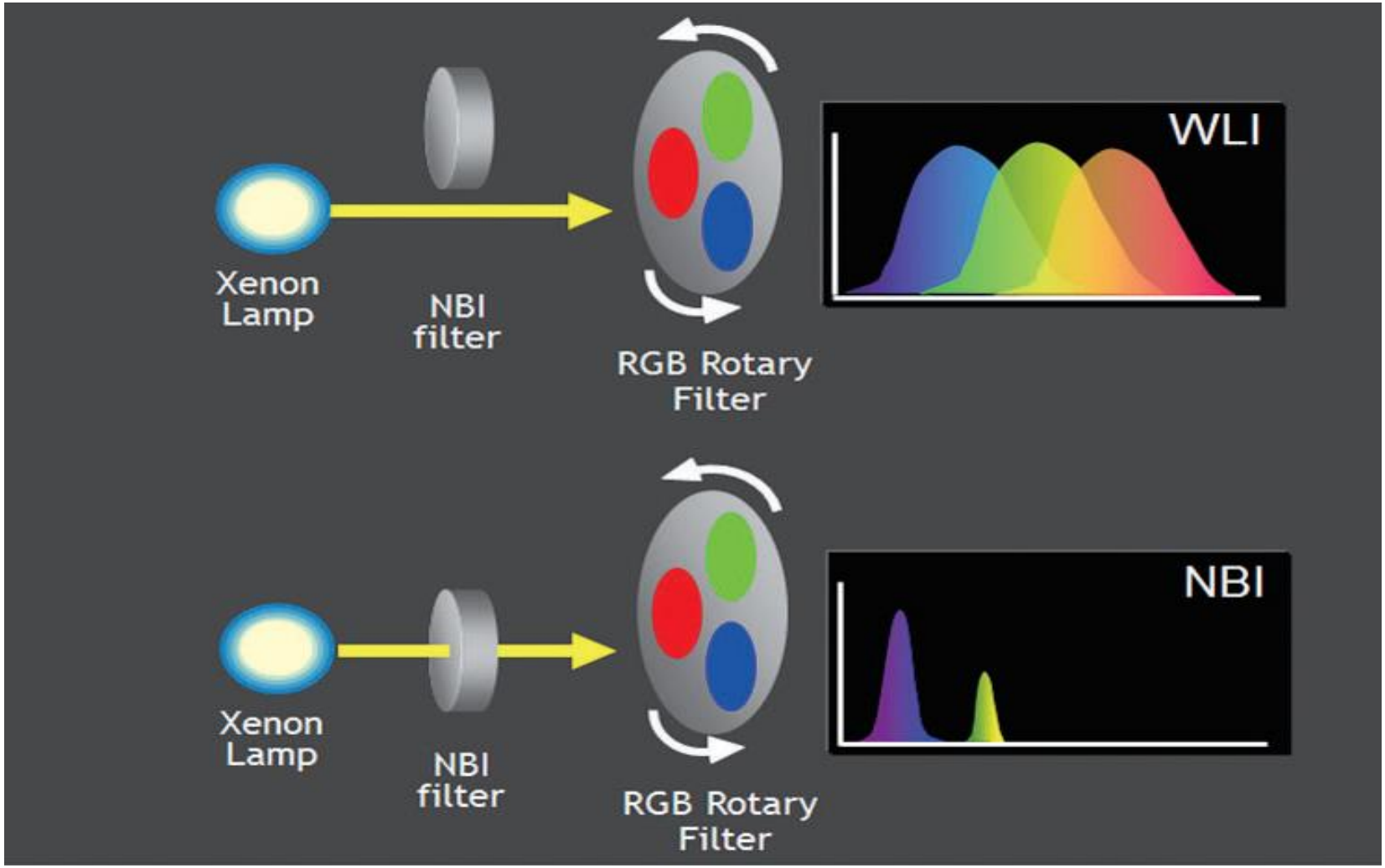
Autofluorescence imaging



Cho, Clin Endo 2015, 48:503

Narrow band imaging (NBI)



Gono, Clin Endo 2015, 48:476

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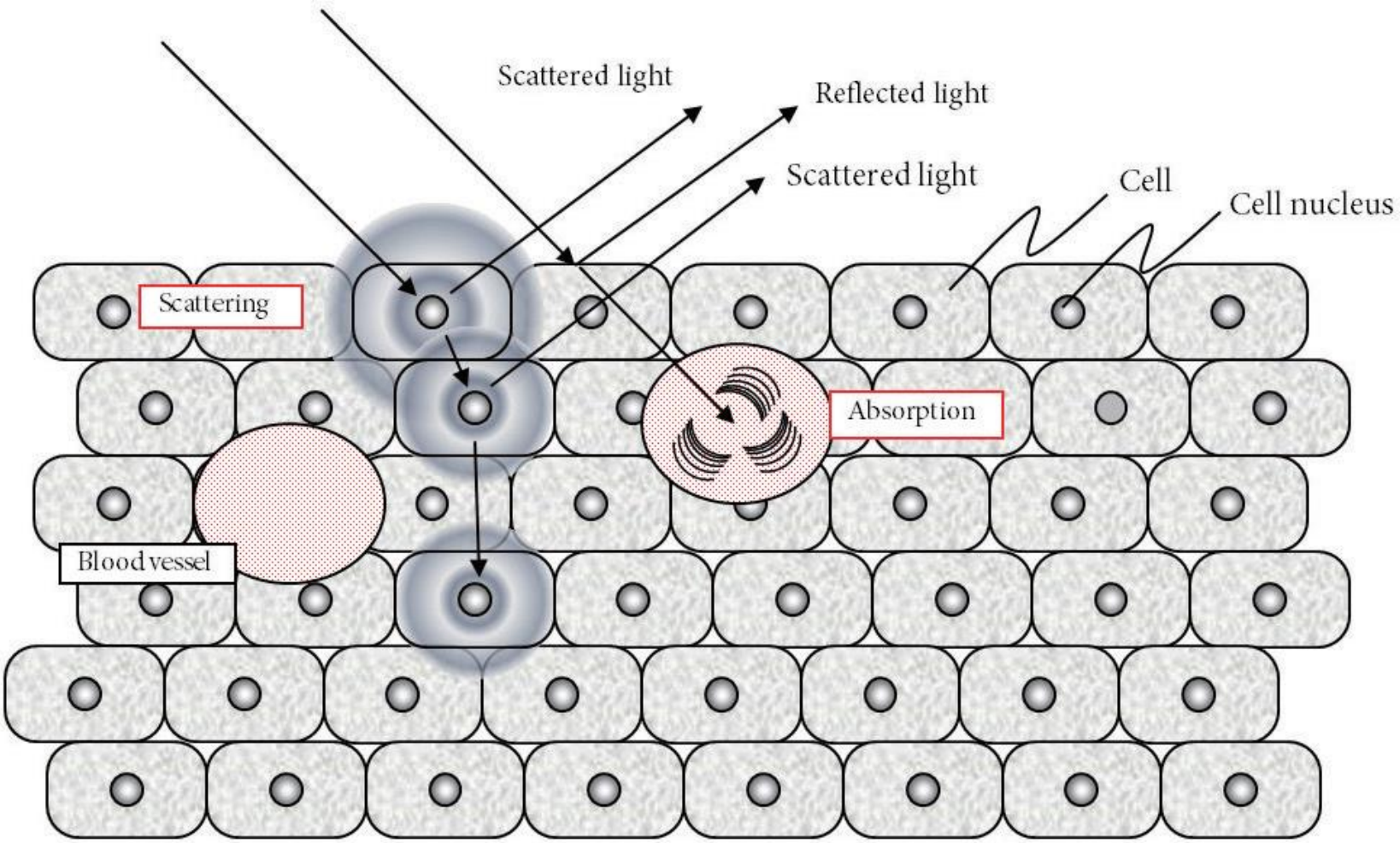
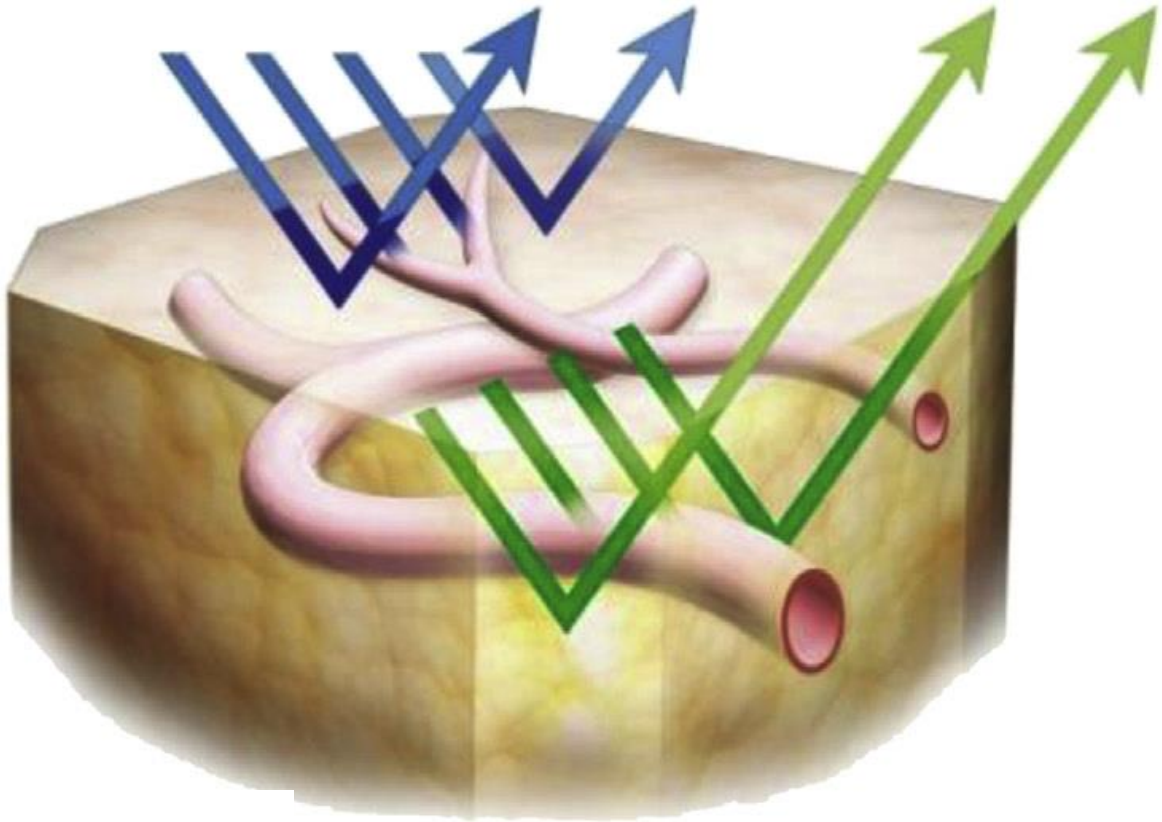
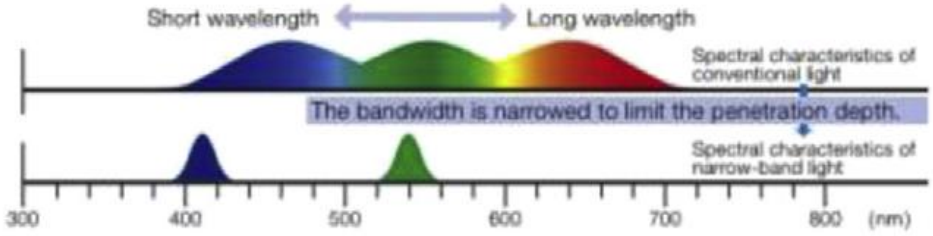


