How to improve adenoma detection

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Retroflex Colonoscopy
Hewett B and Douglas R. Gastrointest Endosc 2011;74:246-52

- 1000 patients with screening or surveillance colonoscopy
- Withdrawal from cecum to left flexure
- Subsequently, retroflexion within the cecum and again withdrawal to the left flexure
- Outcome: Amount of missed adenomas
- Technical success Retroflexion: 94.4% (no adverse events)
Retroflexion Colonoscopy

Hewett B and Douglas R. Gastrointest Endosc 2011;74:246-52

Missed adenomas: 9.8% - per patient: 4.4%

<table>
<thead>
<tr>
<th>Adenomas</th>
<th>Polyps found on forward examination</th>
<th>Polyps found on retroflexion</th>
<th>Miss rate* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>497</td>
<td>54</td>
<td>0.098 (0.075-0.126)</td>
</tr>
<tr>
<td>1-5 mm</td>
<td>410</td>
<td>48</td>
<td>0.105 (0.078-0.137)</td>
</tr>
<tr>
<td>6-9 mm</td>
<td>65</td>
<td>3</td>
<td>0.044 (0.009-0.124)</td>
</tr>
<tr>
<td>≥10 mm</td>
<td>22</td>
<td>3</td>
<td>0.120 (0.026-0.312)</td>
</tr>
</tbody>
</table>

Conclusions:
Retroflex colonoscopy of an experienced endoscopist is a safe and effective way to reduce the miss rate of adenomas within the right side of the colon.
Third eye Retroscopy

Third Eye; retrograde viewing device

3 studies – 2 study designs

- Design 1: Withdrawal with Third Eye\(^1,2\)
- Design 2: Tandem Colonoscopy (randomization of second colonoscopy: with or without third eye)\(^3\)

1. De Marco DC et al. Gastrointest Endosc 2010
2. Waye JD et al. Gastrointest Endosc 2010
3. Leufkens A et al. Gastrointest Endosc 2011
Third eye Retroscopy

- **Study** | **Patients** | **Missed adenomas**
- De Marco et al. | 298 | 16%
- Waye et al. | 249 | 11%
- Leufkens et al. | 448 | 23%

2. Waye JD et al. Gastrointest Endosc 2010;71:551-6

**Conclusions:**
The amount of missed adenomas of standard colonoscopy is surprisingly high. Tandem colonoscopies or retroscopy colonoscopy will increase the safety of the patient.
Serrated lesions

Hiraoka S et al. Gastroenterology 2010;139:1503–1510

- Hyperplastic polyp (diminutive, rectum and sigmoid)
- Sessile Serrated Adenoma SSA (rather flat, right side)
- Traditional Serrated Adenoma TSA (polypoid, left side)
- Mixed Serrated Polyp MP
Observational study
10,199 patients
Risk analysis

Conclusions:
Large serrated lesions (>1cm) are an independent risk factor for the prevalence of colorectal cancer

Multivariate analysis, OR (95% CI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&lt;65 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65 y</td>
<td>2.63</td>
<td>(2.24–3.08)^a</td>
</tr>
<tr>
<td>Gender</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.05</td>
<td>(0.90–1.23)</td>
</tr>
<tr>
<td>Number of adenomas</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>1.65</td>
<td>(1.15–2.32)^c</td>
</tr>
<tr>
<td>Adenomas ≥10 mm</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.56</td>
<td>(1.21–1.99)^b</td>
</tr>
<tr>
<td>LSPs</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3.34</td>
<td>(2.16–5.03)^a</td>
</tr>
</tbody>
</table>
Hyperplastic Polyposis Syndrome
Boparai KS et al. Gut 2010;59:1094-1100

Hyperplastic polyposis syndrome: Patients with multiple hyperplastic polyps and substantial risk for the development of colon cancer (CIMP Mutation)
Hyperplastic Polyposis Syndrom
Boparai KS et al. Gut 2010;59:1094-1100

