Image enhanced endoscopy for neoplasia surveillance in IBD

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Disclosures

None
Learning Objectives

• Review historical concepts guiding IBD neoplasia surveillance recommendations and rationale for advanced surveillance methods

• Review the role of image enhanced endoscopy (IEE) in neoplasia surveillance in IBD, with a focus on chromoendoscopy
Tumorigenesis in IBD

• “Field carcinogenesis” – multifocal genetic aberrations in colitic mucosa
  • ? multifocal tumour development
  • ? accelerated progression

• Irregular lesions that are difficult to delineate with high cancer risk
  • Stricturing lesions
  • Laterally-spreading tumours
  • Irregular plaques and nodules

• “Invisible” flat neoplastic lesions

Rubin, Gastro 1992; Lofberg, Gastro 1992; Soderlund, IBDJ 2011
Flat Neoplastic Growth in IBD
Historical CRC Risk in IBD Dysplasia

High-grade dysplasia
• 40 - 70% rate of synchronous CRC
• 25 - 30% rate of metachronous CRC

DALM
• 42 to 45% rate of synchronous CRC

Low-grade dysplasia
• 20 to 25% rate of synchronous CRC

Perception – IBD colitis is associated with insidious and accelerated neoplasia development that evades endoscopic detection

Rutter et al., Gastro 2006; Bernstein et al., Lancet 1994; Connell et al., Gut 1994; Taylor et al., Dis Col Rectum 1992; Ullman et al., Gastro 2003
Traditional Guidance for Neoplasia Surveillance in IBD

• Interval q 1-3 (U.S.) or q 1-5 (Europe) years, guided by other risk factors
  • Disease duration/extent/severity, family history of CRC, past neoplasia, PSC
  • Annually – PSC, FDR < age 50, previous neoplasia, stricture

• ≥ 33 random biopsies throughout colon to detect “invisible lesions”; targeted biopsies of visible lesions

• Colectomy for any invisible, indistinct, irregular, or high-grade neoplasia, due to fears of being unresectable and harbouring cancer

Laine et al., GIE 2015
Farraye et al., Gastro 2010
Kornbluth et al., AJG 2010
Cairns et al., Gut 2010
Itzkowitz et al. IBDJ 2005
COLITIS SURVEILLANCE

SCREENING COLONOSCOPY AT 10 YEARS
(preferably in remission, panceionic dye-spray)

- **LOWER RISK**
  - Extensive colitis with NO ACTIVE endoscopic/histological inflammation
  - OR left-sided colitis
  - OR Crohn’s colitis of <50% colon

  - 5 Years

- **INTERMEDIATE RISK**
  - Extensive colitis with MILD ACTIVE endoscopic/histological inflammation
  - OR post-inflammatory polyps
  - OR family history CRC in FDR aged 50+

  - 3 Years

- **HIGHER RISK**
  - Extensive colitis with MODERATE/SEVERE ACTIVE endoscopic/histological inflammation
  - OR stricture in past 5 years
  - OR dysplasia in past 5 years declining surgery
  - OR PSC / transplant for PSC
  - OR family history CRC in FDR aged <50

  - 1 Year

**BIOPSY PROTOCOL**
Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended, otherwise 2-4 random biopsies from every 10 cm of the colorectum should be taken

**OTHER CONSIDERATIONS**
Patient preference, multiple post-inflammatory polyps, age & comorbidity, accuracy & completeness of examination
Limitations of Older Studies of CRC Risk

• Effective treatments for IBD $\rightarrow$ T2T (mucosal healing)

• Improved resolution of endoscopes

• Better bowel preparation regimens

• Recognition of quality metrics for colonoscopy (+ ADR, training, etc.)

• Adoption of systematic surveillance protocols before mid-90’s
High-Definition Endoscopy

HDE associated with 2 fold higher neoplasia detection rate in UC

Subramanian et al., IBDJ 2013
Pedunculated sigmoid polyp.

Normal sigmoid colon as seen with colonoscope, showing depth of focus.

Normal sigmoid colon as seen with colonoscope showing details of vascular pattern.

1971 Images obtained from fiberoptic sigmoidoscope

Inflammatory pseudopolyps (rectum).

Carcinoma of rectum.