Gono, Clin Endo 2015, 48:476

Narrow band imaging (NBI)

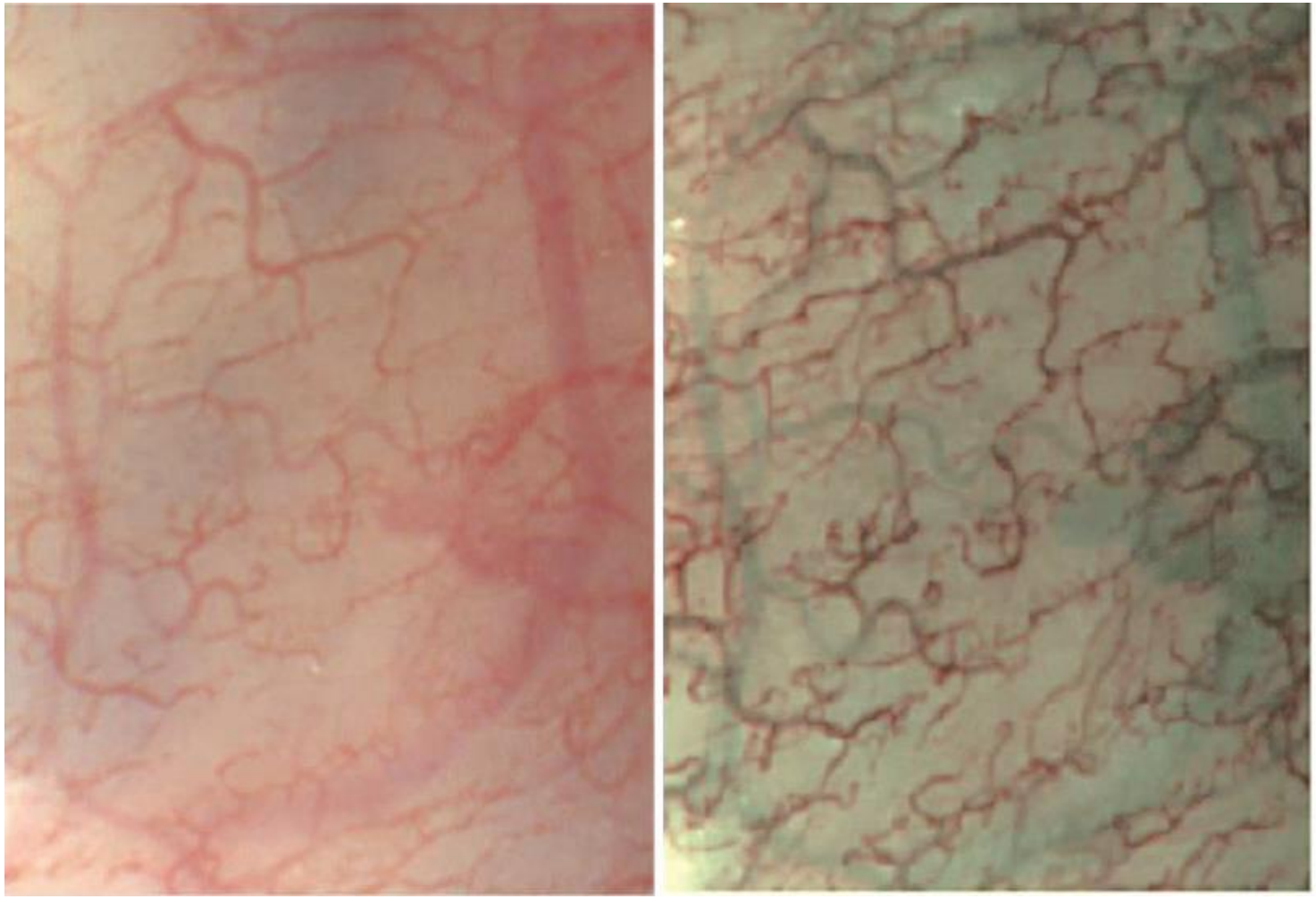
- Penetration properties of light ≈ wavelength





ASGE, GIE 2015, 81(2):249

Tongue: White light vs. NBI



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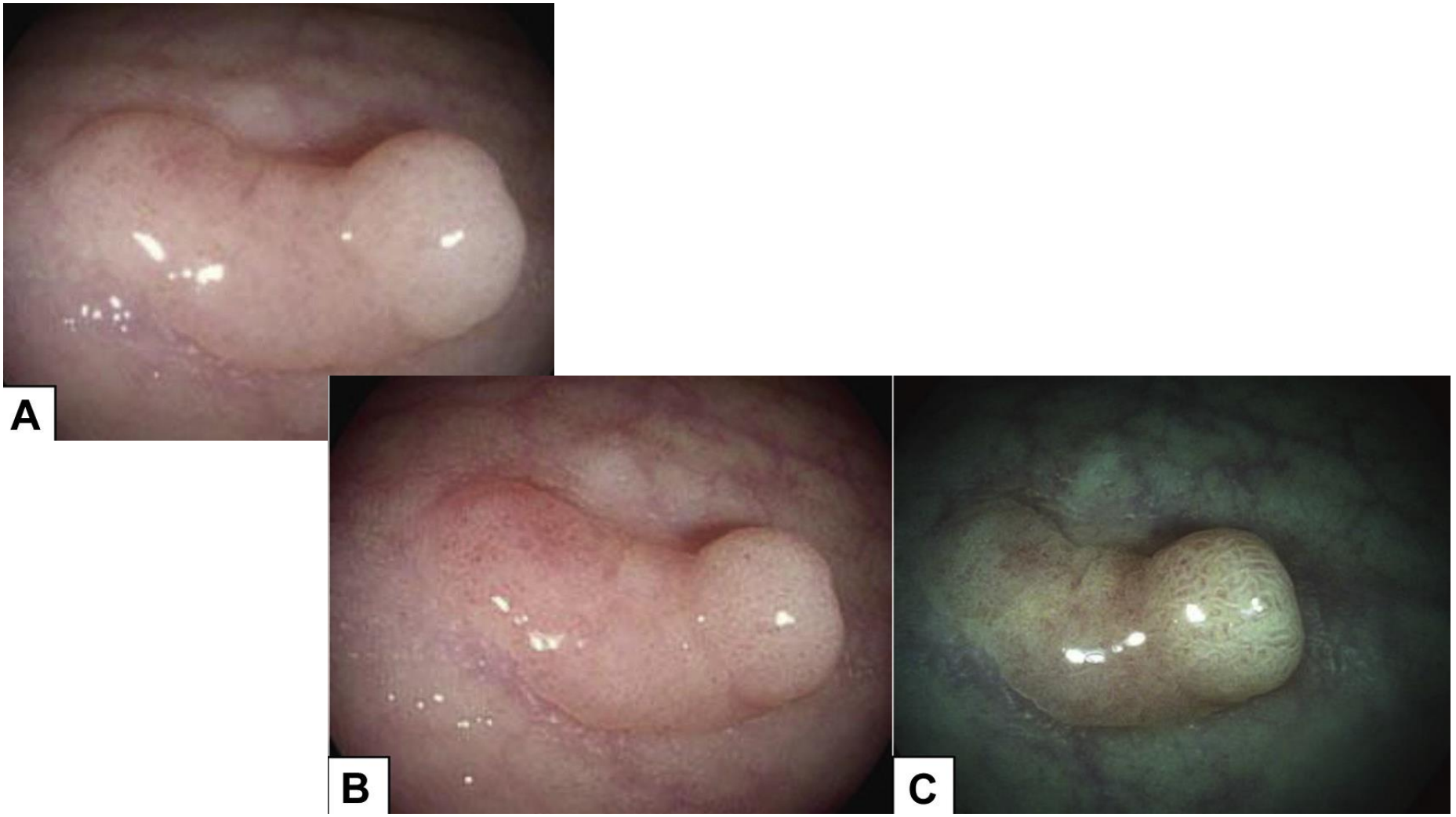
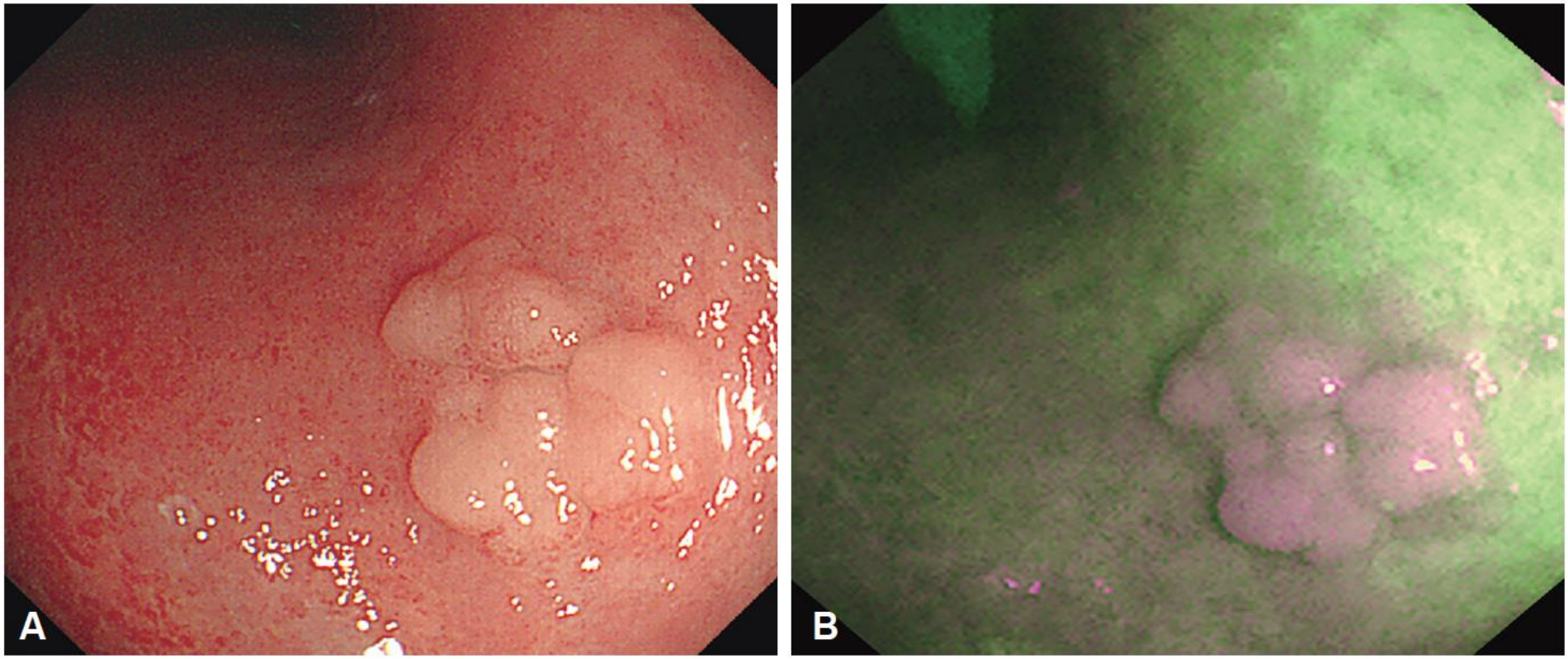
  - Adenoma vs. hyperplasitc
  - Sessile serrated
- “High grade” features?
  - High grade dysplasia?
  - Malignancy?
- Extent of involvement / adequacy of resection

