Advanced Endoscopic Imaging Techniques: Making the Endoscopist Work Smarter not Longer

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Conflicts of Interest

• Research support: Olympus, Fujinon, Ninepoints, Mauna Kea Technology
• Advisory Board: Ninepoints
Goals

• Determine if ADR improves with NBI or high-definition imaging
• Describe how chromoendoscopy may help find in flat adenomas
• Describe how magnification endoscopy can help determine histology

Advanced Endoscopic Imaging

• Detection: Wide Field
  – Finding occult lesions
  – Examples: NBI, I-Scan, Chromoendoscopy
• Diagnosis: Limited field of view
  – Determining nature of lesions
  – Magnification (Zoom), Confocal Laser Endomicroscopy
  – Cross over: Volume laser endomicroscopy
Applications

- Colon
  - Polyp detection and characterization
  - IBD surveillance
- Gastric
  - Intestinal metaplasia surveillance
- Esophagus
  - Barrett’s esophagus surveillance

Wide Field Imaging Techniques

- Chromoendoscopy
- High definition endoscopy
- Hemoglobin enhancement: NBI, FICE, I-Scan
Advanced Imaging Techniques: Caveats

- Rarely find anything significantly different than careful high definition white light examination
- Can enable more rapid assessment of mucosa
  - Decrease random biopsies
- “Look more, biopsy less”

Colon Polyps
What’s the Problem?

![Graph showing mean withdrawal time vs mean number of adenomas detected per subject with a 10-fold variation in ADR.]

Barclay et al. NEJM;2006;355:2533

Cap Assisted Colonoscopy

- Cap-assisted colonoscopy:
  - Lee et al. Gastrointest Endosc 2006; 63:AB226
    - 404 patients in RCT cap vs no cap
    - Cecal intubation time shorter with CAC
    - Increased overall polyp detection
      49.3% vs 39.1% p< 0.05
    - Decreased cecal intubation time
Cap Assisted Colonoscopy

Comparison of the success rate, time and pain for the colonoscope insertion into the cecum

<table>
<thead>
<tr>
<th></th>
<th>With OTC (n= 110)</th>
<th>Without OTC (n=111)</th>
<th>Total (n= 221)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of total colonoscopy</td>
<td>100</td>
<td>102</td>
<td>202</td>
<td>0.8153*</td>
</tr>
<tr>
<td>Success rate (%) ***</td>
<td>90.9%</td>
<td>91.9%</td>
<td>91.4%</td>
<td>0.8153*</td>
</tr>
<tr>
<td>Cecal intubation time (min.)</td>
<td>12.51±6.20</td>
<td>15.8±6.13</td>
<td>14.19±6.36</td>
<td>0.001**</td>
</tr>
<tr>
<td>Pain in patients (VAS) (mm)</td>
<td>37.7±25.17</td>
<td>43.3±30.04</td>
<td>40.54±27.8</td>
<td>0.136**</td>
</tr>
</tbody>
</table>

* $X^2$ test  
** unpaired t-test  
***Percentage of patients in whom the colonoscope could be inserted to the cecum
Indigo Carmine 0.2%, 60 cc

Chromoscopy of Depressed Lesions

Kiesslich R. Gastroenterology 2003;124:880-88
Maruta’s Classification

Depressed Lesions Highest Risk of Malignancy

Depressed has the highest risk to contain HGD or early cancer

Non-Polypoid Colorectal Neoplasia

Characteristics of NP–CRN

1. Subtle Color Differential
2. Slight Hemorrhage-Friability
3. Deformity of the Wall
4. Irregular Vascular Network
5. Absence of Innominate Grooves

Systematic Review

• Cochrane review 5 trials Cochrane Database Syst Rev. 2010 Oct 6;(10)
  – Increased adenoma detection rates OR 1.67 (CI 1.29-2.15)
  – Increased detection of individuals with multiple polyps OR 2.55 (CI 1.49-4.36)
  – Increased time of procedure
Adenoma Detection Rates

Buchner et al. Clin Gastro Hep 09
ACG 2013

High Definition Colonoscopy: A Meta-Analysis

Net effect of HD
- 3.5% [0.9-6.1] increase in all ADR
- -0.1% [-1.7 - 1.6] for advanced ADR
Narrow Band Imaging

- Band-pass ranges of RGB narrowed
- Relatively more contribution of blue light
- Purpose: more superficial (=mucosal) imaging