Colonic IBD is a Risk Factor for Colorectal Cancer (CRC)

<table>
<thead>
<tr>
<th>Population-Based Studies</th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ekbom (NEJM 1990)</td>
<td>5.7 (4.6 – 7.0)</td>
<td>--</td>
</tr>
<tr>
<td>Bernstein (Cancer 2001)</td>
<td>2.75 (1.91 – 3.97)</td>
<td>2.64 (1.69 – 4.12)</td>
</tr>
<tr>
<td>Gillen (Gut 1994)</td>
<td>19.2 (12.9 – 27.5)</td>
<td>18.2 (7.8 – 35.8)</td>
</tr>
<tr>
<td>Herrington (Gastro 2012)</td>
<td>1.6 (1.3 – 2.0)</td>
<td>1.6 (1.2 – 2.0)</td>
</tr>
<tr>
<td>Jess (Gastro 2012)</td>
<td>2.4 (0.6 – 6.0)</td>
<td>1.9 (0.7 – 4.1)</td>
</tr>
</tbody>
</table>

Meta-analyses of recent population-based studies: **CRC risk 1.5 to 2-fold** higher for both Crohn’s disease (CD) and ulcerative colitis (UC)

Shortcomings of Traditional Guidance

• No RCTs evaluating the optimal surveillance technique, timing or frequency or whether surveillance colonoscopy is even effective in IBD

• Low yield of random biopsies with latest technologies
  → ~ 0.1 % of biopsies; ~ 1% of patients Laine et al., GIE 2015

• > 90% of neoplastic lesions are visible using HD-WLE
  Laine et al., GIE 2015

• More sophisticated technologies now exist to allow better detection and management of neoplastic lesions in IBD
Updated Guidance (SCENIC-AGA, ASGE, ECCO, BSG)

• Chromoendoscopy (dye spray colonoscopy, DSC) with targeted biopsies alone is the preferred strategy for neoplasia surveillance

• Random biopsies may be performed if using WLE

• Virtual chromoendoscopy (NBI, iScan, FICE) is not recommended over DSC or WLE for neoplasia detection

• Endoscopic resection with continued surveillance is recommended over colectomy for lesions with (i) clear borders; (ii) no invasive features; and (iii) clear endoscopic and histologic resection margins (complete removal)

• Surveillance with DSC is recommended in the setting of invisible dysplasia
Dye Spray Colonoscopy (DSC)

Contrast or absorptive dyes sprayed throughout colonic mucosal surface during colonoscopy (catheter or water jet)

→ Methylene blue 0.04% (absorptive), indigo carmine 0.03% (contrast)

Enhances borders and surface architecture ("unmasks lesions")

• **Seconds** – dye fills lesion borders and colonic pits → demarcates lesion and highlights surface pattern

• ≥ **1 min** (methylene blue) – dye is taken up preferentially by non-neoplastic epithelial cells → contrasts lesion from surroundings
Technique of DSC

• Cleaning and suctioning during entry – identify if DSC feasible

• Prepare dye if adequate bowel preparation and minimal inflammation → 20 mL of 10mg/mL (1% w/v) stock MB in 500 cc sterile water (0.04%)

• Switch water bottle to dye in cecum

• Apply generously t/o, esp to anti-gravity side in segments (AC, TC, DC, RS)

• Re-intubate each segment, suction excess dye and inspect carefully
SURFACE Criteria for DSC

**Strict patient selection** → Colonic IBD ≥ 8 years’ duration, in clinical remission

**Unmask the mucosal surface** → Excellent bowel preparation

**Reduce peristaltic waves** → Consider spasmolytic agent

**Full length staining of the colon** → Panchromoendoscopy

**Augment detection with dyes** → indigo carmine or methylene blue

**Crypt architecture analysis** → Pit pattern classification

**Endoscopic targeted biopsies of suspicious lesions**

Flat lesion (Paris IIa)

Laterally Spreading Tumour

Murthy et al., GIE 2013
Delineation and Characterization of Neoplastic Lesions with CE

Benefits of DSC
1. Unmasks neoplastic lesions by filling crevices and differential absorption
2. Lesion characterization - differentiate neoplastic and non-neoplastic
3. Facilitates lesion resection by highlighting borders
4. Eliminates need for routine random biopsies
5. Cost-effective relative to WLE + random biopsies Konijeti, GIE 2014

Drawbacks of DSC
1. Requires meticulous bowel preparation
2. Requires near-complete mucosal healing
3. Inconvenient (labour intensive if using catheter spray; messy)
4. Potential increase in procedure time
5. Unclear clinical and/or cost benefit
How Do I Know if a Lesion is Dysplastic?