Adenoma: White light vs. i-SCAN 1 and 2



ASGE, GIE 2015, 81(2):249

Adenoma: White light vs. AFI



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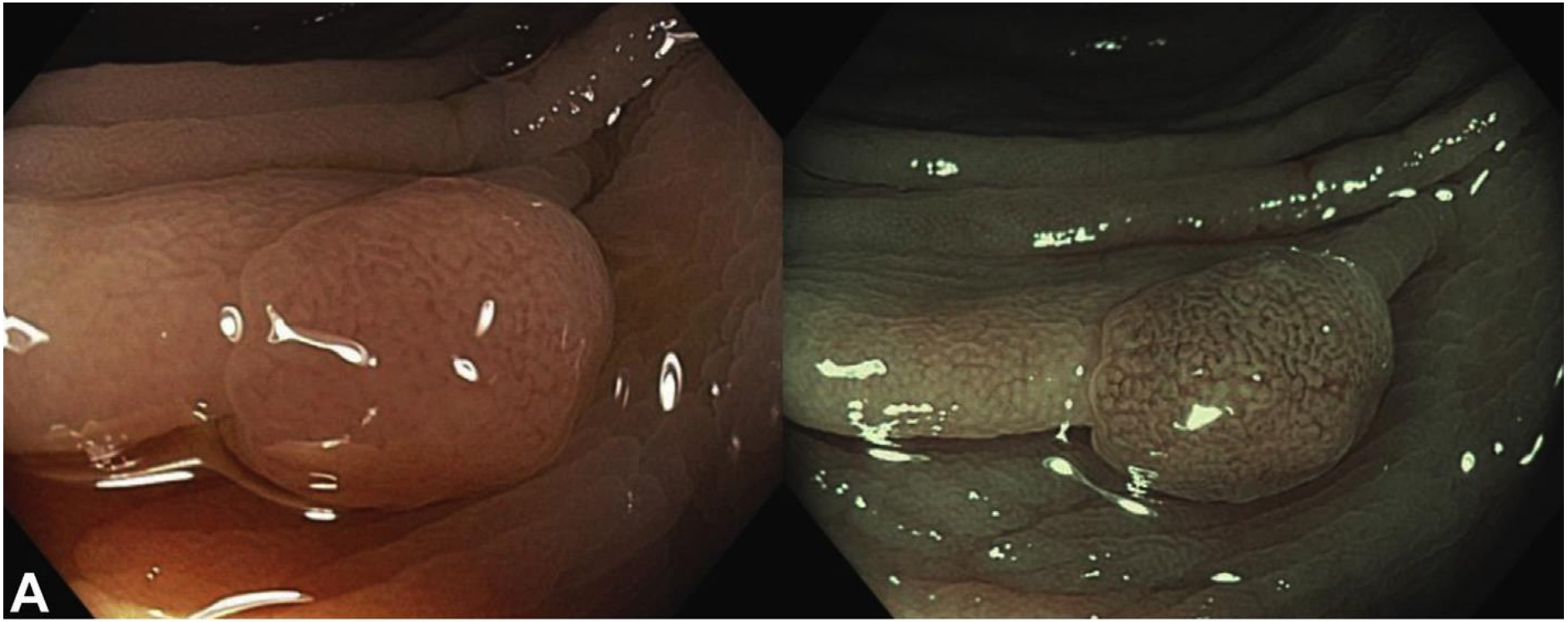
Adenoma: White light vs. NBI



ASGE, GIE 2015, 81(2):249

NBI International Colorectal Endoscopic (NICE) Classification

	Type 1	Type 2
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)
Vessels	None, or isolated lacy vessels may be present coursing across the lesion	Thick brown vessels surrounding white structures
Surface Pattern	Dark spots surrounded by white	Oval, tubular or branched white structures surrounded by brown vessels
Most likely pathology	**Hyperplastic**	**Adenoma**

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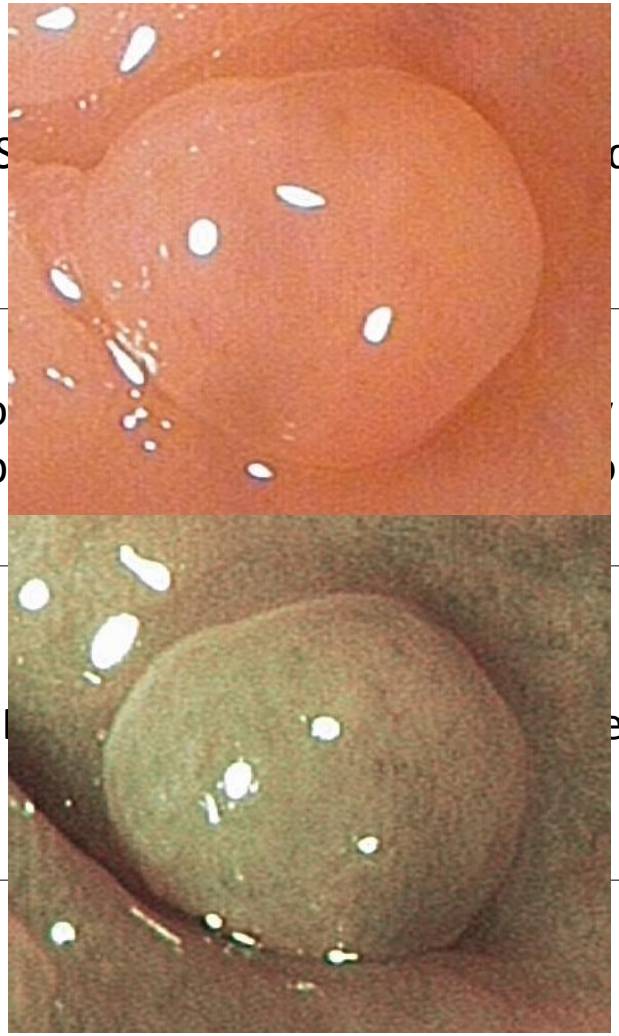
Most likely pathology		**Adenoma**