NBI: Light Absorption by Hemoglobin

Absorption mainly in blue and green spectrum
Depressed Polyp NBI

Depressed HGD, detected by redness

NBI vs White Light Endoscopy for Adenoma Detection: A Meta-Analysis

<table>
<thead>
<tr>
<th>Study ID</th>
<th>RR (95% CI)</th>
<th>Events, Treatment</th>
<th>Events, Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex et al (2007)</td>
<td>0.97 (0.84, 1.11)</td>
<td>141/217</td>
<td>146/217</td>
</tr>
<tr>
<td>Adler et al (2008)</td>
<td>1.36 (0.91, 2.04)</td>
<td>45/198</td>
<td>33/198</td>
</tr>
<tr>
<td>Inoue et al (2008)</td>
<td>1.23 (0.89, 1.71)</td>
<td>51/122</td>
<td>41/121</td>
</tr>
<tr>
<td>Kantenbach et al (2008)</td>
<td>1.15 (0.89, 1.47)</td>
<td>68/135</td>
<td>62/141</td>
</tr>
<tr>
<td>Adler et al (2009)</td>
<td>1.03 (0.84, 1.27)</td>
<td>140/625</td>
<td>137/631</td>
</tr>
<tr>
<td>Paggi et al (2009)</td>
<td>0.98 (0.78, 1.24)</td>
<td>59/103</td>
<td>63/108</td>
</tr>
<tr>
<td>Overall (I-squared = 0.4%, p = 0.413)</td>
<td>1.06 (0.97, 1.16)</td>
<td>504/1400</td>
<td>482/1416</td>
</tr>
</tbody>
</table>

No improvement in:
• Polyp detection,
• Number of adenomas/patient
• Flat polyps
Colonoscopy Surveillance Guidelines

- Pancolitis (or Left-sided): Every 1-2 years after 8-10 years.
- Proctitis: Risk not greater than non-IBD
- Begin surveillance immediately in PSC patients
- Recommendations also apply to Crohn’s disease.

Randomized Controlled Trial of Pan-Chromo vs Standard for CUC-C Surveillance

Kiesslich, Gastro, 2003, 124:880-888

165 patients CUC-C

84 Chromo

81 Standard

Random + Targeted Bx’s

32 Neoplastic sites

10 Neoplastic sites (p=0.003)
Stomach

Chronic Gastritis
Gastric Intestinal Metaplasia

Detection of Intestinal Metaplasia with Methylene Blue

Case

- 58 yo WM with dyspeptic symptoms and recent onset of nausea
- Had a history of H. pylori that was treated 3 years previously
- Weight stable

Magnification Endoscopy with Methylene Blue Staining
What is Your Diagnosis

• Round regular pattern: Intestinal metaplasia
• Irregular pattern: Dysplastic changes

Indigo Carmine

• Indigo carmine has been shown to enhance detection of depressed and flat gastric lesions (Kawahara, Digestive Endoscopy 21:14–19, 2009)
• Intraobserver agreement between observers of pit patterns using indigo carmine is excellent (kappa=0.86) (Dinis-Ribeiro Gastrointest Endosc 57:498–504, 2003)
• Detect the presence of intestinal metaplasia in the gastric cardia (Guelrud, Amer J Gastro 97, 584–589, 2002)
Indigo Carmine

- **Type 1 patterns, regular = normal gastric mucosa**

- **Type 2: Round pits and villi = intestinal metaplasia**

- **Type 3 = Loss of pattern, dysplasia**

Laser Confocal Endomicroscopy

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## Endoscopic Microscopy Systems

<table>
<thead>
<tr>
<th></th>
<th>Confocal Endoscope</th>
<th>Confocal Probe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument</td>
<td>Dedicated Endoscope</td>
<td>Probe via any Endoscope</td>
</tr>
<tr>
<td>Contrast</td>
<td>IV: Fluorescein</td>
<td>IV: Fluorescein</td>
</tr>
<tr>
<td></td>
<td>Topical: acriflavin, cresyl violet</td>
<td></td>
</tr>
<tr>
<td>Magnification</td>
<td>700-1000x</td>
<td>750x</td>
</tr>
<tr>
<td>Image depth</td>
<td>250 microns</td>
<td>70 microns</td>
</tr>
<tr>
<td>Resolution</td>
<td>1 micron</td>
<td>1.2 microns</td>
</tr>
<tr>
<td>Frame Rate</td>
<td>0.8/sec</td>
<td>12/sec</td>
</tr>
</tbody>
</table>

### Endoscope Confocal Laser Endomicroscopy

- N=31 males
- Adenoma accuracy: 94%
- Adenocarcinoma: 95%

Jeon, Gastrointestinal Endoscopy, 74:781-783, 2011
Intestinal metaplasia and gastric cancer.

Laser Confocal Endomicroscopy
Classification of Gastric Polyps

<table>
<thead>
<tr>
<th>Polyp Classification</th>
<th>Fundic gland</th>
<th>Hyperplastic</th>
<th>Adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small round pattern</td>
<td>++++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Prolonged pattern</td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Villous or ridged</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Honeycomb</td>
<td>+++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Dense vascular</td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Core vascular</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Fine network, unclear</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Types of Gastric Polyps

- Caris database
- 121,564 EGD over 2007-2008
- 65% had gastric biopsies
- 6.4% of patients had polyps
  - 77% fundic gland polyps
  - 17% hyperplastic polyps
  - 0.7% adenomas
  - 0.1% inflammatory fibroid polyps