• Look for **circumscribed lesion** or **irregular area** of mucosa → zoom in

• Evaluate **lesion morphology** – finger-like or irregular fleshy projections, or polyps in clusters that are similar in architecture to surrounding mucosa, are typically post-inflammatory polyps

• Evaluate **dye uptake** – dysplastic lesions generally do not take up dye

• Evaluate **surface architecture** and compare to surrounding mucosa → different architecture should be considered suspicious and sampled

• N.B. Kudo classification is not validated in colitis-associated dysplasia
Post-inflammatory polyps

Laterally-spreading tumours
## Evidence for DSC vs SD-WLE in IBD

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Dye</th>
<th>Staining</th>
<th>Design</th>
<th>No. of pts.</th>
<th># Pts. with dysplasia</th>
<th>Outcome (chromo vs. standard)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich</td>
<td>2003</td>
<td>Germany</td>
<td>MB</td>
<td>Pancolonic</td>
<td>Randomized 1:1</td>
<td>165</td>
<td>19</td>
<td>32 vs. 10 dysplastic lesions</td>
</tr>
<tr>
<td>Matsumoto</td>
<td>2003</td>
<td>Japan</td>
<td>IC</td>
<td>Pancolonic</td>
<td>Prospective cohort</td>
<td>57</td>
<td>12</td>
<td>86% versus 38% sensitivity</td>
</tr>
<tr>
<td>Rutter</td>
<td>2004</td>
<td>UK</td>
<td>IC</td>
<td>Pancolonic</td>
<td>Prospective cohort</td>
<td>100</td>
<td>7</td>
<td>9 versus 2 dysplastic lesions</td>
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<tr>
<td>Hurlstone</td>
<td>2005</td>
<td>UK</td>
<td>IC</td>
<td>Targeted</td>
<td>Prospective cohort</td>
<td>700</td>
<td>81</td>
<td>69 versus 24 dysplastic lesions</td>
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<tr>
<td>Kiesslich</td>
<td>2007</td>
<td>Germany</td>
<td>MB</td>
<td>Pancolonic</td>
<td>Randomized 1:1</td>
<td>153</td>
<td>15</td>
<td>19 versus 4 dysplastic lesions</td>
</tr>
<tr>
<td>Marion</td>
<td>2008</td>
<td>US</td>
<td>MB</td>
<td>Pancolonic</td>
<td>Tandem colonoscopy</td>
<td>102</td>
<td>19</td>
<td>17 versus 3 patients with dysplasia</td>
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<tr>
<td>Günther</td>
<td>2011</td>
<td>Germany</td>
<td>IC</td>
<td>Pancolonic</td>
<td>Randomized 1:1:1</td>
<td>150</td>
<td>6</td>
<td>6 versus 0 patients with dysplasia</td>
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<tr>
<td>Hlavaty</td>
<td>2011</td>
<td>Slovakia</td>
<td>IC</td>
<td>Pancolonic</td>
<td>Tandem colonoscopy</td>
<td>30</td>
<td>7</td>
<td>7 versus 0 patients with dysplasia</td>
</tr>
</tbody>
</table>

**SCENIC meta-analysis of 8 studies: Relative benefit 1.8 (1.2-2.6); Absolute benefit 6% (3%-9%)**
**Randomized Controlled Trials**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoendoscopy</th>
<th>White light</th>
<th>Risk Ratio</th>
<th>DSC vs SD-WLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Freire 2014</td>
<td>6</td>
<td>81</td>
<td>4</td>
<td>81</td>
</tr>
<tr>
<td>Kiesslich 2003</td>
<td>13</td>
<td>87</td>
<td>6</td>
<td>87</td>
</tr>
<tr>
<td>Kiesslich 2007</td>
<td>11</td>
<td>81</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>30</td>
<td>249</td>
<td>14</td>
<td>248</td>
</tr>
</tbody>
</table>

Total events: 30 vs 14

Heterogeneity: Tau² = 0.00; Chi² = 0.50, df = 2 (P = .78); I² = 0%

Test for overall effect: Z = 2.41 (P = .02)