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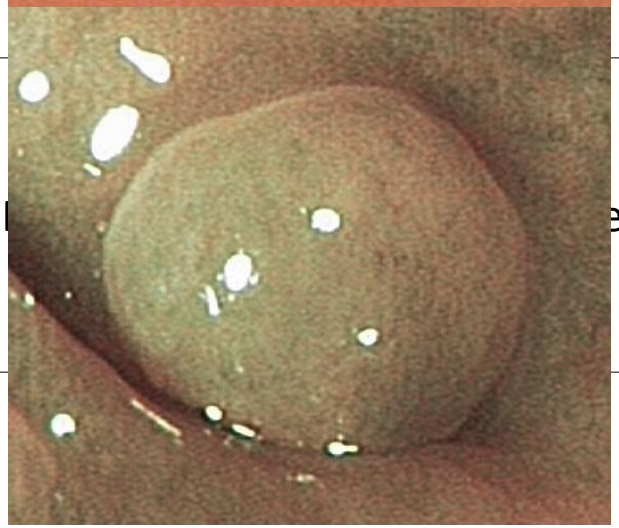
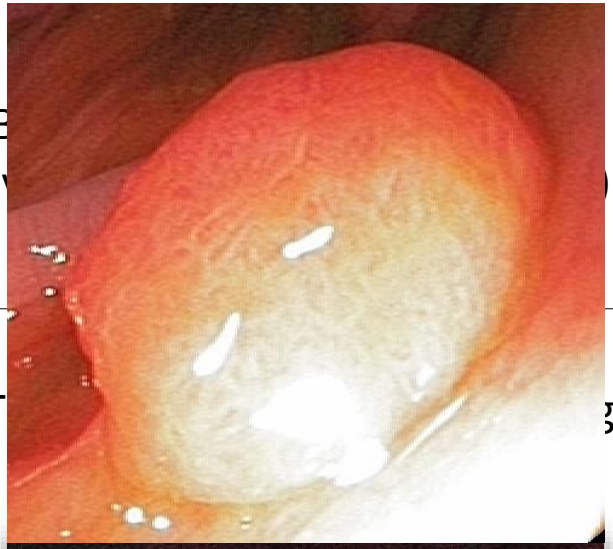
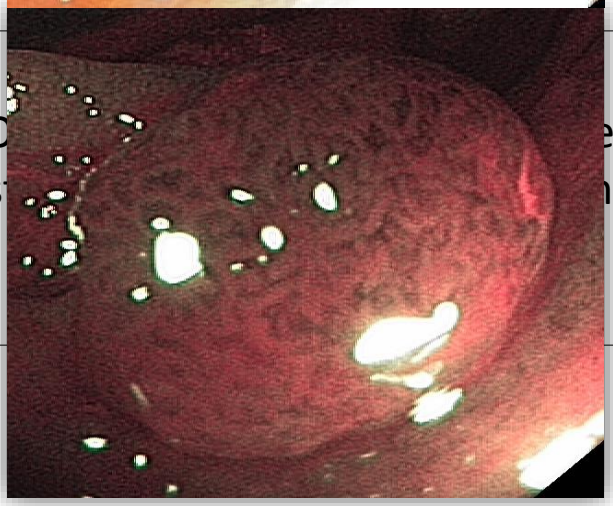
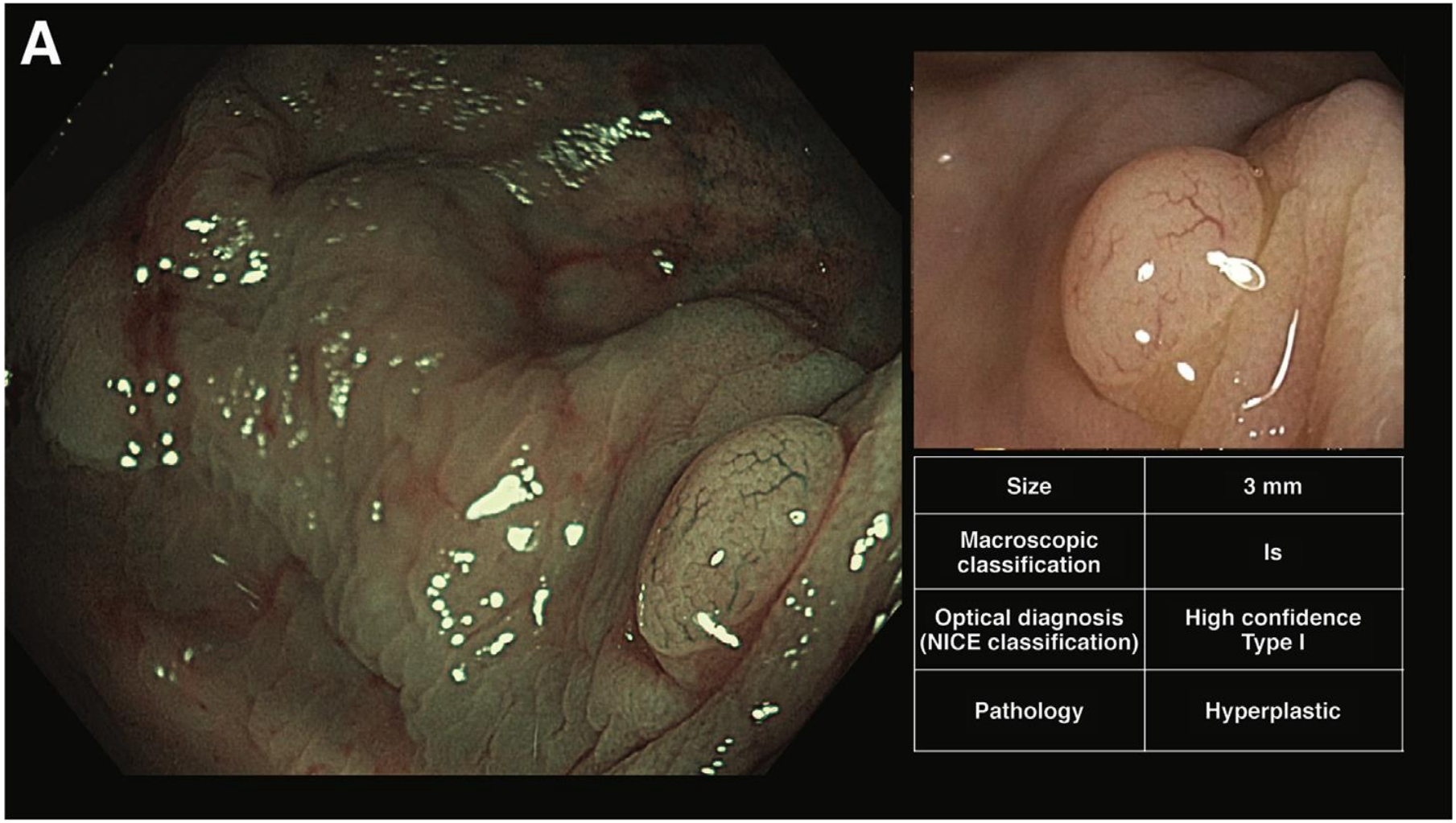




