New Technology of Barrett’s and Colon Cancer/Polyps Detection and Surveillance

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Learning Objectives

• Identify methods associated with increased adenoma detection rate
• Identify methods associated with higher dysplasia detection rates in Barrett’s
• Distinguish hyperplastic, adenoma, and advanced neoplasia in colon polyps based on optical imaging without pathology
• Recognize paradigm shift from random biopsy to image guided therapeutics
### Endoscopic Guided Therapeutics

<table>
<thead>
<tr>
<th>Detect</th>
<th>Characterize</th>
<th>Diagnose</th>
<th>Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Endoscopy</td>
<td></td>
<td></td>
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<tr>
<td>High Def Endoscopy</td>
<td></td>
<td></td>
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<tr>
<td>Chromo-NBI-FICE</td>
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<tr>
<td>Zoom Endoscopy</td>
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<tr>
<td>Confocal Endoscopy</td>
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<tr>
<td>Resect/Ablate</td>
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</table>

### Some Simple Principals

- Eyes and hands are “best” technology
- More looking, less biopsy
- Broad field techniques to detect
- Small field techniques to characterize
- “Microscopy” to diagnose
Applications

• Polyp detection and classification
  – Polypectomy for only adenomas
  – Remove and discard tubular adenomas
  – Real time guide to Rx (EMR)
• Colitis dysplasia detection
  – Eliminating random biopsy
  – EMR for ALMs
• Barrett’s dysplasia detection and Rx
  – Eliminating random biopsy
  – Real time guide to Rx (ablation/EMR)

How Good Does a Technology Have to be?

• PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) frameworks
• Defines threshold values for accuracy for
  – Colon polyps: to avoid removal of hyperplastic polyps
  – Barrett’s: to avoid random biopsy
Barrett’s PIVI

Thresholds to Eliminate Random Bx

- Patients without known dysplasia
  - Per-patient sensitivity ≥ 90% for HGD
  - Negative predictive value ≥ 98% for HGD
  - Specificity ≥ 80%

- Current systems (NBI, FICE, Iscan, CLE)
  - Sensitivity 33-100%
  - NPV: 79-100%
  - Specificity: 56-100%

- Overall NBI + CLE have best performance

Sharma et al. GIE 2012; 76:252

Endoscopic Imaging and Ablation of Barrett’s Esophagus:
BE High Grade Dysplasia
Effect of NBI

HD White light
HD NBI

Prospective, controlled tandem endoscopy study of NBI for dysplasia detection

EGD (standard def)

Same day procedures “back to back”

EGD (HD+ NBI)

Wolfsen et al Gastro 2008;135:24
NBI vs Standard EGD in Barrett’s

- NBI Detects More Patients with Dysplasia
  - NBI 57%
  - Standard 43%  p < 0.001

- NBI Detects Higher Grade of Dysplasia
  - NBI 12/65
  - Standard 0/65  p < 0.001

- Fewer Biopsies Required with NBI
  - NBI 4.7 bx/pt
  - Standard 8.4 bx/pt  p < 0.001

Wolfsen et al, Gastro 2008

Confocal: Barrett’s neoplasia

- Neoplastic Cells
- Squamous Cell Epithelium

Kiesslich CGH, 2006;4:979
Meta Analysis of NBI for HGD

- Sensitivity: 95%
- Specificity: 97%
- Estimated NPV: 99.9%* (assumes prevalence 2%)


Future Directions: BE Imaging

- Whole esophagus endomicroscopy
- Direct image guided ablation
- Non-endoscopic screening/surveillance
Optical Frequency Domain Imaging (OFDI)

Whole Esophagus Endomicroscopy

- Variant of OCT
- Much faster frame rate (100x) than OCT
  - Whole esophagus imaging ~ 90 seconds
- 7 micron resolution
- 3D imaging to 3.5mm (muscularis propria)

Vakoc, GIE, 2007;6:901
Suter GIE 2008; 64:745
Suter, GIE; 2010;71:346
Volume Esophageal Imaging with OFDI

Balloon Insertion

Volume Microscopy

Identify Suspect Areas

Guided Biopsy Paradigm

Mark Suspect Areas

Histopathology

Biopsy at Marks
OFDI in Practice

Volumetric Laser Endomicroscopy

An example case of High Grade Dysplasia

Can Advanced Imaging Increase Adenoma Detection in Screening Colonoscopy?
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>Kaltenbach et al (2008)</td>
<td>1.13 (0.89, 1.47)</td>
<td>68/155</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>Pagli 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>

Dinesen et al. GIE 2012;75:604

High Definition Colonoscopy: A Meta-Analysis

<table>
<thead>
<tr>
<th>Study Name</th>
<th>N (std def)</th>
<th>N (HD)</th>
<th>ADR (total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>East 2008</td>
<td>72</td>
<td>58</td>
<td>65%</td>
</tr>
<tr>
<td>Pellise 2008</td>
<td>310</td>
<td>310</td>
<td>26%</td>
</tr>
<tr>
<td>Burke 2010</td>
<td>426</td>
<td>426</td>
<td>23%</td>
</tr>
<tr>
<td>Buchner 2010</td>
<td>1226</td>
<td>1204</td>
<td>27%</td>
</tr>
<tr>
<td>Tribonias 2009</td>
<td>197</td>
<td>193</td>
<td>54%</td>
</tr>
</tbody>
</table>

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

Subramanian et al. Endoscopy 2011;43:499
Are Multimodal Improvements (High Def, NBI) Additive?