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<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoendoscopy</th>
<th>White light</th>
<th>Risk Ratio</th>
<th>DSC vs HD-WLE</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Iacucci 2017</td>
<td>22</td>
<td>90</td>
<td>23</td>
<td>90</td>
</tr>
<tr>
<td>Mohammed 2015</td>
<td>11</td>
<td>53</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>Park 2016</td>
<td>21</td>
<td>102</td>
<td>13</td>
<td>108</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>54</td>
<td>245</td>
<td>41</td>
<td>248</td>
</tr>
</tbody>
</table>

Total events: 54 vs 41

Heterogeneity: Tau² = 0.06; Chi² = 3.02, df = 2 (P = .22); I² = 34%

Test for overall effect: Z = 1.26 (P = .21)

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Total (95% CI): 494 vs 496

Total events: 84 vs 55

Heterogeneity: Tau² = 0.01; Chi² = 5.40, df = 5 (P = .37); I² = 7%

Test for overall effect: Z = 2.39 (P = .02)

Test for subgroup differences: Chi² = 1.27, df = 1 (P = .26), I² = 21.5%

Feuerstein et al., GIE 2019
Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CE Events</th>
<th>CE Total</th>
<th>HD-WLE Events</th>
<th>HD-WLE Total</th>
<th>Weight</th>
<th>Risk ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iacucci 2018</td>
<td>11</td>
<td>45</td>
<td>23</td>
<td>90</td>
<td>38.5%</td>
<td>0.96 (0.51, 1.78)</td>
</tr>
<tr>
<td>Mohammed 2015</td>
<td>11</td>
<td>50</td>
<td>5</td>
<td>53</td>
<td>12.2%</td>
<td>2.33 (0.87, 6.24)</td>
</tr>
<tr>
<td>Park 2016</td>
<td>21</td>
<td>102</td>
<td>13</td>
<td>108</td>
<td>31.7%</td>
<td>1.71 (0.91, 3.23)</td>
</tr>
<tr>
<td>Picco 2013</td>
<td>16</td>
<td>75</td>
<td>7</td>
<td>75</td>
<td>17.6%</td>
<td>2.29 (1.00, 5.23)</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>272</strong></td>
<td><strong>326</strong></td>
<td></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>1.60 (1.11, 2.29)</strong></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>59</strong></td>
<td><strong>48</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 3.93, df = 3 (P = 0.27); I² = 24%

Test for overall effect: Z = 2.55 (P = 0.01)

Wan et al., JDD 2019
## Non-Randomized Controlled Trials

### Chromoendoscopy vs Standard-definition White-light Endoscopy Non-randomized

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>M-H Ratio, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gasia 2016</td>
<td>9</td>
<td>28</td>
<td>6</td>
<td>126</td>
</tr>
<tr>
<td>Hlavaty 2011 (1)</td>
<td>7</td>
<td>30</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>16</td>
<td>58</td>
<td>141</td>
<td>30.8%</td>
</tr>
</tbody>
</table>

Total events 16, 6
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.01$, df = 1 ($P = .92$); $I^2 = 0$
Test for overall effect: $Z = 4.20$ ($P < .0001$)

### Chromoendoscopy vs High-definition White-light Endoscopy Non-randomized

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>M-H Ratio, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gasia 2016</td>
<td>9</td>
<td>28</td>
<td>22</td>
<td>182</td>
</tr>
<tr>
<td>Gunther 2011</td>
<td>2</td>
<td>50</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>Iacucci 2014</td>
<td>5</td>
<td>35</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>113</td>
<td>257</td>
<td>69.2%</td>
<td>2.57 [1.41-4.68]</td>
</tr>
</tbody>
</table>

Total events 16, 24
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.41$, df = 2 ($P = .82$); $I^2 = 0$
Test for overall effect: $Z = 3.08$ ($P = .002$)

Total (95% CI) 171, 398 100.0% 3.48 [2.11-5.73]

Total events 32, 30
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.61$, df = 4 ($P = .46$); $I^2 = 0$
Test for overall effect: $Z = 4.90$ ($P < .00001$)
Test for subgroup differences: $\chi^2 = 3.16$, df = 1 ($P = .08$), $I^2 = 68.4$

**Footnotes**
(1) Chromoendoscopy arm included use of both chromoendoscopy and confocal microscopy

**Feuerstein et al., GIE 2019**
Reasons for Limited Uptake of DSC

- Uncertain benefit over HD-WLE
- Uncertain impact on CRC or CRC-related mortality
- Uncertainty of surveillance intervals if dysplasia detected
- Uncertain cost implications (with more frequent surveillance)
- Inadequate training and/or experience
- Requirement for healed bowel, meticulous cleansing
- Inconvenient → time-consuming, messy
- Lack of re-imbursement
- Availability of dye, staining of colonoscopes
- Patient reticence → bluish-green discoloration of stool and urine
However, please consider that . . .