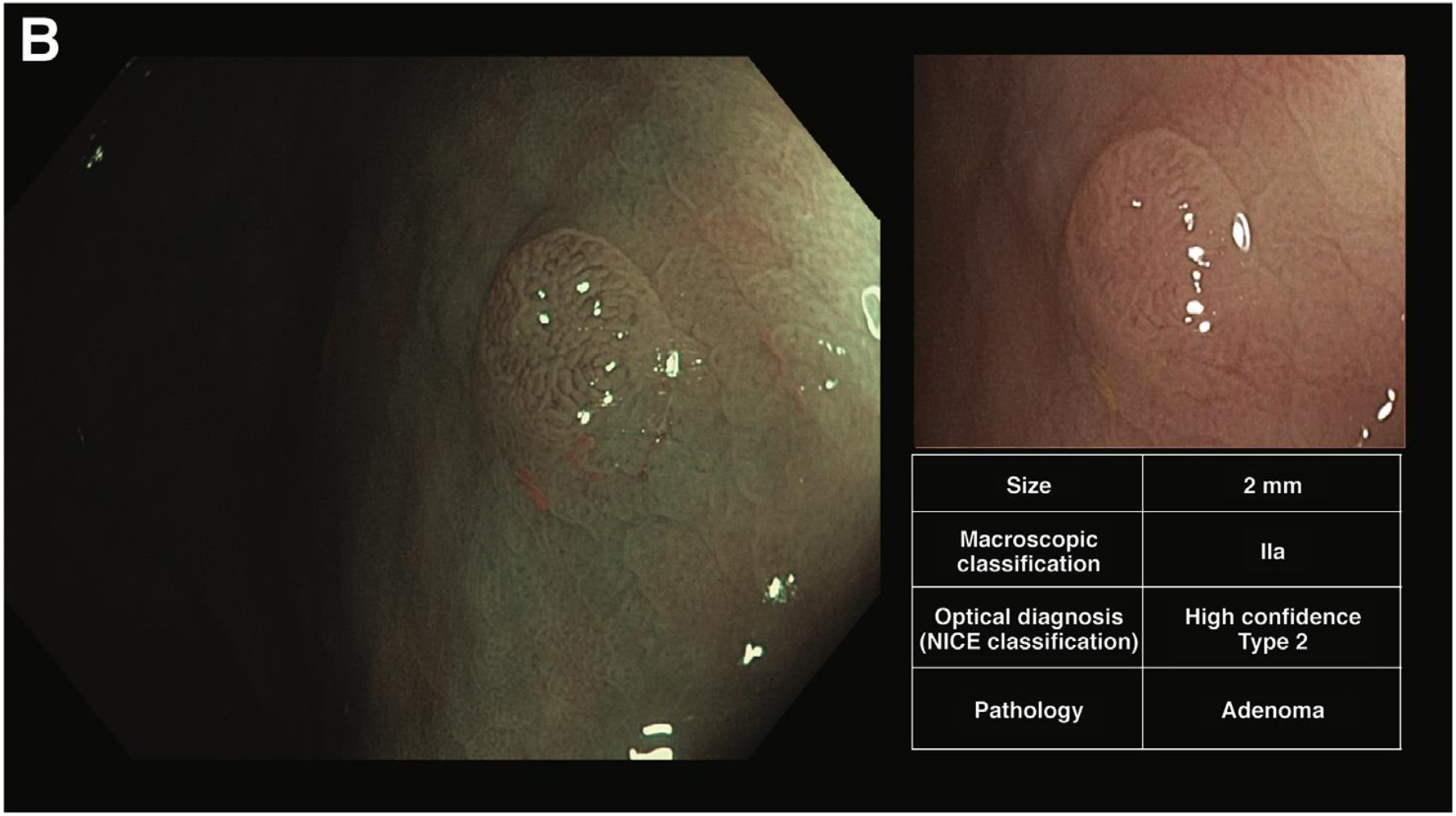


Hyperplastic Polyp: NBI vs. White Light



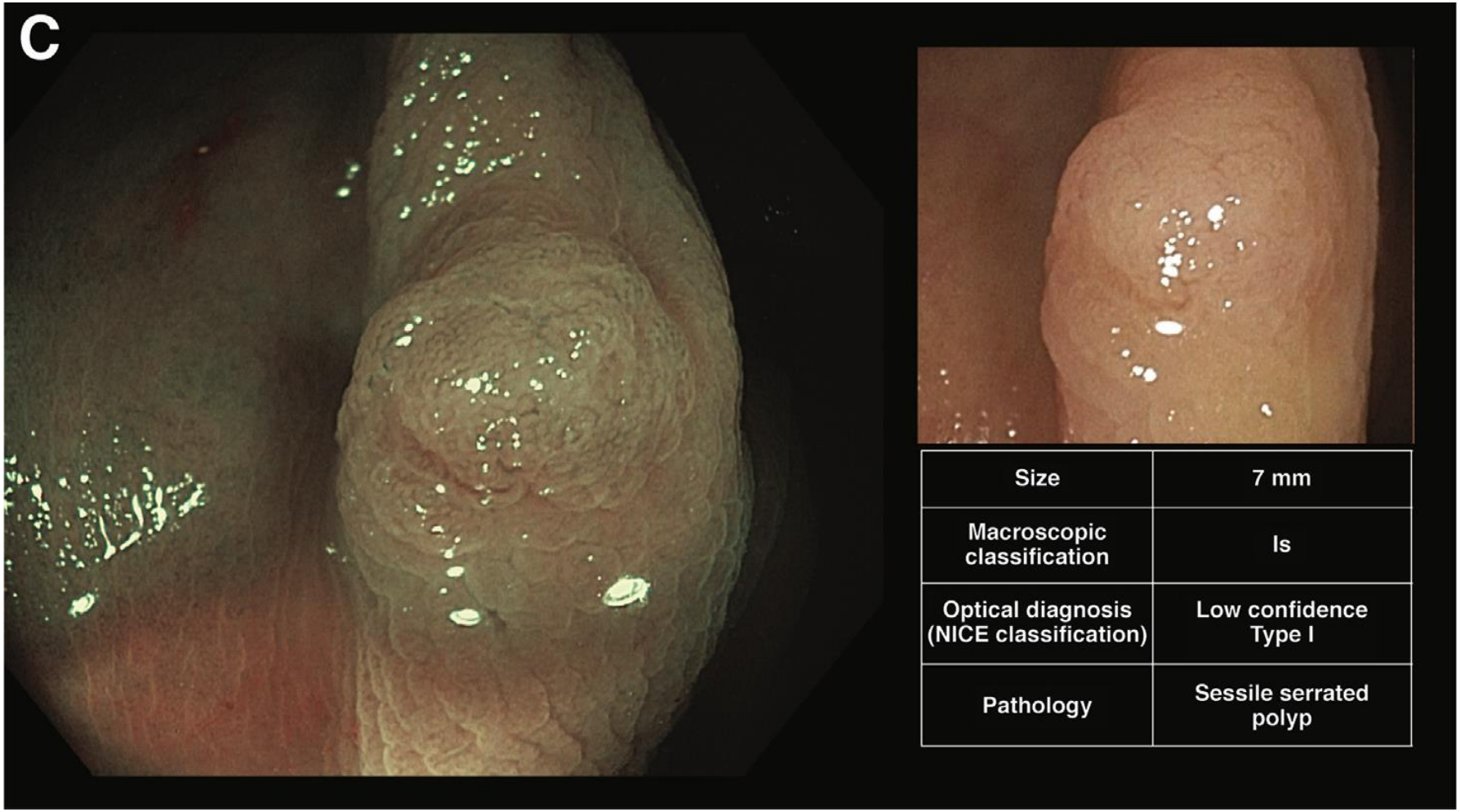
Kaltenback et al, CGH 2015, 13(6):10

Adenoma: NBI vs. White Light



Kaltenback et al, CGH 2015, 13(6):10

Sessile Serrated Polyp: NBI vs. White Light



Kaltenback et al, CGH 2015, 13(6):10

ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

- PIVI: “Preservation and Incorporation of Valuable Endoscopic Innovations”

Rex et al., GIE 2011, 73(3):419

ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

1. In order for polyps ≤5 mm to be resected and discarded without pathologic assessment, endoscopic technology (when used with high confidence*) used to determine histology of polyps ≤5 mm in size, when combined with the histopathologic assessment of polyps >5 mm in size, should provide a ≥90% agreement in assignment of post-polypectomy surveillance intervals when compared to decisions based on pathology assessment of all identified polyps.

Rex et al., GIE 2011, 73(3):419

ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

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ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

2. In order for a technology to be used to guide the decision to leave suspected rectosigmoid hyperplastic polyps ≤5 mm in size in place (without resection), the technology should provide ≥90% negative predictive value (when used with high confidence*) for adenomatous histology.

Rex et al., GIE 2011, 73(3):419

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Rex et al., GIE 2011, 73(3):419

What the PIVI boils down to…

1. If you resect and discard diminutive polyps, get the surveillance recommendation right…
2. If you leave diminutive rectosigmoid polyps in place, make sure they are hyperplastic...

Rex et al., GIE 2011, 73(3):419

ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

- Supporting considerations:
  - Pathology gold standard is imperfect
    - 85-95% accuracy for adenoma vs. hyperplastic
  - Several factors already affect optimal adherence to surveillance guidelines
    - In this context, some error due to endoscopic histology assessment is acceptable

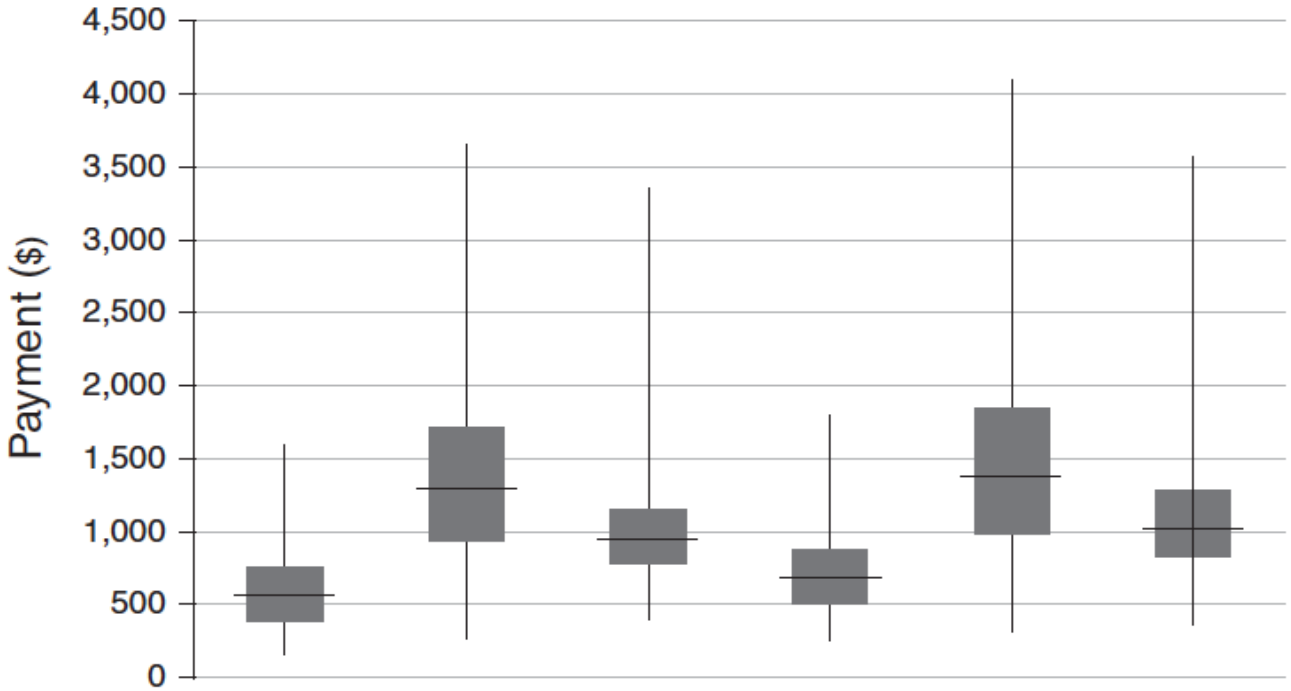
Rex et al., GIE 2011, 73(3):419

ASGE PIVI: real-time endoscopic assessment of histology of diminutive colorectal polyps

- Rationale for “resect diminutive and discard” and “diagnose distal hyperplastic and don’t resect”:
  - May reduce cost
    - $33 million/year in US? (Hassan et al., CGH 2010, 8:865)
    - $1 billion/year in US? (Kessler et al., Endo 2011, 43:683)
  - May improve patient safety
  - May avoid delay in making surveillance recommendation

ASGE, GIE 2015, 81(2):249

Colonoscopy: commercial payments



	Diagnostic colonoscopy			Colonoscopy with intervention		
	Office	OPH	ASC	Office	OPH	ASC
Median	$565	$1,290	$949	$693	$1,371	$1,031
1st percentile	$156	$262	$400	$249	$322	$377
25th percentile	$401	$945	$781	$531	$990	$833
75th percentile	$753	$1,709	$1,156	$871	$1,847	$1,280
99th percentile	$1,600	$3,676	$3,344	$1,800	$4,097	$3,577

Ladabaum et al., AJG 2014, 109:1513

Colonoscopy: commercial payments for pathology

	Pathology Claim within 7 Days		
	Proportion of all procedures (%)	Mean (s.d.)	Median (10–90th percentiles)
Colonoscopy			
Office	55	$232 ($239)	$148 ($67–481)
OP Hosp	46	$352 ($346)	$243 ($90–745)
ASC	47	$228 ($215)	$161 ($72–450)
Overall	52	$272 ($284)	$185 ($69–576)

Ladabaum et al., AJG 2014, 109:1513

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Performance characteristics: Systematic review and meta-analysis

NBI

ASGE Tech Cte, GIE 2015, 81:502

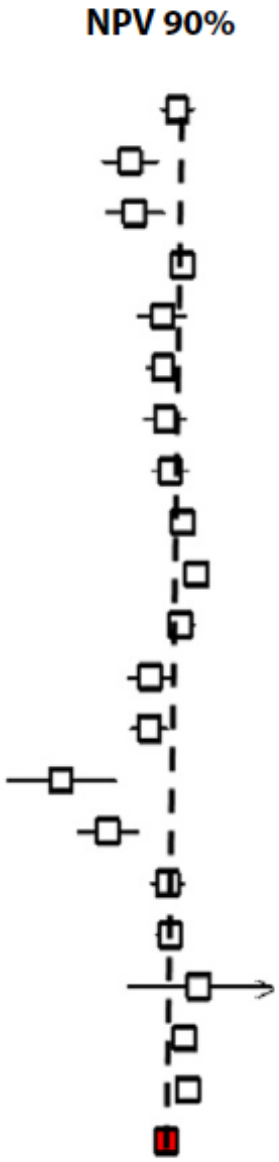
Performance characteristics: Systematic review and meta-analysis