Sampling Protocols

• Devries et al 2010: 12 non-targeted biopsies and additional biopsies of any lesions
  – Primarily found in incisura
  – Second most common antrum
  – Third was less curve
• A protocol of 7 biopsies found 97% of IM/dysplasia
  – 3 antrum
  – 1 incisura
  – 3 body (1 greater, 2 lesser curve)

Endoscope Confocal Laser Endomicroscopy

<table>
<thead>
<tr>
<th>Post-ESD histopathology</th>
<th>Optical biopsy by CLE, no.</th>
<th>Endoscopic biopsy, no.</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adenoma</td>
<td>Adenocarcinoma</td>
<td>Adenoma</td>
</tr>
<tr>
<td>Adenoma</td>
<td>11</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>2</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Overall accuracy</td>
<td>94.2% (95% CI, 81.3-98.4)</td>
<td>85.7% (95% CI, 70.6-93.7)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>Differentiated</td>
<td>Undifferentiated</td>
<td>Differentiated</td>
</tr>
<tr>
<td>Differentiated</td>
<td>17</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>1</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Overall accuracy</td>
<td>95.4% (95% CI, 78.2-99.1)</td>
<td>94.2% (95% CI, 62.4-94.4)</td>
<td></td>
</tr>
</tbody>
</table>

Jeon, Gastrointestinal Endoscopy, 74:781-783, 2011
Esophagus

Methylene Blue

- 450 pts with BE in 9 studies
- No incremental yield with methylene blue

Gastrointestinal Endoscopy 2009;69:1021-8
Non-dysplastic Barrett’s oesophagus

- Regular mucosal pattern
- Regular vascular pattern

High-grade Dysplasia

- Irregular mucosal pattern
- Irregular vascular pattern
- Abnormal blood vessels

Kara et al. Gastrointest. Endosc, 2006

Narrow Band Imaging for Dysplasia

<table>
<thead>
<tr>
<th>Study</th>
<th>Pt # (HGD/Total)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharma 2006</td>
<td>7 / 51</td>
<td>100%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Kara (AFI+NBI) 2006</td>
<td>14 / 20</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>Sharma 2013</td>
<td>14/113</td>
<td>53%*</td>
<td>100%</td>
</tr>
<tr>
<td>Giachino (AFI+NBI) 2013</td>
<td>14/42</td>
<td>71%</td>
<td>46%</td>
</tr>
</tbody>
</table>
Other Systems

• FICE: Fuji Intelligent Chromo Endoscopy
  – Hypersharppness
  – Hypertone
  – Color Emphasis

• I-Scan:
  – CE: Contrast Enhancement
  – SE: Surface Enhancement
  – TE: Tone Enhancement
## I-Scan

![I-Scan Image](image_url)

## CLE and Barrett’s Esophagus

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Instrument</th>
<th>Sites Studied</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich 2006</td>
<td>63</td>
<td>eCLE</td>
<td>156</td>
<td>93%</td>
<td>98%</td>
<td>97%</td>
</tr>
<tr>
<td>Pohl 2008</td>
<td>38</td>
<td>pCLE</td>
<td>296</td>
<td>80%</td>
<td>94%</td>
<td>44%</td>
</tr>
<tr>
<td>Dunbar 2009</td>
<td>39</td>
<td>eCLE</td>
<td>Increased yield of biopsies (17% to 34%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BajBouj 2010</td>
<td>68</td>
<td>pCLE</td>
<td>670</td>
<td>18%</td>
<td>90%</td>
<td>46%</td>
</tr>
<tr>
<td>Sharma 2011</td>
<td>101</td>
<td>pCLE</td>
<td>874</td>
<td>63%</td>
<td>93%</td>
<td>58%</td>
</tr>
</tbody>
</table>
pCLE versus eCLE for Dysplasia Classification

- 16 eCLE stacks (depth imaging) compared with video pCLE

Leggett, DDW 2013

Volumetric Laser Endomicroscopy

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Volumetric Laser Endomicroscopy

Concurrence Between VLE and eCLE

- 22 EMRs were imaged with both VLE and eCLE.
- Diagnostic agreement between VLE and eCLE was found in 18 of the 22 cases.
- VLE found dysplasia characteristics in all (100%) patients with verified dysplasia on histology.
- eCLE showed dysplasia characteristics in 17 (85%) of the 20 dysplasia cases.
Advanced Technology

“One Should Use New Therapy Quickly While It Still Works”

Sir William Osler

Narrow Band Imaging Case 1

• 74 yo WM with 25 years of GERD symptoms
• Barretts esophagus diagnosed 2 years ago, LGD, C6M8
• 6 months ago, HGD found
• Hx CABG, DM, HTN
Video Case 1

Case 2

- 68 yo WM BE with HGD dx 1 year ago
- RFA 360 still HGD
- RFA 90 2 mths ago
- Hx HTN, DM
Case 3

• 58 yo white female with a prior history of a high grade dysplastic polyp in the right side of the colon
• Prior polyp was found to be MSI positive
• Family history of colon cancer