- Retrospective analysis, 7 academic centers (Netherlands)
- Identification of 77 persons with HPS
- 27 colon cancers (28.5%)
- Number of cancer during surveillance: 7% within 5 years
- Risk factors: Number of polyps and number of serrated adenomas

Conclusions: Patients with HPS need intense surveillance
Hyperplastic Polyposis Syndrome
Boparai KS et al. Endoscopy 2011; 43: 676–682

- **HPS: best surveillance option = NBI**
  - 22 patients with HPS – tandem colonoscopy
  - White light endoscopy versus NBI
  - Miss rate: 36% versus 10%
Suboptimal bowel preparation

Lebwohl B et al. Gastrointest Endosc 2011;73:1207-14

- Retrospective study: 12,787 Colonoscopies
- Suboptimal bowel preparation 3047 (24%)
- Early repeat colonoscopy (≤ 3 years after index): 505 patients

Results:
- 216 of 505 patients (43%) with optimal bowel preparation
- 83 „new“ adenomas
- Miss rate: 43%
- Highest risk for patients with adenomas during index colonoscopy

Conclusion: Bowel preparation matters!
Medjet
CO2-Cleaning
Conclusions (I)

- Colonoscopy is the gold standard for colon cancer screening, but:
- Screening sigmoidoscopy is an alternative with similar outcome compared to colonoscopy
- The adenoma miss rate of colonoscopy especially on the right side of the colon is substantial.
- Tandem colonoscopy, retroflexion or third eye are ways for improvement.
- Bowel cleansing can be optimized using intraprocedural cleaning devices
- The individual adenoma detection rate should be above 20%.
Colonoscopy
„Advanced Imaging“
High-Definition Meta-Analysis

Additional diagnostic yield + 3.8%

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Polyps/total</th>
<th>Incremental yield (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IY</td>
<td>Lower limit</td>
<td>Upper limit</td>
</tr>
<tr>
<td>East</td>
<td>0.019</td>
<td>-0.119</td>
<td>0.158</td>
</tr>
<tr>
<td>Pellise</td>
<td>0.048</td>
<td>-0.029</td>
<td>0.126</td>
</tr>
<tr>
<td>Burke</td>
<td>0.031</td>
<td>-0.035</td>
<td>0.096</td>
</tr>
<tr>
<td>Buchner</td>
<td>0.029</td>
<td>-0.010</td>
<td>0.068</td>
</tr>
<tr>
<td>Tribonias</td>
<td>0.109</td>
<td>0.012</td>
<td>0.207</td>
</tr>
<tr>
<td>Pooled</td>
<td>0.038</td>
<td>0.010</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Conclusions:
HD does not provide a higher detection rate of advanced adenomas. However, significant more small polyps (<5mm) can be detected.
Randomized, controlled single center study
Screening or surveillance colonoscopy

Tandem Colonoscopy:
Standard Colonoscopy (SD) versus High Definition Colonoscopy with NBI

<table>
<thead>
<tr>
<th></th>
<th>SD then HD-NBI</th>
<th>HD-NBI then SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>47</td>
<td>49</td>
</tr>
<tr>
<td>Missed adenomas</td>
<td>49% (19/39)</td>
<td>27% (9/33)</td>
</tr>
<tr>
<td>Missed polyps</td>
<td>63% (34/54)</td>
<td>29% (8/28)</td>
</tr>
</tbody>
</table>

Conclusions:
HD-NBI colonoscopy is superior to SD in direct comparison.
Prospective randomized study
High definition (HD), Standard definition (SD) and NBI colonoscopy