- NPV for adenoma with NBI:
  - Overall: 91% (95% CI, 88–94%)
  - Academic medical centers: 91.8% (95% CI, 89-94%)
  - Experts 93%: (95% CI, 91-96%)
  - High confidence 93%: (95% CI, 90-96%)

ASGE Tech Cte, GIE 2015, 81:502

NPV for NBI Optical Biopsy

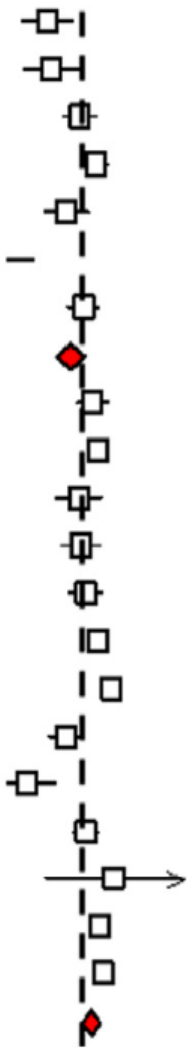
Study name	Mean	Lower limit	Upper limit	Total
East 2008	94.0	89.1	98.9	96
Rogart 2008	81.0	73.0	89.0	265
Ignjatovic 2009	82.3	73.8	90.7	213
Rex 2009	95.4	92.7	98.1	314
Sano 2009	90.0	82.9	97.1	150
Van Den Broek 2009	90.2	85.1	95.4	206
Henry 2010	90.7	84.5	96.9	90
Lee 2011	92.0	86.7	97.3	125
Gupta 2012	95.4	93.1	97.7	516
Hewett_1_2012	99.4	98.8	100.0	201
Hewett_2_2012	95.0	91.0	99.0	178
Kuiper_2012	86.6	79.8	93.3	231
Paggi_2012	86.4	80.9	92.0	399
Sakamoto_2012	62.2	46.9	77.5	270
Shahid_2012	75.0	66.1	83.9	103
Ladabaum_2013	91.4	86.3	96.5	219
Repici_2013	92.0	88.0	96.0	204
Singh_2013	100.0	79.9	100.0	40
Wallace_1_2014	96.0	93.0	99.0	104
Wallace_2_2014	97.0	95.0	99.0	89
Random	91.1	88.7	93.6	



ASGE Tech Cte, GIE 2015, 81:502

Subgroup by Endoscopist Expertise

Group by Expert	Study name	Statistics for each study			NPV 90%
		Mean	Lower limit	Upper limit	
No	Rogart 2008	81.0	73.0	89.0	
No	Ignjatovic 2009	82.3	73.8	90.7	
No	Van Den Broek 2009	90.2	85.1	95.4	
No	Hewett_2_2012	95.0	91.0	99.0	
No	Kuiper_2012	86.6	79.8	93.3	
No	Sakamoto_2012	62.2	46.9	77.5	
No	Ladabaum_2013	91.4	86.3	96.5	
Random	No	87.3	83.3	91.3	
Yes	East 2008	94.0	89.1	98.9	
Yes	Rex 2009	95.4	92.7	98.1	
Yes	Sano 2009	90.0	82.9	97.1	
Yes	Henry 2010	90.7	84.5	96.9	
Yes	Lee 2011	92.0	86.7	97.3	
Yes	Gupta 2012	95.4	93.1	97.7	
Yes	Hewett_1_2012	99.4	98.8	100.0	
Yes	Paggi_2012	86.4	80.9	92.0	
Yes	Shahid_2012	75.0	66.1	83.9	
Yes	Repici_2013	92.0	88.0	96.0	
Yes	Singh_2013	100.0	79.9	100.0	
Yes	Wallace_1_2014	96.0	93.0	99.0	
Yes	Wallace_2_2014	97.0	95.0	99.0	
Random	Yes	93.2	90.6	95.8	



ASGE Tech Cte, GIE 2015, 81:502

Performance characteristics: Systematic review and meta-analysis

- Agreement in surveillance intervals with NBI:
  - Overall: 89% (95% CI, 85-92%)
  - Academic settings: 91% (95% CI, 86-95%)
  - Experienced endoscopists: 92% (95% CI, 88-96%)
  - High confidence 91%: (95% CI, 88-95%)

ASGE Tech Cte, GIE 2015, 81:502

Agreement with Surveillance Intervals Outcome for NBI Optical Biopsy

Study name	Mean	Lower limit	Upper limit	Total
Ignjatovic 2009	95.00	91.06	98.94	82
Rex 2009	94.12	91.27	96.97	136
Gupta 2012	86.10	82.91	89.29	410
Paggi 2012	85.28	80.69	89.87	197
Kuiper 2012	81.48	72.44	90.52	54
Coe 2012	70.00	65.32	74.68	317
Repici 2013	92.00	88.02	95.98	212
Singh 2013	96.55	94.13	98.97	87
Ladabaum 2013	79.90	72.51	87.29	1065
Wallace-1 2014	95.00	93.01	96.99	264
Wallace-2 2014	94.00	91.01	96.99	258
Random	88.63	84.57	92.70	

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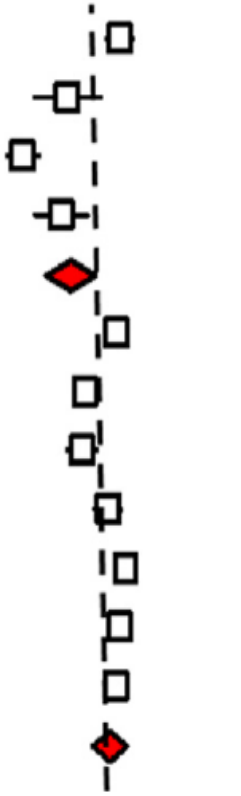
Subgroup by Endoscopist Expertise

Group by Expert	Study name	Statistics for each study		
		Mean	Lower limit	Upper limit
No	Ignjatovic 2009	95.00	91.06	98.94
No	Kuiper2012	81.48	72.44	90.52
No	Coe2012	70.00	65.32	74.68
No	Ladabaum2013	79.90	72.51	87.29
Random No		81.87	75.50	88.24
Yes	Rex 2009	94.12	91.27	96.97
Yes	Gupta 2012	86.10	82.91	89.29
Yes	Paggi 2012	85.28	80.69	89.87
Yes	Repici 2013	92.00	88.02	95.98
Yes	Singh 2013	96.55	94.13	98.97
Yes	Wallace-1 2014	95.00	93.01	96.99
Yes	Wallace-2 2014	94.00	91.01	96.99
Random Yes		91.99	87.62	96.35



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Performance characteristics: Systematic review and meta-analysis

i-SCAN

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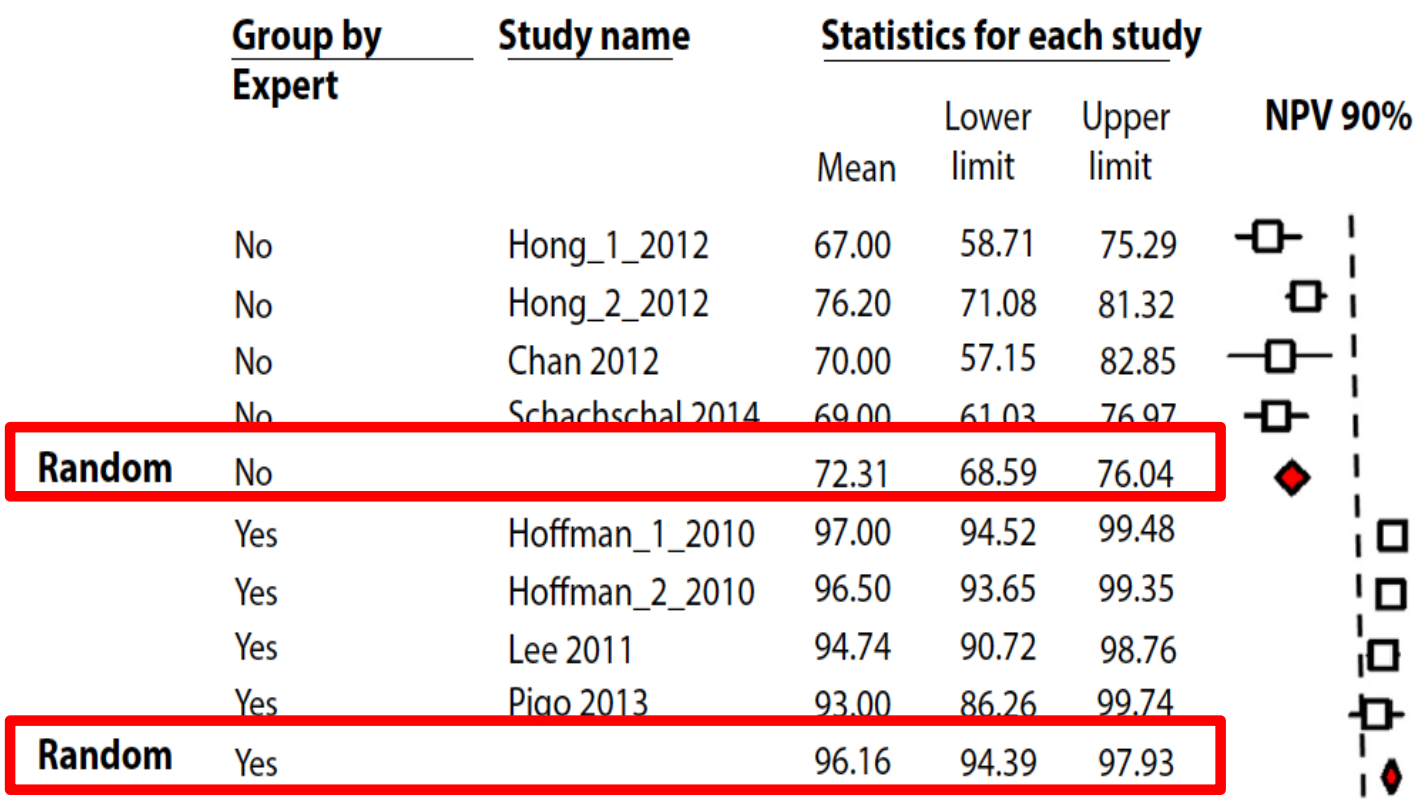
NPV for i-SCAN Optical Biopsy