- DSC is extremely easy to do

- Time to clean and stain the colon ≈ time to take and document 32+ random biopsies

- DSC with targeted biopsies forces careful inspection of mucosa

- DSC aids in the detection and resection of flat lesions

- Methylene blue is cheap ($60/250 mL at Amazon) = < $5 per procedure

- On a per-procedure basis, DSC with targeted biopsies is much cheaper than WLE with non-targeted and targeted biopsies (~50% cheaper)

- Unmasking lesions with DSC may identify patients at increased risk of CRC
Virtual Chromoendoscopy

• Light filters (NBI) or post-image processing (i-scan, FICE) to focus on narrow wavelengths of light

• Highlights vascular pattern → indirect appreciation of pit pattern

• Earlier studies showed that NBI was not superior to SD-WLE or HD-WLE for lesion detection, but similar to DSC for lesion characterization
  Chiu et al., Gut 2007; Rastogi et al., GIE 2007; Ignjatovic et al., AJG 2012; van de Broek et al., Endoscopy 2011

• Recent RCTs in IBD and non-IBD have shown more promising results
  Bisschops et al., Gut 2018; Iaccuci et al., AJG 2018; Atkinson et al., Gastroenterology 2019
Narrow Band Imaging

(a) WL endoscopy
(b) i-Scan 1
(c) i-Scan 2
(d) i-Scan 3
(e) C
(f) C-i-Scan1
(g) C-i-Scan2
(h) C-i-Scan3

iScan
RCTs of VCE vs WLE

6.1 Virtual chromoendoscopy vs. SD white light endoscopy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Virtual chromoendoscopy</th>
<th>White light colonoscopy</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Freire 2014</td>
<td>6</td>
<td>72</td>
<td>4</td>
</tr>
<tr>
<td>Kieslisch 2007</td>
<td>11</td>
<td>80</td>
<td>4</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>152</td>
<td>146</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Total events: 17, Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.36, df = 1 (P = 0.55); I^2 = 0%
Test for overall effect: Z = 1.67 (P = 0.10)

6.2 Virtual chromoendoscopy vs. HD white light endoscopy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Virtual chromoendoscopy</th>
<th>White light colonoscopy</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Lacucci 2017</td>
<td>14</td>
<td>90</td>
<td>23</td>
</tr>
<tr>
<td>Ignojovic 2012</td>
<td>5</td>
<td>56</td>
<td>5</td>
</tr>
<tr>
<td>Van den 2010</td>
<td>5</td>
<td>23</td>
<td>6</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>169</td>
<td>171</td>
<td>160.0%</td>
</tr>
</tbody>
</table>

Total events: 24, Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.79, df = 2 (P = 0.67); I^2 = 0%
Test for overall effect: Z = 1.38 (P = 0.17)

Test for subgroup differences: Chi^2 = 4.57, df = 1 (P = 0.03), I^2 = 78.1%

El-Dallal M. et al., IBDJ 2020
RCTs of VCE vs DSC

El-Dallal M. et al., IBDJ 2020
RCTs of VCE vs CE and HD-WLE in non-IBD

Individual patient level data meta-analysis for high definition White Light Endoscopy (WLE) vs Narrow Band Imaging (NBI) stratified by bowel preparation

11 international centers

4491 individual patient datasets

Odds ratio (95% CI)

<table>
<thead>
<tr>
<th>All</th>
<th>Adequate prep</th>
<th>Best prep</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.14 (1.01–1.29)</td>
<td>1.07 (0.92–1.24)</td>
<td>1.30 (1.04–1.62)</td>
</tr>
</tbody>
</table>

Also improved adenoma detection only with second-generation bright NBI

Atkinson et al., Gastroenterology 2019
Lesion Characterization (CE/VCE)