HD-NBI vs SD-White Light
Randomized Tandem Double Blind Trial

% of all adenomas found on each exam (N=91 patients)

<table>
<thead>
<tr>
<th></th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Std 3/19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBI First</td>
<td>84%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NBI 16/19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBI 16%</td>
<td>16%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard First</td>
<td>58%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard 11/19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBI 8/19</td>
<td>42%</td>
<td></td>
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</tr>
</tbody>
</table>

'Miss rate':
Standard: 42%
NBI: 16%
p = 0.003

Gross et al. Endoscopy 2011
Multi-modal imaging (wide angle, HD, NBI) Improved Adenoma Detection

<table>
<thead>
<tr>
<th></th>
<th>Group I (new scopes) (n = 1256)*</th>
<th>Group II (old scopes) (n = 1400)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomas (n)</td>
<td>416</td>
<td>376</td>
<td>—</td>
</tr>
<tr>
<td>Patients with adenomas</td>
<td>22.1%</td>
<td>18.2%</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>ADR</td>
<td>0.33</td>
<td>0.27</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Adenomas &lt;10 mm</td>
<td>29.1</td>
<td>23.1</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>% with HGIN</td>
<td>1.19</td>
<td>0.57</td>
<td>.06</td>
</tr>
<tr>
<td>Hyperplastic polyp(n)</td>
<td>262</td>
<td>206</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Carcinomas (n)</td>
<td>3</td>
<td>5</td>
<td>.73</td>
</tr>
</tbody>
</table>

*new scopes (Olympus CF H 180), Old scopes; mix of std def Olympus, Fuji, Pentax

Adler et al. CGG 2012;10:155

Optical Diagnosis of Colon Polyps
Can we resect and discard?
Can we ignore small distal hyperplastic polyps?
Colon Polyp PIVI

- To resect and discard polyps ≤ 5mm
  - ≥ 90% agreement with post polypectomy surveillance guidelines (compared with histology)
- To leave behind rectosigmoid hyperplastic appearing polyps ≤5mm
  - ≥ 90% negative predictive value

Advanced Imaging Options

- NBI
- FICE
- iScan
- Confocal
- Chromo
- AFI
On of the most studied questions in colonoscopy

<table>
<thead>
<tr>
<th>Method</th>
<th># pts/# studies</th>
<th>Sens</th>
<th>Spec</th>
<th>Acc</th>
</tr>
</thead>
<tbody>
<tr>
<td>NBI</td>
<td>1615/10</td>
<td>91%</td>
<td>87%</td>
<td>90%</td>
</tr>
<tr>
<td>FICE</td>
<td>1416/7</td>
<td>91%</td>
<td>77%</td>
<td>89%</td>
</tr>
<tr>
<td>Chromo</td>
<td>8230/19</td>
<td>91%</td>
<td>80%</td>
<td>87%</td>
</tr>
<tr>
<td>Confocal</td>
<td>495/7</td>
<td>94%</td>
<td>92%</td>
<td>98%</td>
</tr>
<tr>
<td>AFI</td>
<td>333/3</td>
<td>95%</td>
<td>63%</td>
<td>69%</td>
</tr>
</tbody>
</table>

Rex, D [unpublished summary/ASGE]

Optical Diagnosis in Practice Does Not Yet Meet PIVI Thresholds

- 13 practicing gastroenterologists
- Trained/Tested using standardized module
- Diminutive rectosigmoid Polyps
  - Sensitivity: 85%, Specificity: 78%,
  - NPV: 91% (threshold 90%)
- Agreement b/w image vs pathology for surveillance intervals
  - 80% (Threshold 90%)

Ladabaum et al. Gastro 2012;144:81
Future Directions

• Next generation imaging (Dual Focus 190/Exera 3)

Next Generation NBI-Dual Focus (Olympus 190/Exera 3)
Serrated Adenoma HD WL NBI Near Focus

Can Advanced Imaging Replace Random Biopsy in IBD Surveillance?
Randomized Controlled Trial of Pan-Chromo vs Standard for CUC-C Surveillance

Kiesslich, Gastro, 2003, 124:880-888

165 patients CUC-C

84 Chromo

Random + Targeted Bx’s

32 Neoplastic sites

81 Standard

10 Neoplastic sites (p-0.003)

Meta-analysis: Chromoendoscopy for IBD Dysplasia

Compared with random+targeted biopsy w/o chromo

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC</th>
<th>Diagnostic Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled</td>
<td>0.83 [0.76-1.0]</td>
<td>0.91 [0.84-1.0]</td>
<td>0.89</td>
<td>17.5</td>
</tr>
<tr>
<td>Methylene blue</td>
<td>0.74</td>
<td>0.92</td>
<td>0.99</td>
<td>18.33</td>
</tr>
<tr>
<td>Indigocarmine</td>
<td>0.93</td>
<td>0.91</td>
<td>0.86</td>
<td>16.98</td>
</tr>
</tbody>
</table>

Wu L et al. Colorectal Dis 2012;14:416
Summary

• Advances in endoscopic imaging have improved detection in polyps and Barrett’s
  – Multimodal systems are likely additive
• Chromoscopy significantly improves neoplasia detection in IBD
• Currents systems can reduce/eliminate need for random biopsy in expert hands
• Current systems allow on-table diagnoses to guide immediate therapy

Thank you

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