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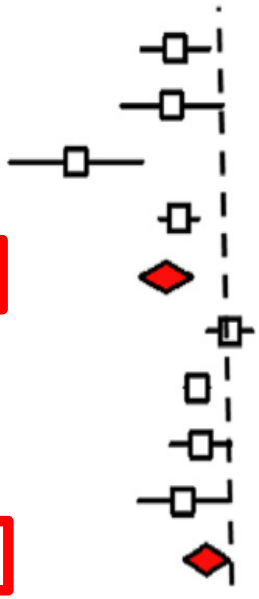
Performance characteristics: Systematic review and meta-analysis

FICE

ASGE Tech Cte, GIE 2015, 81:502

NPV for FICE Optical Biopsy

Group by Magnification	Study name	Statistics for each study			NPV 90%
		Mean	Lower limit	Upper limit	
No	Pohl 2008	77.00	67.06	86.94	
No	Togashi 2009	76.00	61.59	90.41	
No	Buchner 2010	50.00	31.30	68.70	
No	Longcroft 2011	78.00	72.05	83.95	
Random No		73.98	66.69	81.28	
Yes	Dos Santos 2010	92.00	85.08	98.92	
Yes	Kim 2011	83.00	79.21	86.79	
Yes	Longcroft 2012	84.00	75.11	92.89	
Yes	Dos Santos 2012	79.00	66.17	91.83	
Random Yes		85.08	78.93	91.22	



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Optical biopsy of polyps: So, can it be done?

- Test performance = f (technology, operator)
- Optical biopsy *can be done*
- Will most of us be able to do it right?
- Will savings on biopsies be counteracted by inappropriately short surveillance?
- Training?
- Quality assurance?
- What if surveillance recommendations change?

Ladabaum, Lancet Onc 2013, 14:1253

Reality check…

- Surveillance recommendations are evolving…
- Diminutive polyps histology: Much ado about nothing?

US MSTF Surveillance Recommendations

Baseline colonoscopy: most advanced finding(s)	Recommended surveillance interval (*y*)
No polyps	10
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10
1–2 small (<10 mm) tubular adenomas	5–10
3–10 tubular adenomas	3
>10 adenomas	<3
One or more tubular adenomas ≥10 mm	3
One or more villous adenomas	3
Adenoma with HGD	3

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European Surveillance Recommendations

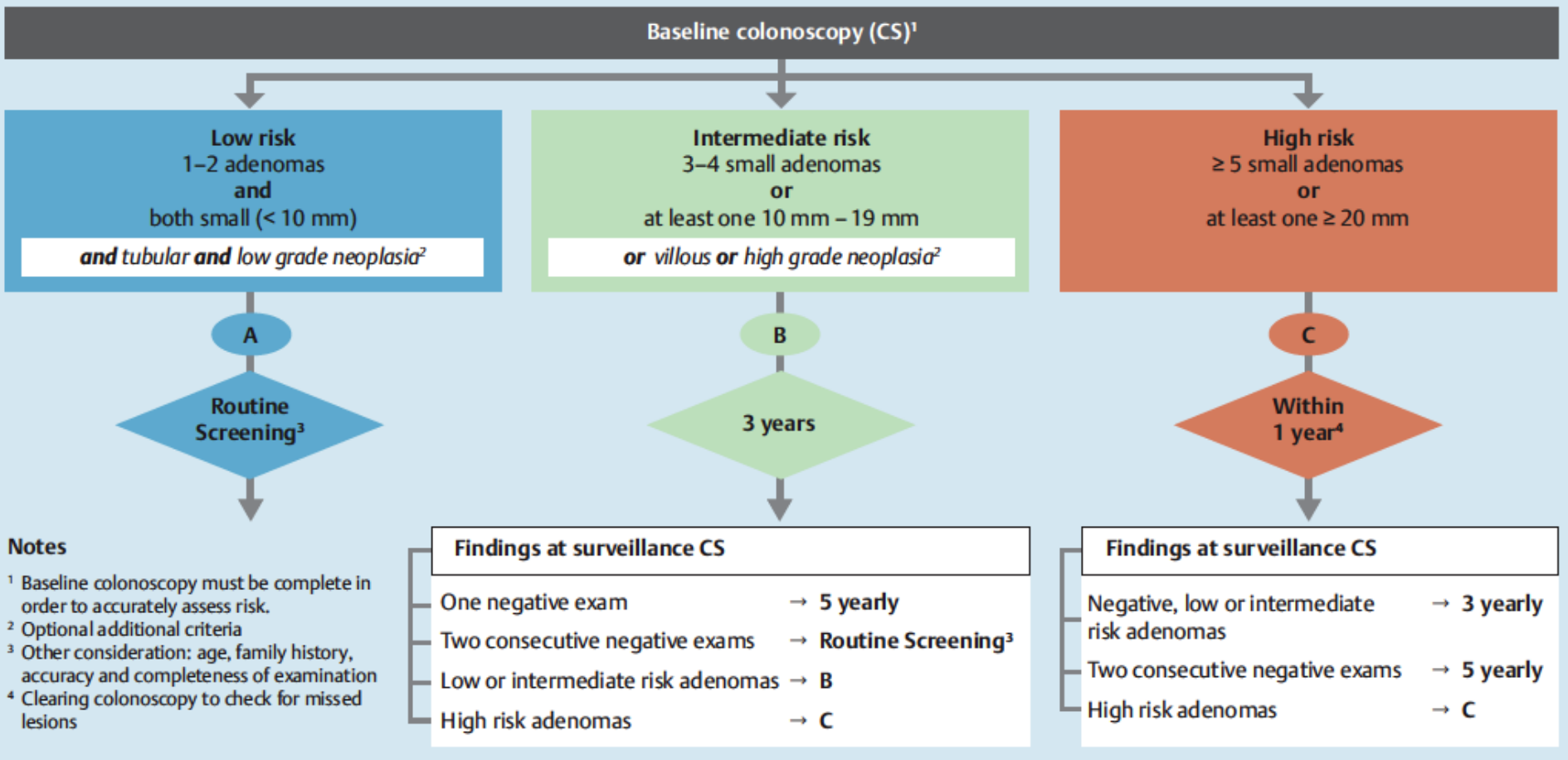


Fig. 9.1 Recommended surveillance following adenoma removal. (For explanation see Recommendations 9.1 – 9.20 and Sections 9.3 – 9.5)

European Surveillance Recommendations

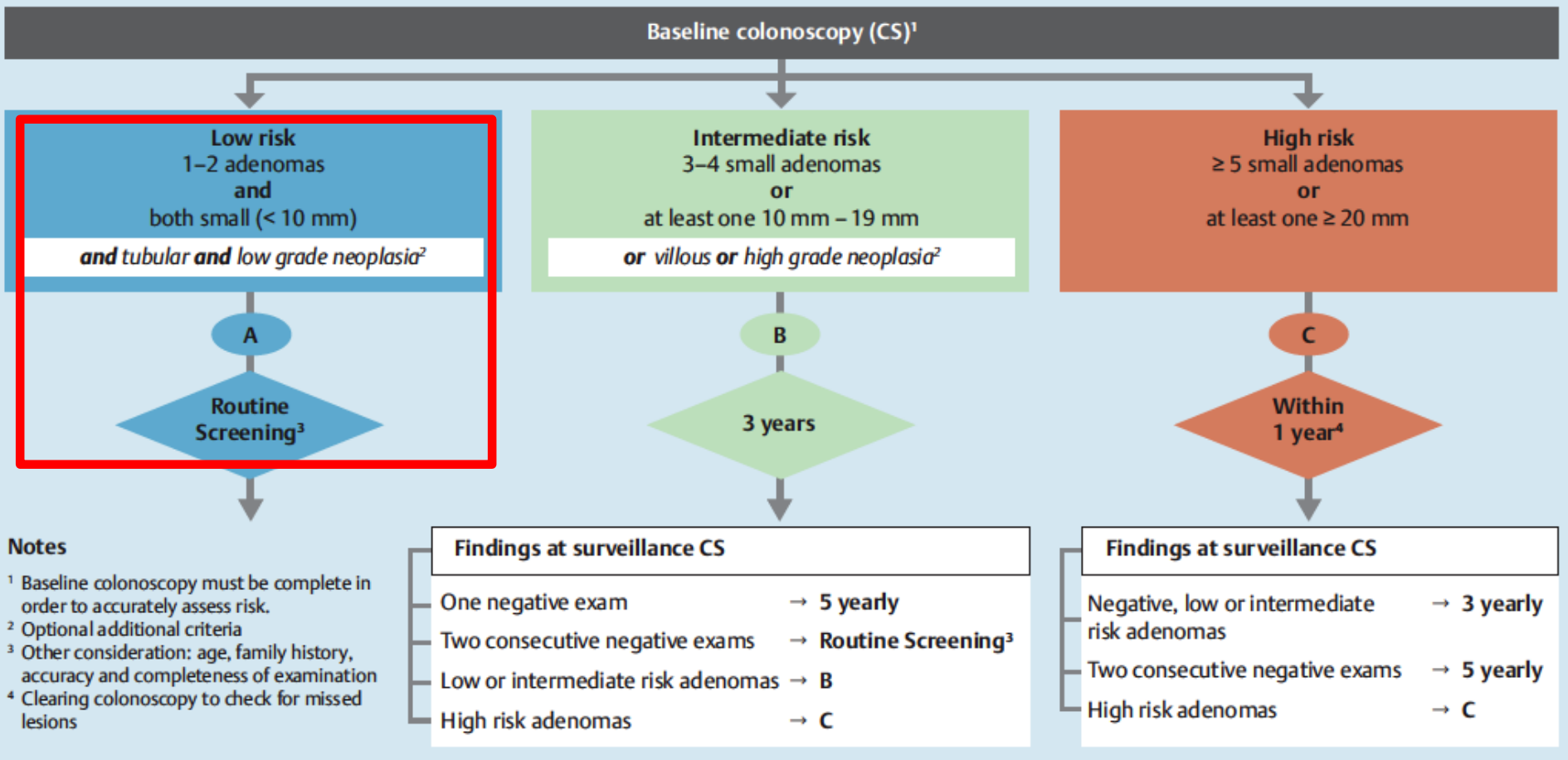


Fig. 9.1 Recommended surveillance following adenoma removal. (For explanation see Recommendations 9.1–9.20 and Sections 9.3–9.5)