<table>
<thead>
<tr>
<th></th>
<th>SD-WL (n = 210)</th>
<th>HD-WL (n = 210)</th>
<th>NBI (n = 210)</th>
<th>HD-WL vs. SD-WL</th>
<th>NBI vs. SD-WL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with adenomas, no. (%)</td>
<td>81 (38.6)</td>
<td>96 (45.7)</td>
<td>97 (46.2)</td>
<td>.166</td>
<td>.138</td>
</tr>
<tr>
<td>Total no. of adenomas</td>
<td>145</td>
<td>235</td>
<td>237</td>
<td>.016</td>
<td>.014</td>
</tr>
<tr>
<td>Adenomas per subject</td>
<td>0.69</td>
<td>1.12</td>
<td>1.13</td>
<td>.016</td>
<td>.014</td>
</tr>
</tbody>
</table>

+ HD and NBI identified more flat and right side adenomas compared to SD

Conclusions:
HD and NBI can identify more adenomas, flat adenomas, especially on the right side of the colon. However, more patients with adenomas could not be identified.
NBI & i-scan, FICE

Narrowing of light spectrum
NBI

Post Processing of emitted light
I-Scan, FICE

Effect:
Vessel analysis

Effects:
Surface analysis
Tissue analysis
Vessel analysis
Comparison between \(i\)-scan and NBI for characterization of small polyps

142 patients, HD colonoscopy for detection, \(i\)-scan or NBI for characterization

<table>
<thead>
<tr>
<th>Mucosal pattern</th>
<th>Hyperplastic polyps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oval, tubular, or elongated pits</td>
<td>No definite pits or circular or dotted pits</td>
</tr>
<tr>
<td>Increased vascular density: short, thick vessels; distinct vascular density surrounding pits; or overall increased vascular contrast to surrounding normal mucosa</td>
<td>Scarce vascular density: no visualized vessels or only minute, thin superficial vessels</td>
</tr>
</tbody>
</table>

![Comparison images](A, B, C, D)
### i-scan versus NBI

Lee CK et al. Gastrointest Endosc 2011;74:603-9

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**Results:** Comparision between HD alone and HD with NBI or i-scan

![Table showing comparison between HD alone and HD with NBI or i-scan](image)

**Conclusions:**

NBI as well as i-scan can characterize better colorectal lesions compared to HD alone. There was no difference between NBI and i-scan.
FICE: Detection and Characterization

Prospective, randomized study – tandem colonoscopies
WLE versus FICE, 359 patients

<table>
<thead>
<tr>
<th>Detected lesions</th>
<th>Missed lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>FICE</td>
<td>WL</td>
</tr>
<tr>
<td>No. of lesions</td>
<td>236</td>
</tr>
</tbody>
</table>

Conclusions: No difference between FICE and WLE for detection of adenomas

232 polyps:
Characterization with WLE (75%), FICE (88%) and indigo carmine (94%)

Conclusions: Characterization of polyps is similar accurate with FICE (88%), NBI (88%) and i-scan (91%).
**Randomized study:**
Pan-Chromoendoscopy versus WLE for the detection of adenomas and cancer (1008 patients)

<table>
<thead>
<tr>
<th>Methods</th>
<th>Patients</th>
<th>Adenomas</th>
<th>Pat. with ≥ 1 adenoma</th>
<th>Withdrawal (min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromoendoscopy</td>
<td>496</td>
<td>501</td>
<td>46.2%</td>
<td>11.2</td>
</tr>
<tr>
<td>WLE</td>
<td>512</td>
<td>338</td>
<td>36.3%</td>
<td>9.8</td>
</tr>
</tbody>
</table>

+ significant flat adenomas and serrated lesions using Pan-Chromoendoscopy

**Conclusions:**
Chromoendoscopy is significantly increasing adenoma detection rate and seems to be superior to virtual chromoendoscopy (detection)
Chromoendoscopy – meta-analysis