<table>
<thead>
<tr>
<th>NBI International Colorectal Endoscopic (NICE) Classification*</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td>Same or lighter than background</td>
<td>Browner relative to background (vestigial color arises from vessels)</td>
<td>Brown to dark brown relative to background, sometimes patchy whiter areas</td>
</tr>
<tr>
<td><strong>Vessels</strong></td>
<td>None, or isolated lacunar vessels coursing across the lesion</td>
<td>Brown vessels surrounding white structures**</td>
<td>Has area(s) of disrupted or missing vessels</td>
</tr>
<tr>
<td><strong>Surface Pattern</strong></td>
<td>Dark or white spots of uniform size, or homogeneous absence of pattern</td>
<td>Oval, tubular or branched white structure surrounded by brown vessels**</td>
<td>Amorphous or absent surface pattern</td>
</tr>
<tr>
<td><strong>Most likely pathology</strong></td>
<td>Hyperplastic</td>
<td>Adenoma***</td>
<td>Deep submucosal invasive cancer</td>
</tr>
</tbody>
</table>

* Can be applied using colonoscopes with or without optical (zoom) magnification.
** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.
*** Type 2 consists of villosa classification types 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area).
Other Methods (not currently in routine use)

- **Autofluorescence** → shown to be inferior to DSC in recent pilot RCT (Vleugels et al., Lancet Gastroenterol Hepatol 2018)
- **Confocal Endomicroscopy** – allows real-time in vivo histology
  → Not useful for improving detection over large surface areas
  → Improves lesion characterization slightly over current IEE methods
  → Time-consuming, costly, large training curve
  → Unclear cost advantage over current methods
  → Not practical for commercial use
### Real-Time Lesion Characterization

<table>
<thead>
<tr>
<th>Technique</th>
<th>Setting</th>
<th>SENS</th>
<th>SPEC</th>
<th>Accuracy</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromoendoscopy</td>
<td>UC</td>
<td>93%</td>
<td>88-93%</td>
<td>~90%</td>
<td>Kiesslich, Gastro 2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hurlstone, Endoscopy 2005</td>
</tr>
<tr>
<td>Chromoendoscopy</td>
<td>Non-IBD</td>
<td>83-96%</td>
<td>83-93%</td>
<td>85-94%</td>
<td>Van den Broek, GIE 2009</td>
</tr>
<tr>
<td>NBI</td>
<td>UC</td>
<td>75-80%</td>
<td>65-81%</td>
<td>~70%</td>
<td>Van den Broek, Gut 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Van den Broek; Endoscopy 2011</td>
</tr>
<tr>
<td>NBI</td>
<td>Non-IBD</td>
<td>89-94%</td>
<td>80-91%</td>
<td>87-91%</td>
<td>Van den Broek, GIE 2009</td>
</tr>
<tr>
<td>Endomicroscopy</td>
<td>UC</td>
<td></td>
<td>97%</td>
<td></td>
<td>Hurlstone, CGH 2007</td>
</tr>
<tr>
<td></td>
<td>Non-IBD</td>
<td>97</td>
<td>99</td>
<td>99%</td>
<td>Kiesslich, Gastro 2004</td>
</tr>
</tbody>
</table>
Summary

• Neoplasia surveillance techniques in IBD are evolving

• DSC with targeted biopsies offers a safe, simple and economical alternative to WLE with non-targeted and targeted biopsies

• Further data is required to define the utility of DSC in the context of HD-WLE and the impact of DSC on CRC rates

• Further data is required to define the utility of random biopsies with either strategy and to better define optimal surveillance intervals
Modified Algorithm for Neoplasia Surveillance in IBD

Targeted neoplasia screening with HD-WLE + DSC + Targeted Sampling

Circumscribed lesion without advanced features

Endoscopic resection

Histology:
Clear resection margins
No submucosal invasion

No neoplastic lesions Identified

Continued endoscopic surveillance q 1-5 years

Simple lesion with low-grade neoplastic changes
Highly irregular lesion or high-grade neoplastic changes

Ill-defined lesions
Features of invasive cancer
HGD on random biopsies
Multifocal invisible neoplasia

Colectomy

Accelerated endoscopic surveillance with targeted CE (3-6 mo)
THE END 😊