Requirements for viability in clinical practice

- Professional society endorsement
- Development of credentialing protocols
- Development of validated training tools
- Documentation of endoscopic decision making (image storage)
  - Medical-legal coverage
  - Documentation of adenoma detection rate[2]
- Revision of institutional policies on requirements to submit tissue to pathology[2]
- Reimbursement or other financial incentives for endoscopic determination of pathology

Rex, Endosc Int Open 2015, 03:E186

ESGE Guideline:
Advanced imaging for colorectal neoplasia

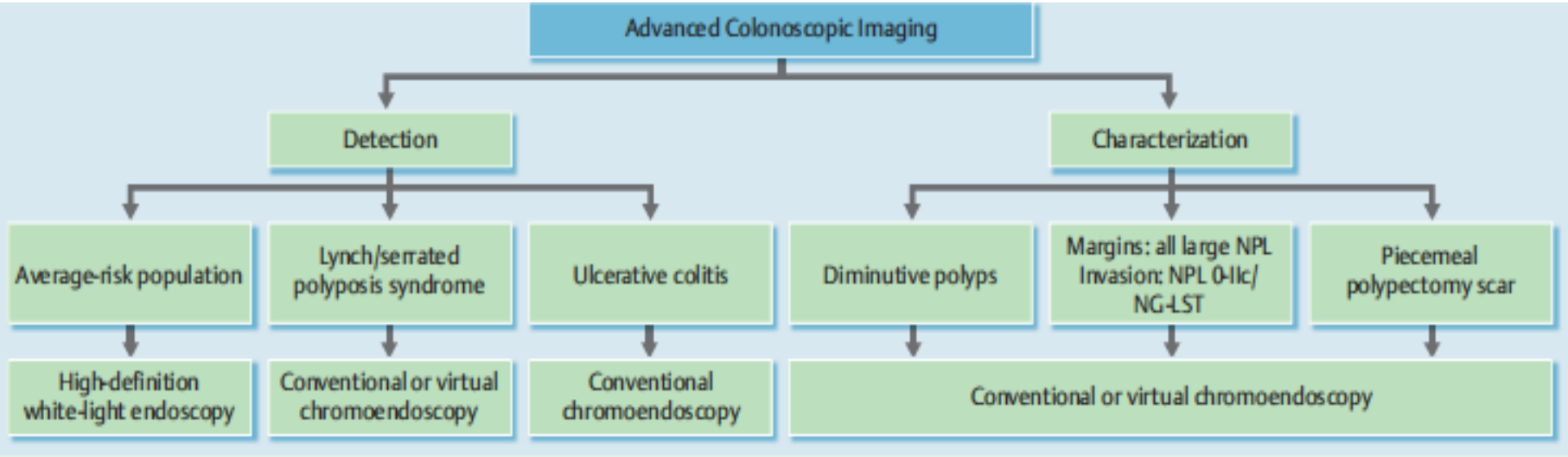


Fig. 1 Summary of the recommendations. NPL, nonpolypoid lesion; 0-IIc, lesions with a depressed component; NG-LST, non-granular laterally spreading tumor.

Kaminski et al, Endo 2014, 46:435

ESGE Guideline:
Advanced imaging for colorectal neoplasia

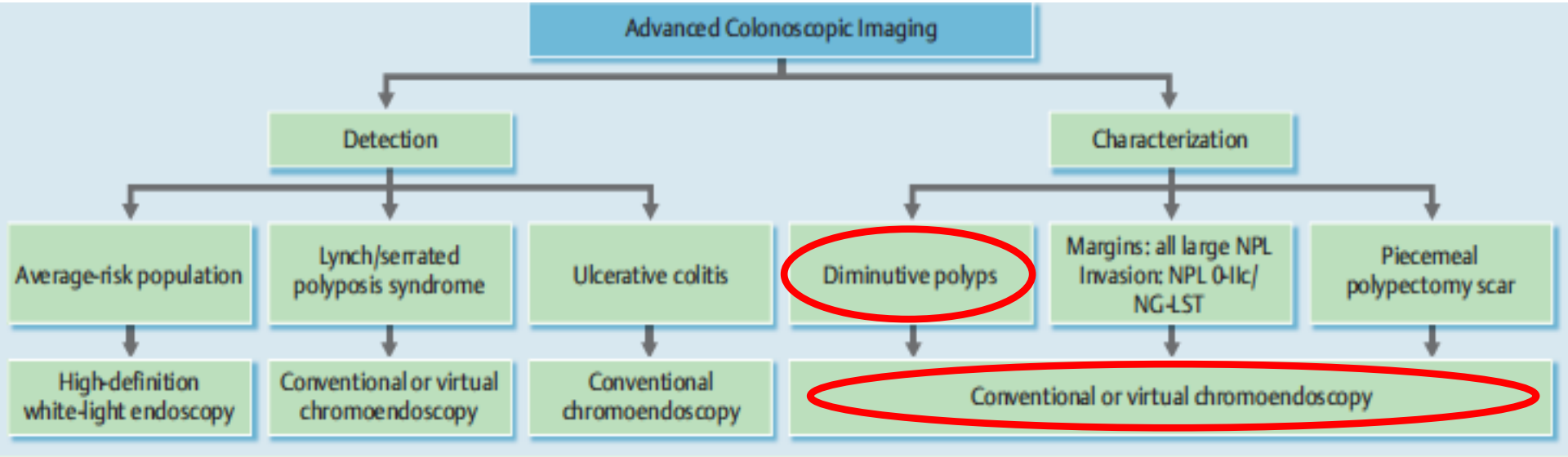


Fig. 1 Summary of the recommendations. NPL, nonpolypoid lesion; 0-IIc, lesions with a depressed component; NG-LST, non-granular laterally spreading tumor.

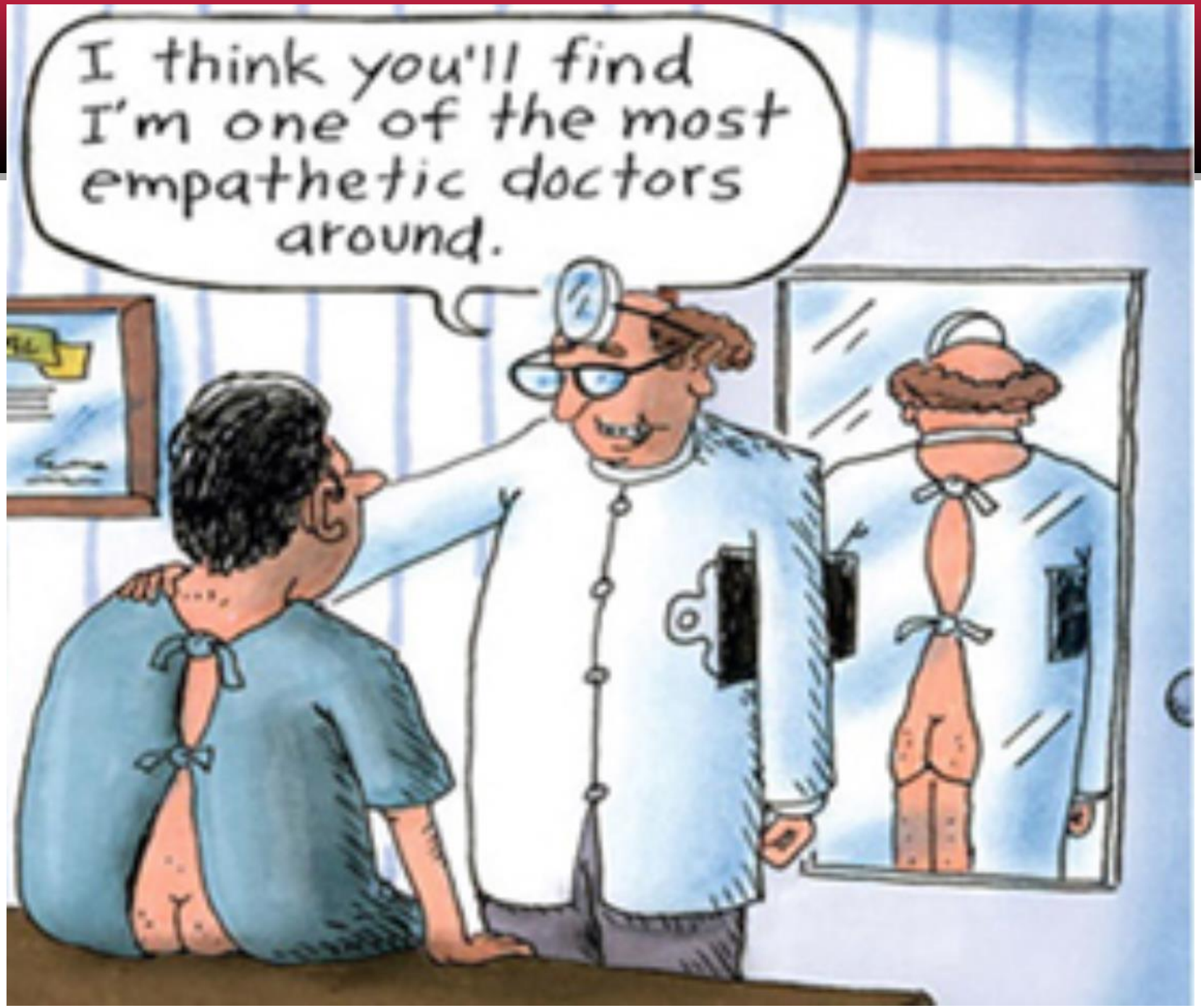
Kaminski et al, Endo 2014, 46:435

Outline

- What is optical biopsy?
- Available modalities
- Applications to colon polyps
- Ready for practice?

When we look,

what can we see?


I think you'll find I'm one of the most empathetic doctors around.