1277 patients

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Incremental yield (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IY</td>
<td>Lower limit</td>
</tr>
<tr>
<td>Kiesslich 2003</td>
<td>0.08</td>
<td>-0.015</td>
</tr>
<tr>
<td>Matsumoto 2003</td>
<td>0.00</td>
<td>-0.150</td>
</tr>
<tr>
<td>Rutter 2004</td>
<td>0.03</td>
<td>-0.021</td>
</tr>
<tr>
<td>Hurlstone 2005</td>
<td>0.12</td>
<td>0.076</td>
</tr>
<tr>
<td>Kiesslich 2007</td>
<td>0.08</td>
<td>-0.009</td>
</tr>
<tr>
<td>Marion 2008</td>
<td>0.06</td>
<td>-0.034</td>
</tr>
<tr>
<td>Pooled</td>
<td>0.07</td>
<td>0.032</td>
</tr>
</tbody>
</table>

NNT 14.3

The difference in proportion of lesions detected by targeted biopsies was 44% (95% CI 28.6–59.1) and flat lesions was 27% (95% CI 11.2–41.9) in favour of chromoendoscopy

V. Subramanian et al. APT 2011

Quality in Endoscopy: Colonoscopy, Berlin 2012
Advanced Imaging – Conclusions II

- HD Colonoscopy is the upcoming standard even if the first meta-analysis shows only a minor increase of the diagnostic yield.
- Virtual chromoendoscopy (NBI, i-scan, FICE) is of no proven benefit for the detection of colorectal adenomas. However, characterization of lesions is more reliable than WLE.
- Pan-Chromoendoscopy significantly increases the adenoma detection rate and is standard of care in patients with long lasting ulcerative colitis.
Colonoscopy
Cellular Imaging
In vivo Histology

In vivo histology is a new diagnostic concept of GI-Endoscopy providing cellular analysis during ongoing endoscopy

- **Endocytoscopy (Olympus)**
  - Super magnification of the mucosal surface
- **Probe based Endomicroscopy (MaunaKea)**
  - Fixed imaging plane depth, high speed image acquisition
- **Endomicroscopy integrated in an endoscope (Pentax)**
  - Dynamic microscopic imaging of the whole mucosal layer
Endocytoscopy

Hyperplasia  Tubular adenoma
Endocytoscopy

- New endocytoscopic classification based on 213 colorectal lesions
- Comparision between WLE and endocytoscopy

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificcity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>WLE</td>
<td>60%</td>
<td>98,5%</td>
<td>96,7%</td>
</tr>
<tr>
<td>Endozyto</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusions:
Impressive images and results. However, The additional diagnostic yield seems to be modest in „japanese hands“.
Endomicroscopy

pCLE

eCLE
Endomicroscopy – in vivo Histology
Xie XJ et al. Endoscopy 2011; 43: 87–93

- Modified Mainz Classification based on 150 colonic lesions (vascular and tissue pattern)
  - Accuracy: 95%
  - Sensitivity: 94%
  - Specificity: 96%
  - Kappa: 0.93

Conclusions:
Endomicroscopy is as accurate as standard histology after mucosal biopsies (differentiation between neoplastic and non-neoplastic tissue)
Endomicroscopy versus virtual chromoendoscopy

- 75 patients with 119 polyps
- Characterization with FICE or NBI, followed by Endomicroscopy (pCLE)

<table>
<thead>
<tr>
<th></th>
<th>pCLE</th>
<th>NBI &amp; FICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>91%</td>
<td>77%</td>
</tr>
<tr>
<td>Specificity</td>
<td>76%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Conclusions:
Endomicroscopy can judge colorectal lesions more accurate than virtual chromoendoscopy.
Molecular targets and expression profiles can be determined using fluorescein labeled antibodies (e.g. EGFR, VEGF)

Conclusions:
Functional and molecular imaging a new and unique diagnostic options for gastrointestinal endoscopy. However, more studies are needed before these options will be embedded into clinical routine.
Cellular imaging – Conclusions (III)

- The diagnostic yield of endomicroscopy is comparable to conventional histology after mucosal biopsies.
- Endomicroscopy is more accurate compared to virtual chromoendoscopy defining intraepithelial neoplasia.
- Functional and molecular imaging are new diagnostic options of gastrointestinal endoscopy.
- Future goals are prediction of disease and therapeutic outcome.